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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*.

You are welcome to publish your basic, medical and pharmaceutical science articles in *Journal of Medical Science*.

Ethical guidelines

The Journal of Medical Science applies the ethical principles and procedures recommended by COPE (Committee on Conduct Ethics), contained in the Code of Conduct and Best Practice Guidelines for Journal Editors, Peer Reviewers and Authors available on the COPE website: <https://publicationethics.org/resources/guidelines>

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ORIGINAL PAPER

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The impact of pollution on the mental health of the population

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
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ABSTRACT

This paper analyzes the relationship between pollution of the natural environment and the population's mental health, based on the example of three urban agglomerations: Gdańsk, Poznań, and Katowice. The following factors were analyzed: air quality, the quality of water from the municipal waterworks, data concerning social pathologies, number of private psychological, psychotherapeutic, and psychiatric practices, as well as statistics concerning psychiatric healthcare in the Pomeranian, Greater Poland, and Silesian voivodships in 2011. Based on the collected data, presented in a descriptive manner, a hypothesis was drawn that natural environment pollutions may influence the mental health of the population. This conclusion was drawn from the fact that worse air quality in Katowice correlates to a higher percentage of social pathologies and a higher demand for psychiatric healthcare than in Poznań or Gdańsk.

Keywords: environmental pollution; mental health; ecological psychiatry.

Introduction

Natural environment pollution influences, to a large extent, the degradation of Earth's biosphere; it also has a significant impact on the broadly understood public health. Taking into account the inextricable connection of human beings to the environment, it should be concluded that the environment strongly influences human health. Pollution is one of the natural environment factors that most influence human health and occur in all elements of the environment, i.e.: water, soil, along with noise or light pollution. Environmental toxins have a negative impact on the physical health of the population, but it can

also be assumed that they have similar influence on their mental health. It is widely established in the public and environmental health literatures that primarily exposure to air pollution is hazardous to human health.

In the analyzed period – the year 2011 – more and more social pathologies (acts of violence, murder, alcoholism, and others) were related to an increase of concentration of pollutants in the air and water and adverse weather conditions [1]. In scientific literature [2, 3] papers suggesting a cause-and-effect relationship between the high suicide rates and ecological threat in the analyzed area were published. Bandiera et al. [4]

also point to a strong dependency between passive smoking and risk of depression, and Wueve et al. [5] the decrease in cognitive intelligence in a group of elderly women. Lundberg [6] correlates the following variables: increase in air pollutants and a number of psychiatric emergency calls and psychiatric admissions, indicating a statistically significant relationship.

In this paper, an analysis is carried out, covering the following parameters for urban agglomerations of Gdańsk, Poznań, and Katowice in 2011:

- › atmospheric air quality,
- › tap water quality,
- › social pathology statistics,
- › numerical data relating to private psychiatric practices, private psychotherapeutic and psychological offices.

Moreover, statistics concerning psychiatric healthcare in the Pomeranian, Greater Poland, and Silesian voivodships were considered.

Aim

The general objective of the study was to find a relationship between the presence of environmental pollution and the mental health status of the population, as a response to the unsatisfactory level of current knowledge in the field of ecopsychiatry, which poses a threat to public health in the face of constantly progressing degradation of the natural environment.

The detailed objectives were formulated in the form of the following questions:

- › Do environmental pollution affect the mental health of the population?
- › Does the level of toxins in atmospheric air correlate with a higher percentage of recorded social pathologies?
- › Is there a connection between the demand for private and state psychiatric health care and the quality of atmospheric air?

Materials and Methods

The object of research were data concerning populations of urban agglomerations of Gdańsk, Poznań, and Katowice in 2011. Those cities were selected due to differences in environmental conditions (stemming from their geographical situation) and the degree of industrialization. The research material were numerical data from

2011, concerning selected natural environment pollution indicators and the mental health of the population obtained from the following databases: Voivodship Inspectorates for Environmental Protection (WIOŚ), Voivodship Sanitary and Epidemiological Stations (WSSE), Municipal Police Stations, Centre of Health Information Systems (CSIOZ), Central Electronic Register and Information on Economic Activity (CEIDG) and Local Databank. Furthermore, information from Polish Psychological Association and Municipal Police Stations were obtained by electronic correspondence and personal interviews. The most relevant environment pollution indicators, influencing the entire population of abovementioned cities, was air quality (monitored by the WIOŚ), as well as physical and chemical parameters of tap water (on the basis of results of review monitoring carried out by the WSSE). The mental health of the population was evaluated based on statistics provided by: Municipal Police Stations, CSIOZ, CEIDG, and the Local Databank. The paper presents only selected, most important results that have the most significant impact on the result of research conducted.

The air quality was evaluated through an analysis of automatic pollution measurements. Besides the visible differences in concentration of the analyzed substances for the studied urban agglomeration, differences are also marked in the scope of measurements taken and their publication: for Gdańsk, only 5 parameters were taken, for Poznań – 21, and for Katowice – 23. An analysis of that problem in this article was therefore limited to 5 parameters. The tap water quality evaluation was obtained from Voivodship Sanitary and Epidemiological Stations which conducted a control and review monitoring. The number of parameters taken was 36 for Gdańsk, 60 for Poznań, and as many as 71 for Katowice, which in turn influenced the final scope of the research material.

Since mental health is a very complex issue, difficult to analyze, a multidimensional approach was adopted. One of the studied markers were social pathologies (deviations). Information concerning the number of social pathologies occurring: homicide, suicide (resulting in death), domestic violence, fights or battery (Art. 158 and 159 of the Polish Penal Code) for 2011 were provided by Municipal Police Stations in Gdańsk,

Poznań and Katowice. The absence of data concerning the number of suicides in the city of Katowice for 2011 was justified by the fact that very often, suicide was not included in the statistical system due to protocol [7]. As concerns domestic violence, data was only collected in relation to persons (not exclusively women) who have decided to report a crime, which resulted in an actual initiation of penal procedure. Statistics did not include the so-called "blue cards" (Polish Domestic Violence Police Intervention Protocols) which do not necessarily entail the initiation of pre-trial proceedings.

The assessment of mental health of the population was also carried out on the basis of data obtained from the Centre of Health Information Systems concerning the number of private practices ran by psychiatrists in Poznań, Gdańsk, and Katowice.

In the same manner, data concerning private psychological and psychotherapeutic offices in the studied urban agglomerations was generated from the resources of the Central Electronic Register and Information on Economic Activity.

Data concerning psychiatric care were complemented by statistics from the Central Statistical Office's Local Databank [8]. Although they concern entire voivodships, and not specific cities, they may contribute to our understanding of

the problem, as each of the discussed agglomerations is the biggest city in a given region.

Statistical analysis methods

Numerical results were expressed in arithmetical mean, standard deviations, and coefficients calculated per number of inhabitants. Due to the limited amount of numerical data and their pre-processing (absence of results of single measurements), it was not possible to carry out statistical tests. Therefore, results are presented in a descriptive manner, using tables.

Results and Discussion

Air quality

Table 1 presents annual average pollutant concentrations in the analyzed urban agglomerations. The highest concentration of sulfur dioxide (SO₂) in 2011 was noted in Katowice, and the lowest in Poznań, with only slightly higher concentration in Gdańsk. In concerns nitrogen dioxide concentration (NO₂), it was also highest in Katowice, and lowest in Gdańsk. Average carbon oxide (CO) concentrations were identical for Gdańsk and Poznań and highest for Katowice. Both the concentrations of ozone (O₃) and particular matter (PM 10) are similar: the highest annual average concentra-

Table 1. Annual average and standard deviation of concentrations of selected air pollutants and physical and chemical parameters of tap water in urban agglomerations of Gdańsk, Poznań and Katowice [9–14]

Substance	City	Gdańsk	Poznań	Katowice
		$\bar{x} \pm SD$	$\bar{x} \pm SD$	$\bar{x} \pm SD$
SO ₂ [$\mu\text{g}/\text{m}^3$]		5.96 ± 2.31	3.84 ± 2.46	15.92 ± 7.96
NO ₂ [$\mu\text{g}/\text{m}^3$]		18.92 ± 3.57	24.79 ± 7.14	47.96 ± 16.83
CO [mg/m^3]		0.36 ± 0.13	0.36 ± 0.11	2.10 ± 1.22
O ₃ [$\mu\text{g}/\text{m}^3$]		40.9 ± 16.48	45.44 ± 15.26	110.83 ± 36.23
Particular matter PM 10 [$\mu\text{g}/\text{m}^3$]		28.82 ± 5.55	39.42 ± 18.95	58.92 ± 26.68
Selected physical and chemical parameters of tap water in Gdańsk, Poznań and Katowice				
Nitrates (NO ₃) [mg/l]		2.10 ± 1.98	n/o	3.76 ± 1.08
Manganese (Mn) [$\mu\text{g}/\text{l}$]		5.20 ± 9.63	8.42 ± 7.80	5.87 ± 6.01
Ferrum (Fe) [$\mu\text{g}/\text{l}$]		44.25 ± 47.0	41.67 ± 55.04	104.75 ± 60.80
Fluorides (F) [mg/l]		0.37 ± 0.46	0.22 ± 0.02	0.09 ± 0.04
Chlorides (Cl) [mg/l]		31.7 ± 34.38	42.39 ± 1.59	9.25 ± 1.08
Sulfides (SO ₄) [mg/l]		41.15 ± 27.20	90.63 ± 12.31	25.51 ± 2.19
Boron (B) [mg/l]		0.15 ± 0.26	0.07 ± 0.03	nd
Aluminium (Al) [$\mu\text{g}/\text{l}$]		4.97 ± 8.81	n/o	26.45 ± 35.12
Nickel (Ni) [$\mu\text{g}/\text{l}$]		1.13 ± 1.10	3.58 ± 1.25	n/o
Chromium (Cr) [$\mu\text{g}/\text{l}$]		2.95 ± 2.10	1.29 ± 1.02	n/o
Copper (Cu) [mg/l]		0.04 ± 0.11	0.005 ± 0.01	n/o
Arsenic (As) [$\mu\text{g}/\text{l}$]		0.39 ± 0.62	0.65 ± 0.80	nd
Trihalomethanes THM [$\mu\text{g}/\text{l}$]		2.75 ± 5.20	29.33 ± 7.31	13.94 ± 6.75

n/o – indeterminable, nd – no data

tion of those pollutants were observed in Katowice, and lowest in Gdańsk. Both parameters were slightly higher in Poznań. Concentrations of all 5 analyzed parameters were highest in Katowice.

Quality of tap water

Table 1 summarizes selected physical and chemical parameters of water from public waterworks in the analyzed cities. The highest concentration of nitrates (NO₃) in the studied period was noted in Gdańsk, and lowest in Katowice. In Poznań, the level of that substance was indeterminable. Annual average concentration of manganese (Mn) was highest in Poznań, lowest in Gdańsk, with slightly higher concentration in Katowice. The level of iron in tap water was highest in Katowice and lowest in Poznań. The highest concentration of fluorides (F) was determined in the city of Gdańsk, lowest in Katowice, and slightly higher in Poznań. Concentrations of chlorides (Cl) and sulfides (SO₄) were highest in Poznań, lowest in Katowice, and in Gdańsk, their level was a little higher than in Katowice. As concerns concentrations of boron (B), the lowest was observed in Poznań, higher in Gdańsk, and in Katowice, the level of that substance was not measured. The level of aluminum (Al) was indeterminable in Poznań, high in Katowice, and lower in Gdańsk. 3 other parameters – nickel (Ni), chromium (Cr), and copper (Cu), were indeterminable in Katowice. The nickel concentration

was lower in Gdańsk than in Poznań, as opposed to chromium, whose level was lower in the water in Poznań than in Gdańsk, similarly to the levels of copper for Poznań and slightly higher level for Gdańsk. The concentration of arsenic (As) was not measured in Katowice, and in Poznań, it was higher than in Gdańsk. The sum of trihalomethanes (Σ THM) was determined as lowest in Gdańsk, highest in Poznań, and slightly lower in Katowice.

Social pathologies

Table 2 shows the data concerning selected social pathologies in the analyzed cities in 2011. In police databases, 11 homicide cases were noted in Katowice and Gdańsk, with 10 in Poznań. Calculated per 10 thousand inhabitants, this indicator is highest in Katowice, lowest in Poznań, and slightly higher in Gdańsk. As regards suicide, we do not dispose of any statistics concerning Katowice; in Gdańsk, the indicator is higher than in Poznań, despite the fact that the overall number of events was slightly higher in the capital of Greater Poland than in the main metropolis of the Pomerania.

Cases of domestic violence were reported most often in Gdańsk; their rate, per 10 thousand persons, was also highest. The lowest number of reports was noted by the Katowice police, although when calculated per the number of inhabitants, the rate is higher than in Poznań. In 2011, brawls and battery occurred most often in Poznań, least

Table 2. Selected social pathologies, number of private psychiatric practices, number of private psychological and psychotherapeutic in Gdańsk, Poznań and Katowice in 2011 [7, 8, 15, 16, 18]

		City		
		Gdańsk	Poznań	Katowice
		Total number	Total number	Total number
		Rate per 10 thousand inhabitants	Rate per 10 thousand inhabitants	Rate per 10 thousand inhabitants
Selected social pathologies	Homicide	11 0.24	10 0.18	11 0.36
	Suicide (resulting in death)	37 0.80	38 0.69	nd nd
	Domestic violence	247 5.36	175 3.17	105 3.41
	Brawl, battery (art. 158 and 159 of the Polish Penal Code)	85 1.85	153 2.77	120 3.89
	Number of private psychiatric practices	64 1.39	68 1.23	50 1.62
Number of private psychological and psychotherapeutic	Psychological offices	138 3.00	213 3.86	70 2.27
	Psychotherapeutic offices	66 1.43	65 1.18	42 1.36

nd – no data

often in Gdańsk, and slightly more often in Katowice. Considering the size of the population, the lowest rate was also noted in Gdańsk, the highest in Katowice, and slightly lower in Poznań.

The overall number of offenses per 1000 Polish citizens in 2011 (rate for Poland – 3036) indicates that the highest level of crime was noted in the western provinces, and the lowest – in the eastern part of the country. Among the analyzed regions of Poland, the highest number of offenses per 1000 inhabitants was noted in the Silesian voivodship (3712), the lowest – in the Greater Poland voivodship (2965), and slightly higher in the Pomeranian province (3325).

Private psychiatric practices

Table 2 presents the data concerning private practices ran by psychiatrists in 2011 in the studied urban agglomerations. The number of practices in that period was lowest in Katowice, highest in Poznań, and minimally lower in Gdańsk. Per 10 thousand inhabitants, the rate was lowest in Poznań and highest in Katowice.

Private psychological and psychotherapeutic offices

Table 2 contains the data obtained from the Central Electronic Register and Information on Economic Activity, concerning the number of private psychological and psychiatric practices in the analyzed urban agglomerations. Psychological offices are most numerous (both in terms of their overall number and per number of inhabitants) in Poznań, least numerous in Katowice, and slightly more in Gdańsk.

The number of psychotherapeutic offices was highest in Gdańsk, minimally lower in Poznań, and lowest in Katowice; an taking into account

the size of population, the rate per 10 thousand inhabitants was also highest in Gdańsk, lower in Katowice, and lowest in Poznań.

Psychiatric healthcare

Table 3 shows the data concerning psychiatric healthcare in Pomeranian, Greater Poland, and Silesian voivodships. The overall number of beds in psychiatric hospitals and their departments is highest in the Silesian voivodship, lowest in Pomeranian, and slightly higher in the Greater Poland province. Per 100 thousand inhabitants, the highest bed rate is also in Silesia, minimally lower in Pomerania, and lowest in the Greater Poland. The number of persons treated in psychiatric hospitals in 2011 was highest (also per number of inhabitants) in the Greater Poland voivodship, slightly lower in the Silesian province, and lowest in Pomerania. Persons addicted to alcohol (registered in clinics) in 2011 were most numerous in Silesia, least numerous in the Greater Poland, and slightly more numerous in Pomerania. The number of people with mental and behavioral disorders registered in clinics, and their distribution, is identical – their number was highest in the Silesian province, the lowest in Greater Poland, and slightly higher in Pomerania.

Conclusions

The analysis of the data presented above did not provide conclusive evidence as to the impact of the natural environment pollution on the mental health of the population.

