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The Editorial Board kindly informs that since 2014 *Nowiny Lekarskie* has been renamed to *Journal of Medical Science*.

The renaming was caused by using English as the language of publications and by a wide range of other organisational changes. They were necessary to follow dynamic transformations on the publishing market. The Editors also wanted to improve the factual and publishing standard of the journal. We wish to assure our readers that we will continue the good tradition of *Nowiny Lekarskie*.

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ORIGINAL PAPER

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Increased neopterin concentration in patients with primary arterial hypertension

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ABSTRACT

Introduction. The data on the safety profile of anti-tumor necrosis factor (anti-TNF) therapy in real-life patients cohorts with inflammatory bowel disease (IBD) still are lacking.

Neopterin is a pteridine derivative produced from guanosine triphosphate mainly by activated monocytes and macrophages in response to cytokines produced by T-lymphocytes and natural killer cells. Changes in neopterin level reflect the stage of activation of cellular immune system and can be associated with various diseases. Low-grade inflammation is also an important factor in the pathophysiology of hypertension. In presented study we assessed neopterin concentration in 63 patients with primary arterial hypertension compared to 14 control healthy volunteers. Obtained results confirmed increased neopterin level in patients group.

Keywords: neopterin, hypertension, inflammation.

Introduction

Neopterin (2-amino-4-hydroxy-6-(D-erythro-1',2',3'-trihydroxypropyl)-pteridine) is a pteridine derivative produced from guanosine triphosphate by activated monocytes, macrophages, dendritic cells, and endothelial cells and to a lesser extent in renal epithelial cells, fibroblasts, and vascular smooth muscle stimulated by interferon gamma. Because it is released in response to cytokines produced by T-lymphocytes and natural killer cells, neopterin is an indicator of activation of cell mediated immunity [1-2]. Neopterin can be assessed in blood serum, plasma, urine, cerebrospinal fluid, pancreatic juice, saliva and gastric juices. Neopterin is a light-sensitive substance, so probes collected for measurement must be protected from light. Physiological serum concentration is lesser than 10 nmol/L and is different in various age groups (Table 1) [21]. Other factors that can influence neopterin level include gender, race, BMI, and percentage of body fat. [3]. Changes in neopterin level reflect the stage of activation of cellular immune system and can be associated with various diseases. For example, increase neopterin level was observed in patients with coronary artery diseases and was associated with the progression of the disease [4–5]. Therefore, the inflammation system, in association with other cardiovascular pathways, can be the central pathway in the development and progression of cardiovascular diseases [6].

Essential hypertension can be characterized by increased peripheral vascular resistance to blood flow and is one of important risk factors for developing cardiovascular disease [7]. Most of this resistance results from resistance arteries, which are vessels with lumen diameters < 400 μ m [8]. These arteries undergo structural, mechanical or functional vascular remodeling in hypertensive patients – a process that involves extracellular matrix deposition and inflammation. In case of chronic vasoconstriction the vessels may become embedded in the remodeled extracellular matrix and

| Age (years) | Average neopterin concentration [nmol/L] |
|-------------|--|
| < 18 | 6.8 ± 3.6 |
| 19–75 | 5.3 ± 2.7 |
| > 75 | 9.7 ± 5.0 |

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may not return to their vasodilated state. Moreover, endothelial dysfunction - an early determinant in the development of hypertension may also participate to the increased vascular tone in hypertension with reduced vasodilation associated with proinflammatory and prothrombotic state [9]. Chronic low-grade inflammation has been recently mentioned to be an integral part in the pathogenesis of vascular disease [10]. Several clinical studies have revealed that pro-inflammatory markers, such as IL-6, ICAM-1 or CRP may be independent risk factors for the development of hypertension [9]. Neopterin is one of inflammatory mediators, which role in hypertension has not yet been sufficiently studied. Numerous studies have confirmed the usefulness of neopterin level measurement in such cases as transplant rejection, viral infections, intracellular bacteria infections, coronary artery disease, angina pectoris and some autoimmune diseases (arthritis, type 1 diabetes, Crohn's disease, autoimmune thyroiditis) [11]. As mentioned earlier, low-grade inflammation is an important factor in the pathophysiology of hypertension. Therefore, the aim of the study was to assess neopterin level in patients with primary arterial hypertension.

standard deviation: 10.58) were enrolled to the study. Patients' weight ranged from 59 to 167 kg (mean: 98.15; standard deviation: 21.50). Patients with acute coronary syndrome, cancer, heart failure, severe renal failure, severe hepatic insufficiency or pregnancy were excluded from the study. The control group consisted of 14 healthy volunteers (6 men, 8 women), aged from 25 to 59 years (mean: 42.57, standard deviation: 11.80), weighed from 50 to 83 kg (mean: 65.21; standard deviation: 9.18). Arterial blood pressure was measured in both groups. Blood samples were collected from elbow vein for biochemical measurements. Neopterin level was assessed using ELISA immunoassay (DRG International Inc., USA). Statistical analyses were carried out using Statsoft Statistica 10.0 software. Normality of distribution was tested with Shapiro-Wilk Test. Statistical significance was assessed using Mann-Whitney U test.

Results

Estimated sample size for statistical power = 0.95 was 56 individuals. Shapiro-Wilk test of normality revealed that most of studied parameters (including neopterin) did not have normal distribution (**Table 2**). As a result, non-parametric Mann-Whitney U test was chosen as a measure of statistical significance (p < 0.05).

Material and methods

63 patients (31 men, 32 women) with primary arterial hypertension, aged from 25 to 67 years (mean: 50.37;

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|--------------------------------------|--|

| Table 2. Anthropometric and biochemical characteristic of the participants | | | | | | | | | |
|--|-------------------|--------|--------------------|----|--------|--------------------|--------------|-------|--|
| | Patients Controls | | | | | Normality of | | | |
| | N | Mean | Standard deviation | Ν | Mean | Standard deviation | distribution | Р | |
| Age [years] | 63 | 50.37 | 10.58 | 14 | 42.57 | 11.80 | no | 0.029 | |
| Weight [kg] | 63 | 98.15 | 21.50 | 14 | 65.21 | 9.18 | no | 0.000 | |
| Height [cm] | 63 | 169.94 | 9.16 | 14 | 168.50 | 9.09 | no | 0.644 | |
| BMI [kg/m ²] | 63 | 33.95 | 6.90 | 14 | 22.91 | 2.03 | no | 0.000 | |
| Waist [cm] | 63 | 111.40 | 16.04 | 14 | 73.43 | 3.50 | yes | 0.000 | |
| Hips [cm] | 63 | 114.56 | 14.19 | 14 | 93.71 | 5.53 | yes | 0.000 | |
| SBP [mmHg] | 63 | 158.49 | 29.16 | 14 | 110.36 | 6.34 | no | 0.000 | |
| DBP [mmHg] | 63 | 91.98 | 11.20 | 14 | 72.50 | 5.46 | no | 0.000 | |
| Creatinine [µmol/L] | 63 | 81.68 | 16.31 | 14 | 70.50 | 10.38 | no | 0.015 | |
| Tchol [mmol/L] | 63 | 5.84 | 1.36 | 14 | 5.11 | 0.61 | yes | 0.019 | |
| LDL [mmol/L] | 63 | 3.70 | 1.13 | 14 | 2.76 | 0.61 | yes | 0.002 | |
| HDL [mmol/L] | 63 | 1.19 | 0.32 | 14 | 1.65 | 0.32 | no | 0.000 | |
| TG [mmol/L] | 63 | 2.13 | 0.88 | 14 | 1.02 | 0.39 | no | 0.000 | |
| Glucose [mmol/L] | 63 | 5.09 | 0.42 | 14 | 4.99 | 0.47 | no | 0.373 | |
| CRP [mg/L] | 63 | 5.73 | 4.44 | 14 | 2.51 | 1.80 | no | 0.001 | |
| ESR [mm/h] | 63 | 9.24 | 5.65 | 14 | 6.64 | 4.97 | no | 0.104 | |
| ALAT [U/L] | 63 | 34.05 | 16.38 | 14 | 26.57 | 9.19 | no | 0.109 | |
| ASPAT [U/L] | 63 | 29.41 | 15.35 | 14 | 20.64 | 3.37 | no | 0.002 | |
| Neopterin [nmol/L] | 63 | 6.50 | 2.510 | 14 | 5.17 | 0.72 | no | 0.001 | |

Ιοι

Anthropometric and biochemical characteristic of the participants is presented in **Table 2**. Patients and control groups did not differ in height, glucose, ESR and ALAT. Statistically significant differences between these groups were observed for such parameters as: age, weight, BMI, waist and hips circumference, blood pressure, creatinine, total cholesterol, LDL and HDL fraction, triglycerides, CRP, ASPAT and neopterin level. Higher level of neopterin was observed in patients with hypertension compared to healthy controls (**Figure 1**).

Discussion

According to WHO data, approximately 20% of adults (1 billion people in the world) are estimated to have hypertension, defined as blood pressure > 140/90 mm Hg. In the elderly, the prevalence of hypertension can be up to 50% [12]. For example, in the United States 1 per 3 adults have hypertension, while the prevalence increases to 50% for people aged 60 – 69 years and to 75% for patients older than 70 years [13].

Essential hypertension is a multifactorial disease caused by combined action of genetic, environmental,

and behavioral factors. A pro-hypertensive change in a single factor can be probably compensated by other control mechanisms. However, any significant disturbance in the balance between the factors which increase and normalize the blood pressure can result in development of essential hypertension [14]. One of the factors which can contribute to the development of hypertension is inflammation [15]. Inflammatory cells accumulate in kidneys and vasculature of patients with hypertension. It was observed in animal models that loss of adaptive immune cells decreases the blood pressure response to such stimuli as ANG II, high salt, and norepinephrine. Moreover, agonistic antibodies to ANG II receptor (produced by B-cells) contribute to hypertension in experimental models of preeclampsia. Also, production of cytokines, such as TNF- α , interleukin-17, and interleukin-6 influences hypertension, possibly due to effects on both the kidney and vasculature. The innate immune system also appears to contribute to hypertension. Therefore, studies concerning immune cell activation could be helpful in understanding this disease [16]. There are only few studies trying to evaluate neopterin level in hyperten-



Figure 1. Mean neopterin concentration observed in patients and controls

sive patients. Avanzas et al. [17] assessed prognostic value of neopterin in the group of treated patients with hypertension, typical exertional chest pain and coronary artery stenosis of < 50% but without obstructive coronary artery disease, revealing that patients who developed adverse events during one year follow-up had significantly higher neopterin levels than patients without events (7.6 nmol/L vs. 5.4 nmol/L). Asci et al. [18] evaluated neopterin level in patients undergoing hemodialysis. The control group of that study consisted of three subgroups: healthy, diabetic and hypertensive subjects. Hypertensive control group had significantly higher serum neopterin level (16 +/- 1 nmol/L) than healthy control group (11 +/- 1 nmol/L). A recent study of Wang et al. [19] showed that plasma neopterin and hsCRP levels were increased in hypertensive patients with obstructive sleep apnea syndrome (OSAS) and correlated with severity of OSAS.

A similar tendency has been observed in our study: neopterin concentration was higher in hypertensive patients than in healthy controls (6.89 +/- 2.793 vs. 5.08 +/- 0.438); this result is consistent with the hypothesis on the role of inflammation processes in hypertension.

It should be also noted that assessed neopterin level seems to fall within the normal range, which is considered 8.7 nmol/L for 95th percentile of healthy population, according to Werner et al. [20]. However, it is usually recommended to estimate neopterin referential values for each study as they can differ significantly due to measurement method or population diversity.

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Conflict of interest statement

The authors declare that there is no conflict of interest in the authorship or publication of contribution.

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ORIGINAL PAPER

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Assessment of effectiveness of complex treatment of apical and marginal periodontitis with thiotriazoline and chloramphenicol ointment

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ABSTRACT

Introduction. Chronic combined periodontal and periapical lesions have a negative impact on the human organism, since they are a source of intoxication and sensitization causing progression of infection, development of focal sequelae and secondary immunodeficiency. Problem of successful treatment of apical and marginal periodontitis is associated with a significant prevalence of these diseases, a complexity of medical procedures, a substantial proportion of failures and complications, and with a lack of long-term stability of gained results.

Aim. The aim of this work was to investigate clinical effectiveness of drug formulation with thiotriazoline and chloramphenicol in the integrated treatment of combined apical and marginal periodontitis.

Meterial and methods. The condition of oral cavity of the 65 patients with combined lesions of periodontal and endodontic tissues before and after treatment was studied. Outcomes measured were X-ray examination, probing depth, OHI-S, PMA, PI, SBI indices. The complex treatment has been worked out in the patients of main group and the ointment with thiotriazoline and chloramphenicol was introduced in the scheme of periodontal treatment

Results and conclusions. Results of applied treatment indicated to the acceleration of healing process, reduction of exudation period and decrease of exacerbations frequency in the patients of main group. Clinical experience also demonstrated positive dynamic in changes of periodontal indices after the conducted treatment.

Keywords: chronic generalized periodontitis, apical periodontitis, treatment, ointment with thiotriazoline and chloramphenicol.

Introduction

Anatomical and functional interrelationship between the endodontium and periodontium causes a high probability of their simultaneous involvement in the pathological process [1]. Diseases of the periodontal tissues may have a damaging effect on the pulp or the apical periodontium through the system of apical and lateral canals, dentinal tubules [2, 3]. Finally, periodontal surgery procedures with removal of damaged cement of the tooth root can contribute to the opening of the lateral canals and dentinal tubules, resulting in the pulp destruction. Progressive periodontal pathology can lead to the pulp necrosis [4]. Chronic combined periodontal and periapical lesions have a negative impact on the human organism, since they are a source of intoxication and sensitization causing progression of infection, development of focal sequelae and secondary immunodeficiency [5, 6].

Problem of successful treatment of apical and marginal periodontitis is associated with a significant prevalence of these diseases, a complexity of medical procedures, a substantial proportion of failures and complications, and with a lack of long-term stability of gained results [7].

Endodontic treatment in patients with pathology of periodontal tissues is of particular importance: it is impossible to achieve a long-lasting remission and stabilization of pathological process without an appropriate endodontic treatment; on the other hand, incomplete endodontic therapy may result in the aggravation of periodontal status at the early stages of periodontitis [8, 9].

Aim

The aim of this work was to investigate clinical effectiveness of drug formulation with thiotriazoline and chloramphenicol [10] in the integrated treatment of combined apical and marginal periodontitis.

Material and methods

Status of oral cavity of 105 patients with apical and marginal periodontitis, who were given complex treatment and a dynamic supervision, was studied. 46 patients were diagnosed with chronic generalized periodontitis (GP) of the I stage of severity; the rest 59 patients had the GP of the II stage of severity. All patients were also diagnosed as carrying lesions of chronic apical infections, among which were granulating (45%), fibrous (37%) and granulomatous (28%) periodontitis.

Clinical examination was performed according to the standard scheme. The diagnosis was made based on the complaints, anamnesis, and assessment of general and local health of patients. The anatomical features of the oral vestibule, the condition of the gingival mucous membrane, the depth of the periodontal pockets, the extent of the gingival recession and pathological tooth mobility were considered during the physical examination of the periodontal tissues. Local irritating factors such as trauma, tooth extraction, incorrect fillings, unstable dental prosthesis, plaque, calculus were also registered. The simplified oral hygiene index (OHI-S) [11], the sulcus bleeding index (SBI) [12], the papillary-marginal-alveolar index (PMA) [13], the periodontal index (PI) [14], and probing depth [15] were evaluated during the index assessment. Among the complaints of the patients with periodontitis a special attention was paid to the spontaneous pain in the causal tooth, the pain on biting, the presence of a fistula.

The duration of the disease, the occurrence of exacerbations, the previous treatment and its effectiveness were determined from the anamnesis. During the physical examination the tooth percussion sensitivity was evaluated, the alveolar bone in the root apex projection was palpated, and symptoms of angioparesis, edema and mucous membrane hyperemia were also determined. The status of the alveolar process and the periapical tissues was assessed using the X-rays examination. Patient's examination was performed before and after treatment, and in the later periods – after 6 months.

All patients received endodontic and periodontal treatment. The patients were divided into two groups according to the given therapy. 52 patients of the main group were treated with thiotriazoline and chloramphenicol ointment after the basic therapy. 53 patients of the control group were given standard treatment.

Providing the endodontic care for patients with combined marginal and apical periodontitis was a priority task. Complex treatment of patients with different clinical forms of apical periodontits, besides mechanical tooth cleaning, disinfection and reliable obturation of the root canals, should include pharmacotherapy of the apical periodontal lesions for pharmacological correction of inflammatory process. Scheme of the endodontic treatment included the following procedures: the creation of an optimal access to the root canals, the evacuation of the degradation products, the mechanical and antiseptic root canal treatment with sodium hypochlorite 5.25%. Apical therapy was finished by additional administration of the ointment with thiotriazoline and chloramphenicol into the root canal of patients from the main group, followed by closing with temporary filling; in patients from control group 0.2% chlorhexidine digluconate solution was introduced into root canal and teeth were temporarily closed.

After 2–3 days the drug preparation inside the root canal was changed into the fresh one, which was repeated 2–3 times. After the drug therapy patients without complications were exposed to obturation of root canals by sealer "Apexit" (Vivadent) and technique of cold lateral gutapercha condensation. Quality of obturation was radiographically assessed.

Periodontal treatment was performed according to the standard principles with consideration of the severity of the periodontitis and the patients' individual characteristics. Periodontal treatment included professional hygiene of oral cavity, scaling, root planning, open and closed curettage, medicamental treatment. Treatment of the control group was finished with conventional therapy. Patients in the main group were given the applications with thiotriazoline and chloramphenicol preparation in the periodontal pockets and marginal gums for 15–20 min. Number of visits depended on the severity of the inflammation.

Results of the study were statistically processed using Wilcoxon signed-rank test.

Ethical Committee Approval: 29.10.2007, protocol number 8.

Results

After the started complex treatment patients in the main group subjectively noticed an improvement in the periapical tissues and gums, and the inflammation reduction was determined objectively. In the next visit the situation was markedly better: pain was gradually disappearing, the exudation was decreasing, the vertical percussion was negative and the paper points used for the root canal were clean. Only 5 patients within the first 2–3 days suffered a discomfort while eating solid foods. 65% patients in the control group who were treated by traditional endodontic treatment, felt the pain when biting on the causative tooth within 3–4 days. The pain syndrome in patients with GP of the II stage lasted for 5–6 days.

The proposed method of medicated influence on lesions of apical periodontal tissues enabled us to reduce the number of visits in the main group from 4.2 to 2.4 and decrease the treatment time 1.8 times.

This was confirmed by more rapid disappearance of clinical symptoms such as spontaneous pain, pain to palpation of the gums or percussion of the teeth, symptoms of angioparesis, edema and hyperemia of the gums in projection of root apex of affected tooth; if the fistula had been present, it was quickly closed. The number of exacerbations that occurred during the treatment and after the root canal dressing in patients of the main group was much less than in the control group.

6 months after root canal treatment the mild tenderness to percussion was detected in 5 patients of control group. Control roentgenograms showed widening of periodontal slit and increasing of bone loss in the apical part of the tooth root in 8 patients. Clinical picture in main group was better: complaints on discomfort and pain were absent; destructive lesions in the apical part of bone had tendency of decrease.

A positive dynamics in patients of the main group was also observed in periodontal tissues: pain, gingival hyperemia and hemorrhage were gradually decreased. Objective examinations showed marginal gingiva induration, decrease of periodontal pocket's depth and tooth mobility, color of gums was gradually changing into light pink.

We determined a positive dynamics of clinical indices. All indices, which describe the status of periodontal tissues of GP of the I stage of severity are shown in **Table 1**. For example, OHI-S index by Green-Vermillion in patients of the main group with chronic GP of the I stage decreased from 1.69 ± 0.04 points (before treatment) to 0.34 ± 0.02 points (after treatment). After the ointment with thiotriazoline and chloramphenicol the parameters decreased 5 times, in the patients of control group – 3 times. 6 months later OHI-S increased a little both in main group (to 0.51 ± 0.03 points), and in control group (to 0.84 ± 0.03 points) that may be explained by reduction in hygienic skills of patients.

