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The use of combined pharmacotherapy and hyperbaric oxygen in the treatment of sudden sensorineural hearing loss

Zastosowanie skojarzonej farmakoterapii i tlenu hiperbarycznego w leczeniu nagłego niedosłuchu czuciowo-nerwowego

Authors' Contribution:
A Study Design
B Data Collection
C Statistical Analysis
D Data Interpretation
E Manuscript Preparation
F Literature Search
G Funds Collection

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Summary

Aim: Sudden sensorineural hearing loss (SSNHL) involves acute unexplained hearing loss, nearly always one-sided of 30dB or greater over at least three contiguous audiometric frequencies. The aetiology of SSNHL is mostly unknown. According to the literature, the causes include vascular, microbial and autoimmune problems. There is still no agreed standard treatment. The aim of the paper was to evaluate the results of combined pharmacotherapy and hyperbaric oxygen therapy in patients with idiopathic sudden deafness.

Material/Methods: The study was carried out on 40 patients with SSNHL. The patients were divided into two groups: group I – 24 patients treated with the combined pharmacotherapy and hyperbaric oxygen therapy and group II – 16 patients treated only pharmacologically. The patients from Group 1 were treated in the Centre of Hyperbaric Therapy CREATOR Ltd. in Lodz, Poland. Each patient underwent 15 sessions in a hyperbaric chamber. In all patients, the percentage of hearing loss for the selected frequencies was assessed before and after the therapy according to Sabine and Fowler.

Results: The group of 40 patie nts aged from 33 to 77 years (mean 52.4) included 21 females and 19 males. Group I consisted of 24 patients, 11 females and 13 males, group II consisted of 16 patients, 10 females, and 6 males. After therapy, the mean hearing level in all patients improved by 27.14%, in Group I – by 34.34%, in Group II – by 16.3%.

Conclusions: Early hyperbaric oxygen therapy combined with steroid therapy improves prognosis and shows good results in sudden hearing loss treatment.

Keywords: **Sudden deafness • Hyperbaric oxygen • Steroid therapy**

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Abbreviations: **ATA** – atmosphere absolute; **HBO** – hyperbaric oxygenation; **ISSNHL** – idiopathic sudden sensorineural hearing loss; **ITS** – intratympanic steroid injection; **NRS** – numeric rating scale; **PTA** – pure-tone average; **SSNHL** – sudden sensorineural hearing loss; **WRS** – word recognition score.

INTRODUCTION

Sudden hearing loss (sudden sensorineural hearing loss) (SSNHL) is defined as sudden hearing loss in one or rarely in both ears (less than 2% of patients have bilateral involvement) of 30dB or greater over at least three contiguous audiometric frequencies. The incidence of the disease is 5–20 persons per 100.000 inhabitants. According to literature data, it occurs with equal incidence in males and females and mostly affects individuals between 30–60 years of age [3, 6, 7]. Sudden sensorineural hearing loss in about 90% of the patients is an idiopathic disease despite detailed evaluation. It is thought to be related to vascular disorders, such as acute vascular haemorrhage, vascular disease, vasospasm and change in blood viscosity. Important reasons for the onset of this are infections caused by bacteria and fungi as *Borrelia burgdorferi*, *Treponema pallidum*, Mycoplasma, *Cryptococcus* spp., by viruses as viral haemorrhagic fever (Lassa fever) or HIV and also by protozoa *Toxoplasma gondii* mainly. Sudden sensorineural hearing loss can also occur in the course of auto-immune disease, e.g. Behcet's disease or Cogan syndrome and metabolic disorders of the endocrine system or diabetes. The remaining 10% manifest symptoms of other diseases, e.g. cerebellopontine angle tumours, brain strokes or cancer of CNS [7, 15]. Prodromal symptoms comprise a sensation of fullness in the ear; the accompanying symptoms are tinnitus and vertigo (in about 40% of patients).

In clinical practice, guidelines for SSNHL treatment recommend using oral steroid therapy and intratympanic steroid ITS infiltration. Glucocorticoids are first-choice drugs, administered systemically or via ITS injection. ITS is used as a combined treatment with oral therapy or as a singular treatment when oral therapy is contraindicated [1, 8, 18]. According to the Polish Society of Audiology and Phoniatrics guidelines 2015, treatment of sudden hearing loss should be instituted within 2 weeks from the onset of the disease; otherwise, the chance of hearing improvement is slight. There is still no evidence confirming the effectiveness of treatment, as in most cases the cause of sudden hearing loss remains unknown, thus only symptoms are treated [9, 11]. Guidelines of the American Academy of Otolaryngology-Head and Neck Surgery recommended hyperbaric oxygen (HBO) therapy within 3 months of diagnosis in ISSNHL [18]. The use of HBO therapy is recommended by the European Committee for Hyperbaric Medicine and by the Polish Society of Audiology and Phoniatrics, but the Undersea and Hyperbaric Medical Society does not include this method [5, 16, 17, 19, 20]. Other treatments are also used, such as multidirectional models of pharmacotherapy, which comprise antimicrobial drugs, drugs to improve microcirculation, diuretics, vascular medicines and vitamin preparations. Although the panel of the American Academy of Otolaryngology-Head and Neck Surgery in the recommendation issued a warning against routinely prescribing antivirals, thrombolytics, vasodilators, vasoactive substances, or antioxidants to patients with idiopathic sudden sensorineural hearing loss (ISSNHL) by clinicians [18].