Studying the numerical data obtained from WIOŚ [9–11], we have observed that the quality of atmospheric air is decidedly worst in Katowice, where average concentrations of all 5 hazardous

Table 3. Statistics concerning psychiatric healthcare in Pomeranian, Greater Poland and Silesian voivodships [19]

	Pomeranian	Greater Poland	Silesian
	Total	Total	Total
	Rate per 10 thousand inhabitants	Rate per 10 thousand inhabitants	Rate per 10 thousand inhabitants
Beds in psychiatric hospitals and departments	1125	1457	2297
	0.49	0.42	0.50
Patients in psychiatric hospitals	10145	22410	21550
	4.44	6.50	4.66
Persons addicted to alcohol (registered in clinics for the mentally disordered)	73567	66279	174920
	32.22	19.22	37.86
Mental and behavioral disorders (without addictions) –registered in clinics	63408	54876	146259
	27.77	15.92	31.65

substances were significantly higher than in other analyzed cities.

On the other hand, in the case of water, no significant differences are visible in water quality of each city. In Katowice, we lack data concerning certain parameters, and some of them is indeterminable. It should be noted that an analysis of all results provided in WSSE reports concerning exceeding the acceptable limits of parameter values (in accordance with – applicable then – Regulation of the Minister of Health of 29 March 2007 (Journal of Laws no. 61, item 417, as amended) has shown that it occurred only three times in 2011: in Gdańsk (1 x ammonium ion and 1 x fluorides) and in Poznań (1 x turbidity). In Katowice, deviation from the accepted norms was found in none of the samples. This may suggest that water in Gdańsk should, perhaps, be classified as the worst among the studied cities. The abovementioned missing markers of certain parameters as well as differences in measurement methodology indicate, however, that such conclusions should not be drawn too hastily.

Information provided by Municipal Police Stations [7, 15, 16] show that in two cases out of four, the highest social pathology rate (per 10 thousand inhabitants) occurred in Katowice (homicide, brawls, battery). It correlates with the situation in the entire country, as, according to the Minister of Interior [62], the threat of crime was, in 2011, higher in Silesia than in the remaining regions of Poland.

A confirmation of the results obtained may be found e.g. in a publication by Mordawa [22], who, in his thorough analyses, shows that in the period from 2008 to 2011, the highest crime level among the analyzed agglomerations was noted in the Katowice region (40.3 thousand offenses), slightly lower in Pomerania (37.8 thousand), and lowest in Poznań (27 thousand).

Katowice is also the leading centre as concerns the number of private psychiatric practices (per 10 thousand inhabitants). However, data obtained from CSIOZ [8] are imprecise and do not allow to accurately determine the number of offices. Physician Chambers do not maintain records concerning those offices, and therefore the statistics are unreliable. Similar problems arose with psychological and psychotherapeutic offices. Acting in accordance with the Act of 8 June 2001 on the profession of psychologist and the profes-

sional self-government of psychologists (Journal of Laws no. 73, item 763), we tried to determine the exact number of psychological practices on the basis of the list of psychologists authorized to practice that should be held by the Council of the Regional Chamber of Psychologists. According to information provided by Polish Psychological Society, however, it is a dead letter. There is no self-government of psychologists, Regional Chambers existed only in residual form (practically only in Podlaskie region) and there was no entity holding a register of psychologists for the studied urban agglomerations.

Figures generated from the CEIDG [18] indicate that the highest number of psychological offices (per number of inhabitants) functioned in Poznań, and psychotherapeutic – in Gdańsk. The data, however, is incomplete, as the PKD code (Polish Classification of Activity) is the same for several medical professions. In view of the above, the generated numerical data reflect reality only to some extent. They may, however, serve as indicative material.

In the process of completion of data concerning psychiatric healthcare, we intended to compare statistics for psychiatric clinics located in the analyzed urban agglomerations, in terms of e.g.: percentage of bed use or the number of patients classified in each ICD-10 diagnosis groups. This information (complete) was provided only by Poznań. The institution from Gdańsk sent only a small fragment of necessary statistics, whereas the center in Katowice (despite numerous requests) did not agree to cooperate with us. Therefore, research plans were modified and limited to statistics from Statistical Office's Database (the only data publicly available) [19]. When analyzing data obtained from that database, it is easy to notice that in three categories out of four, the Silesian voivodship was in the lead: it had the highest number of beds in psychiatric hospitals, and clinics registered the highest number of alcohol-addicted persons and patients with mental and behavioral disorders. Only the number of patients of psychiatric hospitals was slightly higher in the Greater Poland region.

Information and conclusions demonstrated above, concerning mental health of the discussed voivodships and agglomerations, matched the results of research by Langiewicz and Pasiorowska [27], who found that in 2006, the rate of "under sec-

tion" cases per 10 thousand inhabitants was highest in the Silesian voivodship (4.1), slightly lower in Pomerania (4.0), and lowest in Greater Poland (2.7).

The results presented above may lead to a hypothesis that pollution of the environment may influence mental health of the population. Considering the fact that in Katowice in 2011, the air quality was worst among the analyzed cities, the number of social pathologies was highest, as was the demand for psychiatric healthcare (private practices, mental health clinic), there is a possible dependence of these variables. It is, however, no more than a conjecture. Due to different methodologies and larger extent of research cited above, one should proceed carefully when correlating the results with those we obtained. Nonetheless, it should be noted that in Katowice, where the air is most polluted, homicide, brawls, and battery occur more frequently than in other cities. It may also stem from the unemployment problem against which that area struggled at the time.

If we obtained complete statistical data on suicide, the relationship between the condition of the environment might turn out to be the same as in the case of research conducted by Korean scientists [24]: Changsoo et al. demonstrated a visible correlation between a transient PM concentration in air with a higher risk of suicide, especially in persons suffering from cardiovascular diseases. Considering the fact that in Katowice, PM 10 pollution is decidedly higher than in Poznań or Gdańsk, one may assume that police statistics concerning suicide may also be higher than in other cities.

Allen et al. [25] conducted research that may, to some extent, explain the higher number of persons registered in Silesian mental health clinics. The authors have proven that mice that grow breathing polluted urban air are more impatient than mice breathing the air purified by filters. When they reached maturity, animals from group 1 expected immediate gratification, whereas those which breathed clean air did not. This study is noteworthy, as mice were exposed in early periods of life, but consequences of that exposure were observed in adulthood. Mice exposed to toxins after puberty did not demonstrate any change in their behavior, which may suggest that the damage to the growing brain was critical for the observed behavioral effect. The inability to wait and acting on impulses is always related to impairment of cognitive func-

tions and behavioral disorders, including addictions. Hence the assumption that a similar mechanism may occur in the population of Silesians who, exposed to air of poor quality, need help treating alcohol addictions or mental and behavioral disorders more often than the inhabitants of Greater Poland or Pomerania. Hypotheses formulated in this paper are confirmed in scientific research presented above.

Victoria Sass et al. [26] conducted research that was the first study of its kind to utilize longitudinal, nationally representative panel data from the United States to assess the relationship between exposure to air pollution and reports of psychological distress. Using annual-average measures of air pollution in respondents' census blocks of residence we find that over the period 1999–2011 particulate matter 2.5 is significantly associated with increased psychological distress; this association remains even after controlling for a robust set of demographic, socioeconomic, and health-related covariates. This study suggests that public health efforts to reduce the personal and societal costs of mental illness should consider addressing not only individual characteristics and factors in the social environment, but also underexplored facets of the physical environment such as air pollution.

As the number of factors influencing human organism is overwhelming, it is extremely difficult to prove that one of them (drinking water/air/soil, etc.) determines one specific illness. It is easier to prove in the case of physical health, where somatic symptoms are more pronounced and specific. The definition itself of physical health is narrower and more precise than that of mental health. Therefore, if there are publications reporting the harmful impact of natural environment pollutions on human organism, they are mostly focused on physical aspects. Mental health is conditional on many aspects and one cannot determine with absolute certainty which factor prevails in a given specimen. And an attempt at extending this conclusion to the entire population is even more risky.

One can only assume that there is a relationship between environmental pollution and the mental health of the population. Neither was it possible to unequivocally prove the connection between the atmospheric air quality and the rate of social pathologies, although there are indications that suggest it exists.

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ORIGINAL PAPER

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Monitoring of conductive hearing loss due to eustachian tube dysfunction preservative treated with the Otovent pneumotherapy method

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ABSTRACT

Introduction. A conductive hearing loss is a very common problem in childhood. It is possible to indicate many reasons for the problem, but most of the times it is caused by the infectious process, as well as the typical adenoid hypertrophy in children. Very often this disease is associated with obstruction of the eustachian tube.

Aim. In this study, the authors present the results of the hearing tests of patients who underwent the treatment of the eustachian tube obstruction by pneumotherapy with otovent. The aim of the work was to monitor the effectiveness of this method of OME treatment.

Material and Methods. The research group consisted of 54 children aged 4 to 15 years, including 23 girls and 31 boys. The control group consisted of 16 children. Pure tone audiometry and impedance audiometry were performed before and after the therapy, for all of the participants.

Results. Obtained results of the study showed improvement in hearing in children correctly using the Otovent set. Hearing improvement was recorded both in the results of pure tone audiometry and impedance audiometry.

Conclusions. The obtained results showed the effectiveness of the pneumotherapy method. In the case of the research group, 81.4% of children achieved the auditory norm (44 people). In the case of the control group, after a fixed period of application of the Otovent set, this value was 0%. The intergroup comparative analysis clearly shows that the research group obtained significantly better results within all of the parameters assessed, than the control group.

Keywords: conductive loss, exudative otitis media, OME, pneumotherapy, obstruction of the eustachian tube.

Introduction

A conductive hearing loss is a very common problem in childhood. It is possible to indicate many reasons for its formation, but most often it is caused by the infectious process, as well as the typical adenoid hypertrophy in children. Very often this problem is associated with obstruction of the eustachian tube.

Dysfunction of the eustachian tube is one of the causes of otitis media with effusion (OME). During this disease, exudation accumulates in the middle ear spaces – mainly in the tympanic cavity – but without the features of acute inflammation [1, 2]. It is considered that the frequency of fluctuating conductive hearing problems depends on latitude. In Poland, it is associated with humidity

and periodically cold climate [3]. It is estimated that in the first years of life, up to 90% of children are affected at least once. Studies show that the natural course of otitis media is mild, self-limiting and transient, with a tendency to recovery (in 30–40% of patients). However, in 10–20% of cases, the symptOME may last even over a year [4].

The cause of exudate has been studied for over 150 years. Initially, it was perceived by Adam Politzer as a consequence of a blocked eustachian tube. Today, however, it is recognized that etiopathogenesis is more complex – infectious, with ciliary transport disorder and metaplastic changes in the mucous membrane [5, 6, 7].

The history of the first recorded cases of OME is very long. In the 70s of the last century, a human skull of 40,000 years was found. After the analysis, temporal bone defects characteristic of otitis media were found [7]. Other studies show a significant increase in cases from the second half of the last century. This is probably due to the limitation of acute infections through the use of antibiotics and the tendency to form bacterial biofilms. It seems that changing the bacterial environment caused by the use of antibiotics may be conducive to the spread of OME [9].

An additional risk factor for OME is gastro-oesophageal reflux (GERD). This phenomenon consists of throwing gastric acid into the oesophagus. Secondly, it may cause inflammation within the larynx, throat, paranasal sinuses and the Eustachian tube. The consequence is swelling of the mucous membrane, overproduction of exudation, impaired mobility of the cilia. It is also believed that an additional manifestation of GERD is the infection of *helicobacter pylori*, whose presence has been detected in the middle ear aspirants [10].

Both conservative and invasive methods are used in the treatment of OME. Conservative methods include the administration of antihistamines, antibiotic therapy [11], steroid therapy [12], and self-inflation via the Eustachian tube [13]. Myringotomy and drainage is the invasive treatment [14].

Regardless of the choice of procedure, the treatment should lead to a removal of residual fluid from the tympanic cavity and restoration of proper air pressure in the middle ear and, consequently, improvement of hearing.

Conservative methods aim to remove the exudate from the tympanic cavity the natural way, i.e.

through the eustachian tube. This is to be done, for example, by reducing oedema or inflammation through the use of pharmacotherapy or mechanical opening of the tube, which is what we deal with in case of pneumotherapy.

It has been noted that conductive hearing loss in a child, even a small degree, negatively affects the development of speech and communication [15]. These types of auditory fluctuation problems may affect the central auditory processing. Early intervention can eliminate auditory deprivation [16]. For this reason, most children with conductive hearing loss attend speech therapists.

Method of pneumotherapy

Pneumotherapy is one of the conservative methods of removal of exudate from the tympanic cavity. The method used is based on a repetitive, regular and self-performed exercise with the use of an inflatable balloon. This exercise consists of two stages: inflation and deflation [17].

The first stage consists of blowing air – through the nostrils – into the closed space of the balloon (Valsalva maneuver). This leads to an increase in pressure in the nasal part of the throat by about 400–600 dPa [18].

In the second stage, the air from the inflated balloon is forced back into the nasopharynx (similar to the Politzer method), and the patient's task is to swallow, during which the eustachian tube opens and air enters the middle ear. By that means, the natural passage of evacuating the exudate from the tympanic cavity is cleared, which allows the reduction of inflammation and consequent treatment of conductive hearing loss.

The combination of two ways of producing hypertension in the nasopharynx multiplies the desired effect. Research and experience on the use of only the Valsalva in children test shows its ineffectiveness. The introduction of an additional source of air by the Politzer method (retracting from the balloon space) forces a higher value of overpressure [19, 20].

Aim

In this work, we analyze the effectiveness of pneumomassage (performed using the Otovent balloon) in the treatment of conductive hearing loss caused by hearing tube dysfunction.

Material and Methods

Diagnosis and treatment of patients took place in 2016 and 2017 at the Department of Phoniatics and Audiology in Poznań and at the Audiological and Phoniatic Clinic of NZOZ CTS KIND.

54 children were examined, with conductive hearing loss of various severity and otoscopic features of OME, aged 4 to 15 years (median 8 years), including 23 girls and 31 boys. The control group consisted of 16 people. All patients underwent pure tone audiometry and impedance audiometry tests in the beginning of treatment (as part of the initial diagnosis) and after the recommended period of treatment with Otovent.

These patients were advised to use the pneumomassage method. Parents or family have been instructed in carrying out the exercise, i.e.: several times inflating the balloon two to four times a day.

On the follow up appointment, the parents or legal guardians from the research group reported, that the treatment was carried out as recommended. In contrast, the control group consisted of children who did not receive the recommended therapy. Some children with accompanying disorders of speech development and problems of articulation underwent speech therapy and hearing training.

Outpatient treatment lasted 5.4 months on average (median 5.5).

Results

In pure tone audiometry, the average of four frequencies was determined: 500 Hz, 1 kHz, 2 kHz and 4 kHz. Air and bone conduction thresholds were analyzed. The test results, both in the research and control group, confirmed a conductive hearing loss before the treatment. There were no mixed hearing losses.

1. Presentation of test results before treatment

1.1. Pure tone audiometry

The tonal audiometry showed an average degree of hearing loss (out of all 70 subjects) at the level of 33.16 dB. The minimum loss (average calculated for the four above-mentioned frequencies) was 26.59 dB, while the maximum loss was 40.14 dB. The average value of the cochlear reserve was 33.05 dB.

1.2. Impedance audiometry

The analysis of impedance audiometry results included the measurement of pressure changes

in the middle ear, the tympanogram shape and the registration of stapedius reflex.

1.2.1. Tympanogram

Tympanometry shows us the condition of the middle ear. The results obtained are classified due to the shape of the tympanogram, the tympanogram type A means the correct result (from 0 to -50 dPa), the tympanograms B and C show the pathology of the functioning of the middle ear.

Before treatment in the research group, 7 cases of type A tympanogram, 85 type B tympanograms and 48 cases of type C tympanogram were recorded. The average susceptibility value was -328.06 dPa.

1.2.2. Stapedius reflex

The reflex of the stapedial muscle in the study group was noted in 7.86% of subjects.

2. Presentation of the test results after the treatment

2.1. Pure tone audiometry

In pure tone audiometry, the average loss recorded in the research group was 15.64 dB (minimum loss 9.9 dB, maximum loss 22.08 dB).

In the control group, the average loss was 29.60 dB (minimal loss 22.03 dB, maximal loss 37.97 dB).

2.2. Impedance audiometry

2.2.1 Tympanogram

After treatment, 64 cases of type A tympanogram, 12 cases of type B tympanogram and 32 cases of type C tympanogram were recorded in the study group. In the control group, the results were as follows: 2 cases of type A tympanogram, 20 cases of type B tympanogram and 10 cases of the tympanogram type C. The mean value of the tympanic membrane susceptibility for the research group was 159 dPa, and for the control group 318 dPa.

2.2.2. Acoustic reflex

A reflex of stapes muscle was recorded in 67.59% of subjects in the research group and 6.25% in the control group.

Intergroup comparative analysis

The research results presented above indicate an improvement in hearing in the group of people

using the pneumotherapy of the auditory tube. Mean hearing loss decreased by 13.64 dB (in the control group, the improvement was 7.43 dB).