Similar changes were also found for the SBI. Right after the treatment the SBI in patients of the main group significantly decreased from 1.73 ± 0.06 to 0.51 ± 0.03 points. In the control group the SBI was higher -0.75 ± 0.03 points. But within 6 months it was observed the increasing of the SBI and at the moment of repeated examination the SBI in patients of the main group was 0.66 ± 0.03 points, in patients of control group -0.98 ± 0.04 points.

| | | | - | - | | | |
|--------------------|----------------------|-------------------------|----------------------|-------------------------|--------------------------|-------------------------|--|
| | Before tr | eatment | After tr | eatment | 6 months after treatment | | |
| Indices | Main group n = 24 | Control group n = 22 | Main group n = 24 | Control group n = 22 | Main group n = 22 | Control group n = 21 | |
| OHI-S (points) | 1.69 ± 0.04 | 1.74 ± 0.01 | 0.34 ± 0.02 ††† | 0.57 ± 0.02 ***††† | 0.51 ± 0.03 ††† | 0.84 ± 0.03 ***††† | |
| PI (points) | 1.85 ± 0.09 | 1.87 ± 0.08 | 0.81 ± 0.02 ††† | 0.99 ± 0.02 ***††† | 0.94 ± 0.02 ††† | 1.03 ± 0.02 **††† | |
| PMA (%) | 34.46 ± 0.35 | 35.09 ± 0.21 | 3.68 ± 0.16 ††† | 7.10 ± 0.25 ***††† | 4.53 ± 0.13 ††† | 9.63 ± 0.16 ***††† | |
| SBI (points) | 1.73 ± 0.06 | 1.70 ± 0.06 | 0.51 ± 0.03 ††† | 0.75 ± 0.03 **††† | 0.66 ± 0.02 ††† | 0.98 ± 0.04 **††† | |
| Probing depth (mm) | 2.78 ± 0.04 | 2.68 ± 0.05 | 1.65 ± 0.03 ††† | 2.04 ± 0.03 ***††† | 1.32 ± 0.02 ††† | 2.27 ± 0.03 ***††† | |

| Table 1 | . Periodontal | indices in the | patients with | combined | lesions with | GP of | I stage of | heaviness in c | lynamics |
|---------|---------------|----------------|---------------|----------|--------------|-------|------------|----------------|----------|
| | | | | | | | | | |

Difference between the means is signifficant at:

1. Main and control groups: * - p < 0.05, ** - p < 0.01, *** - p < 0.001.

2. Groups before and after treatment: $\uparrow - p < 0.05$, $\uparrow \uparrow - p < 0.01$, $\uparrow \uparrow \uparrow - p < 0.001$.

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| | Before tr | eatment | After tr | eatment | 6 months after treatment | | |
|------------------------------|------------------|-----------------|-------------|---------------|--------------------------|-----------------|--|
| Indices | Main group | Control group | Main group | Control group | Main group | Control group | |
| | n = 28 | n = 31 | n = 28 | n = 31 | n = 26 | n = 28 | |
| OULS (points) | 3.24 ± 0.04 | 3 28 ± 0.04 | 0.53 ± 0.03 | 0.70 ± 0.02 | 0.56 ± 0.03 | 1.71 ± 0.02 | |
| | J.24 ± 0.04 | J.20 ± 0.04 | <u>+++</u> | ***††† | <u>+</u> ++ | ***††† | |
| $Pl(points) = 2.17 \pm 0.00$ | | 3.21 ± 0.00 | 1.43 ± 0.05 | 1.59 ± 0.03 | 1.61 ± 0.03 | 1.90 ± 0.02 | |
| ri (points) | J.17 ± 0.09 | J.21 ± 0.09 | <u>+++</u> | **††† | <u>+</u> ++ | ***††† | |
| DMA(0/a) | 50.31 ± 0.84 | 58 70 ± 0.85 | 8.79 ± 0.14 | 12.22 ± 1.14 | 10.21 ± 0.21 | 15.63 ± 0.18 | |
| FIVIA (70) | J9.J1 ± 0.04 | J0.79 ± 0.0J | <u>+++</u> | ***††† | <u>+</u> ++ | ***††† | |
| (Points) | 3.05 ± 0.07 | 3 13 ± 0.06 | 0.66 ± 0.03 | 0.78 ± 0.02 | 0.90 ± 0.04 | 1.09 ± 0.04 | |
| | 5.05 ± 0.07 | 5.15 ± 0.00 | <u>+++</u> | **††† | <u>+</u> ++ | **††† | |
| Prohing donth (mm) | 1.26 ± 0.03 | 1 23 + 0.03 | 2.65 ± 0.04 | 2.95 ± 0.04 | 2.41 ± 0.04 | 3.24 ± 0.05 | |
| | 4.20 ± 0.03 | 4.23 ± 0.03 | ††† | ***††† | <u>+++</u> | ***††† | |

Table 2. Periodontal indices in the patients with combined lesions with GP of II stage of severity in dynamics

Difference between the means is signifficant at:

1. Main and control groups: * - p < 0.05, ** - p < 0.01, *** - p < 0.001.

2. Groups before and after treatment: † - p < 0.05, †† - p < 0.01, ††+ - p < 0.001.

The value of PMA, which reflects the intensity and the prevalence of inflammation in the periodontal tissues, in patients with GP of the I stage decreased too (in the main group – 9.4 times, in the control group – 5 times), 6 months after the PMA slightly increased. But difference between values of both indices shows the advantage in use of composition with thiotriazoline and chloramphenicol.

The probing depth under the effect of proposed ointment reduced from 2.78 \pm 0.04 mm to 1.65 \pm 0.03 mm, and 6 months later it was 1.32 \pm 0.02 mm.

The PI in patients of the main group was equal to 1.85 ± 0.09 points before treatment, and is decreased 2.3 times after the treatment. In the control group the PI decreased 1.9 times. 6 months after the PI in the main group reduced to 0.94 ± 0.02 points, in the control group – to 1.03 ± 0.02 points. The results of the PI show a statistically significant difference.

Having analyzed the effectiveness of the treatment of patients with chronic GP of the II stage, we got the other results (**Table 2**). The OHI-S, the PI, and the pockets depth decreased markedly, 6 months after the further decrease was significant in patients of main groups.

Use of the composition with thiotriazoline and chloramphenicol significantly improved the effectiveness of the local treatment in patients of the index group, providing the decrease of the OHI-S to 0.53 \pm 0.03 points, whereas the OHI-S in the control group reduced to 0.70 \pm 0.02 points.

Comparison of the SBI in patients of the two experimental groups indicates a strong anti-inflammatory action of the proposed preparation: in patients of the main group the SBI decreased to 0.66 ± 0.03 points, in the control group – to 0.78 ± 0.02 points; after 6

months the SBI was 0.90 \pm 0.04 vs 1.09 \pm 0.04 points, respectively.

The PMA in the main group was $59.31 \pm 0.84\%$ before treatment, and after treatment it changed to $8.79 \pm 0.14\%$. In the control group it was $58.79 \pm 0.85\%$ and $12.22 \pm 0.14\%$, accordingly. 6 months after the treatment with thiotriazlone and chloramphenicol ointment the PMA was $10.21 \pm 0.21\%$; in the control group it amounted to $15.63 \pm 0.18\%$.

The probing depth in patients of the main group was 4.26 ± 0.03 mm before treatment, 2.64 ± 0.06 mm – after treatment, and 2.41 ± 0.04 mm – after 6 months. In patients of the control group the probing depth after 6 months was 3.24 ± 0.05 mm.

The dynamics of the PI was also positive. The PI in the patients of the main group decreased to 1.43 ± 0.05 points, in patients of the control group – to 1.59 ± 0.03 points. 6 months after it was equal to 1.61 ± 0.03 and 1.90 ± 0.02 points, accordingly.

Conclusions

The results of the investigations showed a high effectiveness of the proposed therapeutic scheme for combined apical and marginal periodontitis. This complex treatment including thiotriazoline and chloramphenicol ointment provided the reduction in the recovery time, as well as the positive dynamics in indices (OHI-S, PBI, PMA and PI). Only such complex approach that includes the endodontic and periodontic treatment gives the stable positive result. Results of applied treatment indicated an acceleration of healing process, reduction of exudation period and decrease of exacerbation frequency.

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The impact of factors in work environment (especially shift and night work) on neoplasia of female reproductive organs

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ABSTRACT

Shift work, due to disruption of circadian rhythms, can interfere with a number of physiological functions. It may lead to multiple pathologies (functional gastrointestinal disorders, peptic ulcer disease, hormonal disorders – including impaired melatonin secretion, cardiovascular disease, mental disabilities, neurological disorders etc.). In the last few years, we started to think about the association between disruption in melatonin secretion and the occurrence of certain malignancies. Authors describe and discuss pathophysiology, epidemiological and clinical data concerning influence of shift work to occurrence of some neoplasms.

Keywords: neoplasm, shift work, melatonin.

Introduction

Shift work, due to disruption of circadian rhythms, can interfere with a number of physiological functions. It may lead to multiple pathologies (functional gastrointestinal disorders, peptic ulcer disease, hormonal disorders - including impaired melatonin secretion, cardiovascular disease, mental disabilities, neurological disorders etc.). In the last few years, we started to think about the association between disruption in melatonin secretion and the occurrence of certain malignancies. There are confirming epidemiologic data from almost seventy years before [1]. Melatonin blood level fluctuations may be a factor participating in the development of especially breast and colorectal cancer. Moreover, it seems that the hormone has also an impact on ovary, endometrium, and prostate neoplasia occurrence. There is also a suspicion that disturbances in the melatonin secretion may be a factor inducing changes in the physiology of the mucous membranes in gastrointestinal tract (ulcers), hypertension and abnormal irregular menstrual cycle – frequent diseases in shift workers [1].

Physiology, pathophysiology and results from experimental studies

Suprachiasmatic nucleus, situated in the anterior part of hypothalamus, is one of the most important parts of the brain (as well as medulla oblongata, pons and raphe nuclei), affecting the onset of mammalian twenty-four hour rhythm series in physiological functions [2]. Alteration in circadian rhythm causes destruction just in the anterior part of hypothalamus in experimental animals. The optic fibres from the retina reach these structures, and by stimulus may modify the daily rhythm. Alteration in daily rhythm of melatonin secretion by the pineal gland is the consequence of their function. It was found that a significant impact on

the retina of the human eye (including the synthesis of melatonin) has exposure to light with a wavelength between 446 and 484 nm [3]. Light, of less than 1 lux significantly inhibits the synthesis of nocturnal melatonin [3]. Melatonin is produced in a significant amount in the pineal gland. Amino acid L-tryptophan is the substrate for this synthesis. Its secretion by the pineal gland depends on the circadian rhythm, closely related to the changes of the amount of light reaching the retina during the day and at night, increases in darkness and decreases during exposure to natural or artificial light. Increased melatonin production is associated with longer night periods - in an annual rhythm and in higher latitudes. Melatonin allows for organisms adaptation to changes in lighting rhythm. Among commonly known properties of this substance one can distinguish the function of antioxidants, adjusting sleep-wake rhythm, immunomodulatory function, effects on puberty and the process of reproduction, the emergence of mental disorders and diseases of the central nervous system [4]. Furthermore, melatonin has a positive influence on fight against Gram-negative bacterias infections by immune system, reduces the immunosuppressive effects of stress, enhances antitumor activity of interleukin-2 (IL-2), interleukin-6 (IL-6), interleukin-12 (IL-12) interferon (INF-y) and increases level of neutral killers (NK) [4, 5]. It is known, that this substance may be a diagnostic and prognostic marker of neoplasia. In addition, melatonin heals circadian rhythm alteration caused by air travel (jet lag) and shift work [4].

Melatonin is also produced in rich in serotonin enterochromaffine cells (APUD) in the gastrointestinal tract. It gets to the portal circulation (endocrine effect) and lymphatic tissue but has also auto- and paracrine effect. Thus, it affects the function of mucosa and reduces the voltage of smooth muscle of digestive tract. The presence of food, not light stimulation of the retina is the stimulus for melatonin secretion in the gastrointestinal tract [5]. It has been shown that a colon cancer development is associated with decrease of APUD cells number, that synthesize serotonin, melatonin and other peptides [6, 7].

Melatonin may participate in the process of neoplasia in female reproductive system through various ways [9]:

 melatonin has anti-estrogenic properties – reduces estrogen secretion by the ovaries,

There are an evidence that suppression of the hypothalamus-pituitary-ovarian axis reduces LH and 17betha estradiol [10]. Deteriorated levels of melatonin during night-work cause an increased level of estrogen in premenopausal women [11].

- melatonin stimulates the synthesis of progestagens It seems that via an impact on the transcriptional activity of the steroidogenic enzymes melatonin may modulate ovarian theca cell steroidogenesis at the molecular level [12, 13].
- the occurrence of seasonal variability in, e.g. endometrial hyperplasia can be associated with melatonin levels.

According to Dznelashvili (2013) received results, the more complicated the type of endometrial hyperplasia is, the more consistently melatonin is reduced in blood plasma [14].

 melatonin levels decrease rapidly during menopause period – typical period of breast and endometrium cancers occurrence,

Melatonin therapy in menopausal patient causes the decrease of LH and FSH level in the blood and this therapy is under intensive investigation as a kind of pineal-pituitary-ovarian axis control [15, 16].

 obesity is often associated with cancer – such persons have more frequent disturbed daily melatonin levels,

Significant finding is the induction by melatonin of white adipose tissue browning, which may be related to its effects against oxidative stress as well as body weight reduction in experimental animals [17].

 diabetes, which is correlated with the occurrence of certain cancers (e.g. endometrial cancer), causes reducing in secretion of melatonin by the pineal gland and increases the likelihood of calcification of this gland [10, 17].

For example the mean of salivary melatonin level was significantly lower in patients with type II diabetes [18].

During in vitro treatment, it was found, that melatonin inhibits the process of angiogenesis in tumors (decreases the expression of VEGF receptor and increases the expression of epidermal growth factor receptor and insulin growth factor-1), and significantly affects the rate of cell's DNA synthesis in some tumors [19, 20]. As it was mentioned, it has been shown that it may prevent tumor development by enhancement of immune-response: it stimulates proliferation and maturation of immune cells (NK, T/B- lymphocytes, granulocytes monocytes) [20]. In vitro, melatonin significantly inhibits tumor growth of endometrial, stomach and adrenals cancer, and in some cases of renal, colon and

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rectum cancer. In clinical experimental studies on rats, melatonin inhibited the increase of some form of prostate adenocarcinoma [20]. The relationship has been shown between the growth rates of implanted human breast cancer cells in rats (MCF-7) and the rhythm of illumination. The study evaluated melatonin and linolenic acid levels in the two groups of rats – first, which lived alternately twelve hours in light and darkness, and the other exposed to light all day and night. In rats that were exposed to artificial lighting all the time lower concentrations of melatonin levels was found and rapid proliferation of cancer. The proposed mechanism for melatonin, which limits the growth of the tumor is inhibition of the cellular receptors of tumor's cells, thus affecting the metabolic linolenic acid utilization. Another study revealed that melatonin has directly inhibitory effects on MCF7 human breast cancer cell growth in culture, although supra- or subphysiological levels of melatonin are completely ineffective [21]. Also precursors and metabolites of melatonin such as serotonin, N-acetylserotonin and 6-hydroxymelatonin do not inhibit MCF-7 cell growth. It seems that the antiproliferative effect of melatonin may be dependent on the presence of serum and a complex interaction with hormones such as estradiol and/or prolactin because without it melatonin loses antimetabolic function [21]. In terms of breast cancer, population-based case-control study suggests that polymorphisms in circadian genes and melatonin's biosynthesis genes (like CLOCK, MTNR1B, NPAS2 and ARNTL) may be involved in the process of neoplasia [21].

In case of endometrial cancer, the cytostatic effect of melatonin seems to be mediated by melatonin receptor 1 (MT1) but not MT2, and attenuation of estrogen receptor alpha (ER alpha) expression in endometrial cancer cells [22].

Other experimental studies also confirm anticarcinogenic impact of that substance – eg. the administration of melatonin in rats with removed pineal gland results in inhibition of carcinogenesis [23]. It has been found in experimental studies in rats that changes in circadian rhythm significant disturb the functioning of the immune system (inter alia characterized by changes in the blood results) and increase the risk of tumor growth. Melatonin reduced the risk of such effects [23] and we can conclude it has immuno-modulating, anti-carcinogenic, antiproliferative and anti-inflammatory properties.

Interesting study of Qin et al. (2012) has shown one of the possible anti-proliferative and anticarcinogenic mechanism of melatonin. It reveals, that the hormone may reduce the levels of MMP9 (matrix metalloproteinases) mRNA and protein through up-regulation of TIMP1 (MMP9-natural inhibitor) mRNA and protein, via the nuclear factor kB translocation (NFkB/p65) as well as through direct mechanism: inhibition of MMP-9's activity by binding to its active side. MMPs induced by inflammatory cytokines IL1 β might be a potential mechanism that affects endothelial barrier function, so that might be associated with tumor invasion, metastasis, and angiogenesis [24].

The anti-inflammatory mechanism has been also examined. Melatonin inhibits lipopolysaccharide (LPS)-induced cyclooxygenase-2 (COX-2) and inducible nitric oxide synthase (iNOS) protein levels via inhibition of p300 histone acetyltransferase (p300 HAT) activity and p52 acetylation. Interestingly, in experimental studies, some carcinogens eq. 7.12-dimethyl- [a] anthracene (DMBA) caused growth of the maximum level of melatonin present in the blood during the night, which could indicate a physiological mechanism, which enables the synthesis of melatonin in the case of significant exposure to the carcinogen. In experimental studies in rodents, it was found that other peptides of the pineal gland (epitalamina) and similar synthetic tetrapeptide - epitalon (Ala-Glu-Asp-Gly) are potential inhibitors of carcinogenesis in breast cancer [25].

Clinical and epidemiological data

Shift work affects daily level of melatonin in the blood as well as certain hormones participating in the process of carcinogenesis. Three years lasting research on the relationship between labor rhythm and expulsion of melatonin metabolite in morning urine (6-sulfatoxymelatonin) and levels of steroid hormones in plasma, in 80 women before menopause, showed an increased levels of serum estradiol. It concerned women who have been employed in shift work for at least fifteen years (mean concentration of serum estradiol 10.1 pg / ml) compared with those who have never worked like that (8.8 pg / ml) (p = 0.03). It revealed a statistically significant inverse relationship between the number of worked nights within two weeks and the concentration of melatonin metabolite in urine (r = -0.30, p = 0.008) [26]. Melatonin seems to have anti-estrogenic and anti-aromatase activity as well as may affect fat metabolism, which are risk factors of endometrial cancer. Viswanathan et al. conducted a study consisting of the 121,701 women, where 53,487 had night shift work and 515 of them developed invasive endometrial cancer. The study revealed that women who worked

20+ years of rotating night shifts had a significantly increased risk of endometrial cancer (multivariate relative risks MVRR: 1.47) and obese women doubled their baseline risk of endometrial cancer (MVRR, 2.09) [27]. Because of the fact that darkness increases the plasma concentrations of melatonin (treated as an anti-cancer substance), epidemiological studies were conducted among populations without the effect of light on melatonin secretion - the blind and visually impaired. In the Swedish study, 1567 completely blind and 13 292 visually impaired persons were found to have much lower risk of cancer (RR = 0.69; 95% CI = 0.59-0.82) respectively to general population [27]. It was also revealed that the average concentration of melatonin in the blood is significantly lower in patients with prostate and breast cancer [28]. Epidemiological studies in the population of 78.586 women (nurses) working in shifts for 14 years (at least three night shifts a month), comparing to women who have never been working in shifts, showed that the risk of colorectal cancer was not increased (RR = 1.00; 95% CI: 0.84-1.19). Whereas, in the analysed population the risk was definitely growing on average by 35% (95% CI = 1.3-1.77), after working more than 15 years in the night-shift system [29]. In the same population, the risk of breast cancer grew moderately with the time of shift work (at least 3 night shifts a month). The risk of breast cancer grew in population with the work experience from one to 29 years for about 8% (95% CI = 0.99-1.18 in the population with work experience from one year to 14 years and 0.90-1.30 in the population with experience of 15 to 29 years). Only long-term shift work (above 30 years) caused the risk significantly increased on average by 36% (95% CI = 1.04-1.78) [29]. However, other study of Schernhammer et al. showed that already more than 20 years of rotating night shift work was related with elevated risk (30). When it comes to breast cancer Hansen examined also nurses and revealed confirming data: nurses who worked rotating shifts after midnight had a significantly increased odds ratio OR (1.8; CI 1.2-2.8) for breast cancer compared to nurses with permanent day work. No association was found in a small group of nurses with evening work and without night work (OR = 0.9; 0.4–1.9) [31]. Jia et al. in metaanalysis of epidemiological studies confirmed association between night shift work and breast cancer. Nevertheless, Kamdar et al. in their meta-analysis conclude that there is weak evidence to support previous reports. Using random-effects models, the pooled relative risk (RR) for individuals with ever night-shift work exposure was 1.21, for short-term night-shift workers (< 8 years)

it was 1.13 and for long-term night-shift workers (\geq 8 years) it was 1.04 [32]. Clinical case control study in Seattle analysed night habits at work of 813 women with breast cancer and 793 women as a group control. The study showed that increased by an average of 14% breast cancer risk applies to people who often do not sleep at night in the 10 years prior to the analysis (95% CI = 1.011.28). The risk of this disease did not grow in the case of people who usually have often intermittent sleep with lightening artificial light [33]. In relation to ovarian cancer, large prospective study of 181.548 women revealed no association between duration of rotating night shift work and risk of ovarian cancer [34].