Thus, pharmacotherapy combined with HBO therapy can be a good method of effective ISSNHL treatment perhaps allowing clinicians to reduce effective doses of steroids.

The aim of the study was to evaluate the effectiveness of pharmacotherapy combined with hyperbaric oxygen therapy in the treatment of idiopathic sudden sensorineural hearing loss.

MATERIALS AND METHODS

The study was carried out on 40 patients with sudden hearing loss, admitted to the Department of Otolaryngology, Laryngological Oncology, Audiology, and Phoniatrics of the Military Medical Academy Teaching Hospital in Lodz. The patients were divided into two groups: group I with 24 patients treated with the pharmacotherapy combined with hyperbaric oxygen therapy and group II with 16 patients treated only pharmacologically.

The history of the disease was taken from all patients and laryngological examination, audiometric screening, blood tests, chest radiographs and ECG were per-

Table 1. Treatment regimen for pharmacotherapy and hyperbaric oxygen therapy

	Drug	Dose
Pharmacotherapy	Prednisone p.o.	Immediately, after admission to the hospital, in the morning, after a meal 60 mg p.o. once a day for 7 days and next 10 mg less per every 2 days
	Ranitidine	2 x 150 mg p.o.
	Vinpocetine	5 mg/ml i.v. 2 times a day 1 amp.
	Piracetam	200 mg/ml i.v. once a day 1 amp.
Hyperbaric oxygen therapy	15 of compression in condition 2,5 ATA – 90 min.	

formed. Because of the risk of additional noise overload of the injured ear, magnetic resonance imaging (MRI) and auditory brainstem response testing (ABR) were not performed until a week or later after the acute hearing loss. The protocol of pharmacotherapy included steroids, nootropics (the management is shown in Table 1).

In all patients, the percentage of hearing loss for the selected frequencies was assessed according to the Sabine and Fowler method before and after the therapy. The patients from Group 1 were treated in the Centre of Hyperbaric Therapy CREATOR Ltd. in Lodz. They were given a combination of hyperbaric oxygen therapy with steroid therapy. Hyperbaric oxygen therapy was conducted in a multiplace chamber (12 patients). Each patient had 15 sessions on 15 subsequent days with a weekend break. The procedure started with gradual increase in air pressure up to 2.5 ATA, which took about 10 min. In the pressurized chamber, the patients were exposed to 100% oxygen for 20 minutes, three times within a session, with a 5-minute break between treatments. Each session lasted about 90 minutes. After each session, hearing was evaluated with the use of tone audiometry and auditory evoked potentials in all patients. Each patient subjectively assessed hearing recovery using Numeric Rating Scale (NRS 0-10) from 0 to 10 points, where 0 means no improvement and 10 means the best possible hearing improvement.

The results of the audiometry obtained before and after the therapy were statistically analysed with the use of non-parametric tests: Kruskal-Wallis H test, Mann-Whitney U test, and multivariate regression model with mixed effects and flexible standard errors were used to assess the statistical significance of the investigated variables. The results were accepted as statistically significant when $p < 0.05$. Stata®/Special Edition 14.2 (Stata Corp LLC, College Station, Texas, USA) was used for calculations.