Analyzing subsequent data, it can be noticed that impedance audiometry showed an improvement in the type of tympanograms and air pressure compensation in the tympanic

cavity. Type A tympanogram was recovered in 68.52% of children. A wider analysis showed that in 21 cases the type B tympanogram improved to the tympanogram type A. Improvement from the tympanogram type C to type A was obtained in 37 cases, while from type B to type C – in 27 cases.

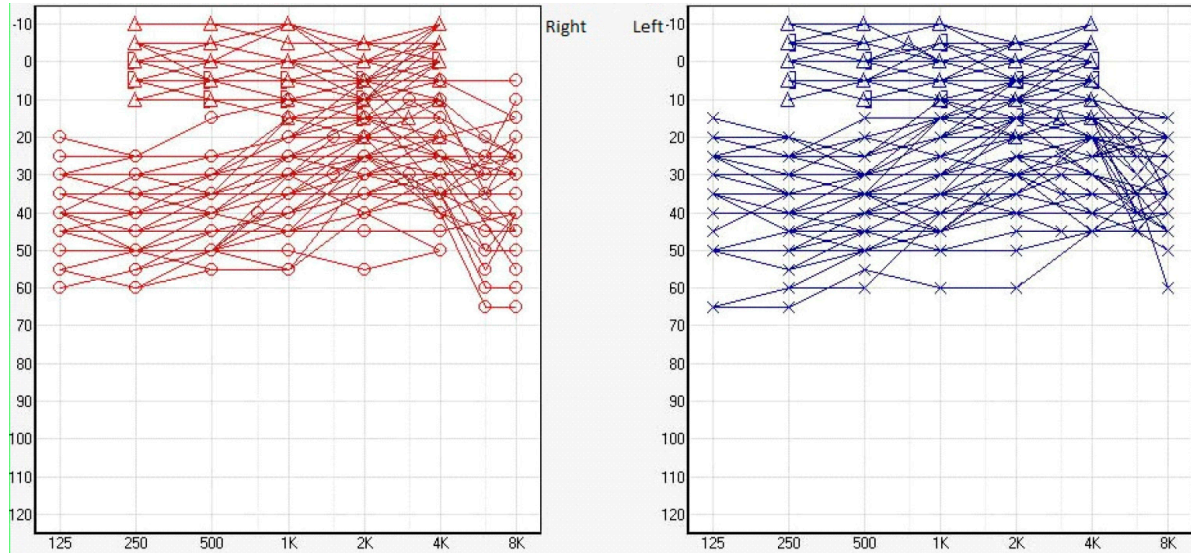


Figure 1. The results of pure tone audiometry before treatment

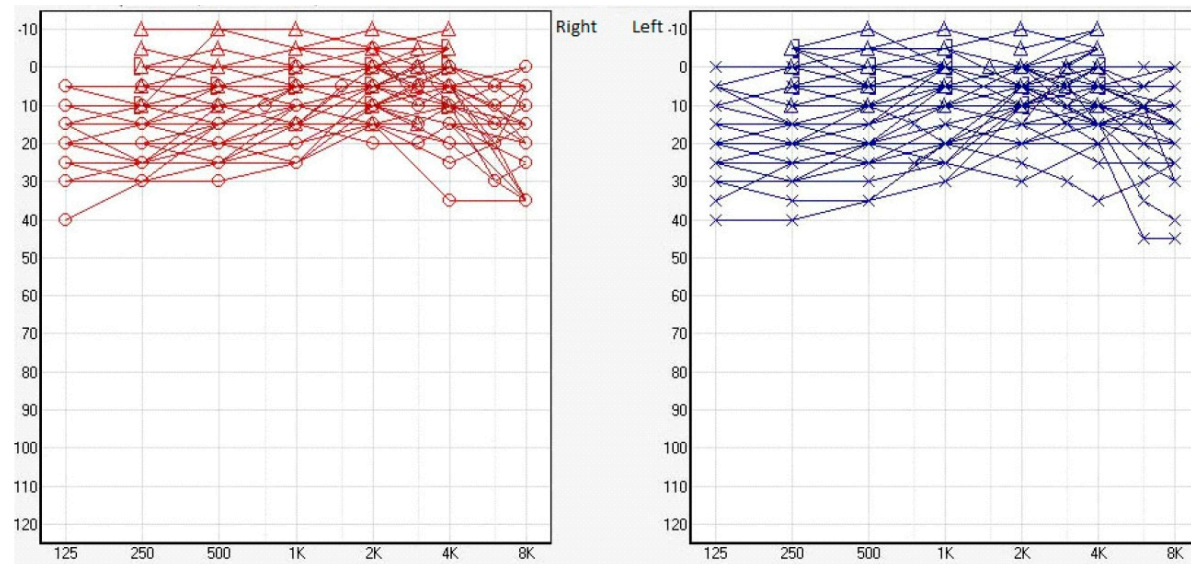


Figure 2. The results of pure tone audiometry after the end of the treatment

Table 1. Comparative analysis of the research group and the control group

	Research group (number of patients = 54)	Control group (number of patients = 16)
The number of people who improved their hearing	44	0
The value of improvement in the average hearing threshold in dB	13,63 dB	7,43 dB
Sound pressure improvement value in the middle ear	139 dPa	40 dPa
Change of the tympanogram	21	0

On the other hand, in the group of children not using the recommended method, the tympanogram type A was recovered in 6.25% of children. Type B tympanogram was not improved in any case. Type A to type C tympanogram changes were obtained in 2 cases, while type B to type C changes – in 6 cases. The rest of the patients did not get any improvement.

The pressure at the top of the maximum susceptibility of the eardrum improved in the research group by 139 dPa, while in the control group only by 40 dPa (**Table 1**).

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ORIGINAL PAPER

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Comparative characteristics of chosen aspects of tobacco smoking among the students of Poznan University of Medical Sciences and students of vocational medical colleges in Poznań

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ABSTRACT

Aim. Medical doctors, nurses, pharmacists, and paramedics are professions placing themselves highest in the rankings of occupations granted public trust. The knowledge of the negative impact of tobacco use on physical condition possessed by those occupational groups ought to limit the addiction among this population, which should constitute a benchmark of health-promoting attitude for the public. Many health-promoting decisions are made during the period of studies. The study aimed to establish the scale of tobacco smoking and the profile of chosen aspects of this issue among students of Poznan University of Medical Sciences and students of vocational medical colleges in Poznań.

Material and Methods. An author questionnaire was conducted. 586 students (471 University students, 115 college students) aged between 19 and 65 completed the survey.

Results. The majority (76.62%) of the surveyed students were non-smokers. Smokers were predominately male (the entire surveyed population, University students). Medical college students smoked more cigarettes daily compared to the University students. The most commonly declared reason for smoking was the social purpose. Among former smokers, female more often than male indicated health considerations and the knowledge of harmful effects of smoking as reasons for quitting; among college students, the most common reason was health considerations, whereas University students listed knowledge of the harmfulness of smoking, health considerations, and other motives most often.

Conclusions. Both University students and medical college students smoked more rarely than their contemporaries in the general population. The respondents constitute a group displaying relatively high prevalence of health-promoting attitudes.

Keywords: smoking, addiction, behaviors, medical university, medical school.

Introduction

In 2015, in a nationwide survey regarding attitudes towards tobacco smoking, almost one-fourth of Poles (24%) admitted to smoking compulsive-

ly (daily), which indicated that the proportion of smokers was slightly lower than in previous editions of the survey – in 2009, 2011 and 2013 [1]. A comparison with the results of the previous

surveys also indicated a downward trend in the quota of chain-smokers - respectively 4 (2013 vs. 2011) and 3 (2015 vs. 2013) percentage points less [1]. The smoking addiction affected men more often than women (31% vs. 18%), among whom a reduction of the percentage of smokers, in comparison to the previous surveys, could be observed [1]. Among everyday smokers, 13% began smoking in the year anteceding the survey. The highest percentage of smokers was represented in groups with vocational education (39% male, 25% female) and primary education - in this group, 36% of men and 24% of women admitted to chain-smoking [1]. Women and men possessing higher education smoked compulsively the least often - respectively 8% and 14%. Compared to the previous survey, a drop in the percentage of smokers among better-educated groups was to be observed - in the groups with secondary, post-secondary and higher education [1]. Medical doctors, nurses, pharmacists, and paramedics are professions placing themselves highest in the rankings of occupations granted public trust [2]. The knowledge of the negative impact of tobacco use on physical condition possessed by those occupational groups ought to limit the addiction among this population, which should constitute a benchmark of health-promoting attitude for the public [3]. Their attitudes and behaviors concerning smoking also influence the readiness and effectiveness of the advice provided to the smoking patients. Moreover, extensive knowledge enables representatives of the professions mentioned above to employ diverse methods in the treatment of tobacco addiction in their professional work [4]. Many health-promoting decisions are made during the period of studies. Health habits presented by the students correspond with their knowledge, beliefs, and needs or might be a result of imitation or experimenting.

Aim

The study aimed to establish the scale of tobacco smoking and the profile of chosen aspects of this issue among students of Poznan University of Medical Sciences and students of medical vocational colleges in Poznań.

Material and Methods

An author questionnaire was conducted. 586 students (471 University students, 115 college students) aged between 19 and 65 completed the survey. Characteristics of the group are presented in **Table 1**.

Statistical analysis was performed using Statsoft Statistica 12.0. The Chi-square test of independence was used to evaluate statistical significance. A P-value of 0.05 was used to determine significance.

Results

The surveyed students from both groups were predominately non-smokers (76.62%, **Figure 1**).

Among all smokers and smokers from the University, male students preponderated statistically significantly (**Figure 1, Table 4**). In both institution types, the most individuals declared smoking between 1 and 5 cigarettes daily (**Table 2**). The number of cigarettes consumed daily differed statistically significantly between University students (< 1) and vocational college students (1-5 cigarettes, **Tables 1 and 4**). Female smokers from medical college consumed statistically more cigarettes daily (5–10). The vast majority of students (69.81%) had been smoking between 1 and 5 years and for social purposes (68.61%). This reason for smoking was statisti-

Table 1. Characteristics of the studied group

Number of individuals	586	
Gender	416 females (71%)	170 males (29%)
Age [years]	Average: 25.2 ± 5.5	Median: 24
Place of education	471 university Pharmacy – 164 (35 %) Dentistry – 142 (30%) Medical – 67 (14%) Emergency Medical Service – 41 (9%) Foreigners – 30 (6%) Dietetics – 27 (6%)	115 medical college Dental technician – 27 (24%) Emergency Medical Service – 24 (21%) Pharmacy technician – 22 (19%) Medical caregiver – 21(18%) Dental assistant – 13 (11%) Dental hygienist – 8 (7%)

cally more often mentioned by all surveyed women and female students of the University.

Former smokers constituted 18.77% of the studied population. Statistically significantly more female than male declared health considerations and the knowledge of harmful effects of smoking as reasons for quitting smoking, both in

the entire surveyed population and in the group of University students. Also, statistically significantly more University students than medical vocational college students indicated health considerations, knowledge of the harmful effects of smoking and other motives as reasons for quitting smoking. A statistically significant difference

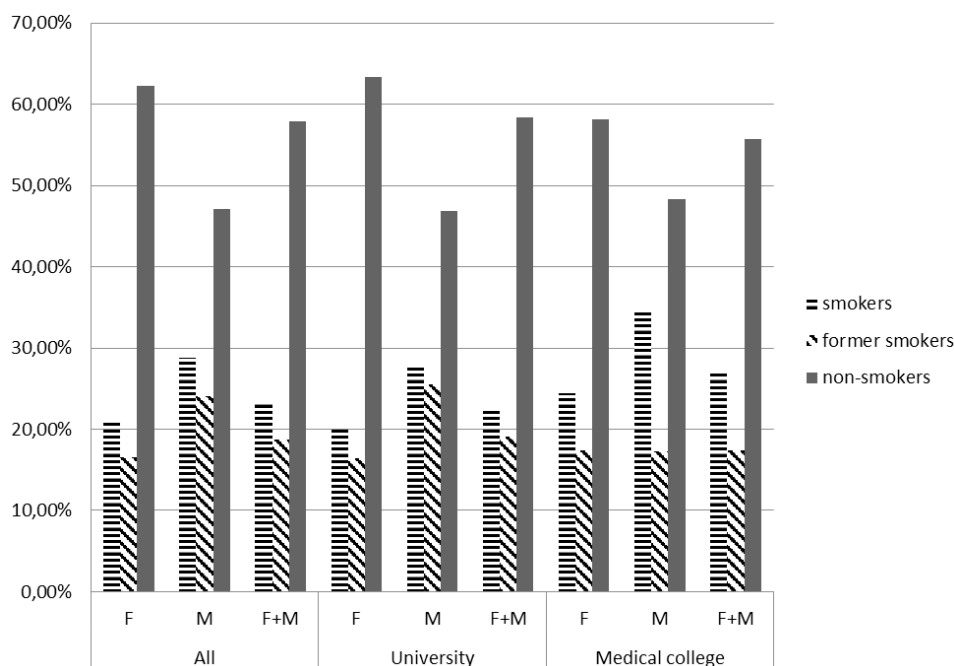


Figure 1. The percentage share of smokers, former smokers, and non-smokers. (F – female population, M – male population)

Table 2. Characteristics of the smoking group. (F – female population, M – male population)

	All			University			Medical college		
	F	M	F+M	F	M	F+M	F	M	F+M
Number of cigarettes daily									
< 1	39.77%	22.45%	33.58%	44.78%	28.21%	38.68%	23.81%	0.00%	16.13%
1-5	31.82%	51.02%	38.69%	32.84%	43.59%	36.79%	28.57%	80.00%	45.16%
5-10	15.91%	14.29%	15.33%	10.45%	12.82%	11.32%	33.33%	20.00%	29.03%
11-20	11.36%	12.24%	11.68%	10.45%	15.38%	12.26%	14.29%	0.00%	9.68%
> 20	1.14%	0.00%	0.73%	1.49%	0.00%	0.94%	0.00%	0.00%	0.00%
Duration of addiction									
< 1 year	1.14%	0.00%	0.73%	1.49%	0.00%	0.94%	0.00%	0.00%	0.00%
1-5 years	68.18%	61.22%	65.69%	74.63%	61.54%	69.81%	47.62%	60.00%	51.61%
6-10 years	11.36%	26.53%	16.79%	8.96%	23.08%	14.15%	19.05%	40.00%	25.81%
11-15 years	4.55%	2.04%	3.65%	4.48%	2.56%	3.77%	4.76%	0.00%	3.23%
16-20 years	1.14%	2.04%	1.46%	1.49%	2.56%	1.89%	0.00%	0.00%	0.00%
> 20 years	5.68%	0.00%	3.65%	2.99%	0.00%	1.89%	14.29%	0.00%	9.68%
The reason for smoking									
Stress	36.36%	30.61%	34.31%	35.82%	33.33%	34.91%	38.10%	20.00%	32.26%
Socializing	75.00%	57.14%	68.61%	77.61%	58.97%	70.75%	66.67%	50.00%	61.29%
No reason	26.14%	22.45%	24.82%	23.88%	17.95%	21.70%	33.33%	40.00%	35.48%
Pleasure	32.95%	42.86%	36.50%	31.34%	46.15%	36.79%	38.10%	30.00%	35.48%

Table 3. Characteristics of the group of former smokers (F – female population, M – male population)

	All			University			Medical college		
	F	M	F+M	F	M	F+M	F	M	F+M
Reason for quitting smoking									
Desire to quit addiction	7.25%	0.00%	4.55%	9.26%	0.00%	5.56%	0.00%	0.00%	0.00%
Pregnancy	5.80%	0.00%	3.64%	7.41%	0.00%	4.44%	0.00%	0.00%	0.00%
Social pressure	1.45%	17.07%	7.27%	1.85%	16.67%	7.78%	0.00%	20.00%	5.00%
Costs	11.59%	12.20%	11.82%	5.56%	13.89%	8.89%	33.33%	0.00%	25.00%
Health	33.33%	7.32%	23.64%	27.78%	5.56%	18.89%	53.33%	20.00%	45.00%
Costs + health	1.45%	14.63%	6.36%	1.85%	11.11%	5.56%	0.00%	40.00%	10.00%
Knowledge of the harmfulness of smoking	17.39%	17.07%	17.27%	22.22%	19.44%	21.11%	0.00%	0.00%	0.00%
No pleasure	2.90%	2.44%	2.73%	3.70%	2.78%	3.33%	0.00%	0.00%	0.00%
Unpleasant smell and taste	1.45%	2.44%	1.82%	1.85%	2.78%	2.22%	0.00%	0.00%	0.00%
No reason	1.45%	4.88%	2.73%	1.85%	5.56%	3.33%	0.00%	0.00%	0.00%
Sport	0.00%	9.76%	3.64%	0.00%	8.33%	3.33%	0.00%	20.00%	5.00%
No need for smoking	2.90%	0.00%	1.82%	1.85%	0.00%	1.11%	6.67%	0.00%	5.00%
Change of lifestyle	1.45%	4.88%	2.73%	0.00%	5.56%	2.22%	6.67%	0.00%	5.00%
Other	8.70%	12.20%	10.00%	11.11%	13.89%	12.22%	0.00%	0.00%	0.00%
Methods of quitting									
Strong will	47.83%	48.78%	48.18%	42.59%	44.44%	43.33%	66.67%	80.00%	70.00%
None	37.68%	36.59%	37.27%	44.44%	41.67%	43.33%	13.33%	0.00%	10.00%
Nicotine patches, tablets, gumms, e-cigarettes	1.45%	12.20%	5.45%	0.00%	11.11%	4.44%	6.67%	20.00%	10.00%
Sudden quitting	2.90%	2.44%	2.73%	0.00%	2.78%	1.11%	13.33%	0.00%	10.00%
Other	7.25%	4.88%	6.36%	9.26%	5.56%	7.78%	0.00%	0.00%	0.00%

Table 4. Statistical differences between the studied groups (F – female population, M – male population)

Parametr	p
F vs M; all participants	
Is smoking?	p =.00333
Reason: socializing	p =.02463
Reason for quitting smoking	p =.00002
University vs Medical college	
Number of cigarettes daily	p =.04840
Reason for quitting smoking	p =.00919
Methods for quitting smoking	p =.00349
F vs M; University	
Is smoking?	p =.00365
Reason: socializing	p =.03155
Reason for quitting smoking	p =.00025
F vs M; Medical college	
Number of cigarettes daily	p =.03523

was also observed in applied methods of smoking cessation – University students indicated 'strong will' and 'none' most commonly, whereas college students mostly pointed to 'strong will' (**Table 3**).