Other occupational factors affecting level of melatonin

One of the professional factor affecting melatonin secretion is exposure to electromagnetic fields. There have been a number of studies attempting to correlate the relationship between the effects of exposure to this factor and the epidemiology of breast cancer [35]. Most of these studies have not shown any strong relationship between these factors. Future studies should focus on a comprehensive assessment of the impact and interdependence of different exposure parameters, field frequency, and co-occurrence of shift work and the individual factors like age and hormonal factors (eg. estrogen receptors). Norwegian study of 2619 women is an example of a significant impact of occupational exposure to electromagnetic fields and simultaneous shift work on carcinogenesis. The relative risk for carcinogenesis in this population was significantly increased by 20% compared to the general population, and in the case of breast cancer increased by 50%! [35].

Melatonin in treatment

There is some evidence that high-dose of melatonin may be beneficial in the combined cancer's treatment (e.g. with chemotherapy). Regression of tumor mass was described for breast cancer and prostate cancer but also lung, kidney, liver, pancreatic, stomach and colon cancer. Worth noticed is the conclusion from the Lissoni's study that melatonin plus chemotherapy in patients with metastatic solid tumors seems to increase regression rate and one-year survival rate by approximately 50% compared to chemotherapy alone. Lung cancer – 104 cases, breast cancer – 77, gastrointestinal tract neoplasms- 42 and head and neck cancers-27 were taken into consideration. Another thing is that melatonin seems to reduce side effect of chemotherapy. For example, it is proven to enhance platelet number in patients with thrombocytopenia due to chemotherapy of metastatic breast cancer [7, 36]. It has an impact on other haematopoietic cells as well as may diminish neurotoxicity, cardiotoxicity, stomatitis and asthenia [36].

Summary

Circadian rhythm disorders caused by work in the night work shift system seems to be the interesting issue in practical occupational medicine. It requires further detailed epidemiological studies and clinical trials. Please note that, for mentioned cancers, there are many other, highly significant risk factors. It is worth noting, that there is a higher risk of a malignant tumor occurrence while working in shifts for many years, especially when there are other unresponsive risk factors (eq. age, genetic factors) and customisable ones. Practically, the exogenous supplementation of melatonin seems to be important in reducing the negative shift work's impact [32, 37]. Interesting would be the analysis of the effectiveness of such therapy in relation to other health problems associated with such a system work, especially because recent studies showed different activity of melatonin transcription in endometrial cancer. It could provide new diagnostic and prognostic markers od the disease [37].

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ORIGINAL PAPER

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"UnderstAID – a platform that helps informal caregivers to understand and aid their demented relatives" – assessment of informal caregivers – a pilot study

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ABSTRACT

Introduction. The number of people with dementia increases. Patients are dependent of informal care provided by their family members, especially spouses, children and friends. As the disease progresses caregiving becomes more complex, stressful and demanding. The needs of informal caregivers are related to the lack of professional support in care, including information about the disease, advise of management of its symptoms and social and financial support. It is therefore important to create an information tool which will assist caregivers in their daily work with people with dementia.

Aim. The aim of the study was the technical evaluation of the information platform for caregivers of patients with dementia.

Material and methods. The study involved 18 caregivers of patients with Alzheimer's disease. The level of GDS scale comprised those between 4 and 7. Platform testing had been carried out from 15 February to 15 March 2015. Evaluation of the platform was made using a technical questionnaire depending on the result of the GDS and the Zarit scale.

Results and conclusions. Platform was rated positively by caregivers (average score 4 out of 5) with the exception of a few areas which received an average rating of 3. These areas include: usefulness of the guidance provided for the application (26% of respondents assessed it negatively), ease to find the relevant information (25% negative assessments), application responsiveness (24% negative assessments) and the quality of the media files (23% negative assessments). Respondents assessed the platform positively, although some technical issues need improvement.

Keywords: dementia, caregivers, software.

Introduction

Dementia is defined as a set of symptoms caused by a chronic and progressive brain disease. As the disease develops, all life functions are affected and independent functioning in the society is disabled. Those responsible for direct and long-term caretaking are most often informal caregivers, i.e. caregivers not related in any way to health care [1–3]. Carrying out such duties is associated with intense stress caused by the lack of professional background, emotional attitude towards the demented person or insufficient help by the state or medical institutions [3–5]. This great physical, mental and emotional burden negatively impacts the health of caregivers themselves [6–8]. It may lead to depression, persistent feeling of not being able to

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cope with the existing situation or an impression of life quality decline [1, 9, 10]. Owing to the incidence rate and the difficulties in organising and financing care of demented people, dementia has become one of the top challenges of healthcare system in the 21st century. Even though more than a half (65%) of dementia patients live in developed countries, the escalation of the above-mentioned problems is directly proportional to an increase in the percentage of the elderly in the global population [2, 11]. In Poland, almost 92% of dementia patients stay at their family homes and most often are taken care of by their spouses, who are at similar age and of failing health, at times even disabled. Frequently, caregivers are left on their own, with no professional help or mental support [2, 12]. In Poland, visits of a public health nurse are a form of help for caregivers of demented relatives. However, this kind of help takes the form of everyday nursing care and wound dressing [13]. Only 6% of Polish dementia caregivers, who participated in studies, described the level of help that the patient receives from the state as satisfactory [12]. To help cope with this status quo, the UnderstAID platform has been created, which was aimed at developing a tool which would support informal caregivers in understanding their demented relatives and in aiding them. The project was awarded in the 5th edition of the Ambient Assisted Living (AAL) Joint Programme.

The participants in the programme are: Sekoia Assisted Living ApS; Faculty of Health Science, VIA University College; Danish Alzheimer Association; Skanderborg Municipality; Instituto de Salud Carlos III and The Centre of Supercomputing of Galicia (CESGA); Balidea Consulting and Programming; Provincial Association of Pensioners and Retired People (UDP) from A Coruña, Poznan University of Medical Sciences (PUMS); and Wiktor Dega's Orthopaedic and Rehabilitation Clinical Hospital (ORSK) of Poznan University of Medical Sciences.

Aim

The study was aimed at the technical assessment of the UnderstAID platform by informal caregivers of persons suffering from dementia.

Material and methods

18 informal caregivers of individuals with Alzheimer's disease, including 2 men and 16 women aged 34-76 (mean age 57 + 10.7) participated in the study. To the

study, the caregivers who met the following inclusion criteria were qualified:

- informal caregivers, who took care of dementia individuals for more than 16 months,
- informal caregivers were the main non-professional caregivers of the demented individual and did not get paid for caretaking,
- informal caregivers had constant access to computer and the Internet at home,
- patient's dementia was assessed to be 4 or more in the GDS scale.

The exclusion criteria were cognitive impairment, illiteracy and visual or motor dysfunctions.

The study was conducted in accordance with the Declaration of Helsinki and consent of the Bioethical Committee of Poznan University of Medical Sciences dated 8 October 2012 (no. 990/12) was obtained. Before participation, all subjects gave their written consent to participate. The study is part of the Ambient Assisted Living (AAL) Joint Programme financed by the European Union and dedicated to National Financing Institutions – Agreement no. AAL-2012–5-107.

Method description

The study was conducted from 15 February to 15 March 2015 at homes of the caregivers on the territory of Poland. All subjects were given 2-month access to the pilot version of the platform. Before the subjects started to use the platform, they filled in the Zarit Caregiver Burden Scale questionnaire. On the scale, 0–20 points indicate no or mild burden that the caregiver experiences as a result of everyday caretaking of a demented relative, 21–40 points mean mild to moderate burden, whereas above 40 – severe burden.

The subjects were taught how to properly use the UnderstAID platform. They were to download and instal the application by themsleves in order to assess its usability. It was possible to test the platform on a PC, smartphone or tablet. When the testing was over, the subjects evaluated the UnderstAID platform using the author's technical assessment questionnaire (approved by Ambient Assisted Living – AAL). The questionnaire included 11 statements related to technical aspects of the application.

Results

In the study group, moderate burden in the Zarit scale (20.4 points) was confirmed for 28% of subjects and severe burden for the remaining part (53.2 points).

All the subjects with moderate burden (group I) and more than a half of those showing severe burden (group II) confirmed that the buttons were appropriately located in the application (**Figure 1**).

Answers to question no. 2 of the technical assessment questionnaire gave similar results. The whole of the group I and most of the caregivers from group II agreed that the layout of images in the application was adequate. All the subjects of group I said that the instructions on how to use the application were valuable. In group II, half of the subjects confirmed that the instructions were useful. However, 16% of the group disagreed on the matter. The caregivers with moderate burden claimed that the application was easy to use. Some of the caregivers (42%) from the group of severe burden agreed with this statement, whereas



Figure 1. Answers to question no. 1 of the technical assessment questionnaire given by the caregivers depending on the level of burden



Figure 2. Answers to question no. 5 of the technical assessment questionnaire given by the caregivers depending on the level of burden

25% disapproved of it. For the majority of the subjects from both groups, the application was intuitive. On the other hand, 8% of the subjects from group II were not able to tell how a given action performed in the application would end (**Figure 2**).

All of the subjects from group I and a big percentage of the subjects from group II confirmed that contrasting colours (text on a given background, colours of illustrations) and the size of the text make the application easy to use. In group II, 16% of the subjects opposed this statement. For the majority of the subjects from both groups, the way the application could be operated was well adapted to the devices they used. In the group of severe burden, 8% the of subjects disagreed. The whole of group I and some of the caregivers (41%) from group II confirmed that they had practically no difficulty finding information they were looking for. In group II, however, some of the subjects (33%) were not able to find the information they required. Caregivers from group I, unanimously claimed that the quality of multimedia files (videos, images, sound) used in the application was adequate. In group II, only a small number of subjects agreed with this statement. In this group, there were also individuals for whom the quality of the files was insufficient (Figure 3).

The majority of the subjects from group I and some of the subjects from group II said that the application worked fast and without any problems. However, in both groups there were also subjects who disagreed with this statement (**Figure 4**).

More than a half of the subjects from both groups confirmed that the support option in the application



Figure 3. Answers to question no. 9 of the technical assessment questionnaire given by the caregivers depending on the level of burden



Figure 4. Answers to question no. 10 of the technical assessment questionnaire given by the caregivers depending on the level of burden



Figure 5. Answers to question no. 11 of the technical assessment questionnaire given by the caregivers depending on the level of burden

was useful. In both groups, however, there were also a few caregivers not satisfied with the "Help" option (Figure 5).

Discussion

The overall technical assessment of the platform conducted by the informal caregivers is satisfactory. Nevertheless, some technical shortcomings were revealed. Reduced utility of the "Help" function, difficulty in finding specific information, as well as problems with application performance or multimedia files quality were confirmed. A similar e-learning tool proposed by Chambers et al. was assessed much higher [14]. The UnderstAID platform was not evaluated that well owing to some technical aspects, which in the caregivers' opinion have not been sufficiently worked up. In the case of UnderstAID, the quality of multimedia files needs to be improved, even though the contrast between colours and font size were evaluated as adequate. Moreover, according to the caregivers the application should be faster and more efficient.

An automated psycho-educational program for caregivers of persons with Alzheimer's disease called Diapason may be another example of such tools. It was assessed to be useful (95%), comprehesible (100%) and complex (85%) but since the study sample was narrow the results cannot be treated as decisive. During the evaluation of the Diapason project, not only quantity but also guality measurements were conducted, which indicated that the approval of the program was little and the expectations of caregivers towards this type of tools were big. These expectations concerned functions such as performance, intuition in using the application or level of personalisation. Caregives do not reject such initiatives and they will be interested in them as soon as such functions are present and their expectations indeed satisfied [15]. The above-mentioned study was another one to indicate that the expectations of potential beneficiaries are high as regards this kind of applications. The results of the pilot study concerning the UnderstAID platform are similar to the results of the two studies just mentioned. Caregivers expect that the platform will be improved as far as the parameters of the application that they were negative about, such as performance and efficiency of the application, are concerned. On the contrary, the majority of the subjects were moderately satisfied with the fact that the application was intuitive for them and all subjects felt that the buttons and images were adequately laid out.

Among the assessed technical aspects of the platform, there were also those on which opinions were divided, namely ease of use of the application or its adaptation to different devices used by caregivers (computers/tablets). A training portal STAR, which is a multilingual e-learning tool and was evaluated by dementia caregivers as very useful and easy to use, can serve as an example to follow [16].

Research done by Vaigankar [17] in a group of informal caregivers of older adults showed that dementia increases the caregiver's burden measured in the Zarit scale to a significant extent. The study on the UnderstAID platform confirmed the same. The majority of subjects experienced severe burden as a result of taking care of a demented person.

The UnderstAID platform obtained a positive opinion from the informal caregivers also because of the utility of the platform as an e-learning tool. The caregivers admitted that it is an accessible and a comfortable way of gaining information. Studies by Leslie P. Kernisan et al. confirmed that caregivers of older adults very often treat the Internet as a basic source of information. No age range was given, however, and this is why it cannot be assumed that this conclusion applies also to caregivers advanced in age, who were included in the study group of the UnderstAID project [18]. Similar results were obtained by Hughes et al., which confirms that visiting the websites of Alzheimer Associations significantly enhances knowledge about the disease [19]. The study compares the knowledge of people visiting this kind of websites with the knowledge of those who do not use such sources of information [19]. The most popular keywords looked up by caregivers in the Internet include: "health information", "practical care" and "support". Those who visit the sites usually browse for some general information about caretaking or for more specific issues concerning symptom interpretation, probable disease symptoms or the impact of the disease on the patient's behaviour and the relationship with the diseased person [18]. This kind of information can be found in the UnderstAID platform.

The available literature gives numerous descriptions of initiatives similar to the present study. The EU-financed project STAR, during which an Internet portal aimed at providing online training for dementia caregivers was developed, is a good example [20]. A study by Dillon et al., on the other hand, evaluated 7 websites that gave information about dementia [21]. The study showed [21] that only 3 out of all the tested websites were a source of relatively complex and high-quality information. Therefore, special emphasis should be given to the reliability and scientific relevance of any initiatives aimed at supporting dementia caregivers.

The number of people suffering from dementia is still growing. Together with the progress of Alzheimer's disease or other forms of dementia, institutional care risk is also increasing, which is very often in contrast to patients' desire to stay at their homes [22]. Because of this, it is so crucial to develop a complex online tool through which informal caregivers could gain knowledge about taking care of demented relatives at home. The UnderstAID platform that was tested during the study was proven to provide a great deal of substantive support to the caregivers. However, no studies on alleviating fear or depression in caregivers have been conducted so far. This idea will be taken up, though, in the second phase of the pilot testing.

Conclusions

The caregivers' assessment of the platform was moderately positive. Data provided by the informal caregivers by means of the technical questionnaire are being currently analysed to be included in a report. The report will form a basis for the modifications to the prototype that is to be tested in the next phase of the pilot testing.

The caregivers expect the UnderstAID platform to be improved with respect to the following technical aspects: the utility of the "Help" option in the application, ease in finding the required information, performance and efficiency of the application, as well as multimedia files quality.

To recapitulate, the platform is most probable to be a useful tool for dementia caregivers but some technical aspects need to be improved.

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Conflict of interest statement

The authors declare that there is no conflict of interest in the authorship or publication of contribution.

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The benefits and risks of short-term diet changes on the example of the use a 5-week long lactoovovegetarian diet. Analysis of 7-day nutritional surveys of women – preliminary study

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ABSTRACT

Aim. Due to more frequent incidence of diet related diseases, alternative methods of nutrition become more popular. The aim of this paper is to determine the degree of balance of a short-term lactoovovegetarian diet followed by those who do not have any previous experience with such a diet. Moreover, the study aims at comparing its findings with results of a nutritional analysis carried out in the case of volunteers following a long-term lactoovovegetarian diet.

Material and methods. The method chosen in this study is a nutritional analysis based on 7-day long nutritional surveys. Diet 5.0 software was used analyze this data. The tests were conducted among 9 lactoovovegetarians females (LVD – long-term vegetarian diet) and 9 females who decided to follow a lactoovovegetarian diet for the duration of 5 weeks (SVD – short-term vegetarian diet). In the latter case, nutritional surveys were performed in the week preceding the experiment (SVD1/control group) and the last week of the diet (SVD2).

Results. In LVD group, when compared with SVD1, significant differences in average daily intake of vitamin E, fat and plant fiber have transpired. After analyzing data from nutritional surveys of SVD2 group, significant differences in the amount of basic nutritional elements (e.g. smaller amount of fat and fiber), microelements (e.g. lower supply of calcium, iron, magnesium) and vitamins (vitamin E, thiamine, niacin) have been noted, as compared to LVD group. When comparing data within SVD group, i.e. a traditional diet and a 5 week long lactoovovegetarian diet significantly lower supplies of vitamins B1, B3, B12 and D were observed than before starting the experiment.

Conclusions. A short-term change of eating habits from a traditional diet into a lactoovovegetarian one may result in insufficient supply of numerous nutrients.

Keywords: short-term diet, lactoovovegetarians, nutritional survey.

Introduction

There has been a great interest recently in a range of short-term and long-term diets. This is due to the fact that they are closely connected with the rising frequency of civilization diseases, their prevention and treatment, as well as a desire to achieve quick dietary results in the form of body mass reduction and maintenance of proper body mass. Pathologies such as obesity, diabetes and diseases related to circulation system, like atherosclerosis or ischaemic heart disease are on the rise [1]. In many cases, pharmaceutical treatment of these diseases is not effective and it is necessary for the patient to follow a short-term or long-term diet very restrictively. Increased physical or mental activity and stress require a change in one's eating habits to suit one's organism's needs. A proper diet may have a very beneficial influence on one's overall health state, physical shape and immune system, and this may concern both the sick and the healthy. However, it is crucial to emphasize the fact that introducing new eating habits, especially without regular control of a dietician, may result in undesired side effects, such as nutritional deficiencies among others. Moreover, professional supervision by a dietician is still a very uncommon procedure for those who decide to change their eating habits.

A lactoovovegetarian diet is considered to be a beneficial alternative eating habit for women, men and children of all ages [2]. This diet involves eliminating meat and fish products from one's menu, whereas dairy products and eggs are allowed. Numerous research has proven its positive influence inter alia on regulation of blood glucose level in diabetic patients, as well as on parameters of one's lipid profile and body mass reduction [1, 3-8]. At the same time, it has been researched that vegetarianism may play a role in increased risk of nutritional deficiencies [6, 9, 10]. Most of this research has been based on an analysis of long-term diets, ones that were applied for many weeks or even years. It should be noticed that a lactoovovegetarian diet may be considered rich in nutritional antioxidants [11], which play a crucial role in prevention of numerous illnesses and in recovery process, e.g. after poisoning caused by medicine or extreme physical activity. In these cases, a short-term change of diet into a lactoovovegetarian one may have a beneficial effect on one's antioxidant-oxidant profile. Moreover, relatively lenient dietary restrictions decrease the risk of an insufficient supply of essential vitamins and minerals.

