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The influence of pulmonary rehabilitation in the Wieliczka Salt Mine on asthma control – preliminary results

Wpływ rehabilitacji pulmonologicznej w Kopalni Soli "Wieliczka" na kontrolę astmy – doniesienie wstępne

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According to asthma treatment guidelines the main goal of pulmonary rehabilitation is optimum asthma control. The Asthma Control Test (ACT) is a standardised five-item questionnaire for the assessment of asthma control. The study compares the pre- and post-treatment (subterraneotherapy) ACT score with other conventional respiratory parameters.

The study included 21 patients with bronchial asthma who underwent a 3-week long subterraneotherapy programme in the 'Wieliczka' Salt Mine. The patients completed the ACT questionnaire before and 2 weeks after subterraneotherapy. At the same time, they underwent testing for concentration of nitric oxide in exhaled breath (FENO), peak expiratory flow (PEF) and spirometry.

Subterraneotherapy influenced significantly the change of MEF75 (p=0.03255) and improvement of ACT score (N=21, p=0.0016). The differences in other parameters were not statistically important, but in the case of FEV1 and VC parameters, the differences found were close to the statistical significance (0.05 < p < 0.10).

The differences of results before and after subterraneotherapy were higher in the group assigned as patient with poor or moderate asthma control (ACT score <20, N=10) than in the group with good control of asthma (ACT score ≥20, N=11). For parameters FEV1, VC, MEF75 and ACT score the improvement was significantly higher in the poor control group.

The pulmonary rehabilitation programme combined with subterraneotherapy helps to control asthma especially in patients suffering from poorly or moderate controlled asthma.

Zgodnie z wytycznymi postępowania w astmie, podstawowym celem rehabilitacji pulmonologicznej jest optymalna kontrola przebiegu astmy. Test Kontroli Astmy (ACT - *Asthma Control Test*) jest standaryzowanym, 5-elementowym kwestionariuszem, służącym do oceny kontroli astmy. Badanie porównuje wyniki uzyskane w teście ACT przed i po subterraneoterapii z wynikami pomiarów parametrów oddechowych.

Badaniem objęto 21 pacjentów z astmą oskrzelową. Uczestniczyli oni w 3 tygodniowym programie subterraneoterapii w Kopalni Soli „Wieliczka". Pacjenci wypełniali kwestionariusz ACT przed rozpoczęciem zjazdów i 2 tygodnie po ich zakończeniu. Jednocześnie mierzono poziom tlenku azotu w powietrzu wydychanym (FENO), szczytowy przepływ wydechowy (PEF) oraz wykonywano spirometrię.

Subterraneoterapia wpłynęła w sposób znamienny na wzrost MEF75 (p=0,03255) oraz zwiększenie wyniku ACT (N=21, p=0,0016). Wzrost innych badanych parametrów nie był znamienny, lecz w przypadku FEV1 i VC był na granicy istotności statystycznej (0,05 < p < 0,10).

Po wydzieleniu podgrupy pacjentów z astmą słabo lub umiarkowanie kontrolowaną (wynik ACT<20, N=10) stwierdzono, że różnica wyników przed i po subterraneoterapii była u nich wyższa niż w grupie z astmą dobrze kontrolowaną (wynik ACT ≥20, N=11) a różnice między grupami były znamienne dla testu ACT, FEV1, VC i MEF75.

Program rehabilitacji pulmonologicznej w połączeniu z subterraneoterapią pomaga uzyskać lepszą kontrolę astmy szczególnie u pacjentów z astmą słabo lub umiarkowanie kontrolowaną.

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Introduction

Asthma is a common chronic disease and affects 1-18% of the population in different countries [1]. According to the Global Initiative for Asthma (GINA) definition "Asthma is a heterogeneous disease, usually characterized by chronic airway inflammation. It is defined by history of respiratory symptoms such as wheeze, shortness of breath, chest tightness and cough that vary over time and in intensity, together with variable expiratory limitation" [1]. Asthma imposes a substantial burden on patients, their families and the community. It causes respiratory symptoms, limitation of activity, and exacerbations that sometimes require urgent health care or hospitalizations [2]. According to the asthma guidelines the main goal of treatment is

symptoms control and future risk reduction of exacerbations [1].