Discussion

Tobacco smoking has been a subject of research in the medical community for many years, since

the attitudes of medical doctors, pharmacists, nurses, paramedics and other healthcare professionals towards nicotine and their behaviors concerning smoking influence the readiness and effectiveness of the advice provided to the smoking patients. It has been proven that active counseling provided by medical doctors and nurses and their assistance results in quit attempts even in patients with low baseline motivation [5]. Moreover, the same research demonstrated that tobacco smoking or lack thereof among medical professionals influences their ability to assist patients in controlling nicotine dependence. Medical professionals ought to both identify addicted patients and provide them with adequate counseling and support. Research has shown that especially professionals within the area of stomatology might play an important role in the process of early detection of smokers since they often notice signs of addiction such as halitosis, dental discoloration or difficulties in maintaining proper oral hygiene earlier than other professions [6, 7]. They are therefore well suited to implement early anti-smoking interventions. Educational and informational actions also constitute an element of everyday work of a pharmacist, who

often helps the patients with the choice of a suitable nicotine replacement therapy [8]. Moreover, the pharmacist can prevent potential drug interactions and difficulties during tobacco addiction therapy by controlling the patient's use of medications, OTCs, and dietary supplements [9, 10]. The prevalence of tobacco addiction among physicians has regularly been analyzed in the USA and most of the European countries. An example of a country closely monitoring cigarette smoking among medical doctors in Sweden, where nationwide epidemiological research on a large, representative group of physicians has been conducted every five years by the Karolinska Institute in Stockholm since 1969. In the last research conducted in 2001, 1367 medical doctors, that is 5% of all Swedish doctors, were randomly chosen to participate [11]. A research on an impressive scale was also conducted in Japan – questionnaires about active smoking, attitude towards tobacco smoking and the knowledge of the topic were distributed to 4500 physicians, that is 63% of all Japanese doctors, of whom 3771 completed the survey [12]. A research carried out by Zinonos and coauthors enabled distinguishing specific risk factors for nicotine addiction among healthcare workers [5]. Those were: male gender, age younger than 34, being unmarried and the prevalence of nicotine addiction in the family of the subject. Studies on the prevalence of tobacco addiction were also conducted in Poland – both among healthcare professionals and students of medical colleges. One of them was research published by Siemińska and coauthors in 2010, evaluating the prevalence and attitudes towards nicotine addiction among medical students of the first and sixth year [13]. The presented results demonstrated both optimistic and alarming trends. The percentage of the sixth year medical students of Medical University of Gdańsk smoking cigarettes (13%) was significantly lower than in the general Polish population (32%). In the same time, research on the prevalence of tobacco smoking among fifth-year students of the Medical University of Warsaw demonstrated a similar percentage of smokers – 14.4%. In comparison, students of the fifth year of the medical faculty of the University of Strasbourg smoked more often – 17.5%, whereas students of Teheran University of Medical Sciences a lot less often – only 4% of them [13]. Another favorable trend was determining that during medical studies the percentage of

smokers diminished from 21% in the first year to 13% in the sixth. The downward tendency in the prevalence of nicotine addiction over studying time was confirmed both among Polish and French medical students. Unsettling was the fact that every fifth person smoking cigarettes in the sixth year of medical faculty had begun smoking during the studying period, and 17% had increased the number of smoked cigarettes during that period. The results of our study indicate that among students of Poznan University of Medical Sciences and vocational medical colleges in Poznań smoking is a less frequent phenomenon than in the general population of the corresponding age [14]. This tendency has a positive connotation in the context of the subjects being future healthcare professionals, allowing them to propagate health-promoting attitudes among the patients. Moreover, among the smoking group of respondents subjects smoking a few cigarettes daily were predominant, suggesting that the “heavy smokers” percentage in the studied group was negligible. Another positive trend to be noticed in the context of forming anti-nicotine attitudes were successful attempts at quitting smoking in the studied group – despite the young age of the respondents, almost a fifth of them had successfully given up smoking. Similarly to the general population, males dominated in the smoking subgroup of the studied group – which was an interesting development in relation to a study carried out in 2012 among the students of Poznań, in which the proportion of smokers did not differ significantly depending on the gender of the subject [15]. Females in the studied group declared smoking for social reasons significantly more often than males. It might suggest that a predominant component of their nicotine addiction is behavioral, rather than physical addiction. That would justify a need to apply different therapeutic interventions in both smoking groups, according to the gender of the subject. The comparison between University students and college students revealed a few significant differences. An interesting finding was a lack of statistically significant deviations in the number of smokers between those two subgroups. In the smoking populations statistically more cigarettes daily were smoked by medical colleges students, which may suggest a higher level of physical addiction (as measured by means of Fagerstrom Test for

Nicotine Dependence) among this subgroup of subjects. The motivation regarding smoking cessation also differentiated both groups – University students listed health considerations more often. Surprisingly, that difference did not significantly affect the quota of smokers among both studied groups. The surveyed group was characterized by a high declarative level of knowledge of the harmfulness of tobacco consumption, which resulted in it being the most common motivation for quitting. Despite that fact, the respondents very rarely used pharmaceuticals facilitating maintaining nicotine abstinence. This creates a potential possibility of increasing the number of persons successfully quitting smoking by implementing an informative campaign on that topic, as well as interventions of primary care physicians regarding the pharmacotherapy of nicotine dependence. In conclusion to our research, a positive tendency is to be noticed taking into account both the percentage of students addicted to tobacco consumption, especially regarding the number of persons who successfully ceased smoking, and the declared motivations for quitting – mainly health considerations and knowledge of the harmful effects of smoking. Students who have previously unsuccessfully attempted quitting smoking should remain the area of particular interest – in this subgroup anti-nicotine counselling and interventions enhancing motivation towards nicotine abstinence ought to be implemented.

Conclusions

- › Among the surveyed students of both types of schools, non-smokers constituted the majority.
- › Males were predominant in the smokers subgroup (the whole population, University students).
- › More cigarettes daily were smoked by the students of medical colleges.
- › The most commonly declared reason for smoking was the social purpose.
- › Among former smokers, females more often than males indicated health considerations and the knowledge of harmful effects of smoking as reasons for quitting; among college students, the most common reason was health considerations, whereas University students listed knowledge of the harmfulness of smoking, health considerations, and other motives most often.

- › Regarding the method of quitting, college students indicated strong will most commonly, while University students – strong will and 'none'.

Perspectives

A prospective, longitudinal study of the population of medical students would be advantageous in order to establish the further development of their attitudes towards tobacco smoking in the years following graduation. Future studies ought to inquire changes in the smoking behaviors resulting from the gain of clinical experience among the studied group.

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Conflict of interest statement

The authors declare no conflict of interest.

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ORIGINAL PAPER


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
Are risk factors of cerebral small vessel disease differ from those in patients with high atherothrombotic risk without cerebrovascular disease?


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
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ABSTRACT

Knowledge of risk factors for cerebral small vessel disease (CSVD) may generate hypothesis regarding possible targets for prevention. Our aim was to evaluate if atherothrombotic risk factors differ between patients with CSVD and with subjects without cerebrovascular disease but with high cardiovascular (CVD) risk. A single-center, cohort study was performed in consecutive patients with different CSVD manifestations. The study group consisted of 205 patients: 52 with lacunar stroke (LS), 20 with subcortical hemorrhagic stroke (HS), 50 with vascular dementia (VaD), 28 with vascular parkinsonism (VaP) and 55 controls (CG) with high CVD risk (35 with atherosclerotic CVD, 20 with 10-year risk of CVD with SCORE \geq 5). Logistic regression was used to analyze the influence of clinical and laboratory data on the occurrence of CSVD. Mean age, sex distribution, prevalence of smoking, hyperlipidemia, peripheral artery disease and obesity were similar in CSVD and CG. The factors significantly associated with CSVD compared to controls were diabetes mellitus, polymetabolic syndrome, elevated systolic blood pressure, low levels of eGFR, HDL, albumin and high uric acid, fibrinogen, fasting glucose, HbA1c and intima media thickness ($p < 0.05$). Hypertension, chronic kidney disease and elevated fasting blood glucose were related to LS and HS ($p < 0.1$). Diabetes was significantly associated with LS and VaD while smoking and low total cholesterol were related to HS ($p < 0.1$). The study confirms that risk factors profile for CSVD differs from subjects with proatherogenic profile without history of cerebrovascular disease. Our results also support that unique risk factors profiles exist for different manifestations of the CSVD.

Keywords: cerebral small vessel disease, risk factors, lacunar stroke, vascular dementia, vascular parkinsonism.

Introduction

Cerebral small vessel disease (CSVD) is one of the most important and common microangiopathy [1]. It can cause several different types of distinct or overlapping clinical presentations: recur-

rent lacunar strokes (LS), deep haemorrhagic strokes (HS), vascular dementia (VaD) and vascular parkinsonism (VaP). The main MRI imaging features are inter-related and include lacunes, intracerebral hemorrhages and white matter

lesions (WMLs) which are frequently found even in asymptomatic elderly people. Although CSVD is considered to result from cerebral arteriolar occlusive disease, classical cardiovascular risk factors are not consistently common in patients with CSVD and latest studies provided evidence, that they can explain only minority of the variance in radiological features [2]. These findings are challenging the traditional view that classical risk factors play a role in CSVD genesis and indicate that pathophysiology of CSVD may be independent from that of atherosclerotic large artery disease [3]. It is also speculated that the exact mechanisms of distinct clinical CSVD manifestations differ and they may be attributable to either burden, lack of control of traditional vascular risk factors and also are influenced by other hemodynamic or inflammatory factors [4]. Due to lack of effective casual treatment, the control and identification of CSVD-specific modifiable risk factors is of increased importance for secondary prevention of ischemic brain lesions [5]. Although asymptomatic radiological CSVD markers e.g. WMLs or lacunes are frequently found in patients with coronary or peripheral artery disease, the comparisons of risk factor profiles between patients with different manifestations of CSVD and patients with high vascular risk but without cerebrovascular disease have not been reported so far. If atherosclerosis were important in CSVD as a whole or in one particular subtype, one would expect the risk factor profile to be similar or even aggravated to that of large vessel disease. Considering the wide spectrum of radiological and clinical picture of CSVD, we hypothesized that associated atherothrombotic risk factors differ between patients with CSVD and subjects without cerebrovascular disease but with high vascular risk.

In this single-center, prospective, cohort study, we compared prevalence of traditional risk factor profiles between patients with different CSVD manifestations and controls with high atherothrombotic risk free of clinical and radiological markers of CSVD.

Material and Methods

Participants

The present investigation is nested in the of SHEF-CSVD Study (Significance of HEmodynamic

and hemostatic Factors in the course of different manifestations of Cerebral Small Vessel Disease) [6]. The studied group consisted of 150 consecutive patients: with first-ever recent LS (n = 52) or deep HS (n = 20), VaP (n = 28) and VaD (n = 50) and 55 controls (CG) recruited between December 2011 and June 2014 from patients treated in the Outpatient Department. The study protocol and methods have been thoroughly described elsewhere [5].

In brief, the SVD group consisted of consecutive patients with a first ever recent LS or HS or newly diagnosed VaD and VaP presumed to be caused by CSVD with evidence of typical findings on neuroimaging (MRI). All patients were independent (total Barthel Index ≥ 80 points) and did not have severe dementia (MMSE ≥ 12 points) [7]. The patients were diagnosed according to typical radiological and clinical picture: LS - according to the OCSP Criteria; VaD and VaP after exclusion of other neurodegenerative conditions with the use of clinical tools easily applied in clinical practice: Hurtig criteria or NINDS-AIREN criteria with Modified Hachinski Ischemic Scale ≥ 7 points, respectively [8, 9, 10]. Patients with recurrent LS or strategic single-infarct dementia or with post-stroke VaD or VaP were excluded. The mean time from first symptoms of cognitive impairment or appearance of parkinsonian symptoms to enrollment was 23.2 ± 10 months in VaD and 25 ± 10 months in VaP ($p = 0.5$). The control group consisted of patients without history of cerebrovascular disease and with high cardiovascular risk assessed according to the European Society of Cardiology and the European Atherosclerosis Society Guidelines (2011) [11]. High risk was recognized in patients with: documented cardiovascular disease (CVD) – coronary artery disease (CAD) or peripheral arterial disease (PAD); diabetes (type 2 or type 1 diabetes with target organ damage e.g. microalbuminuria); moderate to severe chronic kidney disease (CKD; glomerular filtration rate (GFR) ≤ 60 ml/min/1.73 m²); or markedly elevated single risk factors such as familial dyslipidemias and severe hypertension (systolic blood pressure (SBP) ≥ 180 mm Hg and/or diastolic blood pressure (DBP) ≥ 110 mm Hg); or 10-year risk of total CVD $\geq 5\%$ (estimated using the Systemic Coronary Risk Estimation (SCORE) risk assessment charts according to gender, smoking status, age, blood pressure (BP) and total cholesterol (TC))

[12]. All participants were aged between 60 and 90 years. Patients with significant stenosis ($\geq 50\%$) of a major extracranial or intracranial artery, atrial fibrillation, non-SVD related WMLs, life expectancy of less than 6 months, and MRI contraindications were excluded.

Study procedures

To prevent confounding by hyperacute phase responses, all LS and HS patients underwent study procedures at least 2 weeks (mean 19.4 ± 4.1 days) after their index strokes. We assessed eGFR and serum total cholesterol (TC), HDL, LDL, triglycerides (TG), fasting glucose (FG), HbA1c, homocysteine, fibrinogen (FBG), albumin and uric acid (UA) levels for all participants. All patients had MRI examination before entering the study. We categorized MRI findings according to STRIVE (Standards for Reporting Vascular Changes on Neuroimaging) guidelines as a reference standard [13]. The simple modified Fazekas rating scale was used to estimate the extent of the periventricular and deep WMLs. Grade 2 ($n = 83$; 55.3%) or 3 ($n = 45$; 30%) WMLs were present in 80.3% patients with CSVD. There was no significant difference between mean Fazekas score in LS, HS, VaD and VaP (respectively, 2.18 ± 0.6 , 2.3 ± 0.65 , 2.04 ± 0.78 , 2.11 ± 0.68 ; $p > 0.1$). Controls were included only in case of normal MRI scans (Grade 0). To determine baseline BP control (24h mean systolic (SBP) and diastolic BP (DBP) we performed 24h ABPM using a validated portable non-invasive oscillometric device (Schiller MT-300). Assessments of carotid intima-media thickness (IMT) were performed according to previously validated criteria by colour-flow B-mode Doppler ultrasonography by a same experienced sonographer. The IMT was defined as the distance between the leading edge of the lumen-intima echo and the leading edge of the media-adventitia echo [14].