There is scarce research that describes the influence of short-term vegetarian diets. Thus, the aim of this paper is to determine the degree of balance of a short-term lactoovovegetarian diet followed by those who do not have any previous experience with such a diet, but who decided to change their traditional eating habits into lactoovovegetarian ones. This paper specifically aims at comparing its findings with results of a nutritional analysis carried out in the case of volunteers with traditional eating habits and interviews with volunteers following a long-term lactoovovegetarian diet. This paper presents results of studies based on an analysis of 7 day long nutritional surveys among 18 females, 9 females undergoing a short-term 5 day long lactoovovegetarian diet (surveys collected before the dietary intervention and while it was in progress) and 9 long-term vegetarian females. In all cases, the factors to be compared included: dietary energy density, average consumption of carbohydrates, fats and protein and prominent vitamins and minerals.

Material and methods

The method chosen in this study is a nutritional analysis based on 7-day long nutritional surveys. Diet 5.0 software was used to collect and analyze this data. The tests were the following: 9 experienced female lactoovovegetarians (group I, LVD – long-term vegetarian diet), who have been on this type of diet for minimum 3 years and 9 females who decided to change their eating habits into a lactoovovegetarian diet for the duration of 5 weeks (group II, SVD – short-term vegetarian diet). In the latter case, nutritional surveys were performed in the week preceding the experiment (SVD1/ control group) and the last week of the diet (SVD2).

Only 18 females agreed to take part in this research, due to the fact that it would greatly interfere with their lifestyle. When choosing the sex of volunteers, the fact that vegetarian diets are most popular among women has been taken into account. Moreover, it is women who are more ready to change their eating habits for a short time than men. All volunteers were aged 18 to 30, were healthy and not very physically active. In Group I, females were students while taking part in the examination, 5 had a Master's degree. In Group II, 6 women were students and other 3 had a Master's degree. Before this research, all of them underwent a medical examination and were instructed how to follow a balanced lactoovovegetarian diet. They were also presented examples of proper vegetarian meals. All candidates agreed to exclude meat products, gelatin and fish from their diets for the duration of 5 weeks. They have not, however, committed themselves to a menu that had been prepared by a dietician, with respect to the type and amount of food products to be consumed. This was due to the fact that most tested volunteers were students and thus could not devote enough time to following a strict menu. The basic criterion for all of them was to eliminate meat and fish products from their menus. In the week preceding the experiment, all volunteers kept a nutritional survey in which they noted down exact amounts and types of food products they consumed. They were asked to follow the same procedure in the last week of the experiment. If a person stopped the diet half way into the experiment or developed a disease, they would be excluded from it. The data analyzed on the basis of these surveys included a daily intake of minerals and vitamins (characteristic of a stable diet) and the percentage of fats, carbohydrates and protein, both before and during the experiment. Long-term vegetarians had the same data analyzed. Statistica software was used for statistical analysis.

Results

The findings showed that the daily amount of nutritional elements in volunteers' diet changed and differed between two groups (LVD, SVD), as well as among SVD group, before starting the lactoovovegetarian diet (SVD1/control group) and while its duration (SVD2). In LVD group, when compared with those on a traditional diet, i.e. SVD1 (control group), significant differences in average daily intake of vitamin E, fat and plant fiber have transpired (**Table 1**). Vitamin E and fiber intake was higher, and the percentage of animal and plant fiber in the diet was more beneficial (taking norms into consideration) in LDV group.

After analyzing data from nutritional surveys of LVD group, significant differences in the amount of basic nutritional elements and microelements and vitamins have also been noted, as compared to data from nutritional interviews in SVD2 group, in the last week of the experiment (**Table 2**). These differences concerned lower dietary energy density, smaller amount of fat, fiber and lower supply of sodium, calcium, iron, magnesium, zinc, and vitamin E, thiamine, niacin and polyunsaturated fatty acids and fiber in SVD2 Group.

Table 1. Comparison of average daily intake of particular nutritional elements by long-term vegetarians (LVD) and people with traditional diets (SVD1/ control group), before starting the dietary intervention (level of significance p < 0.05)

| Mariah la | SVD1 | | | LVD | | | | D |
|--|---------|---------|--------|---------|---------|---------|----|--------|
| variable | Average | Median | SD | Average | Median | SD | u | r |
| Energy [kcal] | 1732.42 | 1661.92 | 621.80 | 1837.65 | 1660.37 | 625.51 | 42 | 0.6027 |
| Protein in total [g] | 65.84 | 60.12 | 20.50 | 59.14 | 56.47 | 18.89 | 38 | 0.4119 |
| Animal protein [g] | 42.49 | 38.09 | 12.70 | 28.16 | 29.03 | 14.47 | 22 | 0.0381 |
| Plant protein [g] | 22.89 | 19.08 | 9.92 | 30.17 | 27.70 | 6.50 | 20 | 0.0251 |
| FAT [g] | 61.12 | 53.60 | 25.06 | 65.89 | 60.17 | 30.77 | 45 | 0.7664 |
| Carbohydrates in total [g] | 233.72 | 213.76 | 81.61 | 264.53 | 240.63 | 87.41 | 33 | 0.2299 |
| Sodium [mg] | 2565.32 | 2590.00 | 831.76 | 2756.43 | 2779.35 | 979.73 | 39 | 0.4561 |
| Potassium [mg] | 2902.09 | 2756.65 | 670.53 | 3186.58 | 3067.87 | 1070.48 | 42 | 0.6027 |
| Calcium [mg] | 738.10 | 724.37 | 295.06 | 1045.00 | 848.28 | 523.25 | 30 | 0.1519 |
| Phosphorus [mg] | 1167.86 | 1090.13 | 272.14 | 1268.45 | 1185.97 | 435.73 | 45 | 0.7664 |
| Magnesium [mg] | 294.54 | 278.33 | 69.70 | 370.09 | 374.63 | 131.51 | 33 | 0.2299 |
| Iron [mg] | 9.59 | 8.73 | 2.69 | 11.52 | 11.65 | 2.77 | 28 | 0.1119 |
| Zinc [mg] | 8.27 | 8.38 | 1.80 | 8.56 | 7.80 | 3.20 | 48 | 0.9408 |
| Manganese [mg] | 4.15 | 4.37 | 1.75 | 5.54 | 6.05 | 2.18 | 36 | 0.3312 |
| Vitamin A (retinol equivalent/ [µg]) | 815.49 | 668.08 | 420.81 | 1269.26 | 1109.61 | 742.20 | 29 | 0.1308 |
| Vitamin E(alfa- tocopherol equivalent, [mg]) | 7.60 | 7.02 | 3.03 | 12.08 | 13.37 | 3.23 | 15 | 0.0074 |
| Thiamine [mg] | 0.95 | 0.87 | 0.32 | 0.98 | 1.01 | 0.22 | 42 | 0.6027 |
| Niacin [mg] | 16.76 | 14.04 | 5.81 | 13.92 | 11.98 | 9.29 | 27 | 0.0952 |
| Vitamin C [mg] | 109.34 | 75.39 | 89.34 | 131.95 | 133.54 | 71.68 | 38 | 0.4119 |
| Saturated acids [g] | 23.18 | 21.70 | 9.91 | 22.86 | 22.06 | 9.17 | 47 | 0.8820 |
| Monosaturated acids [g] | 24.49 | 22.05 | 10.50 | 22.41 | 21.34 | 7.76 | 44 | 0.7103 |
| Polysaturated acids [g] | 8.77 | 8.08 | 3.86 | 11.90 | 11.88 | 4.11 | 26 | 0.0804 |
| Cholesterol [mg] | 228.60 | 201.42 | 89.90 | 171.66 | 169.75 | 123.32 | 28 | 0.1119 |
| Fibre [g] | 14.60 | 14.11 | 3.66 | 21.65 | 22.31 | 6.65 | 18 | 0.0159 |
| Folate [µg] | 243.28 | 216.19 | 92.86 | 306.25 | 256.03 | 116.30 | 32 | 0.2014 |
| Vitamin B12 [µg] | 3.28 | 2.64 | 1.42 | 2.93 | 2.20 | 2.49 | 35 | 0.2947 |
| Vitamin D [µg] | 2.66 | 1.76 | 2.11 | 1.50 | 1.33 | 1.07 | 33 | 0.2299 |
| Percentage of protein energy | 15.81 | 16.85 | 2.56 | 13.55 | 11.40 | 3.88 | 30 | 0.1519 |
| Percentage of fat energy | 30.71 | 30.82 | 3.69 | 30.69 | 29.44 | 4.92 | 43 | 0.6556 |
| Percentage of carbohydrates energy | 52.03 | 50.58 | 6.05 | 53.97 | 53.89 | 5.57 | 39 | 0.4561 |

| Variable | SVD2 | | | LVD | | | | D |
|--|---------|---------|--------|---------|---------|---------|----|--------|
| Valiable | Average | Median | SD | Average | Median | SD | u | ſ |
| Energy [kcal] | 1328.25 | 1429.28 | 352.27 | 1837.65 | 1660.37 | 625.51 | 23 | 0.0465 |
| Protein in total [g] | 46.15 | 52.19 | 13.03 | 59.14 | 56.47 | 18.89 | 32 | 0.2014 |
| Animal protein [g] | 24.81 | 25.85 | 7.50 | 28.16 | 29.03 | 14.47 | 44 | 0.7103 |
| Plant protein [g] | 21.04 | 20.64 | 7.62 | 30.17 | 27.70 | 6.50 | 17 | 0.0125 |
| Fat [g] | 43.22 | 43.09 | 10.25 | 65.89 | 60.17 | 30.77 | 18 | 0.0159 |
| Carbohydrates in total [g] | 197.35 | 212.92 | 60.94 | 264.53 | 240.63 | 87.41 | 26 | 0.0804 |
| Sodium [mg] | 1887.10 | 1919.61 | 636.53 | 2756.43 | 2779.35 | 979.73 | 20 | 0.0251 |
| Potassium [mg] | 2363.64 | 2358.33 | 706.28 | 3186.58 | 3067.87 | 1070.48 | 26 | 0.0804 |
| Calcium [mg] | 594.66 | 534.32 | 174.77 | 1045.00 | 848.28 | 523.25 | 17 | 0.0125 |
| Phosphorus [mg] | 935.54 | 867.37 | 288.85 | 1268.45 | 1185.97 | 435.73 | 29 | 0.1308 |
| Magnesium [mg] | 240.81 | 237.32 | 80.48 | 370.09 | 374.63 | 131.51 | 21 | 0.0310 |
| Iron [mg] | 7.68 | 7.38 | 2.66 | 11.52 | 11.65 | 2.77 | 16 | 0.0097 |
| Zinc [mg] | 6.25 | 5.98 | 1.85 | 8.56 | 7.80 | 3.20 | 23 | 0.0465 |
| Manganese [mg] | 4.13 | 3.76 | 2.18 | 5.54 | 6.05 | 2.18 | 32 | 0.2014 |
| Vitamin A (retinol equivalent [µg]) | 825.35 | 606.61 | 539.24 | 1269.26 | 1109.61 | 742.20 | 31 | 0.1754 |
| Vitamin E(alfa tocopherol equivalent, [mg] | 6.75 | 6.07 | 2.56 | 12.08 | 13.37 | 3.23 | 11 | 0.0023 |
| Thiamine [mg] | 0.68 | 0.64 | 0.22 | 0.98 | 1.01 | 0.22 | 17 | 0.0125 |
| Niacin [mg] | 9.63 | 8.42 | 5.18 | 13.92 | 11.98 | 9.29 | 23 | 0.0465 |
| Vitamin C [mg] | 92.91 | 79.49 | 50.56 | 131.95 | 133.54 | 71.68 | 34 | 0.2610 |
| Saturated acids [g] | 17.05 | 15.48 | 3.62 | 22.86 | 22.06 | 9.17 | 27 | 0.0952 |
| Polysaturated acids [g] | 16.10 | 15.02 | 4.30 | 22.41 | 21.34 | 7.76 | 25 | 0.0674 |
| Monosaturated acids [g] | 7.14 | 6.67 | 3.46 | 11.90 | 11.88 | 4.11 | 16 | 0.0097 |
| Cholesterol [mg] | 178.78 | 184.16 | 72.03 | 171.66 | 169.75 | 123.32 | 41 | 0.5516 |
| Fibre [g] | 15.15 | 13.83 | 5.88 | 21.65 | 22.31 | 6.65 | 21 | 0.0310 |
| Folate [µg] | 221.06 | 217.68 | 67.95 | 306.25 | 256.03 | 116.30 | 27 | 0.0952 |
| Vitamin B12 [µg[| 2.19 | 1.77 | 0.92 | 2.93 | 2.20 | 2.49 | 45 | 0.7664 |
| Vitamin D [µg] | 0.91 | 1.01 | 0.36 | 1.50 | 1.33 | 1.07 | 30 | 0.1519 |
| Percentage of protein energy | 14.19 | 14.48 | 1.39 | 13.55 | 11.40 | 3.88 | 34 | 0.2610 |
| Percentage of fat energy | 28.67 | 29.29 | 4.26 | 30.69 | 29.44 | 4.92 | 46 | 0.8238 |
| Percentage of carbohydrates energy | 56.13 | 55.41 | 4.68 | 53.97 | 53.89 | 5.57 | 39 | 0.4561 |

Table 2. Comparison of average daily intake of particular nutritional elements by long-term vegetarians (LVD) and people on a short-term lactoovovegetarian diet (SVD2) (level of significance p < 0.05)

When comparing data within SVD group, i.e. a traditional diet (SVD1/control group) and a 5 week long lactoovovegetarian diet (SVD2), significantly lower amounts of vitamins B1, B3, B12 and D were observed than before starting the experiment (**Table 3**). A lactoovovegetarian diet has also shown lower amounts of zinc. The most beneficial change concerned the percentage of plant protein when compared to the amount of animal protein in the diet.

When comparing eating habits of long-term, experienced female lactoovovegetarians (LVD) and those with traditional eating habits – SVD1/control group (a diet including meat and fish) one can claim that the differences which are visible in this research show a more balanced and healthy way of eating on the part of female vegetarians (**Table 4**). What is worth noticing is the percentage of animal and plant protein in this group, which represents the recommended percentage (1:1). The intake of vitamin E by vegetarians was also higher than that in traditional diets, which in fact are characterized by a deficiency of this vitamin. What is more, experienced vegetarians consumed much more fiber, an amount recommended by Polish Institute of Nutrition and Food IŻŻ [12].

After comparing traditional eating habits (SVD1/ control group) and a short-term lactoovovegetarian diet (SVD2) applied by females who had not had any previous experience with changing their diets, the diet which contains meat and fish products turned out to be a more balanced kind of nutrition. The results of this research showed a significant decline in dietary energy density of a daily food ration. Moreover, the 5 week long vegetarian diet resulted in lower intake of B1, B3 and B12 vitamins, as well as zinc and vitamin D (the intake was below recommended norms). The beneficial result of this type of diet was proportionate consump-

| Variable | SVD1 | | | SVD2 | | | т | D |
|---|---------|---------|--------|---------|---------|--------|-----|--------|
| Valiable | Average | Median | SD | Average | Median | SD | · · | Г |
| Energy [kcal] | 1732.42 | 1661.92 | 621.80 | 1328.25 | 1429.28 | 352.27 | 7 | 0.0663 |
| Protein in total [g] | 65.84 | 60.12 | 20.50 | 46.15 | 52.19 | 13.03 | 3 | 0.0209 |
| Animal protein [g] | 42.49 | 38.09 | 12.70 | 24.81 | 25.85 | 7.50 | 1 | 0.0109 |
| Plant protein [g] | 22.89 | 19.08 | 9.92 | 21.04 | 20.64 | 7.62 | 20 | 0.7671 |
| FAT [g] | 61.12 | 53.60 | 25.06 | 43.22 | 43.09 | 10.25 | 7 | 0.0663 |
| Carbohydrates in total [g] | 233.72 | 213.76 | 81.61 | 197.35 | 212.92 | 60.94 | 12 | 0.2135 |
| Sodium [mg] | 2565.32 | 2590.00 | 831.76 | 1887.10 | 1919.61 | 636.53 | 8 | 0.0858 |
| Potassium [mg] | 2902.09 | 2756.65 | 670.53 | 2363.64 | 2358.33 | 706.28 | 7 | 0.0663 |
| Calcium [mg] | 738.10 | 724.37 | 295.06 | 594.66 | 534.32 | 174.77 | 11 | 0.1731 |
| Phosphorus [mg] | 1167.86 | 1090.13 | 272.14 | 935.54 | 867.37 | 288.85 | 6 | 0.0506 |
| Magnesium [mg] | 294.54 | 278.33 | 69.70 | 240.81 | 237.32 | 80.48 | 8 | 0.0858 |
| Iron [mg] | 9.59 | 8.73 | 2.69 | 7.68 | 7.38 | 2.66 | 7 | 0.0663 |
| Zinc [mg] | 8.27 | 8.38 | 1.80 | 6.25 | 5.98 | 1.85 | 3 | 0.0209 |
| Manganese [mg] | 4.15 | 4.37 | 1.75 | 4.13 | 3.76 | 2.18 | 21 | 0.8590 |
| Vitamin A(retinol equivalent/ [µg]) | 815.49 | 668.08 | 420.81 | 825.35 | 606.61 | 539.24 | 21 | 0.8590 |
| Vitamin E (alfa-tocopherol equivalent [mg]) | 7.60 | 7.02 | 3.03 | 6.75 | 6.07 | 2.56 | 16 | 0.4413 |
| Thiamine [mg] | 0.95 | 0.87 | 0.32 | 0.68 | 0.64 | 0.22 | 3 | 0.0209 |
| Niacin [mg] | 16.76 | 14.04 | 5.81 | 9.63 | 8.42 | 5.18 | 3 | 0.0209 |
| Vitamin C [mg] | 109.34 | 75.39 | 89.34 | 92.91 | 79.49 | 50.56 | 20 | 0.7671 |
| Saturated acids [g] | 23.18 | 21.70 | 9.91 | 17.05 | 15.48 | 3.62 | 12 | 0.2135 |
| Monosaturated acids [g] | 24.49 | 22.05 | 10.50 | 16.10 | 15.02 | 4.30 | 6 | 0.0506 |
| Polysaturated acids [g] | 8.77 | 8.08 | 3.86 | 7.14 | 6.67 | 3.46 | 14 | 0.3139 |
| Cholesterol [mg] | 228.60 | 201.42 | 89.90 | 178.78 | 184.16 | 72.03 | 6 | 0.0506 |
| Fibre [g] | 14.60 | 14.11 | 3.66 | 15.15 | 13.83 | 5.88 | 22 | 0.9528 |
| Folate [µg] | 243.28 | 216.19 | 92.86 | 221.06 | 217.68 | 67.95 | 15 | 0.3743 |
| Vitamin B12 [µg] | 3.28 | 2.64 | 1.42 | 2.19 | 1.77 | 0.92 | 0 | 0.0077 |
| Vitamin D [µg] | 2.66 | 1.76 | 2.11 | 0.91 | 1.01 | 0.36 | 1 | 0.0109 |
| Percentage of protein energy | 15.81 | 16.85 | 2.56 | 14.19 | 14.48 | 1.39 | 10 | 0.1386 |
| Percentage of fat energy | 30.71 | 30.82 | 3.69 | 28.67 | 29.29 | 4.26 | 13 | 0.2604 |
| Percentage of carbohydrates energy | 52.03 | 50.58 | 6.05 | 56.13 | 55.41 | 4.68 | 9 | 0.1097 |

Table 3. Comparison of average daily intake of particular nutritional elements in the duration of traditional diet (SVD1/control group) and lactoovovegetarian diet (SVD2) (level of significance p < 0.05)

tion of animal and plant protein. On analyzing two variants of lactoovovegetarian diets: short-term (LVD) and 5 week long (SVD2), it has been noticed that females who do not have any previous experience with preparing and composing vegetarian meals consumed insufficient amounts of basic microelements and vitamins, specifically calcium, magnesium, zinc, iron, B vitamins of group B, D vitamins and polysaturated fatty acids (**Tables 3, 4**).