Asthma is a multifaceted disease, and therefore it is a number of markers or measurements to assess its severity. Among them there are functional parameters (spirometry), clinical assessment (symptoms and quality of life) and biomarkers of inflammation or indirect markers of inflammation (fractional exhaled nitric oxide - FENO measurement) [3]. In the last decade a new instrument for evaluation of asthma control – Asthma Control Test (ACT) was introduced. It is a self-reported questionnaire that includes 5 items assessment each concerning the previous 4 weeks. It refers to the frequency of shortness of breath, asthma caused sleeping problems, use of rescue medicines, the influence of asthma symptoms on daily duties and self-assessment of asthma control. Each question has five possible answers scored from 1 (the worst) to 5 (the best). The higher the ACT score a patient achieves, the better control of asthma is reached [4].

One of the treatment methods indicated for patients with asthma is subterraneotherapy . The 'Wieliczka' Salt Mine is one of the few places in the world where specialized treatment is carried out in underground saline cavities. Natural salt caverns climate is favourable for patients with chronic respiratory diseases [5-8]. In Europe, outside Poland, this type of treatment is performed in Germany (Berchtesgaden, Klutterthöhle), Austria (Bad Gastein), Romania (Turda), the Czech Republic (Zlate Hory) and Slovakia (Banska Bystrica) [9-11]. However, the Wieliczka Salt Mine is the cradle of scientific research in this field. The history of subterraneotherapy in Poland dates back to the thirties of the nineteenth century, when Dr Feliks Boczkowski demonstrated the therapeutic effects of stays in salt chambers in people with airway obstruction. The first study in patients with asthma were conducted by Prof. Mieczyslaw Skulimowski in the fifties and sixties of the twentieth century, who was the first to introduce regular treatment in salt caverns. He showed that subterraneotherapy can alleviate the symptoms of chronic bronchitis. Studies continued in the seventies demonstrated that this type of therapy is beneficial in the treatment of pollen allergy, allergic rhinitis, chronic sinusitis, rhinitis and allergic eczema [12-15].

In the 90's research focused on the analysis of aerosol composition and the microclimate of the Wieliczka salt mine chambers in terms of their value for health purposes [16-18]. Between the years 2006 and 2007 a research on the effectiveness of subterraneotherapy as a complementary method in the treatment of asthma was carried out. The intensity of inflammation in the airways was assessed by measuring the amount of exhaled nitric oxide (NO). Nitric oxide produced by the constitutive isoform of nitric oxide synthase (NOS) has a beneficial and desirable effect on the airways. In asthma NO synthesis is not sufficient what is compensated by the increase in the production of NO by inducible isoform of NOS (iNOS). Its expression has been demonstrated in bronchial epithelial cells, inflammatory cells (macrophages, eosinophils, neutrophils, mast cells), endothelial cells, fibroblast, type II pneumocytes and myocytes. Asthma patients demonstrated an increased expression of iNOS and increased levels of NO in exhaled air. iNOS expression is induced by endo- and exogenous factors, such as bacterial lipopolysaccharides, proinflammatory cytokines (IL-1, INFγ, TNF) and exposure to allergens and oxidants (as a response to the atmospheric pollutant - ozone and nitrogen dioxide) [19-20].