Based on clinical history, documented investigations and physical examination at baseline, we evaluated major atherothrombotic risk factors. Hypertension was defined as persistent elevation of systolic blood pressure (SBP) ≥ 140 mmHg or diastolic blood pressure (DBP) ≥ 90 mmHg at least 1 week from stroke onset, or current treatment with antihypertensive drugs. Diabetes mellitus was defined as a previous diagnosis of type I or type II diabetes, or at least two random glu-

cose readings of ≥ 200 mg/dL or FG ≥ 126 mg/dL. Hypercholesterolaemia was defined as a serum TC ≥ 200 mg/dL or current treatment with a statin. The following criteria were used to diagnose polymetabolic syndrome (PS): waist circumference ≥ 102 cm in men or ≥ 88 cm in women; HDL ≤ 40 mg/dL in men and ≤ 50 mg/dL in women or on drug treatment; elevated SBP ≥ 130 mmHg or ≥ 85 mmHg DBP or on drug treatment; elevated TG ≥ 150 mg/dL or on drug treatment; and elevated FG ≥ 100 mg/dL or on treatment for diabetes [15]. Coronary artery disease was defined in patients with stable angina, prior MI, prior percutaneous revascularization, coronary artery bypass graft, angiographically proven coronary atherosclerosis, or reliable non-invasive evidence of myocardial ischemia [16].

Statistical analysis

Quantitative and qualitative demographic characteristics were summarized, and data were tabulated and tested for normality with the Shapiro-Wilk test. Categorical data were presented as frequencies and compared using the Chi-square, factorial logistic regression, or Fisher's exact test, where appropriate. Continuous data were reported as means \pm SD and compared using paired t tests, non-normal data were analyzed using non parametric tests. The one way ANOVA and chi-square test were used to assess statistical differences of data between study groups with *post hoc* Tukey's HSD test used for comparisons between CSVD subgroups. Logistic regression was used to calculate odds ratios (ORs) with 95% confidence intervals (CI) to assess the strength of association between clinical and laboratory data with CSVD vs CG (gender and age-adjusted). For continuous variables the ORs per 1-SD increase was used. A probability value of $p < 0.05$ was considered significant. All data are presented as mean \pm SD values. All analyses were performed using Statistica 12 software (StatSoft Inc, USA).

This study complied with the Declaration of Helsinki. All participants signed an informed consent form. This study was approved by the local Medical Ethics Committee.

Results

The comparison of risk factors between patients with CSVD and CG is presented in **Table 1**. Mean

age, sex distribution, prevalence of smoking and hyperlipidemia, PAD and obesity were similar in both groups. Patients with CSVD had a higher prevalence of PS, diabetes, hypertension with elevated 24h SBP, CKD, and lower prevalence of CAD compared to CG ($p < 0.05$). All controls had high CVD risk: 35 patients (63%) had documented symptomatic large artery disease (CAD or PAD), 3 (5.5%) had diabetes and CKD, 2 (3.6%) had diabetes alone, and the remaining 15 (27%) patients had elevated 10-year risk of CVD (SCORE $\geq 5\%$) caused by other cardiovascular risk factors. Patients with CSVD ($n = 94$, 62.6%) less often than CG (100%) met criteria for high CVD risk, however the difference was not statistically significant ($p = 0.1$). Among all patients with CSVD 30

(26%) had CAD or PAD, 16 (10.6%) had diabetes and CKD, 65 (43%) had diabetes alone, 17 (11.3%) had calculated SCORE $\geq 5\%$. No patients from either group had severe hypertension or familial dyslipidemia. The frequency of antiplatelet use in CG and LS, VaP or VaD (respectively, 43.6% vs 83%, 50%, 70%, $p = 0.13$) or statin use (57.4% vs 86.5%, 54%, 60%, $p = 0.8$) recorded at baseline was similar. It was however lower in HS comparing to other study groups (respectively, 15% and 10%, $p < 0.05$). Mean levels of fibrinogen, FG and HbA1c, UA, homocysteine, IMT values were higher and HDL and albumin levels were lower in CSVD than in CG.

There was no difference in frequency of bad control of glycaemia (HbA1c $\geq 7.5\%$) between dia-

Table 1. Comparison of clinical and laboratory data of patients with CSVD and controls

	CG (n = 55)	CSVD (n = 150)	LS (n = 52)	HS (n = 20)	VaP (n = 28)	VaD (n = 50)	p#
Age (y)	72 (5.9)	72.4 (8.4)	69.9 (8.7)	74.1 (10.4)	72.3 (6.24)	74.4 (7.9)**	.04
Female sex n (%)	25 (45.5)	76 (50)	19 (37)	10 (50)	10 (36)	37 (74)**	.01
Hypertension	43 (78.2)	132 (88)*	49 (94)*	19 (95)*	20 (71.4)	44 (88)	.01
24h - MAP (mmHg)	90.64 (9.8)	94.98 (13.05)	95.02 (12.9)	99.77 (19.4)*	91.24 (11.14)	95.24 (11.1)	.46
SBP (mmHg)	125.3 (18)	133.9 (17.2)**	136.5 (18.3)**	137.1 (21.8)*	128.8 (13)	132.9 (15.3)*	.33
DBP (mmHg)	74.8 (8.2)	75.53 (12.5)	74.24 (11.7)	81.1 (19.7)	72.2 (10.3)	77 (10)	.32
CAD	22 (40)	29 (19)*	10 (19)*	3 (15)	3 (11)	13 (26)	.39
Diabetes mellitus	20 (37)	81 (54)*	29 (56)	10 (50)	14 (50)	28 (56)	.9
HbA1c (%)	5.9 (0.6)	6.3 (1)**	6.57 (1.22)**	5.9 (0.4)	6.3 (1)*	6.2 (0.9)*	.1
FG (mg/dL)	103.1 (20)	123.2 (44.9)**	132 (51.47)**	134.2 (44.6)**	113 (32.7)	115 (41.7)*	.12
Current smoking	15 (27.3)	49 (32.7)	18 (34.6)	9 (45)	11 (39.3)	11 (22)	.2
Hyperlipidemia	43 (78)	107 (71.3)	39 (75)	11 (55)*	20 (71.4)	37 (74)	.37
LDL (mg/dL)	114.6 (36.9)	108.6 (36.5)	109.28 (38.8)	112.45 (28.7)	107.4 (34)	109.5 (39.4)	.81
HDL (mg/dL)	56.5 (17.5)	51.3 (16.7)*	45.9 (9.9)**	58.7 (20.3)	54.9 (13.5)	50.8 (21.4)	.01
TG (mg/dL)	126 (142)	126 (76.8)	147.9 (110)	109.5 (46)	126.3 (54.1)	111.8 (46.6)	.06
TC (mg/dL)	192.2 (38.9)	182.9(42.4)	178.6 (42)	185 (34)	187.5 (43.1)	188.5 (45.3)	.51
PAD	13 (23.6)	27 (18)	8 (15)	4 (21)	6 (21.4)	4 (8)	.1
BMI	26.4 (4.3)	27 (5.3)	28.5 (5.99)*	26.4 (5.4)	25.4 (3.6)	26.7 (4.8)	.1
Obesity (BMI > 30)	11 (20)	37 (24.7)	18 (34.6)	2 (10)	5 (18)	12 (24)	.12
PS	13 (23.6)	63 (42)*	25 (48)**	8 (40)	9 (32)	21 (42)	.5
CKD	3 (5.5)	25 (16)*	10 (19)*	5 (25)*	5 (18)*	5 (10)*	.4
eGFR (ml/min)	99.9 (22.3)	77.2 (24.6)**	78.21 (27.87)**	74.3 (19.7)**	70.2 (22.2) **	79.6 (22.4)**	.38
Albumin (g/dL)	4.5 (0.52)	3.7 (0.7)**	3.7 (0.7)*	3.6 (0.6)*	3.9 (0.6)*	3.7 (0.9)*	.5
Fibrinogen (mg/dl)	284.2 (70.2)	352 (86.9)**	349.7 (76.6)*	359.9 (78.9)*	343.4 (99)*	357.7 (95)*	.4
Uric acid (mg/dl)	4.8 (1.2)	5.9 (1.9)**	6.3 (2.4)*	5.8 (1.8)*	5.9 (1.4)*	5.4 (1.6)*	.2
Vit. B12 (pg/ml)	238.5 (90)	232.3 (119)	209.1 (112)	224 (130)*	299.4 (113.5)*	223.9 (117)	.03
Homocysteine (mg/dl)	13.2 (5.1)	15.3 (6.7)*	13.8 (4.6)	16.9 (7.6)*	17.5 (7.5)**	15.1 (7.5)	.1
IMT (mm)	0.9 (0.1)	1 (0.1)**	1.1 (0.2)**	1 (0.1)	1 (0.1)	1.1 (0.2)*	.01
Antiplatelet treatment	24 (43.6)	95 (63)	33 (62)	9 (45)	19 (67.9)	37 (74)	.1
Statin treatment	31 (57.4)	92 (61)	29 (55)	10 (50)	17 (60)	36 (72)	.11

Values are means (\pm SD) for continuously distributed data or numbers (%) for categorical data

ANOVA and χ^2 difference between CSVD groups; *Significant difference between studied group vs control subjects ($p < 0.05$). ** < 0.01
 CSVD – cerebral small vessel disease; CG – control group; LS – lacunar stroke; VaD – vascular dementia; VaP – vascular parkinsonism; CAD – coronary artery disease; BMI – body mass index; FG – fasting glucose; PAD – peripheral artery disease; PS – polymetabolic syndrome; CKD – chronic kidney disease; IMT – intima media thickness; MAP – mean arterial pressure; SBP – systolic blood pressure; DBP – diastolic blood pressure

betic patients from CG and CSVD (8.3% vs 20%; $p = 0.18$), HS (5%, $p = 0.3$), VaP (21%, $p = 0.2$) and VaD (13%, $p = 0.6$) but it was more frequent in patients with LS (31.2%, $p = 0.03$). In CSVD subjects without diabetes or CKD, mean levels of HbA1c, FG were higher and eGFR was decreased compared to CG (respectively, 5.8 ± 0.31 vs $5.6 \pm 0.31\%$, $p < 0.01$; 98.4 ± 10.3 vs 93.2 ± 11.8 mg/dL, $p = 0.02$; 80.4 ± 23.2 vs 99.1 ± 20.7 ml/min, $p < 0.01$).

The results of ANOVA and chi-square tests showed significant differences between CSVD groups with regard to mean age, IMT, levels of HDL, vit.B12 and distribution of gender, and hypertension. Post hoc analyses showed that hypertension was more prevalent in LS and HS than in VaP (respectively, 94% and 95% vs 71.4%, $p < 0.05$). Patients with LS had lower HDL (difference between means, -12.5 ± 4.2 mg/dl, $p = 0.01$) than those with HS and were also younger (-4.5 ± 1.6 years; $p = 0.03$), were more often males (63% vs 26%, $p = 0.01$) and had increased IMT comparing with VaD (0.1 ± 0.03 mm, $p = 0.02$). Mean vit. B12 levels were lower in LS and VaD than in VaP (respectively, -90.2 ± 30.7 and -75.5 ± 30.7 pg/ml, $p < 0.05$). Males predominated in VaP compared to VaD (64.3% vs 24%, $p = 0.01$). There was no significant difference in CSVD groups with regard to levels of homocysteine, LDL, TG, TC and control of blood pressure.

Logistic regression analyzes revealed that in contrast to CG, diabetes (OR 2), PS (OR 2.5), eGFR (OR 0.2), HDL (OR 0.5), albumin (OR 0.1), UA (OR 2.4), fibrinogen (OR 2.6), fasting glucose (OR 2.2), HbA1c (OR 2.1), IMT (1.8) and SBP (OR 1.8) were associated with CSVD (**Figure 1**). All CSVD subgroups demonstrated significant association with low eGFR (OR 0.1–0.3), albumin (OR 0.09–0.3) and high levels of fibrinogen (OR 2.1–3.1) or UA (OR 2.3–3.3). Hypertension (OR 4.4–5), SBP (OR 2–2.1), CKD (5.3–6.6) and FG (OR 2.9–3.8) were related to acute CSVD (LS and HS, $p < 0.1$). Diabetes mellitus was associated with LS (OR 2.2) and VaD (OR 2) while BMI (OR 1.5), PS (OR 3.1) and IMT (OR 3) were exclusively related to LS. Smoking (OR 3.6), low TC (OR 0.6) and prevalence of hyperlipidemia (OR 0.3) were associated solely to HS ($p < 0.1$). Symptomatic large artery disease: PAD (OR 3.7, 95%CI 1.5–9.2, $p < 0.01$) and CAD (OR 2.7, 95%CI 1.3–5.4, $p < 0.01$) were significantly associated with CG.

Discussion

Our study documented that comparing to controls with high CVD risk but free of cerebrovascular disease, PS, diabetes and high SBP were the only clinical factors that significantly influenced the occurrence of CSVD. Moreover, control of modifiable factors appeared to be important as low eGFR, HDL, albumin and high levels of uric acid and fibrinogen significantly increased that risk. Patients with CSVD subgroups shared similar risk factors but there were some differences. Hypertension, SBP, CKD and elevated FG were associated with acute CSVD manifestations (LS and HS), diabetes was related to LS and VaD whilst smoking and low TC were associated with higher risk of HS.

These results are in line with some previous studies. In a systematic review of 16 studies comparing risk factors between patients with different stroke etiology, hypertension and diabetes were more frequent in patients with lacunar than in large vessel strokes [17]. There was no association between smoking and hypercholesterolemia with any type of ischemic stroke. In the study of Khan et al patients with LS more frequently had hypertension whereas smoking, hypercholesterolemia, CAD and PAD were more common in non-lacunar stroke [18]. As we recruited patients with marked WMLs (presumably related to lipohyalinosis) and without ultrasound markers of large vessel disease it is not surprising that the most important risk factors in CSVD group were diabetes and metabolic disturbances (such as decreased eGFR) and not hypercholesterolemia and CAD which are strongly related to large vessel disease. Although patients with CSVD more frequently than CG had diabetes and had higher SBP at baseline, the overall atherothrombotic risk was similar in these groups. High incidence of diabetes (54%) may be surprising but several studies showed that diabetes is an independent risk factor for lacunar strokes and WMLs related to CSVD. Lower prevalence of large artery diseases in CSVD group is also unexpected but it was probably related to previously undiagnosed PAD and CAD as systematic evaluation of these diseases is not currently recommended in asymptomatic patients with cerebrovascular disease.

Higher levels of HbA1c and FG were associated with LS but there was no such association with

other CSVD groups. These findings suggest that patients who have abnormally glycosylated end products, as are present in diabetes, may have more lipohyalinosis resulting in decreased perfusion in the territory of penetrating arteries and responsible for LS. This is in line with cross-sectional ARIC study of 1827 community-dwelling participants, which documented that incident lacunes related to lipohyalinosis were associated with diabetes and HbA1c while LDL, hypertension and smoking were associated with lesions presumably caused by microatheroma [19].

Our results demonstrated that low eGFR and albumin, high uric acid and fibrinogen concentrations were independently associated with all clinical manifestations of CSVD. These results are in line with the Northern Manhattan Study and the Rotterdam Scan Study which found that subjects with reduced eGFR had a greater burden of WMLs volumes after controlling for other factors and there is mounting evidence that CKD increases the risk of different cerebrovascular disease including HS [20, 21, 22]. Also previous studies demonstrated strong correlations of serum UA with WMLs and cognitive decline in elderly adults [23, 24]. Several biologically plausible mechanisms activated by UA and CKD could result in development of WMLs through oxidative stress and inflammation, resulting in endothelial dysfunction and vascular damage [25].

Elevated serum fibrinogen in all CSVD subgroups supports the hypothesis that coagulation pathway contributes to the pathogenesis of CSVD. This association was independent of age and type of CSVD manifestations regardless they were acute or chronic. Fibrinogen is a marker of systemic hypercoagulability, inflammation and acts as an important factor in the coagulation cascade. It is also assumed to be a faithful marker of brain-blood-barrier (BBB) dysfunction. Higher serum fibrinogen levels were independently associated with both WMLs and lacunes and in patients with LS and VaD, it was correlated with the extent of leukoaraiosis [1, 2]. Low albumin level in CSVD was also reported in several previous studies which also suggested an inverse association between serum albumin concentrations and stroke risk [3]. The underlying pathophysiology, however, remains unclear. Albumin increases the plasma oncotic pressure, decreases red blood cell

sedimentation and viscosity which might favor reperfusion and leads to a better microvascular circulation. It is also recognized as an important antioxidant and a marker of chronic systemic inflammation [4].