Each tested group made some nutrition mistakes which resulted in insufficient intake of vitamin D and iron, as well as too low intake of vitamin E and calcium and magnesium (in the case of traditional and short-term vegetarian diets) (**Table 5**) and excess of phosphorus in each variant of the diet in question. The ratio of sodium and potassium content in the diet should also be taken into serious consideration.

Discussion

A properly balanced lactoovovegetarian diet does not cause a greater risk of nutrient deficiencies than in the case of a diet rich in meat and fish products [2]. This fact can be proven by this research based on an analysis of nutritional surveys of long-term experienced vegetarians. The analysis has shown that the level of balance and health benefits of their diet were higher than in the two other groups when it comes to daily consumption of nutritional antioxidants, such as vitamin E and fiber. Some deficiencies that have been observed concerned fewer nutrients than in the case of the other two groups. As noted in the introduction to this paper, this type of diet does not rule out products of animal origin which are rich source vitamins of group B and calcium. Minerals such as magnesium, iron, phosphorus, manganese, zinc and copper can be found in many

| Table 4. Mean value of daily intake of particular mine | rals and vitamins among females on a | traditional diet and a vegetarian diet, | recommended norms |
|--|--------------------------------------|---|-------------------|
| (level of significance $p < 0.05$) | | | |

| Nutrient (average daily intake) | Traditional diet (SVD1/control group) | Long-term vegetarian diet (LDV) | 5-week-long lactovegetarian diet (SVD2) | Recommended dietary allowances for women [12] |
|---|--|------------------------------------|--|---|
| Vitamin B (thiamine) | 0.94 | 0.98 | 0.68 | 1.1 |
| Vitamin B3 (niacin) | 16.76 | 13.92 | 9.62 | 14 |
| Vitamin B12 [µg] | 3.27 | 2.93 | 2.18 | 2.4 |
| Vitamin D [µg] | 2.65 | 1.5 | 0.90 | 5 |
| Zinc [mg] | 8.26 | 8.56 | 6.25 | 8 |
| Animal protein [g] | 42.48 | 28.16 | 24.80 | 0.45g/kg/ body weight /daily |
| Protein in total [g] | 65.84 | 59.14 | 46.14 | 0.9g/kg body weight/daily |
| Magnesium [mg] | 294.53 | 370 | 240.80 | 320 |
| Iron [mg] | 9.58 | 11.52 | 7.67 | 18 |
| Calcium [mg] | 738.09 | 1045 | 594.65 | 1000 |
| Sodium [mg] | 2565.31 | 2756 | 1887.1 | 1500 |
| Potassium [mg] | 2902.09 | 3186.5 | 2363.64 | 4700 |
| Phosphorus [mg] | 1167.8 | 1268.4 | 935 | 700 |
| Manganese [mg] | 4.14 | 5.54 | 4.12 | |
| Vitamin A [µg] | 815.48 | 1269.2 | 825.35 | 700 |
| Vitamin C [mg] | 109.34 | 131.95 | 92.91 | 75 |
| Vitamin E [mg] | 7.60 | 12.08 | 6.75 | 8 |
| % of caloric requirement covered by carbohydrates, protein and fats | Protein:15.81 | 11.40 | 14.19 | <15% |
| | Fats:30.71 | 29.44 | 28.67 | <35% |
| | Carbohydrates:52.03 | 53.89 | 56.13 | 50-70% |
| Dietary energy density [kcal] | 1732 | 1838 | 1328 | - |

Table 5. Types of nutritional deficiencies during nutritional intervention (groups SVD1/control group and SDV2) and in log-term lactoovovegetarian diet (LVD)

| Analysis of nutrition interviews in each group | Nutrients consumed in insufficient amounts | Health benefits |
|--|--|---|
| LVD (long-term vegetarian diet) | Potassium, iron, vitamin D, B1 | High fibre and vitamin E content, beneficial ratio of plant and animal protein consumed |
| SVD1 (traditional diet) | Potassium, iron, vitamin D, vitamin B1, vitamin E, calcium, magnesium | Lower risk of vitamin B3 and B12 deficiencies |
| SVD2 (5 week long vegetarian diet) | B1, B3, B12, D, zinc, magnesium, iron, calcium, potassium, vitamin E | Beneficial ratio of plant and animal protein consumed |

| Table 6. Zinc, vitamin B1 [mg], B3 | [mg], B12 [µg], and vitamin D | IU] content in particular food p | products [per 100 g] |
|------------------------------------|-------------------------------|----------------------------------|----------------------|
|------------------------------------|-------------------------------|----------------------------------|----------------------|

| Zinc [16] | Veal liver (8.40), Ementaler cheese (4.05), beans (3.77), buckwheat (3.50), pork shoulder (3.11), oatmeal (3.10), rye whole-wheat bread (2.54), hen's eggs (1.76) |
|--------------------|--|
| B1 vitamin [21] | Sunflower seeds (1.318), red lentils (1.072), pork (0.98), pistachio nuts (0.82), pea seeds (0.77), millet (0.73), white beans (0.67), peanuts (0.66), buck-wheat (0.54) |
| B3 vitamin [21] | Peanuts (17.2), liver (13.6), pork (0.8–5.6), trout (8.4), plaice (8.3), cheese (1.2), parsley (1.2) |
| B12 vitamin [22] | Liver (25–110), fish (1–15), milk and milk products (0.4–2.2), eggs (1.6) and meat (0.6–1.2) |
| Vitamin D [22, 23] | Fresh eel (1200), fresh cod (480), pickles salmon (540), egg yolk (54), cheese (7.6–28) |

food products of both animal and plant origin. This research has shown that a short-term vegetarian diet has a significant influence on testees' insufficient supply of nutrients as compared to a traditional diet and a long-term vegetarian diet.

One of such nutrients is zinc, the amount of which was not sufficient in the case of volunteers who underwent our dietary intervention. Products rich in this element include: brown bread, buckwheat, eggs, rennet cheese, but also meat and liver (**Table 6**). Eliminating the last two on the list from one's diet without finding a proper substitute may result in lower zinc intake. Moreover, this research has shown that volunteers examined both before and during their diets consumed insufficient amounts of calcium, iron and magnesium, elements which are present in dairy products, eggs, whole grains, groats, fruit and vegetables. As a consequence, eliminating meat and fish (rich in zinc) and eating habits which do not include sufficient amounts of meat-free and rich in zinc products mentioned before led to problems with a balanced amount of zinc in a vegetarian diet. The research also shows a significantly lower supply of vitamins of group B i.e. B1, B3, B12 (during the 5 week long vegetarian diet), which in turn shows too small consumption of meat-free products such as groat, whole grains, seeds and legumes, nuts (vitamin B1, B3) and dairy products (vitamin B12) (Table 6). Lower supply of both zinc and B1, B3, B12 vitamins confirms the fact that a properly balanced vegetarian diet should include a higher consumption of the food products mentioned before [13, 14]. It is worth noticing that vitamin B3 can be synthesized endogenously. Tryptophan is a substrate in this reaction [13]. It has been suggested that the biosynthesis of niacin from this amino acid is sufficient to supply the organism with a proper amount of vitamin B3. However, it is necessary to consume 100 g of protein daily. Volunteers did not include such an amount before or after the experiment. B12 vitamin is present in products of animal origin exclusively. When choosing a vegetarian diet, one should pay particular attention to the consumption of dairy and eggs which substitute meat, which in turn is the primary source of cobalamin (Table 6) [15].

As far as other minerals are concerned, this research has not shown any significant differences in their amounts for those on a vegetarian diet as compared to their diets preceding the experiment. Numerous sources point out, nevertheless, that a properly balanced vegetarian diet supplies more antioxidant A, C, E vitamins in comparison to a traditional diet, which confirms our results for long-term vegetarians [7]. This is due to the fact that a vegetarian diet is richer in fruit and vegetables than a traditional one. Having no proper eating habits before undergoing the vegetarian diet a low intake of fruit and vegetables can influence nutritional behavior while diet is in progress. A relatively small amount of these nutrients in both traditional and 5 week long vegetarian diets correlates with a relatively small amount of fibers.

Another aspect worth noticing is the excessive amount of phosphorus, both before and during the experiment, as well as in the case of the long-term vegetarian diet (**Table 4**). Phosphorus is present in many food products [16] and its excess in one's organism is quite common. It might be suggested, thus, that a diet which eliminates meat and fish products does not influence total phosphorus content, as this element is present to a high extent in seeds and whole grain products. The research has also shown higher amounts of potassium as compared to those supplied in a traditional diet. Consumption of this element was insufficient in all three types of diets discussed in this paper. Compared to a high concentration of sodium, deficiency of potassium was quite significant. However, studies of long-term vegetarians showed that vegetarian diets should include relatively higher amounts of potassium than diets rich in meat and fish. This may be achieved by including dry and fresh fruit and vegetables in one's diet.

Calcium deficiencies in Poles' diets are quite common [17]. It has been calculated that average daily intake of this element equals 50% RDA [18]. The **Table 4** confirms that traditional eating habits in most cases do not supply one's organism with sufficient amounts of calcium required for proper metabolism. Here, the amount of calcium consumed in a traditional diet and in a 5 week long vegetarian diet did not differ and in both cases was below the minimum. However, nutritional surveys with long-term vegetarians confirmed the fact that a lactoovovegetarian diet which included a higher supply of dairy products, as compared to a diet rich in meat and fish, does cover the daily requirements of this nutritional element.

This research has also shown that all tested group did not receive enough vitamin D with their diets. Despite the fact that 90% [12] of this compound is synthesized endogenously, it is claimed that proper supply of this vitamin is indispensable to maintain proper calcium phosphorus ratio of an organism. Vitamin D is present, among others, in fish, eggs but also in products enriched by this element, as well as in mushrooms [19] (**Table 6**). When concentration of vitamin D and calcium in blood is not sufficient, one might suspect that metabolic processes of these two elements may be disturbed, which might result in calcium absorption disorders and inadequate bone mineralization and some cell changes [20].

In both cases of the lactoovovegetarian diet, i.e. a long-term and a short-term example, the analysis of nutritional surveys showed a beneficial change in the amount of consumed animal protein in relation to plant protein. Adequate supply of animal protein is connected with providing the organism with bigger amounts of unsaturated fatty acids and eliminating saturated fats at the same time.

This research also shows a relatively low dietary energy density, especially in the case of volunteers undergoing a dietary change. In all cases, nutritional surveys were performed on women who described the level of their physical activity as low, which explains the data. A significant difference between the dietary energy density before choosing a vegetarian diet as compared to data collected during the dietary change proves that these volunteers' eating habits had not been properly balanced and as a consequence, accounts for the deficient supply of all aforementioned nutrients.

Conclusion

A short-term change of eating habits from a traditional diet into a lactoovovegetarian one by those who do not have previous experience in planning vegetarian meals may result in insufficient supply of numerous nutrients, especially calcium, iron, magnesium and group B vitamins deficiencies. This is mainly due to the fact that those people do not know how to compile a balanced vegetarian diet. In order to prevent them from all the deficiencies mentioned earlier, it is necessary to provide them with regular assistance and consultations of a dietician.

A properly balanced lactoovovegetarian diet, even one applied over many years, may turn out to be a very beneficial eating habit, especially for those at risk of diabetes or heart disease. Consumption of products which comprise this diet, i.e. whole grains, groats, rice, seeds and vegetables and fruit may significantly lower the risk of those diseases. This diet may also have a positive influence on the supply of antioxidants, especially vitamin E. Big dietary awareness and experience in preparing vegetarian meals (which results in adequate supply of dairy and eggs) lowers the risk of many nutritional deficiencies, such as those of calcium.

This research has also proven that each of the diets discussed here may result in deficiencies of some nutrients. Two of such nutrients include vitamin D and iron.

Limitations of the study include small research group as well as inclusion of only female volunteers. Therefore results of this study cannot be attributed to the general population. Moreover the studies did not include any biochemical analysis that could assess the actual nutritional status of respondents.

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Conflict of interest statement

The authors declare that there is no conflict of interest in the authorship or publication of contribution.

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ORIGINAL PAPER

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Legal aspects of a healthy diet for children. Comments on the grounds of the directive on foodstuffs in schools

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ABSTRACT

The aim of this article is to analyze legal solutions for the availability of foodstuffs in schools, binding from Sep 1, 2015, targeted to introduce into school shops and canteens so-called healthy food. The Directive issued by the Minister of Health on Aug 26, 2015 on groups of foodstuffs intended to be sold to children and young people in education system units and requirements for foodstuffs used within collective feeding of children and young people in those units eliminated from school shops provide a list of food which is considered unhealthy. The adopted solutions are an introduction to the legal statutory fight against obesity in children and young people and enhance the protection of the health of children at pre-school and school age by limiting access within kindergartens, schools and tutelary-educational institutions to foodstuffs containing significant quantities of ingredients not recommended for their development.

Keywords: food, obesity, liberty of economic activity, children and young people.

Introduction

The aim of this article is to analyze legal solutions for the availability of foodstuffs in schools, binding from Sep 1, 2015. These new solutions are intended to introduce into trade in school shops and canteens so called healthy food. Like any revolutionary changes, they generate a series of questions regarding their conformity with the Polish Constitution [1] and also contribute to the discussion on overall solutions intended to fight against obesity in children and young people in a broader perspective. The new regulations are protested against by entrepreneurs who run businesses in schools as they state that the list of products approved for sale is too restrictive, due to the fact that it eliminates from students' diets products containing too much sugar. They also point out that students will continue to provide themselves with so called junk food due to the proximity of regular groceries to schools or due to a lack of changes in nutritional habits at home which results in bringing unhealthy food to school.

The Directive issued by the Minister of Health on Aug 26, 2015 on groups of foodstuffs intended to be sold to children and young people in education system units and requirements for foodstuffs used within collective feeding of children and young people in those units [2], which entered into force on Sep 1, 2015, eliminated from school shops food which is considered unhealthy. It needs to be pointed out that the Directive was published in the Journal of Laws of Aug 28, 2015 i.e. three days before it entered into force. The entrepreneurs point out that such a short period of vacatio legis makes it difficult for the addressees of those provisions to adapt to the new legal conditions. The Constitutional Tribunal in its judgment of March 2, 1993 [3] emphasized that "the principle of the rule of law requires that a modification of law binding so far which implies unfavorable effects for the legal situation of entities be in principle introduced under the regime of interim provisions or at least with a proper vacatio legis as they let the entities involved adapt to the new legal conditions. The legislator may abandon them and decide to introduce directly (immediately) a new law - if to do so is justified by an important public interest which cannot be outweighed by the interest of an individual". In this case, although the modification of binding legal provisions had unfavorable effects on businesses such as school shops, the legislator decided not to extend the period which would allow them to adapt to the new legal situation. Pursuant to the provisions of Article 2 of the Act of Nov 28, 2014 on the modification of the Act on food and feeding safety [4], the date of entering into force of Article 52c, which is the basis to issue the Directive in discussion was determined to be Sep 1, 2015. Considering the necessity to adapt by businesses to the new legal situation, the legislator passed a relatively long period of vacatio legis. However, there is still a question about the lawfulness of the basis of the Directive issued. If the Act of Nov 28. 2014 on the modification of the Act on food and feeding safety determined the date of its entrance into force to be Sep 1, 2015 and the Directive of the Minister of Health was issued on Aug 26, 2015 pursuant to Article 52c of the Act on food and feeding safety, this means that it was issued on the basis of an act which had not yet entered into force. Under §127 of legal technicality [5] a directive should enter into force on the date of entrance into force of the act being the basis for the issuance of the directive. Also, under §128, section 1 of the legal technicality a directive may be issued after the act containing a provision which authorizes its issuance is published and before the act enters into force. In such a ase, the date of entrance into force of a directive is determined as a date no sooner than the date of entrance into force of the act that authorizes the issuance of such a directive. Considering the above, it needs to be stated that the directive in discussion conforms with legal technicality. The rules of legislation proceeding provided for in the act are directly binding for the government legislator [6]. Moreover, Article 7 of the Act of July 20, 2000 on the publication of normative deeds and some other legal deeds [7] clearly states that normative deeds issued on the basis of acts may be published within the period between the date of the publication of the act and the date of its entrance into force; such a deed may not enter into force before the act.

Considering the fact that directives are issued on the basis of acts and in order to execute them and their most important function is to enable the execution of the provisions of the act, it is obvious that the executory provisions should enter into force together with the new basic provisions [8]. Furthermore, it needs to be remembered that under §13 of the legal technicality, together with a draft version of an act, the draft directives which are fundamental for its execution are drawn up. The Directive under discussion undoubtedly is a deed on which the execution of the provisions of the act depends. The Constitution in Article 92 section 2 provides that directives are issued by authorities specified in the Constitution on the basis of a detailed authorization contained in the act for the purpose of its execution. The authorization should specify the authority competent to issue the directive and the scope of matters to be regulated and guidelines regarding the content of the deed. This provision results in the fact that the lawfulness of a directive depends on the accomplishment of the constitutional grounds for its issuance. In the case of the Directive of the Minister of Health of Aug 26, 2015 on groups of foodstuffs intended to be sold to children and young people in education system units and requirements for foodstuffs used in the collective feeding of children and young people in those units, it needs to be said that the statutory authorization was complete as it specified the authority competent to issue it and specified in detail the scope of the matters to be regulated.

Pursuant to the content of §1 of the aforementioned directive, it specifies groups of foodstuffs intended to be sold to children and young people in education system units. In practice this means that the foodstuffs enlisted in Schedule 1 of the directive cannot be sold in school shops, canteens or vending machines. Moreover, the directive sets forth the requirements for foodstuffs used in the collective feeding of children and young people in education system units. These requirements result from the principles of a rational diet in collective feeding and are based on norms for feeding children and young people and the nutritional and health values of the different foodstuffs.

The adopted solutions are intended, according to the grounds of the draft directive, to enhance the protection of health in children at pre-school and school age by limiting access within kindergartens, schools and tutelary-educational institutions to foodstuffs containing significant quantities of ingredients not recommended for their development [9]. It needs to be emphasized that proper diets in children and young people are very important considering the fact that excessive consumption in these groups leads to being overweight or obese caused, among others, by incorrect diets, well established in the family which means in particular an overly high calorific value for their everyday diet, too much animal fat and simple sugars accompanied by the limited physical activity of children and young people [10]. Typical irregularities in the diets of school children and young people are monotony, too much consumption of sugar and sweet things as well as meat and meat products, sweet carbonated drinks, fats and fast foods, combined with too little consumption of fruit and vegetables, milk and wholemeal cereal products, as well as fish [11]. In addition, it needs to be pointed out that disorders of energy balance in the body appear when certain physiological stimuli are removed from the person's everyday life e.g. when physical effort is limited [12].

The directive was issued on the basis of a statutory authorization referred to in Article 52c section 6 of the Act of Aug 25, 2006 on food and feeding safety [13], modified with the Act of Nov 28, 2014 on the modification of the Act on food and feeding safety. This Act, in Article 1 point 2, added Part IIA entitled: Foodstuffs and feeding children and young people in education system units. Under Article 52c, section 6 of the Act referred to hereinabove the minister competent for health matters will specify by means of a directive:

- the groups of foodstuffs approved for sale to children and young people in education system units;
- the requirements for foodstuffs used in the collective feeding of children and young people in education system units
- in consideration of the feeding standards for children and young people and the nutritional and health values of foodstuffs.

A violation of those provisions will be penalized with a fine or a civil sanction such as termination of contract. Under Article 52c, section 5 of the Act, if the provisions are violated, the head of a kindergarten, a school head or a head of a unit referred to in Article 2, points 3, 5, 7 of the Act of Sep 7, 1991 on the Education System (i.e. schools and other educational facilities including school youth hostels, centers for rehabilitation, centers of sociotherapy, special school-educational centers, special educational centers as well as facilities that provide care and education to students during education away from their fixed residence) are authorized to terminate, without notice, the contract with the entity responsible for the sale of foodstuffs or the provision of collective feeding to children and young people, without compensation.