The mechanism of subterraneotherapy action is not clear to date. The impact of the specific chambers climate is taken into account. It is characterized by bacteriological purity, high relative humidity (60-75%) and high content of sodium chloride and elements such as magnesium, manganese and calcium [21]. The chamber air does not contain impurities typical for the environment on the surface of the earth. The first complex study on the organic and inorganic particles occurrence in salt chambers of 'Wieliczka' Salt Mine was performed in 2001 [16]. Both, the microbiological and palynological analyses pointed out the high microbiological purity of the air, with only low fungal spores, pollen grains and bacteria concentrations. Similar research was arranged in the Bochnia Salt Mine in 2008 using the Andersen trap. The maximum concentration of bacteria colonies achieved 11.000 cfu/m^3, and the mean fungal spore concentration up to 88 cfu/m^3 [22]. Salt aerosol has an osmotic effect, which together with the high humidity affects the airway secretory function and skin condition. It is not conducive to the development of bacterial flora and fungi. In addition, the chambers climate isolates the patient from allergens present on the surface of the earth. In subterranean biodynamics the differences in oxygen and carbon dioxide concentration and the emergence of new components, such as radon and methane compared to the composition of the atmospheric air, are essential. Constant temperature (12.9-14.5°C), pressure, air movement, negative ionization, the absence of light and electromagnetic radiation and a pH of 4.5 with bacteriostatic properties is also important [21-24]. A stay in the 'Wieliczka' Salt Mine chambers is recommended mainly for people suffering from upper and lower airways diseases, such as atopic and non-atopic asthma in adults and children, chronic obstructive pulmonary disease (COPD), recurrent diseases of the nose, sinuses, pharynx and larynx, chronic bronchitis, pneumonia, and allergic diseases of the skin [5,25,26].

The aim of the study was an evaluation of the subterraneotherapy influence based on asthma control test results. The result of the asthma control test was compared with other conventional parameters including spirometry, PEF rate and FENO.

The results can contribute to the recognition of this method of treatment in asthma therapy consensuses and will refine the subterraneotherapy eligibility criteria.

Materials and methods

The study included 21 patients: 16 females, mean age 49.9 with a range from 12 to 72 years. All the patients were diagnosed with asthma by a specialist (according to GINA guidelines). In 11 cases asthma was well controlled according to a specialist rating of asthma control (Tab. I).

Table I
Baseline characteristic of the group.
Charakterystyka grupy badanej.

	Asthma (n=21)
Age (years)	49.90 (12-72)
Sex (M/F)	5/16
FEV1 (L)	2.32 (0.99 – 3 .67)
FEV1 (% predicted)	82.19 (31 – 103)
VC (L)	3.29 (2.02 – 4.99)
ACT (points)	18.81 (9 – 25)

Patients' qualification for subterraneotherapy (physical examination, general blood tests (morphology, CRP), chest X-ray, electrocardiogram) and their written consent to participate in the study, signed by the patient or a legal guardian (if a patient was a child) was carried out before entering the mine. The protocol of the study was approved by a local Ethics Committee.

In the period between April 2013 and March 2014 patients remained in the Wessel Lake Chamber 6 hours daily for 3 weeks. All patients enrolled for subterraneotherapy were requested to complete the Asthma Control Test before treatment. In addition, spirometry tests (Lungest 1000, module for Lungest) and FENO measurements (Medisoft SA analyser) were performed. All these tests were repeated 2 weeks after subterraneotherapy.

During the study the following respiratory parameters were analysed:

- FEV1 (Forced Expiratory Volume in 1 second)
- VC (Vital Capacity)
- PEF (Peak Expiratory Flow)
- MEF75 (Maximal Expiratory Flow)
- FENO

and an ACT score was gathered (Fig. 1).

The difference between the post- and pre-treatment parameters examined were tested by the nonparametric Wilcoxon test (dependent variables comparison).

The patients database was then divided into two groups, regarding their ACT value: the patients with ACT< 20 were assigned to the asthma poor or moderate control group (PC hereafter), and patients with 20-25 points were assigned to the asthma good control group (GC hereafter). The possible differences between these two groups in final results of parameters examined were tested with ANOVA. In the case of ACT values, the data were coded by adding 1 to each value and then transformed by taking the second root to achieve the normal distribution of data. Finally, all the parameters measured were checked for correlations.