There were some important differences in risk factor profile in between CSVD subgroups which support the concept of multiple mechanisms involved in the pathogenesis of these diseases. Diabetes was significantly related only for LS and VaD. This is in line with community-based cross-sectional studies which failed to find an association between diabetes and WMLs and with Helsinki Aging Brain Study in which WMLs were associated with diabetes only in persons <75 years of age [1, 2]. Patients with VaP had higher homocysteine level while higher BMI and hypertension were less prevalent than in LS group. Hiperhomocysteinemia was only marginally related to LS and VaD and that association was stronger in HS. Elevated level of homocysteine can result from a folate deficiency and it can be aggravated in patients with CKD. Positive association with the presence of WMLs is well documented especially in patients with silent strokes or cognitive impairment [3, 4]. Although smoking was a risk factor for HS, we did not find a correlation with LS, VaD, VaP while majority of studies documented that association with WMLs [5]. We also found that hypertension and low prevalence of hyperlipidemia were related to HS. These results are consistent with previous trials which found that hypertension, smoking, alcohol consumption and low cholesterol are linked to subcortical hemorrhage [6, 7]. However, findings on the association between cholesterol levels and CSVD are not consistent. Total cholesterol, LDL and triglycerides were not significantly associated to any CSVD subgroups in our study. Only low HDL was related to VaD and LS and this was in line with the LADIS study which documented that among 639 elderly subjects with some degree of WMLs, incident lacunes were associated with low HDL. Other studies found that lower TC was associated with CSVD and mid-life lower HDL level was associated with late-life WMLs [8, 9, 10]. Also in a population based cohorts, elevated TG and decreasing LDL were associated with severity of all MRI markers of CSVD [11].

There was a similar risk factors profile between VaP and VaD patients although the later had lower HDL and vit. B12 levels. These different risk factor associations with CSVD subtypes may suggest that concomitant neurodegenerative process play an important role both in the VaD and VaP pathogenesis.

We cannot directly compare our results with others because studies on CSVD usually concentrated on LS patients or asymptomatic patients with WMLs. Knowledge of risk factors for CSVD may generate hypothesis regarding possible targets for prevention. The present study adds new data and demonstrates that risk factor profile for CSVD differs from patients with proatherogenic profile without history of cerebrovascular disease and that modifiable risk factors should be targeted for primary or secondary CSVD prevention. Little is known about role of biochemical markers in CSVD pathophysiology and also of the magnitude of effect of classical vascular risk factors in the disease, which makes our data the more important. The advantages of the current study include the relatively well characterized and simultaneously studied patients with different CSVD manifestations, the use of MRI in controls which enabled us to exclude patients with silent radiological markers of CSVD. We also enrolled a well-phenotyped group of patients with rarely studied chronic VaP and VaD. On the other hand our study has some limitations. The major weakness is the potential for random error or selection bias because of the small number of patients and controls included, and the results may not be generalizable to other populations, however this is also a limiting factor in most published reports on the subject. Although patients with VaP and VaD were included to the present study immediately after diagnosis but they were in an advanced stage of their disease therefore it remains unknown whether our results can be applied to less severely affected patients. The study is therefore regarded as hypothesis generating rather than definitive, and a larger study and replication are needed for more robust conclusions.

In summary, our study showed that the risk factor profile for CSVD as a whole differs from subjects with proatherogenic profile without history of cerebrovascular disease. Our results support the concept that CSVD is not homo-

geneous, and those unique risk factors profiles exist for different clinical manifestations of the disease. Although this observation requires replication to ensure validity, if validated, it lends support to the involvement of multiple or different pathways in the pathogenesis of LS, HS, VaD or VaP. It is important that close association of CSVD with vascular risk factors gives a chance for successful primary and secondary prevention. The identified high-risk patient groups should be subjected to aggressive management of the underlying diseases and closer follow-up.

Figure 1. Impact of risk factors on the occurrence of CSVD adjusted for age and sex (available at request).

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Conflict of interest statement

The authors declare no conflict of interest.

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REVIEW PAPER

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Ausgewählte psychologische-ethische und sexualprobleme in der kinder- und jugendgynäkologie

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ABSTRACT

Zulassung. Die Kinder- und Jugendgynäkologie befasst sich mit angeborenen und entwicklungsbedingten gynäkologischen Störungen im Kindes- und Jugendalter. Eine der wichtigsten-spezifischen Fragen der Gynäkologie des Entwicklungsalters sind die psychologische-ethische Probleme, sehr oft Probleme, die mit einer vorzeitigen sexuellen Initiation zusammenhängen. Zwischen mehreren gynäkologischen somatischen Problemen der jugend Patientinnen sind auch psychologische-ethische Probleme und Probleme, die mit einer vorzeitigen sexuellen Initiation zusammenhängen.

Zielsatzung. Präsentation der Bedeutung der psychologischen-ethischen und sexuologischen Probleme in der Gynäkologie der Pubertät.

Methode. Analyse der Literatur der Problematik der Pubertätsgynäkologie in Bezug auf Sexuologie und Psychologie.

Schlussfolgerung. Die kurze Überprüfung der gewählten sexuologischen Themen in Bezug auf die Kinder- und Jugendgynäkologie weist auf die Bedeutung der sexuologischen Ausbildung, der Gesundheitspromotion, inklusiv sexuelles Wohlstandes hin.

Schlüsselwörter: Kindergynäkologie, Jugendgynäkologie, Psychologie, Sexuologie, Ethic, sexuelle Initiation, Geschlechtskrankheiten.

Gesundheit ist ein Prozess von den Wechselwirkungen in der Relation Körper-Umwelt, das, wenn keine Krankheit vorhanden ist, das Gleichgewicht

zwischen dem Körper und der Umwelt ermöglicht. Gesundheit bildet das Potential der Anpassungsfähigkeiten des Körpers zu den Umweltbe-

dingungen [1, 2]. Gesundheit nach WHO ist: ein Zustand des physischen, psychischen und sozialen Wohlfühlens, und nicht nur Mangel an Krankheit oder Behinderung. Gesundheit bedeutet auch die Fähigkeit, die sozialen Rollen auszufüllen, sich den Umweltveränderungen anzupassen und mit diesen Veränderungen richtig umzugehen [3, 4]. Die Weltgesundheitsorganisation führte auch einen Begriff „das Sexualeben“ ein. Das ist die Integrität von biologischen, emotionellen, intellektuellen und sozialen Faktoren des Sexuallebens, die für die richtige Entfaltung von Persönlichkeit, Kommunikation und Liebe wichtig sind. „Das Geschlecht, Probleme, die mit Geschlecht verbunden sind – hängen mit jeder Lebensphase des Menschen zusammen, von der Kindheit, über Pubertät, Reife, über das Klimakterium bis zum Alter. Der Staatliche Ausschuss für Sexuelle Gesundheit der Jugendlichen (Sexuality Information and Education Council of the United States) betonte, wie wichtig diese Erklärung für die Pubertätsphase ist.

Auch die Konvention für Geschlechtsrechte WHO aus 2002 ist vor allem auf die Jugendlichen gerichtet - über die Hälfte der Population ist unter 25 Jahre alt, und 1/3 ist im Alter von 13–21 Jahren.

Diese Konvention garantiert „Sexualrechte, auch die Rechte jedes Individuums, den höchst erreichbaren Standard des Sexuallebens zu erlangen und das Recht, das Sexualeben befriedigend, sicher und zufriedenstellend zu erleben“ [3, 4, 5].

Die Konvention beruht auf drei grundsätzlichen Annahmen:

1. Sexualität ist ein integraler Bestand der Persönlichkeit jedes Menschen.
2. Sexualität entfaltet sich infolge von Wechselwirkungen zwischen dem Individuum und den gesellschaftlichen Strukturen und die Entfaltung der Sexualität hat eine grundsätzliche Bedeutung für das Allgemeinwohl und das Wohl des Individuums.
3. Die Geschlechtsrechte sind die Universalrechte des Menschen, die auf einer unveräußerlichen Freiheit, Würde und Gleichheit aller Rassen basiert.

Um die gesunde Entwicklung zu erreichen, müssen die Geschlechtsrechte von allen Gesellschaftsgruppen anerkannt, befördert und bewahrt werden.

Zwar bestehen relativ geringe Gesundheitsprobleme in der Altersgruppe unter 15, jedoch

eigentlich in dieser Gruppe gehören die sexuell übertragbaren Krankheiten zu den wichtigsten Problemen [6–11].

Unter den Geschlechtskrankheiten, die auch Venerea (von Venera die Göttin der Liebe) genannt werden, im engeren Sinn soll man die Krankheiten der Geschlechtsorgane als Folge der sexuellen Infektion verstehen.

Sexuell übertragbare Krankheiten, die früher meist als Venerea bezeichnet wurden, resultieren aus Verhaltensweisen, die von sozio-ökonomischen, psychologischen und kulturellen Faktoren beeinflusst werden [12, 13]. Diese Krankheiten stellen ein bedeutender Grund für Besorgnis des Gesundheitswesens und der Gesellschaft im allgemeinen dar. Die Erkrankungszahl von den sexuell übertragbaren Krankheiten in den Vereinigten Staaten und anderen westeuropäischen Ländern erreichte zu dieser Zeit ihr höchstes Niveau. Frauen mehr als Männer sind von der Infektion gefährdet. Die meisten Krankheiten können asymptomatisch verlaufen und die Folgen vom Mangel an Diagnose und Behandlung ernst sein [7, 8, 9].

Bongiovani behauptet „wir sind genau in der Mitte der Seuche von Geschlechtskrankheiten. Sie greifen jede ethnische und gesellschaftliche Gruppe an und ihre Opfer werden meist die Patienten im Alter von 15–20 Jahren. 85% von STD betrifft die Personen unter 25 Jahre alt, 50% bei Personen im Alter von 15–19 Jahren“.

Es gibt unstrittige Beweise für den Zusammenhang zwischen dem frühen Anfang mit dem Geschlechtsverkehr und dem Risiko für Gebärmutterhalskrebs-Erkrankungen – ein unreifes, metaplastisches Epithelium des Gebärmutterhalses ist gegen die onkogene Wirkung von HPV besonders empfänglich.

Der Gesetzgeber, in dem er die psychisch und physisch unreifen Personen vor einem frühen Geschlechtsverkehr schützen will, bestimmte die Altersgrenze, unter der die sexuellen Verhalten gegenüber den Minderjährigen bestraft werden.

In Polen wurde diese Altersgrenze auf 15. Lebensjahr bestimmt. Falls dieses Gesetz verletzt wurde, es steht unter Freiheitsstrafe von 2 bis 12 Jahren. Auf der Welt beträgt das Alter für Geschlechtsverkehr durchschnittlich 15–18. Lebensjahr. In manchen Regionen beträgt das Alter dennoch 9–21. Lebensjahr.

Manche der wichtigsten Ursachen vom Anstieg der sexuell übertragbaren Krankheiten bei Jugendlichen sind:

1. Senkung vom Alter der sexuellen Initiation.
2. Anstieg der sexuellen Aktivität von Jugendlichen.
3. Anstieg der sexuellen Aktivität von Jugendlichen, zugleich mit der niedrigem Niveau der Sexualbildung.
4. Häufige Änderung von Sexualpartnern.
5. Häufige symptomlose Infektionen führen dazu, dass die Geschlechtskrankheiten relativ spät diagnostiziert werden.

Die vorzeitige sexuelle Initiation bildet ein Risikofaktor, dass die Geschlechtskrankheiten und ihre Folgen, ein emotioneller Stress oder eine ungeplante Schwangerschaft aufkommen.

Es gibt unstrittige Beweise für den Zusammenhang zwischen dem frühen Anfang mit dem Geschlechtsverkehr und dem Risiko für Gebärmutterhalskrebs-Erkrankungen [5, 11, 12, 13].

Eine der wichtigsten Problemen der Gynäkologie des Entwicklungsalters sind auch die Psychosomastörungen oft mit Essstörungen- z.B. Ess-Brech-Sucht *H: Bulimia nervosa* Magersucht *Anorexia nervosa*. Die Patientinnen mit Essstörungen (mit Störung der Energiebilanz als Resultat) haben irregular Blutungen (sehr oft oligomenorrhoea oder amenorrhoea) und andere somatische Probleme (z.B. Pubertas tarda, Osteoporosis) In Essstörungen zentral ist *die ständige gedankliche und emotionale Beschäftigung mit dem Thema „Essen“*. Sie betrifft die Nahrungsaufnahme oder deren Verweigerung und hängt mit psychosozialen Störungen und mit der Einstellung zum eigenen Körper zusammen (Psychosomatik) [14].

Viele Probleme (auch Sexualprobleme) der Kinder- Jugendgynäkologie haben Verbindung mit psychologischen und ethischen Aspekten.

Für Ende wir berichten kurz über eine 18-jährige Patientin mit Freeman-Sheldon Syndrom und Labienhypertrophie. Diese Patientin wg Freeman-Sheldon drom (FSS, cranio-carpo-tarsale Dysplasie) bereits mehreren plastischen Operationen unterzogen wurde. Die Vorstellung in unserer Klinik erfolgte bei einer subjektiv störenden Hypertrophie der kleinen Labien. Zu den Hauptsymptomen des FSS gehören Gelenkfehlstellungen und Mikrostomie (whistling-face), ohne kognitive Defizite. Genitalfehlbildungen wurden im

Zusammenhang mit FSS bislang nicht berichtet, sodass wir die Labienhypertrophie im vorliegenden Fall als ein unabhängiges medizinisches Problem betrachtet hatten. Während plastische und rekonstruktive Eingriffe im Falle von offensichtlichen somatischen Fehlbildungen ethisch unbedenklich sind, stellte sich nun die Frage, inwieweit – bei einer mehrfach voroperierten Patientin – eine weitere Korrekturoperation im Genitalbereich die Überzeugung über das gestörte Körperbild stärkt oder – im Gegenteil – zur Besserung des vielfältig beeinträchtigten Körperbildes beiträgt. Wir führten eine ausführliche gynäkologische und sexuologische Beratung der Patientin. Bei offensichtlich fehlender Akzeptanz des äußeren Genitales wurde eine Labienreduktionsplastik nach der in unserer Klinik üblichen „wedge-resection“ Methode durchgeführt. Das gute postoperative Ergebnis trug zu einer subjektiven Stärkung der Selbstakzeptanz und des affirmativen körperlichen Selbstwahrnehmung der Patientin bei.

Das vorliegende Beispiel zeigt, dass eine Intervention im Genitalbereich zur Besserung des Bildes und der Selbsteinschätzung des ganzen Körpers führt, selbst im Falle von koexistenten multiplen, nicht-gynäkologischen Fehlbildungen [15].

Marlene Heinz „Die Kinder- und Jugendgynäkologie ist ein interdisziplinäres Fach: (Kinder-) Gynäkologen, Pädiater, (Kinder-)Psychologen sowie (Kinder-)Urologen, (Kinder-) Chirurgen und andere müssen im Interesse der kleinen und heranwachsenden Mädchen eng zusammenarbeiten“ [16].

Schlussfolgerung

Die kurze Überprüfung der gwehalten sexuellen Themen in Bezug auf die Kinder- und Jugendgynäkologie weist auf die Bedeutung der sexuellen Ausbildung, der Gesundheitspromotion, inklusiv sexuelles Wohlstandes hin..

In der Kinder- und Jugendgynäkologie grosse Rolle spielt die interdisziplinäre Kooperation – das ist stark verbundet mit Sexuologie, Psychologie und auch mit Ethic..

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Genetic background of Meniere's disease


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ABSTRACT

Meniere's disease (MD) as an inner ear disorder including such symptoms as recurrent vertigo attacks, tinnitus, fluctuating or progressive sensorineural hearing loss. Its relatively frequent familial incidence implicates a genetic background. An autosomal dominant inheritance was commonly observed with a few exceptions. It was established that Meniere's disease is not a monogenic disorder. Instead a group of genes of genomic and mitochondrial genes was established as determinants of hearing loss. Another group of genes was associated with inner ear (vestibulum, labyrinth, endolymph) alterations followed by dizziness and tinnitus. Altogether, many studies suggest a multigenic interaction to predispose to develop Meniere's disease.

Keywords: meniere's disease, genetic background, gene identification T.

Meniere's disease (MD) as an inner ear disorder including such symptoms as recurrent vertigo attacks, tinnitus, fluctuating or progressive sensorineural hearing loss, and aural fullness. The latter is associated with an accumulation of endolymph forming endolymphatic hydrops. Further symptoms as nausea and vomiting seem to be a consequence of primary alterations [1, 2]. Migraine attacks observed in a subset of patients are classified as accompanying but separate condition. Altogether, patients present a clinical heterogeneity and not necessarily all particular symptoms are detected at diagnosis. Further, it has been noticed that first three symptoms are currently present in 40% of the patients only. It means a full manifestation of all symptoms is a subject of disease evolution and requires more time [3]. To facilitate diagnosis the American Academy of Otolaryngology – Head and Neck Surgery has proposed the guidelines widely accepted

[1]. Though MD remains in the frame of interest of otolaryngology, neurotology and neurology.