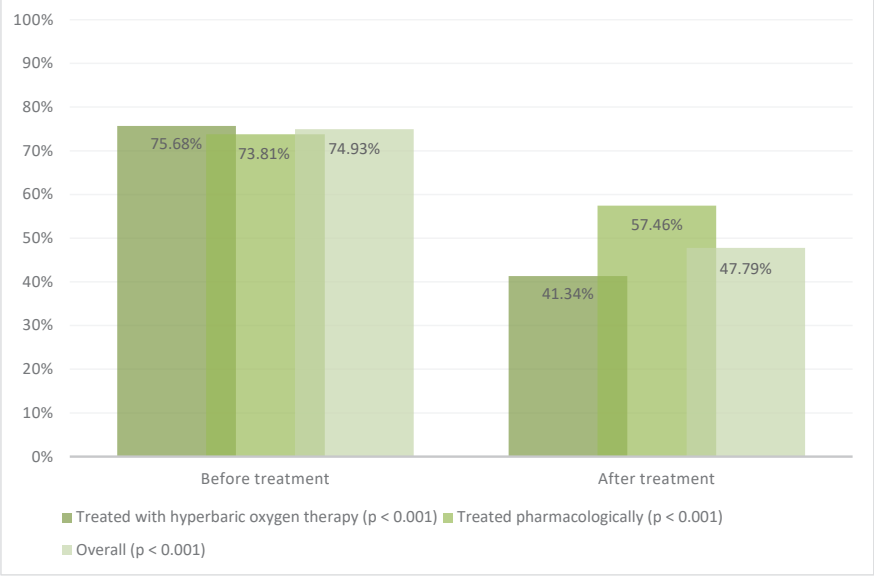

Fig. 1. The average hearing loss (%) before and after treatment in both groups

RESULTS

Patients between 33 and 77 years of age (mean age 52.4 years) included 21 women and 19 men. Group I consisting of 24 patients and it included 11 women and 13 men (mean age 54.3 years), and Group II contained 16 patients – 10 women and 6 men (mean age 49.56 years). In group I, the average hearing loss before the treatment was 75.68% and thereafter 41.34%, in Group II, 73.81% and 57.46%, respectively (Fig. 1). The mean hearing improvement in all patients was 27.14%, in Group I – 34.4% and in Group II – 16.35% (Table 2).

Below, the results of the multivariate analysis of changes in the investigated parameters over time (before and after the treatment), considering age, sex and the duration of the ailments in the examined patients are presented.

Hearing thresholds: at 250 Hz, there were no statistically significant correlations between the frequency and age (p = 0.598), sex (p = 0.177) or duration of symptoms (p = 0.967); at 500 Hz, no statistically significant correlations between the frequency and age (p = 0.601), sex (p = 0.197) or duration of symptoms (p = 0.973) were noted; at 1000 Hz, no statistically significant correlations

Table 2. Descriptive statistics of the age (years) and percentage of hearing loss (%) before *versus* after treatment for group I and II with overall summary

Patient groups	Investigated trait	Statistical parameter			
		M	SD	CI 95%	Min. – max.
Group I – (treated with hyperbaric oxygen therapy and pharmacotherapy, n = 24)	Age (years)	54.3	13.6	48.5–60.0	33.0–77.0
	Hearing loss prior to treatment (%)	75.7	22.9	66.0–85.3	11.1–100.0
	Hearing loss after treatment (%)	41.3	28.9	29.1–53.5	1.0–95.8
	Mean absolute improvement in hearing loss (%)	34.3	24.8	23.9–44.8	2.5–94.1
	Mean relative improvement of hearing loss (%)	48.1	31.9	34.6–61.5	4.1–98.9
Group II – (treated pharmacologically, n = 16)	Age (years)	49.6	13.4	42.4–56.7	26.0–67.0
	Hearing loss prior to treatment (%)	73.8	27.1	59.4–88.2	31.5–100.0
	Hearing loss after treatment (%)	57.5	30.1	41.4–73.5	1.8–94.1
	Mean absolute improvement in hearing loss (%)	13.6	9.8	11.1–21.6	3.8–34.2
	Mean relative improvement of hearing loss (%)	27.7	24.9	14.5–41.0	4.1–94.3
Overall (n = 40)	Age (years)	52.4	13.6	48.1–56.7	26.0–77.0
	Hearing loss prior to treatment (%)	74.9	24.3	67.1–82.7	11.1–100.0
	Hearing loss after treatment (%)	47.8	30.1	38.2–57.4	1.0–95.8
	Mean absolute improvement in hearing loss (%)	27.1	21.9	20.1–34.1	2.5–94.1
	Mean relative improvement of hearing loss (%)	39.9	30.7	30.1–49.7	4.1–98.9

M – mean, SD – standard deviation, 95%CI – confidence interval, min-max – minimum-maximum

between the frequency and age (p = 0.540), sex (p = 0.307) or duration of symptoms (p = 0.896) were present; at 2000 Hz, no statistically significant correlations between the frequency and age (p = 0.407) or sex (p = 0.373) were found, but there was a statistically significant interdependence between the frequency and duration of symptoms (p = 0.035); at 3000 Hz, there were no statistically significant correlations between the frequency and age (p = 0.452) or sex (p = 0.337), but a statistically significant relationship between the frequency and the duration of the disease was found (p = 0.032); at 4000 Hz, there was no statistically significant correlation between the frequency and age (p = 0.234) or sex (p = 0.247), but a statistically significant relationship between the frequency and duration of the disease (p = 0.012) was observed; at 6.000 Hz, there was no statistically significant correlation between the frequency and age (p = 0.099) or sex (p = 0.250), but a statistically significant relationship between the frequency and duration of the disease was found (p = 0.028). Long duration of hearing loss before the treatment with hyperbaric oxygen or pharmacotherapy had a negative effect at high frequencies (2 kHz), i.e. delaying the treatment may decrease the effectiveness of treatment (Table 3).