Results

1. The difference between pre- and post-treatment parameters.

All examined parameters except for FENO tended to have higher values follo-

Figure 1
Scheme of the project.
0 – pre-treatment measurements, 02 – post-treatment measurements.
Schemat procedury badawczej.
0 – pomiary przed subterraneoterapią, 02 – pomiary po subterraneoterapii.

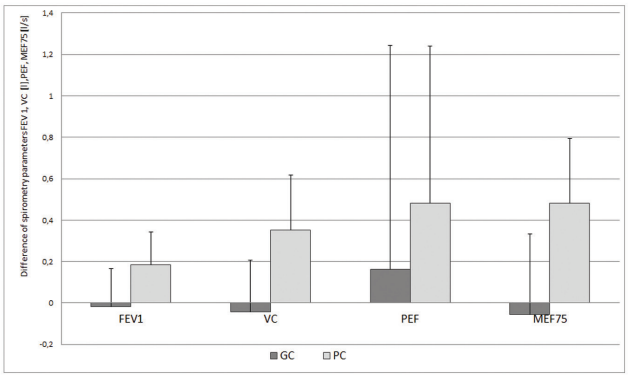

Figure 2
Change of FEV1, VC, PEF and MEF75 parameter in tested groups of patients.
PC – poor or moderate control group, GC – good control group.
Zmiana parametrów FEV1, VC, PEF i MEF75 w badanych grupach pacjentów.
PC – grupa pacjentów z astmą słabo lub umiarkowanie kontrolowaną, GC – grupa pacjentów z astmą dobrze kontrolowaną.

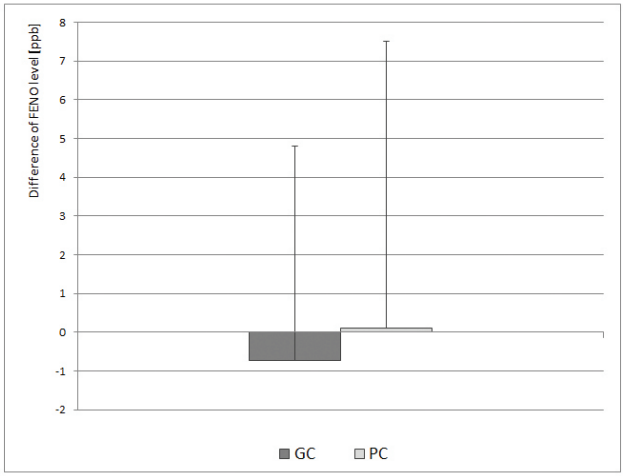

Figure 3
Change of FENO parameter in tested groups of patients.
PC – poor or moderate control group, GC – good control group.
Zmiana parametru FENO w badanych grupach pacjentów.
PC – grupa pacjentów z astmą słabo lub umiarkowanie kontrolowaną, GC – grupa pacjentów z astmą dobrze kontrolowaną.

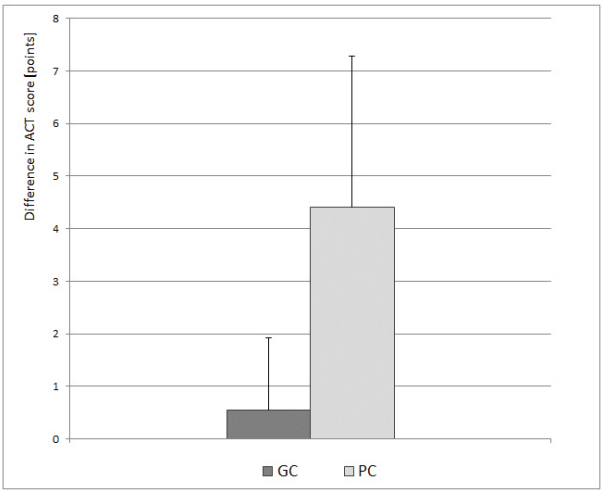

Figure 4
Change of ACT score in tested groups of patients.
PC – poor or moderate control group, GC – good control group.
Zmiana wyniku ACT w badanych grupach pacjentów.
PC – grupa pacjentów z astmą słabo lub umiarkowanie kontrolowaną, GC – grupa pacjentów z astmą dobrze kontrolowaną.

wing therapy.