There are many different options of MD treatment which should be used in a determined order. The first line of treatment should always be medical conservative treatment including modification of the lifestyle (well sleeping, decreasing stress, avoiding coffee, alcohol and tobacco and adopt a low salt diet), vestibular rehabilitation, psychotherapy, pharmacotherapy (diuretic and betahistine) and pressure pulse therapy (Meniett® system). After this treatment 80% of patients are cured or in remission. The second line is intratympanic injections with steroid or with gentamicin. The third line is surgical treatment (endolymphatic sac surgery, vestibular neurectomy and labyrinthectomy), however endolymphatic sac surgery should be indicated before intratympanic gentamicin in cases with efficient hearing [4].

Although it has been described first in the middle XIXth MD poses still a serious medical problem for two reasons. First, the progressing MD contributes to serious health, psychological and social problems. Secondly, the disease affects a relatively high number of subjects. Epidemiologic studies have shown a range of prevalence from 17 (Western Europe) to 513 (Finland) cases per 100 000 individuals. Primarily it is detected in Caucasians and Eurasians. Diagnosis of MD is slightly more frequent in female population [2, 5].

Pathology of MD is not fully recognized yet that means a single or multiple casual factors have not been identified. Nevertheless it concerns inner ear with ion disequilibrium of endolymphatic fluid. An accompanying statement on disturbed ion homeostasis derived from dysfunction of ionic transport cannot serve as a definitive explanation of molecular pathology [6].

Hence further studies went in two directions aiming for a genetic background or immune deregulation in MD. We are aiming at presentation of genetic findings explaining predisposition and manifestation of MD. Clinical observations have shown a strong familial association of MD attributed up to 20% of patients. Pedigree analysis in families of MD carriers indicates an autosomal dominant inheritance with a reduced penetrance and anticipation [7].

Taking into account the above findings an attention was paid first on the already known genes attributed to individual symptoms assembling together Meniere's disease. Genes determining hearing loss provided themselves a broad spectrum of targeted investigations. Within this field vestibular disorders were found to be associated with the following loci: DFNA9, DFNA11, DFNA15, DFNA28 and DFNB102/103. Abbreviation DFNA is coming from deafness and the letter A denominates autosomal dominant tract when the letter B is attributed to autosomal recessive tract. The genes coded by the listed loci are as follows: *COCH*, *MYO7A*, *POU4F3*, *GRHL2* and *GLIC5* and all of them are associated with non-syndromic hearing loss [8]. Such attribution of genes to the symptoms of MD were first done by linkage analysis [9]. According to another publication [10] other mutations of the mentioned genes can be also extended onto vestibular dysfunction. The study was performed in a large Swedish family using whole-exome and targeted sequencing

techniques. *COCH* gene attracted more attention. An early study of Fransen et al. [11] investigating a large Belgium family, localized DFNA9 locus on chromosome 14 narrowing *COCH* (Coagulation Factor C Homolog, coded protein: cochlin) gene to 14q12-13. Gene mutation P51S (Pro-Ser) was found responsible for progressive autosomal dominant sensorineural hearing loss. Similar phenotype effect was established in American family carrying novel heterozygous missense mutation c.362>T>C, p.F121S0 [12]. All found *COCH* mutations were detected in exons 4, 5 and 12. The study of Gallant et al [13] done on large 3 generations American family with MD brought the discovery of another mutation located in 11th exon. This finding reinforced the need for genetic examination of the whole structure of *COCH*.

A specific position is taken by *SLC44A2* (chromosome locus 19p13.1) which product is a membrane transporter protein. It has a strong role in choline transport and uptake in inner ear. The research group of Tom Carey [14] has found disequilibrium at polymorphic loci rs2288904 with rs3087969 responsible for hearing loss. The defect is registered as DFNB68 that means, contrary to majority of genes responsible for hearing loss in MD, it is inherited on the autosomal recessive way. *SLC44A2* polymorphism seems also to be responsible for severity of Meniere's disease [14].

Our own study on hearing loss was done on 250 unrelated Polish subjects including a subgroup of MD patients. A sensitivity to aminoglycoside drugs was established with mutations of mitochondrial *12S rRNA* gene. Mutations m.1555 A>G, m.988 G>C and m.1453 A>G were found in all studied MD patients [15]. Our findings are consistent with the study on deafness-associated mutations by Qian and Guan [16].

Independently on hearing loss genetic studies on MD were focused on tinnitus, dizziness and motion sickness [6, 8, 10]. Initial studies performed on 5 generations Swedish family affected by MD done by genome wide linkage scan (GWAS) indicated chromosome locus 12p12.3 [17]. Later on it was shown that a finding is not having a general character as the familial MD studied in Finland was not linked to this region [18]. Further studies indicated that in very close region there is located *KCNA7* gene (12p13) encoding protein connected with a voltage-gated potassium channel [19].

Another genes also connected with ion homeostasis, aquaporin water channels (*AQP-1*), potassium channel (*KCNE1* and *KCNE3*) and $\text{Na}^+\text{-K}^+$ pump activity (*ADD1*) are under investigative attention [18]. It is necessary to add that a recent meta-analysis concluded that neither of *KCNE* variants is significantly associated with MD [20].

Looking for a background of pathology in MD some studies deal with immune system. There were published reports on association of MD with certain major histocompatibility complex (HLA) genes, namely *MICA-STR A.4* and *HLA-DRB1* [21, 22]. Also *PTPN22* (1p32; protein product: protein tyrosine phosphatase) as an integral part of immune stem could contribute to bilateral MD in east in southern European population [23]. It seems that immunologic hypothesis of MD incidence is not having a sufficient experimental support.

The reviewed list of the established or requiring further studies genes is not full. At this point a leading position in the field of laboratory headed by Jose A. Lopez-Escamez (Granada, Spain) is to be mentioned. In any case, it has become clear that Meniere's disease is not derived from a single mutated gene. A combination of genes responsible for hearing loss [12, 14, 15], dizziness [8, 10, 19] and tinnitus [24] forms a landscape for genetic background of Meniere's disease. A heterogeneous nature of genetic background makes the studies difficult to perform and complicates an interpretation of results [8, 25, 26].

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IMAGES IN CLINICAL MEDICINE


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Superior vena cava syndrome in the CT scanning

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ABSTRACT

Introduction. The study concerns a 67-year-old woman with symptoms such as swelling of the face, neck and upper limbs; bruising in the head and neck region; conjunctival hyperemia; excessive filling of the jugular veins. The CT examination was performed using the SOMATOM Definition AS (Siemens) and analyzed with SYNGO Multi-Modality CT Workstation (Siemens). The study showed a tumoral mass (67 × 91 mm) located in the right upper lobe and adjacent to the mediastinum, simultaneously invades the superior vena cava and causes it to narrow completely.

Keywords: superior vena cava syndrome, CT, tumor.

The study concerns a 67-year-old woman with symptoms such as swelling of the face, neck and upper limbs; bruising in the head and neck region; conjunctival hyperemia; excessive filling of the jugular veins. In addition, the patient complained of symptoms such as dizziness, headache, and blurred vision. The study was conducted using a contrast agent - Omnipaque 350 (contains 755 mg of iohexol equivalent to 350 mg of organic iodine per ml). The CT examination was performed using the SOMATOM Definition AS (Siemens) and analyzed with SYNGO Multi-Modality CT Workstation (Siemens). The study showed tumoral mass (67 × 91 mm) located in the right upper lobe and adjacent to the mediastinum, simultaneously invades the superior vena cava and causes it to narrow completely. The tumoral mass also adheres to the brachiocephalic trunk and compresses the bronchi to the upper lobe. (**Figure 1A**). At the apex of the right lung, a metastatic change of 40 × 27 mm was observed (**Figure 1B**). In the hilum of the right lung, the tumoral mass (size 41 × 30 mm) narrowing the main and lobar bronchi and narrowing the right pulmonary

artery was also observed (**Figure 1C**). According to literature data, the syndrome of the superior vena cava in 90–95% of cases is caused by malignant tumors, and in 5–10% by benign tumors. Superior vena cava syndrome compression usually caused by tumoral masses in the middle or anterior mediastinum and it most often affects the right lung cancer (80%) [1, 2].

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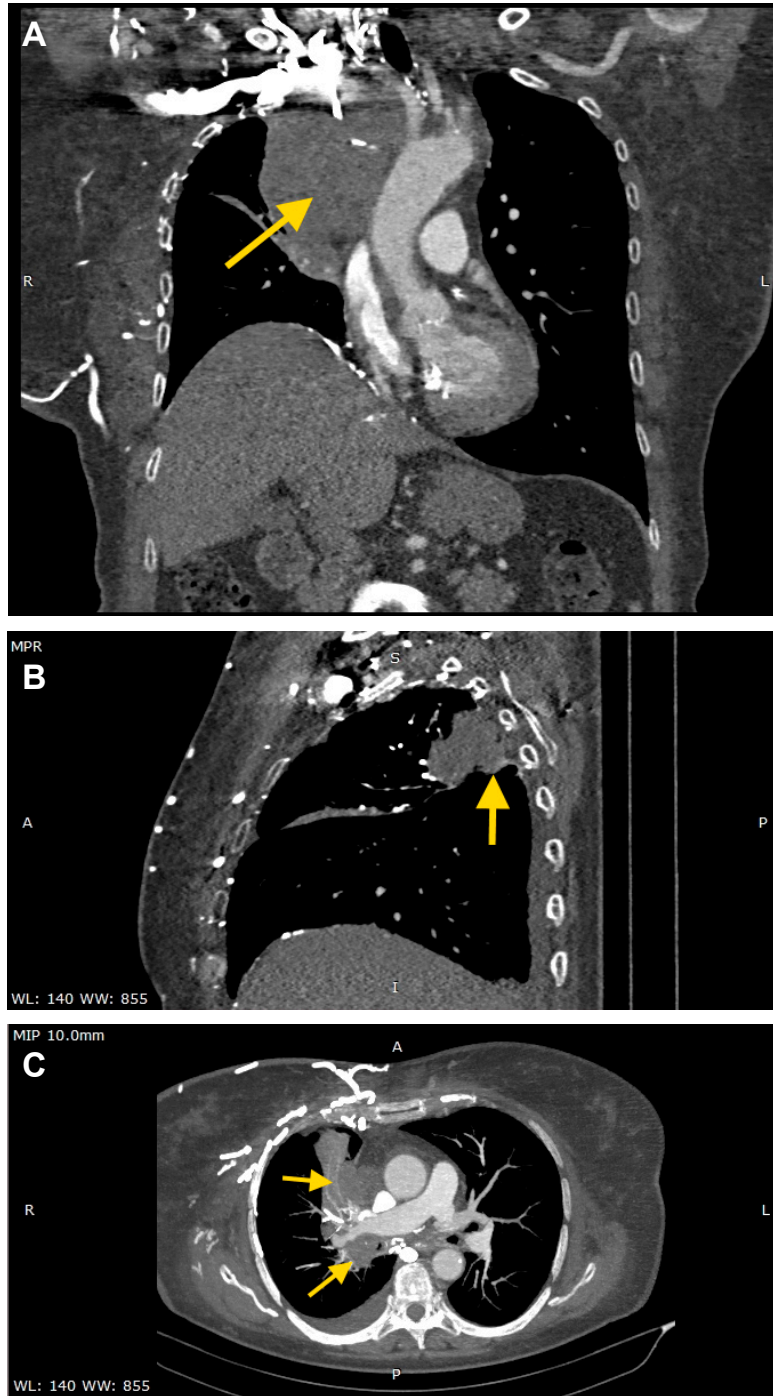


Figure 1. Lung cancer responsible for a superior vena cava syndrome. The CT scan detects the tumoral mass (arrow): A – coronal reconstruction; B – sagittal reconstruction; C – axial reconstruction in maximum intensity projection [MIP]

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CASE STUDY


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Folliculitis decalvans – a case study and an overview of literature


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ABSTRACT

Folliculitis decalvans is a rare disease that leads to alopecia. This disease is a major challenge for physicians due to the therapeutic difficulties. This publication describes the case of a patient in whom a dermatological condition had improved after using doxycycline.

Keywords: folliculitis decalvans, alopecia, treatment.

Introduction

Folliculitis decalvans is a rare disease belonging to the cicatricial alopecia group. It is a big challenge for a dermatologist to treat the disease because there are no clear guidelines concerning effective therapeutic methods. The disease was first described in 1888 by Quinquaud, who wrote that it was a chronic inflammation usually occurring in young adults of both sexes. In 1905 Brocq et al. named it folliculitis decalvans. The aetiopathogenesis of the disease has not been fully investigated. However, it seems that infection with *Staphylococcus aureus* (*S. aureus*) may play a significant role here with an inadequate immune response of the host [2, 4, 12]. Jahns et al. conducted immunofluorescence microscopy and fluorescent in situ hybridisation and proved that apart from *S. aureus*, other microorganisms were often responsible for folliculitis, e.g. *P. acnes* and coagulase-negative staphylococci [9]. There

are a few reports which suggest that head injury might result in predisposition for the disease [8].

Initially, the clinical image is predominated by erythematous papules and perifollicular pustules, which are usually covered by crust. The inflammation of follicles causes the emergence of alopecia foci with the characteristic 'brush symptom, i.e. tufts of residual hair. Progressing scarring alopecia is a characteristic feature of folliculitis decalvans. At the place where hair was lost the skin becomes atrophic and we can also observe erythema, follicular hyperkeratosis as well as erosions and hemorrhagic crusts. The usual locations are: top of the head and the occipital area, occasionally, the face (eyebrow and beard) and nape. Other extracranial locations are very rare. Patients complain about pain, the burning sensation and itchiness. Lesions may bleed periodically.

The disease is diagnosed on the basis of a typical clinical image and dermatoscopy. In

each case the diagnosis needs to be confirmed histologically. Early lesions are characterised by the accumulation of keratin in dilated follicular ostia, destruction of sebaceous glands as well as intra- and perifollicular neutrophilic infiltrates. When the disease is advanced, we can observe lymphocytes, numerous plasma cells and individual multinucleated giant cells. At the final stage of the disease fibrous strands replace hair follicles together with fibrosis in interfollicular skin.

They form overgrown scars, which are thicker and more cohesive than those observed in other diseases with initial perifollicular inflammations resulting in cicatricial alopecia [1, 2, 7, 8]. Differential diagnosis includes dissecting folliculitis of the scalp, acne keloidalis nuchae, erosive pustular dermatitis of the scalp, follicular lichen planus, kerion celsi as well as tufted folliculitis, which may be considered as a variant of folliculitis decalvans [7, 8].

Case study

A 24-year-old female patient was admitted to the Dermatological Clinic to diagnose and treat lesions encompassing the hairy skin on her head and lower legs. The history of the disease spanned a period of few years. In 2008 the patient underwent septoplasty. A few days after the surgery first skin lesions appeared on her head and legs. About 4 years earlier the patient had had a traffic accident and suffered craniocerebral injury, which encompassed the frontoparietal region and the left craniofacial region. Due to the injury she had undergone an operation at the neurosurgical clinic.

Apart from that, the craniocerebral injury the patient suffered in 2004 resulted in blindness of her right eye, restriction of the visual field of her left eye, cerebral circulation disorder and disordered balance. The patient was a student of cosmetology and additionally worked as a cleaner. Her parents suffered from asthma and atopic dermatitis, whereas her sister did not tolerate gluten.

Patient presented with erythematous scaly areas localized on the extremities, with numerous pustules. It was diagnosed as superinfected eczema or folliculitis. Scalp lesions were initially diagnosed as seborrheic dermatitis. Later it was diagnosed as folliculitis decalvans accompanied

by alopecia. Since the beginning of the disease the patient had been suffering from local itchiness.

Histopathological examination of the biopsy taken from the lesioned skin on the patient's right lower leg revealed *acanthotic epidermis with irregular rete ridges with intercellular oedema, infiltrated with neutrophils forming two micro-abscesses in the stratum corneum and moderate, mixed inflammatory infiltrates in the dermis – the image consistent with superinfected eczema*. The bacteriological test of the swab collected from a pustule in the lower leg region revealed infection with methicillin-sensitive *S. aureus* (MSSA), that confirmed the histopathological diagnosis.

Patient was treated with topical steroids and a combination of steroids and antibiotic. A steroid therapy lasting a few days had been included in systemic treatment twice. The patient had received antifungal drugs (itraconazole, probably) as well as antihistamine preparations and she had undergone an antibiotic therapy with doxycycline according to the antibiogram obtained in the microbial test of the swab collected from lesions in her lower legs. On the examination alopecia with tufts of residual hair located in the parietal region was observed (**Figure 1**). In the vicinity papules and perifollicular pustules predominated (**Figure 2**). Occasionally, individual erosions and crust could be found. There was a vast inflammatory infiltration. In the parietal region there were predominant traits of excessive keratosis with stratified scales. Apart from that, the image of the patient's lower legs was similar to that of folliculitis. The dermatological state deteriorated immediately before and during menstruation. The patient's lower legs were swollen then. The exacerbation was accompanied by pain and itchiness in the lesions.