Paternal responsibility for a child is the natural right of each parent. Under Article 48 of the Constitution of the Republic of Poland parents shall have the right to rear their children in accordance with their own convictions. This right, guaranteed in Article 48, section 1, refers to freedom of conscience and belief. Moreover, in Article 72, section 1 the Constitution ensures the protection of the rights of the child. The Constitution recognizes the supreme role of parents in the process of child education and it also covers looking after the child which involves among other things the right to make decisions about the child's diet. It needs to be said that the democratic legislator should respect the parents' right to bring up their children in accordance with their convictions i.e. also those which concern the child's diet. With the introduction of a total ban on the sales of foodstuffs containing excessive quantities of ingredients not recommended for their development, the legislator is interfering too much with the constitutional freedom to educate children in accordance with the parents' own convictions.

Another issue to be considered with respect to the introduction of the new provisions is a question about the lawfulness - in the light of Article 22 of the Constitution - of the limitation of the freedom of economic activity by banning the sales of some foodstuffs in education system units. Undoubtedly, the modification of the Act of Aug 25, 2006 on food and feeding safety introduced a limitation into the discussion upon the freedom of economic activity, which was specified in detail in the directive issued by the Minister of Health on the basis of the provisions of the Act. The legislator has the right to limit economic activity for important public reasons, which in its view includes health prevention in children and young people.

The principle of the freedom of economic activity is among the fundamental legal principles of the Polish legal order. According to the doctrine of business and administrative law it is one of the fundamental pillars of the economy [14]. However, this principle referred to in Article 20 of the Constitution is not absolute and may be limited on the basis of Article 22 of the Constitution pursuant to which a limitation of the freedom of economic activity may be imposed only by means of statute and only for important public reasons. It needs to be emphasized that the provision of Article 22 of the Constitution determines limits to state interference in economic activity. The limits are of two kinds: formal it says that the limitation upon the freedom of economic activity may be imposed "only by means of statute" and material – saying that they may be imposed "only for important public reasons" [15]. The Constitutional Tribunal in its judgment of Apr 8, 1998 [16] stated that freedom of economic activity may be subject to different limitations to a larger degree than personal rights and freedoms. Undoubtedly, such a value is the protection of health referred to in Article 68 of the Constitution and this is an important public reason, which justifies the limitation upon the freedom of economic activity [17]. The conditions of the introduction of limitations are set forth in Article 31, section 3 of the Constitution under which any limitation upon the exercise of constitutional freedoms and rights may be imposed only by statute, and only when necessary in a democratic state for the protection of its security or public order, or to protect the natural environment, health or public morals, or the freedoms and rights of other persons. Such limitations shall not violate the essence of freedoms and rights. The principle of proportionality referred to in Article 31, section 3 of the Constitution is an important barrier which prevents rights and freedom from being limited in an unjustified or excessive manner by the legislative authorities [18]. In conclusion, the limitation upon the freedom of economic activity in order to protect the value of health should be considered acceptable in terms of the principle of proportionality. It is also important to point out that the adopted solution is proportional to its desired purpose because it is impossible to achieve with other, less burdensome methods. Also, the opinion of the government about a draft act - filed by MPs - about the modification of the act on food and feeding safety (files no. 1127 and 1127A) is worth considering. This opinion states that in the statement of reasons for the MPs' draft act it has not been proven that the requirements of proportionality have been met and it is doubtful whether the suggested solutions are capable of guaranteeing the achievement of the desired purpose, considering the fact that children and young people willing to provide themselves with those foodstuffs subject to limitations will be able to acquire them out of units covered by bans, also during breaks between lessons [19].

The legislator assessed in legal terms two values: the freedom of economic activity and the protection of children and young people's health by introducing a ban on the sales of determined foodstuffs in a situation where, in the legislator's view, the full exercise of rights was not possible. The limitation upon the freedom of economic activity should be imposed by means of statute, which took place in the Act on food and feeding safety which in Article 52c indicated an authority competent to issue the directive.

On the basisi of the outlined legal status arises the question of whether the limitation upon the freedom of economic activity for businesses selling food in schools is adequate for the protected values and if it is possible to achieve the purpose set by the legislator by introducing other means aimed to limit the consumption of unhealthy foodstuffs than only by banning their sales in school shops. A possible limitation upon the freedom of economic activity of businesses conducting economic activity in schools and other educational centers needs to be considered. After the modifications enter into force, they will be the only group not to benefit from the ban but on whom the legislator imposes special duties within the scope of the distribution of so called healthy food in schools. It needs to be agreed with the legislator that the introduced bans are targeted to accomplish vital social purposes such as health protection, although the introduction of a statutory ban on the sales of certain foods is not a means necessary to achieve the purpose set by the legislator. Maybe to achieve the desired purpose, it would be sufficient to increase children and young people's awareness through education on healthy dieting or also to increase the volume of physical activity in schools. It is easy to imagine children and young people having access to foodstuffs containing significant quantities of ingredients not recommended for their development at home, after school or by going during school breaks to grocery stores located near their school-educational facilities. It seems that the achievement of the purpose, aside from the adopted legal solutions, could be guaranteed with obesity prevention programs involving, as well as proper dieting, also increased volumes of physical activity for children and young people. Some Polish cities (e.g. in Gdańsk) have introduced programs to fight against obesity in children involving examining children in determined age groups for early detection of civilization diseases.

In conclusion, it needs to be said that the limitation upon the freedom of economic activity imposed in the Act on food and feeding safety and the directive issued on the basis thereof is legally acceptable as the introduction of the solutions discussed herein above by the legislator was motivated by the need to protect children and young people's health, which is a value referred to in Article 31, section 3 of the Constitution. In the margin of this discussion, however, it needs to be added that no later than a month after the directive entered into force, buns reappeared in the list of products admissible in school shops [20] which prompts the question of whether this is only a liberalization of the adopted provisions or the begining of a return to the situation before the modifications. Let us hope that the imposed limitations will be a successful tool in the fight against obesity in children and young people and will lead them to learn and preserve good eating habits. However, it needs to be remembered that the solutions adopted by the legislator are not a complete remedy in the fight against obesity in children and young people.

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REVIEW PAPER

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Liposuction-induced metabolic alterations – the effect on insulin sensitivity, adiponectin, leptin and resistin

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ABSTRACT

Liposuction surgically removes subcutaneous abdominal tissue (SAT) and has almost no effect on visceral abdominal tissue (VAT) depot. However, some authors suggest that deep layers of SAT are functionally similar to VAT and the amount of deep subcutaneous abdominal adipose tissue is strongly related to insulin resistance in a manner nearly identical to that of visceral adiposity. Moreover, SAT determines leptin secretion which indirectly reflects the level of insulin sensitivity in the body. Thus, the immediate removal of SAT could potentially affect metabolic profile of a patient. The current data are conflicting and cannot bring a clear evidence suggesting that liposuction itself results in important metabolic outcomes and, on the other hand, cannot exclude such a possibility. This review summarizes the liposuction-induced metabolic changes with regard to release of major adipokines and insulin sensitivity.

Keywords: liposuction, insulin sensitivity, adiponectin, leptin, resistin, metabolic outcomes.

Introduction

According to International Society of Aesthetic Plastic Surgery liposuction was the second most frequently performed aesthetic operation in 2013. As with any surgery liposuction carries risks, however, in recent years, improved techniques have made liposuction safer, easier, and less painful. Thus, any intervention that immediately decreases adiposity and is relatively safe could be a viable method not only for aesthetic purpose but also for increasing the efficiency of insulin and improving metabolic profile, especially when combined with regular exercise and proper diet. Beneficial change in adipose tissue metabolism may be achieved directly or indirectly by modified release of metabolically active hormones/adipokines, modulated response to these hormones or by increased activity of sympathetic afferents to the fat cell. This paper presents

the current state of knowledge on liposuction-induced metabolic changes with regard to release of major adipokines.

Types, distribution and function of adipose tissue

Adipose tissue is a metabolically active organ involved in multiple functions. It serves as a buffer against influx of dietary fat and energy depot, plays role in the processes of satiety control, thermoregulation, reproduction, and exhibits immunomodulatory and endocrine activities. As an endocrine organ adipose tissue secretes hormonally active factors including leptin, adiponectin, resistin, visfatin, interleukin 6 (IL6), tumor necrosis factor (TNF), and many others, and plays role in hormonal metabolism of sex hormones and glucocorticoids [1]. The division of adipose tissue into two main types, white and brown, reflects functional and anatomical differences. White adipose tissue (WAT) is localized under skin and is designed for energy storage whereas brown adipose tissue (BAT) is present around kidneys, adrenals, aorta, and within mediastinum and neck. BAT plays role in secretion of inflammatory mediators, dissipates energy and generates heat. Energetic utilization of fats is regulated by beta-3 adrenergic receptors activation and/or in the mechanism of postprandial thermogenesis, which is due to leptin activity and signals from ventromedial hypothalamus in response to postprandial levels of glucose and insulin. Depending on body's demands, white adipose tissue acts as a potent buffer maintaining constant level of fatty acids in the circulation by storing lipids in the form of triglycerides and esterified form of cholesterol, and also releasing free fatty acids. WAT is also the major site of leptin and adiponectin production. [2]. The most important localizations of WAT are visceral abdominal tissue (VAT), subcutaneous abdominal tissue (SAT) and femoral and gluteal subcutaneous regions. Different anatomic distribution of WAT is related with different function, metabolic and endocrine activity. 2/3 of WAT is present in SAT, while the rest is found around viscera, in the retroperitoneal and gonadal depots, in the mammary glands, liver and skeletal muscles.

Abdominal obesity, also known as a central obesity, results from accumulation of fat in both SAT and VAT and serves as a risk factor for insulin resistance, which in turn favors development of diabetes type II, dyslipidemia, arteriosclerosis and chronic inflammation with inflammatory cytokines production (eg. TNF alpha, IL6, IL1) and inhibition of anti-inflammatory cytokines release (eq. adiponectin, IL10) [3]. The expression and secretion of adipokines in adipose tissue vary according to the adipocyte size and number and to the adipose tissue depot. For example, adiponectin and leptin expression and secretion are higher in SAT containing larger adipocytes as compared with VAT [4]. Until recently the ideas presenting relationship of regional adiposity with insulin senisitivity/resistance were not consistent and studies differed in the assessment of the importance of WAT and BAT. Some studies have suggested that the majority of metabolic activity in the adipose tissue belongs to WAT which is the most critical determinant of insulin sensitivity [5], whereas others have indicated the dominant role of BAT [6, 7].

The lack of consistent findings is probably attributed to the use of different methodologies (eg. different type of liposuction procedure), small number of subjects, not homogenous study groups, differences in patient's lifestyle (exercise, diet), difficulties in maintaining stable body mass, and low sensitivity of an examination. At the moment, most authors agree that there is a positive correlation between accumulation of VAT and development of insulin resistance, while SAT determines leptin secretion which indirectly reflects the level of insulin sensitivity in the body [8].

Liposuction procedure, metabolic change and maintenance of body weight after surgery

Classic liposuction also known as suction-assisted liposuction (SAL) uses aspiration techniques to break down and draw the fat cells out of the body. In this method small cannula is inserted through a small incision and attached to a vacuum device. There are many different types of liposuction according to the volume of infiltration or wetting solution injected before the surgery: dry, wet, superwet and tumescent technique. Moreover, the surgery could be modified by the new technologies such as power assisted liposuction (PAL), ultrasound assisted liposuction (UAL) and laser assisted liposuction (LAL). According to the volume of solution aspirated liposuction could be divided into two categories: large volume liposuction (> 5 liters aspirated) and small volume liposuction (< 5 liters aspirated). The most popular liposuction types are tumescent and superwet techniques with minimal risk of bleeding complications and small volume fluid infusions during surgery. Tumescent liposuction is performed under local anesthesia after subcutaneous infusion of fluid (most commonly containing saline, lidocaine, and epinephrine, with or without sodium bicarbonate) in a ratio of 2-3 mL of infiltrate to 1 ml of aspirate; the endpoint of infiltration is tissue turgor [9]. For the best results liposuction candidates should be healthy and physically fit and not more than 20 pounds overweight, their skin should be firm and elastic. The major contraindications include and are not limited to: severe cardiovascular disease, severe coagulation disorders, pregnancy or less than 6 months post-partum, eating disorders, psychiatric problems, morbid obesity, serious life stress within last 6 months [10]. The indications and contraindications for liposuction summarizes Table 1.

Liposuction surgically removes only SAT and has almost no effect on VAT depots. Up to 50% of SAT is localized in the deep layer and, during abdominal liposuction, this is the predominant removed tissue. Some

| Table 1. General indications and contrained | dications for I | iposuction |
|---|-----------------|------------|
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| Indications | Absolute contraindications | Relative contraindications |
|--|---|---|
| Aesthetic indications; reduced body mass | Psychiatric diseases; eating disorders | Previous liposuction complications |
| Multiple systemic lipomatosis | Morbid obesity | Some medications which cannot or will not be stopped |
| Dercum's disease | Unrealistic expectations | Previous liposuction in areas "of interest" |
| Lipomas | Ucontrolled drug or alcohol addiction | Lifestyles which cannot or will not be changed |
| Chronic Lymphedema | Use of some specific medications, which cannot be stopped | More than 50 pounds weight loss during last year |
| Axillary hyperhidrosis | Pregnancy or less than 6 months post-partum period | Excessive smoking or alcohol use |
| Post-ablative surgery | Immunosuppressive therapy (steroids) | Some psychiatric and/or social problems |
| Gynecomasty | Anticoagulant therapy | |
| | Major surgery and/or general anesthesia within last 6 months | |
| | Stroke or heart attack within last 6 months | |
| | Allergy to lidocaine | |
| | Serious life stress within last 6 months | |
| | Uncontrolled diabetes | |

authors suggest that deep layers of SAT are functionally similar to VAT and the amount of deep subcutaneous abdominal adipose tissue is strongly related to insulin resistance in a manner nearly identical to that of visceral adiposity [11, 12]. The assessment whether liposuction is successful in a longitudinal weight management is the first step toward potential metabolic benefit analysis. In 2001 Commons et al. reviewed 631 cases of liposuction that was performed in the same hospital by the same surgeon over 12 years, with an average follow up 1 year. More than 80% of patients maintained stable body weight within 12 months from surgical procedure [13]. Contrary to this report, there are studies describing rebuilding of removed fat and its redistribution to the abdominal and visceral regions with negative impact on metabolic parameters and risk factors for coronary artery disease. In prospective analysis of fat distribution Hernandez et al. observed an initial decrease in abdominal SAT (6 weeks after liposuction) with subsequent significant increase in SAT and WAT after 1 year from surgery. Tested metabolic variables (serum adiponectin, free fatty acids, glucose, insulin, triglycerides, sensitivity to insulin) were not significantly changed except an initial drop in leptin level, which after 12 months returned to its basic concentrations. This study, however, was conducted on small study group (n = 14) and the type of surgery was small-volume liposuction (less than 5L of aspirate) [14].

It has been documented that large volume liposuction enhances insulin sensitivity markedly, lowers insulinemia and additionally reduces circulating markers of vascular inflammation [15]. The beneficial effect on insulin sensitivity persists over months from surgery [16, 17].

The number of study participants is one of the major determinants for statistical power and sensitivity of analysis. In a large clinical study (123 obese women) D'Andrea et al. observed positive metabolic changes after 21 and 90 days from large volume liposuction. They noted significantly improved insulin sensitivity, resting metabolic rate, serum adipocytokines, and level of inflammatory markers. The changes were correlated with the decrease in fat mass and waist-hip ratio and remained relatively stable [18]. Rizzo et al. evaluated the effects of dermolipectomy after 40 days from the surgery. They found significant decline in plasma resistin, and inflammatory markers (IL6, IL10, TNF) and an increase in plasma adiponectin. Moreover, observed metabolic changes were accompanied by an improvement in insulin-mediated glucose uptake, substrate oxidation and degree of inflammation [19].

Contrary to these findings, a number of studies reported no, or even diverse effects of liposuction on metabolic profile. They underlined that only negative energy balance induced by diet and/or exercise, not simply a decrease in the mass of adipose tissue, is critical for achieving the metabolic benefits of weight loss. Weight loss in response to energy deficit decreases VAT mass, production of proinflammatory cytokines, size of adipocytes, helps to reduce intrahepatic and myocellular fat, and undoubtedly, these changes bring significant improvement in most of the metabolic parameters [20]. In addition, some authors report post-liposuction adipose tissue regain and redistribution, preferentially in the abdominal regions of VAT, after months from the

| Hormone | Site of production | Metabolic activity |
|-------------|---|--|
| Adiponectin | white adipose tissue | increases fatty acids oxidation inhibits hepatic gluconeogenesis increases insulin sensitivity and glucose uptake has anti-inflammatory and anti-atherogenic activity |
| Leptin | white adipose tissue, brown adipose tissue, stomach, placenta, skeletal muscle | inhibits appetite and enhances thermogenesis stimulates sympathetic activity increasing rate of metabolism inhibits insulin secretion increases insulin sensitivity increases lipolysis decreases hepatocyte lipogenesis preventing from lipotoxicity |
| Resistin | mononuclear blood cells, white adipose tissue, skeletal muscle, pancreas | pro-inflammatory molecule mediates insulin resistance other metabolic functions are still unclear |

Table 2. General metabolic activities of adiponectin, leptin and resistin in humans

surgery. This, in turn, may possibly result in consequences of metabolic dysregulation after surgery [14, 21].

For better understanding of the metabolic alterations after liposuction a number of studies determined its effect on major adipokines: adiponectin, leptin and resistin. These adipose tissue derived hormones are involved in maintenance of metabolic homeostasis (**Table 2**).

Adiponectin

Adiponectin is a hormone/cytokine primarily produced in the WAT. Changes in its serum concentration are associated with metabolic profile and risk factors for cardiovascular disorders. Serum level of adiponectin is reversibly correlated to BMI, insulinemia and triglycerides. The number of studies have shown that adiponectin increases insulin sensitivity via enhancement of fatty acids oxidation and inhibition of hepatic gluconeogenesis, and exhibits anti-inflammatory and antiatherogenic activity in blood vessels [22, 23]. There are three forms of this hormone: LMW (low molecular weight), MMW (middle molecular weight), and HMW (high molecular weight). It has been shown that antidiabetic and antiatherogenic properties of adiponectin are related to HMW activity [24, 25].

A number of authors demonstrated that surgical removal of fat improves metabolic parameters like insulin sensitivity, and increases adiponectin secretion [18, 26]. As reported by Giugliano et al., super wet technique of liposuction was associated with improvement in insulin sensitivity measured by HOMA-IR (Homeostasis Model Assessment - Insulin Resistance), reduction in circulating markers of vascular inflammation (IL6, IL18, TNF alfa, CRP), and elevated serum adiponectin within six months of stable body weight after liposuction. Moreover, there was a positive correlation between the amount of fat aspirate and adiponectin and changes in HOMA [27]. Similar findings were described by Maher et al. after 12 weeks of observation. Using tumescent technique and aspirating more than 5L of fat they noted that insulin sensitivity has greatly improved in obese women with and without coexisting diabetes. The level of adiponectin was increased in both groups, but not significantly in patients without diabetes [28]. It has been shown that weight reduction increases adiponectin plasma level. Thus, after liposuction an inhibitory effect of obesity on its production is possibly "turned off" [26]. On the other hand, there are negative studies that deny the existence of metabolic benefits and elevated adiponectin levels in response to liposuction. They underline that regulation of adipokine production is multifactorial in response to negative energetic balance that could be induced by exercise and/or dietary restriction only. Physical effort as a nonpharmacological and nonsurgical intervention evidently reduces VAT level, even if body mass has not been decreased so markedly [20, 29]. Decreased size of adipocytes decreases leptin release, which is a well known factor inhibiting adiponectin production, the other mechanisms involve improvement in BAT blood flow, antioxidant effects, and high catecholamine level [30]. Most recent data indicate that irrespectively of exercise training small-volume liposuction down regulates the expression of adiponectin genes in SAT and its serum level [31]. To clarify these discrepancies, however, further studies performed on large population cohorts and including mechanistic insights are required.