Among them, statistically significant differences were found for two parameters: MEF75 (p=0.03255) and ACT score (p=0.0016).

In the case of FEV1 and VC parameters, the differences found are close to the statistical significance (0.05< p < 0.10) (Tab. II).

2. The difference in respiratory parameters between examined groups.

The differences of results before and after subterraneotherapy were higher in the group assigned as patient with poor or moderate asthma control (ACT score<20, N=10) than in the group with good control of asthma (ACT score ≥20, N=11).

For parameters FEV1, VC and MEF75 the difference between groups is statistically significant (greater in the PC group) (Tab. III), (Fig. 2-3).

3. The difference in the ACT result between examined groups.

Patients from the PC group (N=10) showed improvement in the ACT result. It amounted to an average of 4.40 points, compared with the 0.55 points mean change of ACT score in the GC group. The differences between groups was significantly important (p=0.0037) (Tab. III), (Fig. 4).

Table II
Differences between pre- and post-treatment parameters. (0 – pre-treatment values, 02 – post-treatment values).
Różnice w badanych parametrach przed i po subterraneoterapii. (0 – pomiary przed subterraneoterapią, 02 – pomiary po subterraneoterapii).

	Wilcoxon Matched Pairs test (dataset)			
Pair of variables	**Valid N**	**T**	**Z**	**p-value**
FEV1_0 and FEV1_02	21	66.5000	1.703125	0.08855
VC_0 and VC_02	21	60.5000	1.911671	0.05592
PEF_0 and PEF_02	21	81.0000	1.199139	0.23048
MEF75_0 and MEF75_02	21	54.0000	0.522657	0.03255*
FENO_0 and FENO _02	20	91.0000	0.522657	0.60121
ACT_0 and ACT_02	15	4.50000	3.152188	0.00162*

* p<0.005 compared with values before treatment

4. Correlations

Correlation analysis carried out for the difference in the individual parameters before and after subterraneotherapy treatment showed that the difference in the obtained result of ACT correlated significantly (p<0.05) with the difference in the measurement result of FEV 1 (r=0.461), VC (r=0.561) and MEF 75 (r=0.532) (Tab. IV).

Discussion

Subterraneotherapy improves asthma control in patients treated in Wieliczka, measured by ACT. The comprehensive therapeutic program, implemented in the Health Resort comprising climate effects,

Table III

Mean change of respiratory parameters and ACT score measured before and after subterraneotherapy in poor or moderate control group (PC) and good control group (GC).

Zmiana badanych parametrów przed i po subterraneoterapii w grupie z astmą słabo lub umiarkowanie kontrolowaną (PC) i w grupie z astmą dobrze kontrolowaną (GC).

Differences between groups - ANOVA test			
	Mean change PC group (N = 10)	Mean change GC group (N=11)	p
FEV 1	0.18	-0.02	0.01490*
VC	0.35	-0.04	0.00225*
PEF	0.48	0.16	0.44710
MEF 75	0.48	-0.05	0.00268*
FENO	0.10	-0.73	0.77348
ACT	4.40	0.55	0.00037*

*p<0.005 (statistical significance)

Table IV

Correlations between the difference of ACT score and the differences of respiratory parameters.

Korelacja pomiędzy różnicą w uzyskanym wyniku ACT a różnicą badanych parametrów oddechowych.