Laboratory investigations conducted during the patient's hospitalisation revealed slightly reduced amounts of haemoglobin (up to 10.7 g/dl) and haematocrit (up to 31.5%), the limit content of erythrocytes ($3.54 \times 10^6/\mu\text{l}$) and potassium (5.11 mmol/l) and a slightly reduced amount of urea (14 mg/dl). The anti-streptolysin O value was 250 IU/ml. Other markers of inflammation as well as the content of thyroid hormones and anti-thyroid antibodies remained normal.

A punch biopsy was taken from the lesional skin of the patient's head. The histopathological examination revealed: Disrupted hair follicles and fragments of hair shafts surrounded with mixed



Figure 1. Alopecia with tufts of residual hair located in the parietal region



Figure 2. Papules and perifollicular pustules

inflammatory infiltrates composed of giant cells, lymphocytes, histiocytes, plasmacytes and neutrophils (**Figure 3**). Epidermis was normal but the upper dermis between hair follicles was also infil-

trated with inflammatory cells and fibroblasts, the features of folliculitis decalvans (**Figure 4**).

The direct immunopathological examination of the skin specimen did not reveal IgA, IgM, IgG

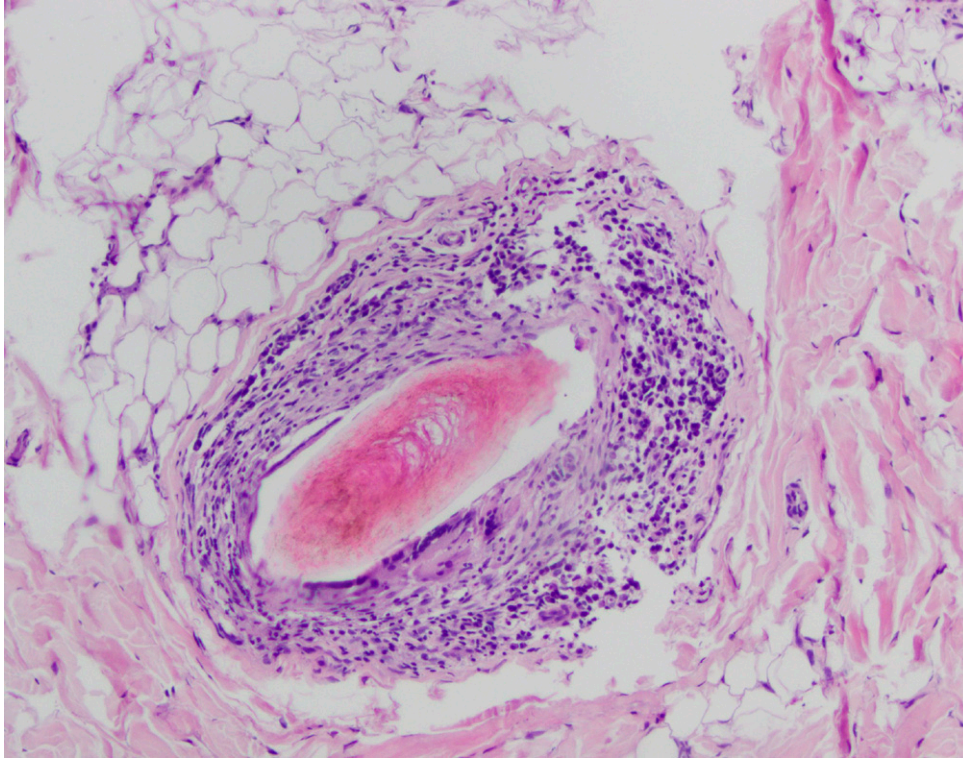


Figure 3. Remnants of disrupted hair follicle surrounded with inflammatory infiltrate with giant cells and plasmacytes

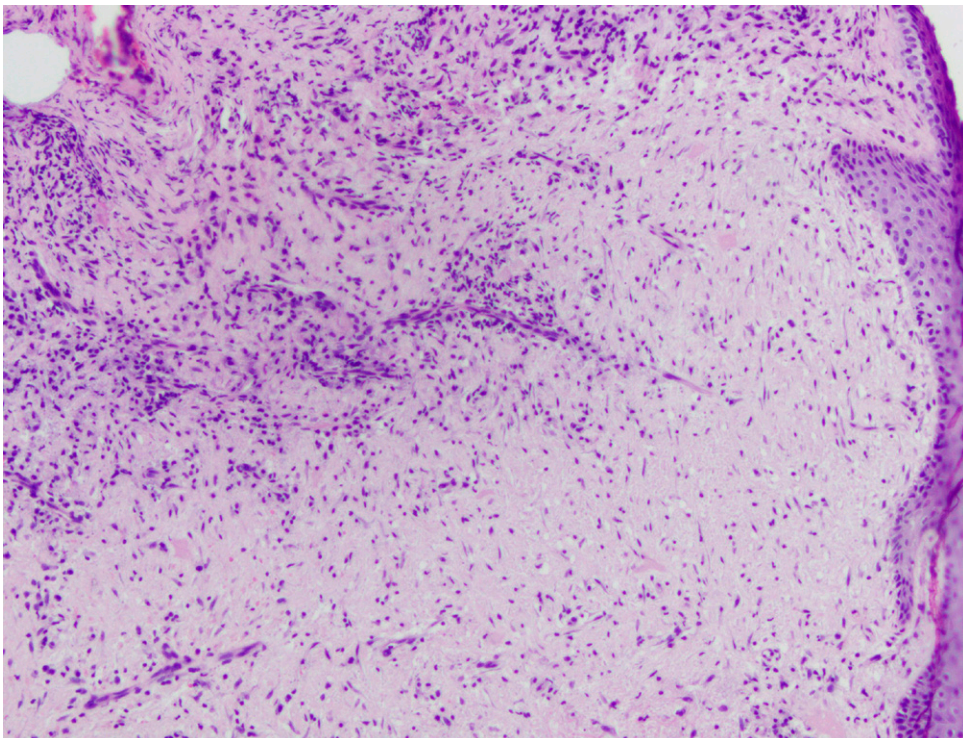


Figure 4. Mixed inflammatory infiltrate and fibroblasts in the upper interfollicular dermis

or C3 deposits. The indirect immunofluorescence test revealed the presence of antinuclear antibodies (ANA) with a titre of 1/320, characterised by granular fluorescence. Laryngological consultation resulted in diagnosing chronic tonsillitis and nasal septum deviation. Bilateral tonsillectomy was recommended in the case of dermatological indications. The dentist did not find potential pockets of infection. The mycological culture was negative.

During hospitalisation (6 days) the patient received doxycycline administered intravenously at a dose of 2 x 100 mg, fluconazole administered orally at a dose of 1 x 50 mg and cetirizine at a dose of 2 x 10 mg. Twice a day fluocinolone acetonide gel was applied locally to the skin on the patient's head. 5% salicylic oil was recommended to be applied twice a day in the occipital region with predominant exfoliation and stratified crusts. Boric cream with 1% hydrocortisone was applied to the patient's lower legs twice a day. Boric cream was also recommended for the patient's arms and torso.

According to the information in the discharge summary, the therapy should be continued in an outpatient setting by applying doxycycline orally at the same dose for few weeks. A preparation with urea was recommended to be applied once a day locally in the occipital region. A regenerative preparation was recommended to be applied to other lesions on the patient's head. Preparations with 15% urea were recommended to be applied to the patient's lower legs.

Discussion

The aetiopathogenesis of folliculitis decalvans has not been explained. It may be a problem to treat the disease.

Vano-Galvan et al. conducted a multi-centre study on 82 patients with symptoms of folliculitis decalvans. Hypotension, dyslipidaemia and thyroiditis were listed as concomitant diseases. Some patients also suffered from atopic dermatitis and hidradenitis suppurativa. None of the patients associated the occurrence of first skin lesions with any drug they received. However, the report described two cases of patients treated with erlotinib due to lung cancer and one case of a patient receiving lapatinib due to breast cancer. The average age of patients with the disease was

35 years. On average the diseases lasted about 4.6 years. There were three cases of positive family history with folliculitis decalvans (there were three male patients whose brothers suffered from the disease). There were two patients in the group who reported an earlier injury in the lesioned region. The researchers specified the scale of intensity of skin lesions, where foci smaller than 2 cm were classified as the first degree, foci ranging between 2 cm and 4.99 cm – as the second degree, whereas efflorescence of 5 cm or larger was classified as the third degree. The degree of classification depended on the maximum size of the largest focus of alopecia. Three groups with a benign (first degree), moderate (second degree) and acute (third degree) course of folliculitis decalvans were identified. There were respectively 40%, 39% and 21% of the patient population in each group. It seems that an early onset of dermatosis, i.e. before the age of 25, and the presence of pustules in alopecia foci prognose the acute course of the disease (third degree). The 'brush symptom' was usually described in the clinical image. Most of the patients had skin itchiness, pustules and scabs. More than a half of the patients had lesions on the top of their heads. Some of the patients had lesions in the parietal, occipital or frontal region. It was rarely found on their eyebrows or chin. In all the cases the diagnoses were confirmed by the histological examination, which showed cicatricial alopecia and different degrees of intra- or perifollicular inflammation and fibrous strands. In most of the patients microbiological tests revealed the presence of *S. aureus* in the swabs collected from pustules. The growth of *S. aureus* in the tested material was observed in all the patients whose nasal swabs were collected and analysed bacteriologically. The research did not confirm any correlation between the intensity of the disease and the patients' sex or location of efflorescence. There was no statistically significant correlation between the patients' sex, age, location of lesions and their response to treatment [4].

Questions about effective therapy cannot be omitted in the discussion on folliculitis decalvans. According to Powell et al., when rifampicin was administered orally twice a day at a dose of 300 mg in combination with clindamycin administered twice a day at a dose of 300 mg for 10 weeks, the patients' health improved. In most of

them pain was gradually relieved, the emergence of new pustules was inhibited and it was possible to control the inflammation. A few patients needed to have the ten-week therapy repeated two or three times. The research also proved that if there were contraindications against clindamycin, it was possible to apply combination therapy, where rifampicin was administered together with doxycycline, ciprofloxacin or clarithromycin. Powell et al. stressed the fact that rifampicin should not be used in monotherapy due to the high risk of drug resistance [2, 3]. Vano-Galvan et al. confirmed good response to treatment with rifampicin and clindamycin, but the remission observed in their research was shorter than in the aforementioned studies. The researchers noted the fact that apart from the strong bactericidal effect on *S. aureus*, rifampicin modified the cellular response of the organism by inhibiting the transformation of T lymphocytes. Vano-Galvan et al. suggested that alternatively doxycycline should be administered orally at a dose of 100 mg a day for 3–6 months, minocycline – at a dose of 100 mg a day for 3–6 months or if the patient exhibited intolerance to these drugs, azithromycin should be administered at a dose of 500 mg three times a week for 3 months. The authors indicated that this therapy reduced the risk of adverse reactions [4].

When corticosteroids were systemically applied, they did not have long-lasting effects although they blocked the inflammatory reaction. They should be taken into consideration as a short-term therapy if there is high intensity of the disease [4].

According to Otberg et al., the disease could be significantly inhibited by eradicating *S. aureus*. The authors recommended a wide range of orally administered antibiotics, such as: doxycycline, erythromycin, minocycline, co-trimoxazole, cloxacillin, sulfamethoxazole – trimethoprim, vancomycin, rifampicin and clindamycin as well as locally administered drugs, such as: fusidic acid, 2% mupirocin, 1% clindamycin and 2% erythromycin. However, it is necessary to remember that local antibiotic therapy is effective if there are very discreet lesions [5].

Steroids applied locally or administered by injection in the region of skin lesions help to reduce inflammation and the resulting itchiness, burning sensation and pain. They should supplement the antibiotic therapy [4, 5].

As far as isotretinoin is concerned, its application is limited due to the risk of adverse reactions and exacerbation of the disease, as was described in a few cases [4]. Gemmeke et al. applied a combination therapy with isotretinoin administered at a dose of 40 mg a day, clindamycin administered at a dose of 300 mg a day for 6 weeks and prednisolone administered at a dose of 20 mg a day for 3 weeks. The therapy was applied to a young patient and produced a good effect and remission during the six months of observation [11]. There are few reports on the application of dapsone. The dermatological state may be improved when the drug is applied at a dose of 50–100 mg daily, but when the therapy is finished, there is usually a relapse [5].

Bastida et al. described four cases where tacrolimus was locally applied in ointment and produced very good effects as inflammatory lesions remitted. When the immunomodulating drug is applied to lesioned skin, it inhibits signal transduction cascade in T lymphocytes. As a result, it prevents the synthesis of selected proinflammatory cytokines and blocks the release of inflammation mediators from mast cells, eosinophils and basophils. Apart from that, according to Bastida et al., tacrolimus increases the keratinocytes capacity to eliminate *S. aureus* by stimulating the expression of antibacterial proteins. However, when the therapy is stopped, the ailments usually remit. Bastida et al. stress the fact that the therapy they suggest does not eradicate *S. aureus*, so simultaneous antibiotic therapy might be helpful [6].

In case of resistance to the aforementioned treatment other methods can be applied, such as: Nd-YAG laser epilation, oral application of L-tyrosine and hydroxychloroquine, surgical treatment, photodynamic therapy or, as results from latest reports, adalimumab and infliximab [4, 5, 10, 11, 13].

Surgical reduction of lesions with hair transplantation can only be taken into consideration if there is a long-term remission after the therapy [5]. Miguel-Gomez et al. confirmed the efficacy of photodynamic therapy. The method consists in applying methyl aminolevulinate cream until occlusion and, after about 3 hours lesioned skin is exposed to radiation at a wavelength of 630 nm and dose of 37 J/cm² for 16 weeks. The photodynamic therapy improved the health of 90% of the patients under study. However, some patients

needed to have another method applied to sustain the effect. Due to the low comfort and uncertain effect of the method photodynamic therapy is reserved for the cases where pharmacotherapy is ineffective [10, 13].

Folliculitis decalvans is a chronic disease, where treatment includes limiting the inflammation and inhibiting alopecia. Hair regrowth should not be expected. The disease may relapse if the therapy is stopped. Therefore, it is important not only to select an adequate method of treatment for each patient with folliculitis decalvans but also to provide intensive psychological care.

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Conflict of interest statement

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Review articles: These articles should describe recent advances in areas within the Journal's scope. Review articles cannot exceed 5000 words length (excluding title page, abstract and references) and contain no more than a combination of 10 tables and/or figures. Authors are encouraged to restrict figures and tables to essential data that cannot be described in the text. The number of references should not exceed 80.

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Acknowledgements

Under acknowledgements please specify contributors to the article other than the authors accredited. List here those individuals who provided help during the research (e.g., providing language help, writing assistance or proof reading the article, etc.). Also acknowledge all sources of support (grants from government agencies, private foundations, etc.). The names of funding organizations should be written in full.

References

All manuscripts should use the 'Vancouver' style for references. References should be numbered consecutively in the order in which they appear in the text **and listed at the end of the paper.** References cited only in Figures/Tables should be listed in the end. Reference citations in the text should be identified by Arabic numbers in square brackets. Some examples:

This result was later contradicted by Smith and Murray [3].

Smith [8] has argued that...

Multiple clinical trials [4–6, 9] show...

List all authors if there are six or fewer; if there are seven or more, list first six followed by "et al.". Journal names should be abbreviated according to Index Medicus.

Some examples

Standard journal articles

1. Fassone E, Rahman S. Complex I deficiency: clinical features, biochemistry and molecular genetics. *J Med Genet.* 2012 Sep;49(9):578–590.
2. Pugh TJ, Morozova O, Attiyeh EF, Asgharzadeh S, Wei JS, Auclair D et al. The genetic landscape of high-risk neuroblastoma. *Nat Genet.* 2013 Mar;45(3):279–284.

Books

Personal author(s)

1. Rang HP, Dale MM, Ritter JM, Moore PK. *Pharmacology.* 5th ed. Edinburgh: Churchill Livingstone; 2003.

Editor(s) or compiler(s) as authors

2. Beers MH, Porter RS, Jones TV, Kaplan JL, Berkwitz M (editors). *The Merck manual of diagnosis and therapy.* 18th ed. Whitehouse Station (NJ): Merck Research Laboratories; 2006.

Chapter in the book

1. Phillips SJ, Whisnant JP. Hypertension and stroke. In: Laragh JH, Brenner BM, editors. *Hypertension: pathophysiology, diagnosis, and management.* 2nd ed. New York: Raven Press; 1995. p. 465–478.

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