Leptin

Leptin is a hormone secreted primarily by WAT. It acts as a satiety factor in signaling whole body energy balance. High levels of circulating leptin signal adequate energy stores whereas low levels are consistent with an energy deficit. At the hypothalamic level leptin inhibits appetite and enhances thermogenesis by decreasing the activity of orexigenic neurons (Npy/AgRP/ GABA containing neurons) and increasing the activity of the anorexigenic neurons (POMC/CART containing neurons). Leptin, through its central activity, favors catabolism in BAT which is partially a consequence of its stimulatory effect on sympathetic nervous system [32]. Barzilai et al. showed that peripheral leptin stimulates its receptors in VAT and selectively decreases visceral adiposity preventing from development of an insulin resistance [33]. The current data clearly indicate counterregulation of insulin by leptin through inhibition of insulin secretion, increase in hepatic insulin extraction, suppression of insulin lipogenesis by leptin lipolysis, and modulation of peripheral tissue and brain sensitivity to insulin action [34, 35]. Decreasing hepatocyte lipogenesis leptin prevents development of lipotoxicity, the condition which often contributes to the insulin resistance. Leptin-mediated inhibitory feedback on insulin secretion is related with decrease in adipogenesis and parallel increase in overall insulin sensitivity. The direct stimulatory effect of leptin on glucose uptake and increased insulin sensitivity is limited to muscle, because prolonged exposure of adipocytes to leptin results in a loss of insulin sensitivity and an inhibition of insulin stimulated lipogenesis. [36, 37]. The reciprocal effects on synthesis of leptin and insulin are regulated by complex mechanisms that occur within adiopoinsular axis. Both insulin and glucose increase the synthesis of leptin, while leptin alone acts as a potent inhibitor for insulin secretion preventing occurrence of hyperinsulinemia and lipotoxicity. On the other hand, hyperinsulinemia interferes with leptin signaling at the peripheral receptor level and facilitates leptin resistance [38].

Normally leptin concentrations tend to increase with increasing adiposity, however, in obese individuals this interaction is somehow inhibited and leptin resistance develops [39]. As suggested by authors, this resistance abolishes only selected actions of leptin. Enriori et al. demonstrated that although hyperleptinemia in obese subjects was linked with resistance to anorexigenic effects of leptin, the ability to activate dorsomedial nucleus of hypothalamus and sympathetic drive to BAT was sustained [40]. Additionally, peripheral resistance to leptin in WAT was also widely described [41]. Peripheral leptin resistance may contribute to decreased leptin ability to modify the adipocyte insulin responsiveness and to maintain normal basal rate of lipolysis. Almost all cases of obesity contribute to increased leptin resistance and deregulation of its central anorexigenic activities. Thus, it has been postulated that liposuction by decreasing adiposity could possibly improve both leptin and insulin sensitivity. Most authors agree that one of the early effects of liposuction is lowered leptin level but the relationship between hypoleptinemia and insulin sensitivity is not so evident. In animal model, Schrebier et al. reported an increasing trend of leptin level at 42 day after liposuction [42]. In humans, SAL liposuction was followed by an early drop in serum leptin concentration (after 1 week), which additionally correlated with voluntary changes in energy intake. The effect was not significant after 6 weeks from surgery [43]. Another study demonstrated the effect of low level laser therapy (LLLT) on serum leptin and lipid profile in overweight and obese women. Authors observed increase in serum triglycerides and decrease in leptin level. However, the effect was limited to overweight patients only (BMI 25-29.9) [44]. In an open parallel-group clinical trial Robles-Cervantes et al. tested metabolic profile in two groups of obese women: "liposuction plus diet" and "diet only". They found a marked decrease in leptin level 1 month after liposuction, however this change was not correlated with insulin sensitivity Described by many authors delayed return of leptin concentrations to the levels before surgery with simultaneous maintenance of body weight (when yo-yo effect is absent) may indicate potential metabolic benefits resulting from improved peripheral and central leptin sensitivity [36]. In meta-analysis of 15 studies on cardiovascular metabolic markers after suction assisted lipectomy only leptin and fasting insulin were the variables that were significantly associated with the amount of aspirated fat, whereas the other factors such as inflammatory markers were not [45].

Resistin

Resistin is yet another cytokine that may contribute to obesity and impaired metabolic profile. It was originally named for its resistance to insulin, and was proposed to impair glucose tolerance and insulin action, but the exact role of this peptide in humans still remains unclear. In animal model, resistin suppresses insulin stimulated glucose uptake and induces insulin resistance [46]. Excessive adiposity increases expression of resistin genes in adipose tissue and resistin works as a feedback regulator of adipogenesis in rats [47]. However, unlike the rodents, human resistin is predominantly expressed in human mononuclear cells in response to inflammatory stimuli and, because of that, cannot be considered as a fat-derived cytokine [48]. On the other hand, in vitro studies on isolated human adipocytes have shown that antigenic stimuli increase secretion of resistin from adipose tissue. Moreover, culturing adipocytes with recombinant human resistin evokes proinflammatory cytokine release and up-regulates mediators of insulin signaling pathway [49]. Most studies on genetic programming confirm the correlation between increased gene expression, inflammatory response and risk for diabetes [50]. In 2001 Stepan et al. described the link between diabetes and level of serum resistin. They have found that administration of anti-resistin antibody improves blood sugar and insulin action in mice with diet-induced obesity. Moreover, treatment of normal mice with recombinant resistin impaired glucose tolerance and insulin action [51]. According to recent large case-controlled clinical studies on humans, elevated levels of resistin are associated with the development of diabetes type 2, possibly through inflammatory processes, but the mechanistic insights require further evaluation [52]. Resistin levels appear to correlate positively with SAT and majority of studies confirm this relationship [53]. A longitudinal analysis of patients on a weight reduction program including dieting and exercise, has brought an evidence that serum resistin change is positively correlated with changes in BMI, body fat, fat mass, visceral fat area, and mean glucose and insulin in patients [54]. Little is known about the effect of abdominal lipoplasty on resistin level. D'Andrea et al. reported decrease in serum resistin after large volume liposuction. Their report was based on observation of a large study group, so they were able to detect even discrete effect of liposuction on levels of studied variables [18]. Ma et al. confirmed beneficial metabolic effects of liposuction describing lowered resistin level with no change in inflammatory markers (CRP and IL6), and improved insulin sensitivity after 3 months from surgery. However, their study group was very small and consisted of 16 individuals only [55]. Similar effect but after dermolipectomy was presented by Rizzo et al. who found that after 40 days following surgery decrease in serum resistin was accompanied by a significant improvement in insulinmediated glucose uptake [19]. Ramos-Gallardo et al. suggested that in patients with impaired lipid profile, liposuction can reduce the metabolism of cholesterol by lowering the level of resistin, which is known to increase the production of LDL and degrades LDL receptors in the liver [56].

Summary

Numerous clinical and experimental studies have brought conflicting findings about abdominal liposuction surgery and its metabolic effects including adipokines secretion and insulin sensitivity. The possible explanation includes differences in a lifestyle of examined subjects (diet, physical activity), difficulties in maintaining stable body mass, experimental methodology (eq. differences in the follow-up time after surgery or the methods used to test for insulin sensitivity), and the type of liposuction procedure used (eq. large vs. small volume liposuction). Moreover, most of published observations was based on examination of the small number of study participants. Thus, the current data cannot bring a clear evidence suggesting that liposuction itself results in important metabolic outcomes, on the other hand, the possibility that liposuction may serve as a new strategy for rapid restoration of impaired metabolic profile cannot be completely excluded. Some of the scientists suggest its additive/facilitating effect when combined with reduced calorie intake and increased energy expenditure [18]. Indeed, more trials performed on large population, that address the long-term effects of SAL on metabolic markers and are similar in experimental design and study homogeneity, are required to evaluate this concept in details.

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REVIEW PAPER

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Institutions of health's care. Aspects European and judicial

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ABSTRACT

Present paper is then a part of a trend to find the premises for the theory's construction. I will try to combine the point of view presented by social sciences, criminology and medical sciences, what will become a starting point for analysis and in further perspective – for research on some theoretical models.

Keywords: European Union, justice, medico-social institutions, convicts' health care.

Introduction

Health protection for people facing jurisdiction in consequence of different types of crime starts to be an issue of great importance, especially in connection with "social" opening of polish penitentiary system after 1989. Although the problem is vital, polish penitentiary thought seems to pass it over, what can be noticed especially in penitentiary sciences, which focuses mainly on the crisis in penitentiary reeducation [1]. From this point of view the problem is a bit "one-tracked". There are many voices pointing the essence, causes and consequences of the mentioned problem for working with people, who came into collision with the law - in the wide perspective for state's penal policy, but solution proposals are still few. Usually they limit to an analysis of single action programs, description of therapeutic activities in a particular prison etc. This perspective lacks of the possibility to generalize mentioned descriptions of successful experiences to the status of scientific theory. This is the main reason why in Polish penitentiary thought standstill prevails. It causes that instead of extrapolating mentioned programs to a higher level than analytic sentences most of theorists tend to reach to penitentiary classics like Michel Foucault [2] or Erving Goffman [3].

The problem of crisis may be defined as the "problem of crisis in scientific thought" about reeducation, it's aims, elements and methods. The solution, however, requires a new theory of influence adequate to nowadays challenges and standards.

Present paper is then a part of a trend to find the premises for the theory's construction. I will try to combine the point of view presented by social sciences, criminology and medical sciences, what will become a starting point for analysis and in further perspective – for research on some theoretical models.

The issue is not as simple as it may seem – it begins on the level of definition of the reeducation itself. It is a fact that to this day it remains impossible to work out one, universal concept of reeducation. In the face of controversies classics always give the best solution – in their understanding reeducation is the process of change done in persons' personality, which aims to eliminate or reduce social disadaptation. For S. Jedlewski, and especially for Cz. Czapów [4], reeducation is a system of caring, educational and therapeutic actions (influences). It seems that mentioned triad is broad in meaning, so it may refer to different age categories in people affected by these actions. Unfortunately confrontation with "real reeducation " especially penitentiary one falls out not really well.

Therefore, despite the fact that possibility of moral revival in people, who are in collision with the law, is nowadays often remonstrated, what may be argued with opinion that the prison didn't improve anybody yet – there appears a question concerning specification of current priorities.

Taking into consideration classical reeducation thought and my former papers on social work [5] I would like to propose here a system of factors influencing people, who are in collision with the penal law:

- Therapy.
- Social reinforcement.
- Education.

It is easy to notice that this system is alike to one presented in my former papers [6], but here appears a legible turn in priorities towards treatment and social support. It goes with trends present in so called "old EU members" especially in United Kingdom and France [7].

More precise characteristics of mentioned actions should be preceded by a comment concerning social reinforcement. So - it can be defined as a supreme aim, which can be realized by i.e. protection of convicts' health. After B. Dubois and K.K. Miley I will present it here as "the way, in which people, institutions and communities obtain control over their lives" [8]. According to J. Rappaport "the idea of reinforcement (authorization) suggests both - person deciding about his/her live and his/her democratic participation in live of community, often realized via institutions like schools, neighborhood, churches and other voluntary organizations. Reinforcement brings psychological sense of control and influence on things that happen with and to a person, it also refers to the possibility of having a real influence on society, politics and law. Therefore it is a multi-level construct, which applies to single citizens and institutions or local communities, it suggests studies on people in a certain context" [9].

Reinforcement is then both – the aim and the process. As an aim it signifies an ultimate state, e.g. when person under charge obtains power to complete integration with surrounding community. As a process it is expressed by facilitating, making possible and favoring or promoting the ability to competent, adaptive functioning. It is obvious that in this process actions aiming to maintain good state of health play leading role. Above mentioned conclusion lays on a belief that: "people, as long as they have proper support from milieu, are fighting, active organisms, able to organize their lives and develop their hidden potentials" [10].

From supporting convicts actions model perspective, direction of efforts to obtain change is determined by basic problem, which is client's "departure" to dregs of society in consequence of committing a crime. In case of juveniles it brings a threat to their physical, mental and social development, so the threat of demoralization, which is often connected with family pathology and upbringing in environment socially downgraded, where health care is usually on a very low level. On latter issue the process of causing change in convict, judged in consequence of getting into collision with penal law, should be oriented.

Initial condition of success is the maintenance relatively good state of convict's health. In already described perspective process of "health repair" should be proceeded on three basic levels:

- Single person work level
- Group work level
- Social institutions level, making no difference for convicts placed in prison, so – in isolation, and those, who are released (especially in the conditions of probation supervision).

The issue of levels needs a few words of comment. It seems that the fact of convict's isolation from society by imprisonment, is not an obstacle for health supporting actions for a convict and family. These actions are complex and may be proceeded simultaneously inside and outsider the prison. The fact that prison system in nowadays more open to society is not meaningless here – this is why the problem of convicts health can not remain hidden from society, as it happened before. Prisons' openness, what is worth emphasizing, enables to include in prisoners supportive actions services and institutions of health care and social assistance, which operate in open environment. Therefore convicts during imprisonment may be interested in cooperation.

Mentioned institutions may also focus on convicts' families. So – casework in health protection is typical for cases commissioned by court. It is taken on a base of legal mandate, like judgment made by court (e.g. absolute imprisonment or conditional stay of the carrying out of a sentence connected with probation). It dominated is old EU member countries and in Poland in 1960s. It pressures direct work with individual. Five basis orientations can be pointed here:

- Traditional, i.e. medical
- Psychosocial
- Functional
- Problem-oriented
- Socio-behavioural.

Focusing on social reeducation of convicts (but – formulated individually) is common for all orientations in the work context.

In the middle 1950s in Western Europe some attention focused on taking care of families of justice administration clients. On the beginning working with family was a part of casework. Still quite soon ward's (prisoner or person under probation in open environment) behaviour started to be perceived not as a personality product, but as an effect of family interactions. It all started familial approach, which is a basis for framework program of taking care of dynamic system individual (patient) – surrounding. British system of helping prisoners based on supporting bonds with family during imprisonment (what is often a difficult situation for relatives, also affecting health [11]) can be an example here.

General familial approach relies on acknowledging the influence of familial processes, roles and the way that state of health in family members affects health of an individual included in executive penal proceedings. On the beginning focus was on individual pathology, but quickly family pathology was centered, especially health negligence – it all caused farming four approaches to work on heath issues with families.

Thus in 1950s psychodynamic approach was used. It involved taking into consideration the influence of family members' personalities on their health and convict's health. In early 1960s theorists initiated approach involving denying the possibility to communicate about health in dysfunctional families. Following was a structure approach, which dominated in 1970s. Its aim was to work with disorganized families and served as a way to study environmental influences, family development stages, and organizational factors like interaction patterns and rules. It served health interventions in cases of family crises using the method of planned, short-term problem solving. In the 1970s eclectic approach to ward's families' health occurred it involved using techniques of evaluation and intervention strategies from different theoretical models, e.g. psychodynamic model, communication theory, structural model or crisis intervention model. Together they presume existence of many factors, which should be taken into consideration by medical and social staff to understand family's functioning, intervention aims and potential possibilities and forms of pro-health actions.

Group-work methods were applied to professional social work in 1930s, and group-work theories were created on 1940s. Group-work is defined as a planned effort made for change, based on a conviction that people experience through interactions and group processes, because group is an organism in which mentioned processes occur on many levels. In other words, people responsible for convicts' health care should use group structure and group processes to evoke change in single group members. Helping practice concerning convicts' health care should then use both – medico-social context of the group itself, and means which are used by group members to sustain or change attitudes, interpersonal relations and develop abilities of effective coping and preserving good state of health in their surroundings. It is necessary to notice that group therapy may be preceded only in little groups.

English author G. Konopka describes in this context group-work as a method of medico-social work. This should help single person to improve functioning in a society through intentional experiencing within a group and lead to more effective coping with one's problems concerning group or community, especially those related with health care [12].

As a method of acting in legal cases in an open environment group-work didn't became popular as much as mentioned above familial approach. One of the main reasons is a peculiar character of criminal circles. They create difficult to modify hermetic systems of values, they are usually closed structures, rarely submitting to interventions. Specific solidarity of its members and following high level of inner integration cause the existence of informal groups, which are an alternative for those created by medico-social staff - directed by administration task groups. Despite all it seems to be a promising method of medico-social work, which meaning will grow with the process of opening prisons' to the society. Prisons were the place where group therapy proved to be effective (e.g. addiction therapy programs like duet for convicted alcoholics) [13]. The character of institutions favours creating by penitentiary service special purpose groups for prisoners.

A version of group-work is combining individual actions taken by every social worker with the work done in interdisciplinary teams. The level of complication in convicts' problems is often high, so social workers face the necessity of cooperating with different specialists (e.g. psychologists, psychiatrists and doctors of many other specialties).

The last level of convicts' health care refers to its institutional dimension. Some comment on organizing local communities' health care seems necessary here. Medico-social staff actions in community involve arrangements, but also assistance organizations development and conducting reforms in health service. It is than acting on macro systems, focusing on community organization models and following conclusions for social policy and the process of its administration.

General philosophy of arranging local communities is based on following assumptions:

 Human communities often require help to satisfy their needs in terms of health care. Like individuals needing help to manage these problems.

- Human communities may develop a capacity of solving their problems, especially those concerning health.
- People wish for change and are able to alter.
- Democracy requires participation in health protection, taking actions concerning community problems and for people to acquire abilities, which enable this participation.
- People should participate in making, adjusting or controlling crucial changes in health protection, in the community premises.
- Changes in communities live, made or prepared by its members, have the meaning and permanence, impossible for imposed ones.
- "Holistic" approach enables dealing with those problems, which are insoluble using "fragmentary" approach. It is crucial for solving health problems.

Holistic model of convicts' health care seems to be the most effective for its protection, especially in the process of social reeducation. The standard of its realization depends on society's wealth i.e. possessed funds, and public opinion support in addition. However European public opinion is not always well oriented in the topic. Furthermore, in the beginning of XXI century it becomes a bit populist towards methods of treating criminals, with an attitude rather towards punishing than supporting [14]. This is why the model probably will come to life [15]. However it may not speak against comparison of engaged in convicts' health protection institutions system in "old EU member-countries" and in Poland. This comparison will be the last part of the present paper. It was based on following documents:

- Rapport from conference "L'insertion des jeunes en difficulte et le fonds social europeen. Approche comparee en Europe", chich took place in Vaucreeson near Paris at 15–17.10.2007 (organization: Centre National de Formation et d'Etudes de la Protecion Judiciaire de la Jeunesse).
- Rapport from "Practice into Policy conference", which took place in London at 20–21.11.2007 (organization: Centre for Economic & Social Inclusion –London).

I took part in both mentioned. Furthermore:

- Studies: Prise en charge Medici psycho sociale.
 Ed. Le Comede. Comite Medical pour les exiles.
 Hopital de Bicetre, Le Cremlin (Paris 2005).
- Administration Penitentiaire. Rapport annual d'activite 2006. Ed. Ministre de la Justice. Paris.
- Le guide de sortant de prison. Observatoire International des prisons. Ed. La Decouverte, Paris 2006.

Analysis presented below is a first stage of comparative analysis mentioned system and Polish institutions, it includes confrontation of information from cited documents and concerning both compared areas.

To characterize present system of health care institutions for convicts in Western Europe it is necessary to notice, that it formed under the influence of tradition developmental social services. Evolution of these services in XXth century in EU countries took place in following 5 basic stages:

- The stage of gradual passage from charity and voluntary work to professional actions (1900–1920).
- The stage of forming working methods based mainly on North-American experiences (1920–1940).
- The stage of inner differentiation of social services, caused by variety of realized tasks (1940–1955).
- The stage of "casework as a basic method of acting" re-discovery (1955–1960).
- The stage of "comprehensive approach" to working methods, based on acting in reliance on group and local communities (after 1960).

French author C. de Robertis notices that equally important moment for social services development, alike to passage from voluntary to professional work, was combining occupation of social assistant and social nurse in one called a social worker. It happened before II World War (in France in 1938) [16]. After II World War to a group of social workers also other specialists and professions working and helping people in difficult situations, which impede integration with society, were included. Although had rather informal character. They were employed in a variety of institutions like social assistance houses and prisons, what caused a fact, that they were not a homogenous group any more, because institutions created new places of actions, aims and tasks.