Correlations (dataset)								
	Means	SD	FEV1 difference	VC difference	PEF difference	MEF75 difference	FENO difference	ACT difference
FEV1 difference	0.07	0.200	-	0.515*	0.622*	0.681*	-0.312	0.461*
VC difference	0.14	0.328	0.515*	-	0.735*	0.323	-0.186	0.561*
PEF difference	0.19	0.762	0.622*	0.735	-	0.406	-0.418	0.400
MEF75 difference	0.20	0.453	0.681*	0.323	0.406	-	-0.177	0.532*
FENO difference	-0.55	6.419	-0.312	-0.186	-0.418	-0.177	-	0.009
ACT difference	1.77	0.694	0.461*	0.561*	0.400	0.532*	0.009	-

Marked (*) correlations are significant at p < 0.05000, N=20, casewise deletion of missing data

pulmonary rehabilitation program and health education, has an influence on obtained results. All patients who, prior to subterraneotherapy treatment, received ACT results indicating low or moderate asthma control (ACT score <20) improved their score by an average of 4.40 points, having completed the stay. According to Schatz [27], Minimally Important Difference (MID) for ACT is 3 points, and therefore the result shows a statistically significant improvement in asthma control.

The improvement of certain respiratory parameters, such as FEV1 and VC, MEF75, was observed in the study, however only MEF75 differences were statistically significant. Maximum expiratory flow (MEF) is considered as an indicator of patent airway and is helpful in the diagnosis and monitoring bronchial asthma [28]. Nevertheless, basing on received results it cannot be concluded which of the factors involved in the therapeutic program, contributed to the change in respiratory parameters. There are many studies investigating the outcomes of pulmonary rehabilitation for asthma, but most of them are uncontrolled trials or case studies [29-30]. Existing data suggest that exercise training and pulmonary rehabilitation improve exercise tolerance and/or quality of life for those suffering from asthma [30-32]. However the effect on spirometric parameters has not been confirmed in a significant way [32]. On that basis, it could be suggested that the element affecting the patency rate of the respiratory system is the underground microclimate, also indicated in studies on the effectiveness of pulmonary rehabilitation in subterraneotherapy conditions in patients with bronchial asthma [6,20].

It was found previously that subterraneotherapy significantly reduces FENO parameter [19-20] yet, this result is noticeable only during the period when the patient stays in the underground atmosphere. Reducing the concentration of nitric oxide in exhaled air was observed during the measurements made on the last day of therapy, whereas in the test performed 7 days after the treatment, this parameter returned to baseline values, which is confirmed by the obtained results (in the measurements carried out 2 weeks after treatment there are no significant differences in relation to measurements taken before the treatment). FENO parameter manifests inflammation in the airways (often allergic), and the presence of salt aerosol, having anti-inflammatory effect, may alleviate this symptom .

There was also observed an increase in the parameter IC [20], FEV1 and VC [6,26]. Growth of spirometric parameters is associated by the authors, with improved patency of the bronchial tree, resulting from the osmotic effect of salt aerosol, as well as different pressure conditions prevailing under the ground [6,15,23].

Achieved, through a subterraneotherapy program, improvement in the ACT result significantly correlates with the improvement of some respiratory parameters (FEV1, VC, MEF 75), suggesting a connection between subjectively experienced symptoms (such as shortness of breath, trouble with sleeping, coping with everyday responsibilities) and objective measurement results of respiratory tract patency [4]. A study on the correlation between the ACT result and respiratory parameters, does not present statistically significant correlation in the case of FEV1 [3] parameter, which, however, does not deny the existing correlation between the change in the parameters mentioned above, revealed in this research.

Analyzing the differences between patients with poorly or moderate controlled asthma and those with good asthma control (control group), participating in the survey, it can be stated that the improvement in the ACT was higher in the former one. Likewise the tested respiratory parameters such as FEV1, VC, and MEF75 improved to a greater extent in a group of patients with moderate asthma control, than in those from the control group.

Conclusions

The obtained results indicate that the subterraneotherapy program can be an effective tool to achieve at least one of the two therapeutic purposes, recommended by GINA [1], this means control of asthmatic symptoms, particularly in patients who have not achieved this result yet. The results should be confirmed through the study of a larger group of patients.

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