Currently medico-social staff works with such a heterogeneous group of people needing help and support like: elderly, disabled, homeless, unemployed, mentally distorted, socially unadapted people or criminals etc. The face the problems like children abuse or neglect, lack of care or incapability of elderly people, lack of accommodation, poverty, addiction from drugs or chemical substances and crime. They prepare rapports for courts concerning topics like: health care, treatment possibilities – original and consequent, health support for families, gerontology, possibilities of creating prevention systems, unemployment counter acting etc. In following presentations I'll focus on this group of socio-medical staff, whose aim is convicts' health protection. The second important developmental factor for modern convicts' health care institutions system was gradual cessation of private funds for medico-social services. In consequence currently the core of health care institutions for this group is located in a public sector. Still, the sector of societies and foundations is an important "supplement". It seems necessary to emphasize that although means for the institutions are transferred from public funds, both institutions and money are administrated by societies themselves or private persons.

To sum up, current division of health care institutions for convicts contains following categories (**Table 1**).

Source: author's own study after: Prise en charge Medici – psycho – sociale. Ed. Le Comede. Comite Medical pour les exiles. Hopital de Bicetre, Le Cremlin (Paris 2005) oraz : Le guide de sortant de prison. Observatoire International des prisons. Ed. La Decouverte, Paris 2006.

From above presented table appears that:

 When we compare institutions of health care for convicts in public and societal sector in "old EU member countries" and in Poland it turns out that in first case both sectors developed proportionally. In Poland there are no departmental services in societal sector, what causes that the public sector is a monopolist in the scope of health services for convicts. In the same time public sector in Poland is inefficient in providing health care for all demanding convicts, especially in situation of prisons overpopulation, so it needs a kind of institutional support. One of the possible ways contains **table 1**.

- Situation looks much better after analysis of both sectors concerning medical services and institutions supporting departmental medical services. Except medical services in schools the rest of services developed in both – old EU member countries and in Poland, however some differences to the detriment of Poland occur [17]. In our country this sector is less extended, what may be caused by a fact that it develops for a quite short time, furthermore old EU member countries are wealthier, so they have greater funds, which may be allocated in health care.
- Situation referring to sanitary services and social assistance is quite alike. In Poland societal sector, although represented on the level of all services and institutions, except those created by religious congregations, is poor. The reasons are resemble to these presented in point 2.

It seems that further evolution of health care institutions for convicts judged by common courts will be

Table 1. Institutions of health protection for jurisdiction clients in old EU member countries and in Poland (state from 2006)

| | Sector's characteristics | | | | |
|--|--------------------------|--------|-------------------|----------|--|
| Types of social services | | Public | | Societal | |
| Types of social services | Old EU members | Poland | Old EU members | Poland | |
| Basic medical and services and institutions | | | | | |
| Departmental | | | | | |
| Prisons' medical services | + | + | + | - | |
| Juridical medical services | + | + | + | - | |
| Supporting (universal health service – medical services for convicts) | | | | | |
| Health care, prevention, and treatment institutions | + | + | + | + | |
| Specialist health institutions (specialist hospitals, clinics, mental hospitals, rehab institutions) | + | + | + | + | |
| Schools' medical services | + | + | + | - | |
| Sanitary and social assistance institutions | | | | | |
| Regional services of social hygiene | + | - | + | - | |
| Social actions of Armed Forces | + | - | - | - | |
| Municipal services and social assistance offices | + | + | + | + | |
| Medical and social services for emigrants and and profit-emigrants | + | + | + | + | |
| Charity institutions | - | - | + | + | |
| Religous Congregations | - | + | - | - | |
| Red Cross | + | + | - | - | |
| Others | - | _ | + | + | |
| + exists | | | | | |

+ EXISIS

– does not exist

Source: author's own study after: Prise en charge Medici-psycho-sociale. Ed. Le Comede. Comite Medical pour les exiles. Hopital de Bicetre, Le Cremlin (Paris 2005) oraz : Le guide de sortant de prison. Observatoire International des prisons. Ed. La Decouverte, Paris 2006

connected with both – consolidation of public sector in old EU member countries and more definite state and social support for societal sector in Poland. Practice and hitherto experiences of old EU member countries prove that this sector has large developmental possibilities. It also enables flexibility in administrating health protection institutions and possessed funds, so it is a vital support for health care institutions system traditionally located in old EU countries and in Poland in the public sector.

Table analysis would be incomplete without an indication of the fact that European health care institutions working for jurisdiction may be divided according to the type of environment they act in or according to subordination to the Ministry of Justice. Concerning the latter organizations located formally inside and outside jurisdiction. First group consists of:

- Medico-social services in probation services.
- Medico-social services in educational institutions and reformatories.
- Medico-social services in prisons organized as autonomic services or as a part of probation services.
- In Poland there are no medico-social services in juridical probation service [18]. In second group following European institutions and medico-social services are located:
- Childcare centers,
- Centers of medical and social service for family,
- Institutions and organizations of common health service,
- Mental health clinics,
- Medical and social services for schools.
 All kinds of these services are present in Poland.

To sum up, institutions and services included in first group may be named as proper medico – social services in Justice (services medico – sociaux aupres de la Justice), those from the second – supporting (subordinate to Ministries, e.g. Ministry of Public Health; services authorized by Justice – services habilites par la Justice).

In practice these services cooperate closely and their tasks often overlap. It is worth emphasizing that courts may order to both, however the scope of competencies is defined by the law and authorizations done by Minister of Justice (habilitation). It is worth to notice that in the first group public sector services prevail, in case of prisons it has monopoly on medical services for people during imprisonment.

In the majority of Western European countries institutions and organizations dealing with health care of convicts are a part of public sector, while those from societal sector are taking care of cases recognized by courts in a guardianship procedure.

To the complete comparison of present medico-social service systems in old EU member countries and in Poland should be added that in both exists separate network of medico-social services for juveniles and adults subordinate to the Ministries of Justice. In Poland this network is less developed. In France it is a organizational part of great system of legal youth protection, which have in the Ministry of Justice own autonomic General Directory (Protection Judiciaire de la Jeunesse) [19].

To summarize all what has been said in present paper concerning the comparison of institutions of health protection for people, who appear before the court in old EU member countries and in Poland I would like to formulate some more general remarks.

The issue of health care for jurisdiction "clients" obtained great meaning in Western Europe after II World War. It remains an integral part of social and penal policy of single EU member countries. In consequence whole system if medico-social institutions located in public and societal sector are harmonizing. Poland seems to be a bit behind, however in the last few years clear progress is observed. Its determinants are e.g. constant extension of public sector and creating and development of societal sector. This direction should hold, because consequences for jurisdiction are consequences for a whole society.

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CASE STUDY

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Presacral schwannoma. Case description

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ABSTRACT

Schwannomas in the presacral region of vertebral column occur sporadically and are usually diagnosed incidentally during diagnostic procedures applied as a response to nonspecific complaints associated with vertebral column or abdominal cavity. This study focuses not only on the presentation of the case of the patient with giant schwannoma in the retrorectal area, but on the highlighting of the problems associated with diagnosis and treatment of tumours located in this anatomic region as well. The presented case involves a 23-year old woman. The diagnosis of the disease was made during gynecological examination accompanied by ultrasonography of pelvic organs. Neurological examination disclosed no deviations from the normal condition. MR imaging allowed to determine precise location of the tumour and its anatomic relations to pelvic visceral and vascular structures. The patient underwent a successful surgery using laparotomy. Histological examination revealed structures of schwannoma. Surgical radicality and the lack of relapse were confirmed by MR imaging taken five years after the surgery.

Keywords: schwannoma, presacral space, surgery.

Introduction

Tumours of the presacral regions occur at the frequency of one case per 40,000 persons admitted to hospital [1]. Schwannoma accounts for 3% to 3.2% tumours in this anatomical region. Abernanthey et al. (1986), working in Mayo Clinic in the period of 33 years collected a series of only 13 giant schwannomas of the presacral region [2].

The presacral region, also referred to as retrorectal region, is frontally confined by the rectum, dorsally by the sacral and coccygeal bones and on the inferior side by muscles of pelvic floor. Lateral limits are marked by ureters and iliac blood vessels [3].

Tumours of the spinal presacral region pose a complex problem, requiring collaboration of specialists in surgery, gynecology, urology and neurosurgery.

The objective of the study is the presentation of the case of a 23-year-old female with a giant schwannoma in the retrorectal region and the analysis of the prob-

lems resulting from diagnosis and surgical treatment of tumours located in this anatomic region.

Case description

23-year-old female patient during routine gynecological examination was diagnosed with a tumour of small pelvis. The tumour was confirmed by per rectum examination and transrectal ultrasonography (T-USG). Magnetic resonance imaging (MR) of abdominal cavity (**Figure 1a, b**) disclosed pathological solid mass (in size of 130 mm x 74 mm x 63 mm) with sharply outlined margins in the presacral area in small pelvis. In sagittal plane the tumour was located beginning at lower edge of L5 vertebral body down to interface of S2–S3 sacral segments, inducing an osteoblastic reaction in the sacral bone on its left side and bulging through widened sacral foramina at the level of S1 and S2 segments on the left side. In T2-weighted images the



Figure 1. MRI in (a) sagittal and (b) axial projections presents location of the tumour in the presacral region

tumour manifested a non-uniform signal intensity and the examination disclosed fine foci of destruction within the tumour. The tumour, out of necrotic areas, demonstrated evident amplification following intravenous administration of paramagnetic contrast agent (gadolinium). The tumour compressed and modelled uterine corpus. The left ovary manifested normal structure, was compressed and frontally and medially displaced. Left parametrium with urinary bladder were also compressed. The radiologist put forward the diagnosis of schwannoma.

The patient was admitted to the Department of Neurosurgery in a good general condition, with no complaints reported. Neurological examination

revealed no pathology. Preoperative supplementary tests were made including urography, which demonstrated unitemporal, normal urinary excretion of contrast agent by both kidneys and a normal calyces/pelvic system in both kidneys. The left ureter was normal in its upper segment while at the level of L5 vertebra and S1 segment of sacral bone it was widened to 9 mm, with no peristaltic movements and from the level of S2 segment to its ostium in the urinary bladder it was narrow, with irregular wall surface. The right ureter in its upper fragment manifested normal course with preserved peristalsis but in its lower portion, beginning at the upper limit of the sacral bone it did not show up. Its bladder ostium was visible but narrow, modelled on the tumour mass. The tumour compression on the urinary bladder resulted in its asymmetric filling with urine. The tests ordered by the consulting surgeon: rectoscopy, sigmoidoscopy and barium enema, demonstrated no lesions within anus and colon.

The surgery by means of laparotomy was made in general endotracheal anesthesia. The vertical incision within abdominal skin was made in the midline, bypassing the umbilliculus. The incision of peritoneum and the separation of intestinal loops enabled the access to prevertebral space, uncovering the division of aorta into common iliac arteries, the outflow of common iliac veins into inferior caval vein, L4, L5 vertebral bodies and a segment of S1 vertebra. The tumour was positioned in front of the vertebral column, between lower margin of L5 vertebral body and S3 segment of the sacral bone. The tumour, (120 mm x 90 mm x 80 mm in size), on its left side was strictly connected to the sacral bone. The ureters passed in the tumour capsule on its both sides. At the next stage of the surgery, by means of microsurgical technique, the ureters were dissected free from the tumour capsule. In the back, on the right side, the inferior caval vein adhered to the tumour capsule. After dissecting the vein from the tumour capsule, the accreting tumour was separated from the sacral bone: using a surgical microscope the pathological mass was separated from roots of S1 and S2 sacral nerves on the left hand side and from the front surface of sacral bone it was fused with. Continuity of the nerve roots was preserved. The tumour was completely dissected, with blood loss of 700 ml. After assuring hemostasis in the site, the wound was closed in layers, with a drain remaining in the retroperitoneal space. To alleviate the pain a drain was introduced to extrameningeal space of the vertebral canal, which provided the potential for the administration of 0.5% Bupivicaine.

The macroscopic dimensions of the dissected tumour were 120 mm x 80 mm x 60 mm (**Figure 2**). The cross-section of the tumour was macroscopically uniform and grey-white in colour. In macro- and micro-scopic evaluation the tumour had an evident capsule of connective tissue, its texture was solid and contained moderately high number of cells. The elongated, spin-



Figure 2. Macroscopic outlook of the tumour

dle-shaped cells manifested a slightly blurred margins of cytoplasm. The cells formed parallel or interwoven bands. The nuclei of cells were elongated, rod-shaped and positioned in the long axis of a cell. Nuclear chromatin had uniform character, with nucleolus noted only occasionally. Palisade set-ups of cell nuclei were not encountered in the examined case. Occasionally, the tumour texture contained fibrous acellular regions and foci of xanthomatous cells. The vascular supply was relatively rich. The blood vessels frequently manifested thickened walls, with the presence of homogenous hyaline masses. Routine histological examination of the surgical material allowed for the diagnosis of schwannoma, manifesting, according to WHO, I degree of biological malignancy (**Figure 3**).

The post-operational course was free of complications. After healing of the post-operational wound, on the ninth day following the operation, the patient showed a normal condition in neurological examination, complained of no pain and was released home. The patient continued her studies, then took up professional work, staying under control in the outpatient clinic. Currently the patient reports no complaints and consecutive neurological examinations demonstrate no deviations from a normal condition. MR control examination of lumbal/sacral vertebral column made 5 years after the operation revealed a condition following a complete removal of the tumour (**Figure 4**).

Discussion

Schwannomas in the retrorectal region are slowly growing tumours leading to transplacement of surrounding anatomic structures. They are observed more frequently among females [4, 5].

The tumour evokes ailments when it reaches a large size. The clinical symptoms result from compression from the tumour on the neighbouring anatomic structures: nervous, vascular and visceral. Most frequently the patient complains of a discomfort in abdominal



Figure 3. Histological preparation of the tumour. H&E staining, magnification 150 x



Figure 4. Control MRI in sagittal projection (a) and axial projection (b) presents the condition following complete excision of the tumour

cavity, lumbosacral pain, pain in the lumbar/sacral region, hypogastric pain radiating to groins, frequent urination or difficulties in passing urine. Some patients complain of unpleasant sensation of a filled anus and constipation. Sporadically, neurological defects are also observed [6, 7].

The symptoms are usually nonspecific and in over 26% the tumours are completely asymptomatic [3]. In such cases presacral schwannomas are recognised during physical examination of the abdominal cavity, gynecological examination "per rectum" or during radiological examination made due to nonspecific complaints [6]. This confirms our case, in which suspicion of a tumour in the presacral region was put forward by a gynecologist during a routine gynecological examination. The presence of a tumour in the retrorectal space may hamper a delivery of a newborn [6, 7].

Tumours located in this anatomic region may manifest an inborn character (meningeal hernias, dysontogenetic tumours), be of primary origin (chordoma, osseous giant cell tumour, chondrosarcoma, immature neuroma), of metastatic or inflammatory character [3, 6].

Apart from the above mentioned tumours, schwannoma has to be distinguished from ovarian tumours, ureteral tumours, retroperitoneal sarcoma or abscess in iliopsoas muscle [8–11].

Nevertheless, despite such broad range of differential diagnosis, similarly to the discussed case, the classical variant of schwannoma presents no diagnostic difficulties in the postoperative material already on the level of routine morphological techniques. In doubtful cases, immunohistochemical techniques and occasionally electron-microscopic techniques turned out to be useful.

Schwannoma stems from ventral roots of sacral nerves. In plain radiography and computer-assisted tomography (CT) lesions of erosion type and irregular destruction of frontal pelvic foramens of sacral bone may be evident [12]. In CT examination and in magnetic resonance imaging (MRI) schwannoma is very well confined, manifests smooth edges and transplaces the neighbouring anatomic structures. The tumour is frequently featured by a heterogenous pattern, with centrally located cysts and it manifests marginal augmentation following administration of a contrast agent [4]. Lesions of cystic type are present much more frequently (in 60%) in schwannomas than in other tumours [4, 13]. MRI patterns of schannomas present hemorrhagic, necrotic and calcified foci. The lesion is hypointense on T1 weighted images and hyperintense on T2 weighted images [14].

Needle biopsy of tumours in the retrorectal region is a safe approach to make the diagnosis strict. Histological evaluation of the obtained material in 95% cases allows to conclude whether the lesion is of a benign or a malignant character. The tumour type can be precisely defined in 81% cases [15]. Indications for needle biopsy in cases of schwannomas are controversial due to their sufficiently distinct image in MRI examination. Proponents of needle biopsy are of the opinion that such a biopsy should be made in patients with the tumour evoking no clinical symptoms and the patient does not decide to undergo surgery [7].

The size and location of the tumour have to be very precisely determined prior to surgery. A particular attention should be paid to position of arterial and venous blood vessels in the anatomic region, to the determination of tumour relationships to ureters, urinary bladder, posterior wall of rectum and other closely positioned anatomic structures. The risk of intraoperative injuries has to be evaluated before taking the decision about the surgery. In our case, this led to the extension of diagnostic procedures (apart from MRI) by rectoscopy, sigmoidoscopy, barium enema to the large intestine.

Depending of tumour location, size, relationships to other anatomic structures and type of tumour in the presacral region various surgical approaches are applied, including frontal access (through the peritoneal cavity), posterior access (through the sacral region), frontal and posterior in parallel, transrectal and transvaginal one [3, 6, 16]. Schwannomas are approached through the frontal access. In the case of small dimension tumours the endoscopic technique is used with transrectal or transvaginal operative approach [17]. Surgical treatment of schwannoma aims at its complete removal. Problems with reaching the aim stem from the size of the tumour, its rich blood supply and vicinity to important anatomic structures. The tumours in this area are usually supplied with blood through sacral arteries, medial and lateral arteries, lumbar arteries and internal iliac arteries.

During the surgery, the surgeon should focus on preserving continuity of sacral nerve roots (S1, S2, S3) which exit from sacral bone through pelvic foramina, fused with the capsule of the tumour. Damage to the nerves results in dysfunction of vesical and anal sphincter muscles, disturbs sexual functions and leads to paresis of greatest gluteal muscle [1]. In order to preserve the continuity of nerve roots S1 to S3 a microsurgical technique has been applied during our operation.

Complete excision of a tumour in the presacral region is possible in cases of benign tumours and in three quarters of cases of malignant tumours. A partial tumour resection is made when there are no chances for a complete removal of the pathological lesion [7]. In such cases relapses if schwannoma are described, usually within a time distance of a few years [18].

Complications occur quite frequently, in 1/3 of the cases, but they are usually of reversible character [3]. They most frequently include the injury to venous or arterial blood vessels, a disturbed function of vesical and anal sphincters and in men disturbances in erection. Deficits in sensation in perineal region and frontal surface of thighs were also described [2, 3, 18].

In patients with asymptomatic schwannoma the possibility of conservative treatment with periodic control of MR examination should be taken into account. Strauss et al. treated 28 patients with schwannoma in retroperitoneal space, out of which 8 had the tumour accidentally detected due to their nonspecific complaints and signs in MR imaging [7]. The diagnosis of schwannoma was established by needle biopsy and the patients were subject to further observation. After 32 months no progression of the tumour was revealed by MRI control, the patients reported no pains and neurological examination detected no abnormalities. However, other authors reported very good results of surgical treatment applied to asymptomatic presacral schwannomas [19, 20].

Application of radiotherapy in cases of incomplete excision of schwannoma is controversial and rather not recommended as it may induce the transformation of schwannoma cells and the development of malignant neuroma [21, 22]. Stereotactic radiosurgery is recommended in cases of small schwannomas,

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with the diameter of less than 30 mm, positioned in the sacral bone [23].

Conclusions

Giant schwannomas of sacral bone occur rarely and pose diagnostic and therapeutic difficulties. They manifest a slow local growth and induce nonspecific symptoms.

Their preoperative procedures require magnetic resonance imaging of lumbosacral vertebral column and multispecialistic evaluation of pelvic visceral structures.

Complete tumour excision is equal to cure.

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Conflict of interest statement

The authors declare that there is no conflict of interest in the authorship or publication of contribution.

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