Table 3. Descriptive statistics of the hearing thresholds (dB) by pulse frequency (Hz) before *versus* after treatment for group I

Stage of the study	Frequency (Hz)	Statistical parameter						
		M	Me	$Q_1 – Q_3$ (IQR)	SD	SE	95% CI	Min. – max.
Before treatment	250	61.2	65.0	40.0–90.0 (50.0)	28.8	5.9	52,0–76.3	20.0–120.0
	500	65.6	60.0	42.5–92.5 (50.0)	29.0	5.9	53.4–77.9	20.0–120.0
	1000	65.6	60.0	40.0–90.0 (50.0)	29.5	6.0	53.2–78.1	20.0–120.0
	2000	74.4	75.0	60.0–90.0 (30.0)	24.9	5.1	63.9–84.9	20.0–120.0
	3000	76.2	80.0	60.0–97.5 (37.5)	26.7	5.4	65.0–87.53	20.0–120.0
	4000	80.2	87.5	60.0–100.0 (40.0)	26.4	5.4	69.1–91.3	30.0–120.0
	6000	81.2	87.5	67.5–100.0 (32.5)	29.2	6.0	68.9–93.6	20.0–120.0
	8000	82.1	85.0	65.0–110.0 (45.0)	30.8	6.3	69.1–95.1	20.0–120.0
After treatment	250	40.6	40.0	20.0–55.0 (35.0)	23.4	4.8	30.8–50.5	10.0–90.0
	500	38.1	35.0	20.0–55.0 (35.0)	24,0	4.9	28,0–48.3	10.0–100.0
	1000	39.6	37.5	25.0–50.0 (25.0)	22.4	4.6	30.1–49.0	10.0–100.0
	2000	45.2	40.0	30.0–62.5 (32.5)	25.2	5.1	34.6–55.8	10.0–90.0
	3000	48.7	45.0	27.5–67.5 (40.0)	26.4	5.4	37.6–59.8	10.0–100.0
	4000	51.7	50.0	30.0–70.0 (40.0)	27.8	5.7	39.9–63.4	10.0–100.0
	6000	55.2	55.0	30.0–75.0 (45.0)	27.7	5.7	43.5–66.9	10.0–100.0
	8000	57.5	60.0	35.0–85.0 (50.0)	28.9	5.9	45.3–69.7	10.0–100.0

M – mean, Me – median, Q1–Q3 (IQR) – interquartile range, SD – standard deviation, SE – standard error, 95%CI – confidence interval, min–max – minimum–maximum. Level of statistical significance (p–value) <0.001

The percentage of hearing loss: at 500 Hz, no statistically significant correlations between the frequency and the investigated variables: age (p = 0.705), sex (p = 0.118) or duration of symptoms (p = 0.822) were found; at 1000 Hz, there was no statistically significant correlation between the frequency and age (p = 0.839), sex (p = 0.185) or duration of symptoms (p = 0.807); at 2000 Hz, there was no statistically significant correlation between the frequency and age (p = 0.341) or sex (p = 0.159), but a statistically significant relationship between the frequency and duration of symptoms (p = 0.022) was found; at 4000 Hz, there was no statistically significant correlation between the frequency and age (p = 0.277) or sex (p = 0.274), but a statistically significant relationship between the frequency and duration of the disease was observed (p = 0.015). The total result showed that no statistically significant correlations between frequencies and age (p = 0.638), sex (p = 0.145) or duration of symptoms (p = 0.107) were found.

Delaying sudden hearing loss treatment decreased the chances of improvement in hearing for the frequencies f = 2 kHz and f = 4 (Table 4).

Evoked potentials: wave I latency, no statistically significant improvement was recorded (p = 262); wave III latency, no statistically significant correlation between latency and age (p = 0.239), sex (p = 0.909) or duration of symptoms (p = 0.256) was observed; wave V latency, no statistically significant relationship between age (p = 0.761) or duration of symptoms (p = 0.542) was noted, while statistically significant correlation between wave V latency and sex (p = 0.042) was found, i.e. a better therapeutic effect was observed in women. Considering I-V inter-peak latency, no significant increase in the interval (p = 0.224) was noticed (Table 5).

Subsidence or decrease in the intensity of symptoms were reported by about 83% of the patients; 33.3% of the patients reported improvement in the numerous rating

Table 4. Descriptive statistics of the percentage of hearing loss (%) by pulse frequency (Hz) before *versus* after treatment and overall summary for group I

Stage of the study	Frequency (Hz)	Statistical parameter						
		M	Me	$Q_1 – Q_3$ (IQR)	SD	SE	95% CI	Min. – max.
Before treatment	500	10.2	11.3	5.6–15.0 (9.4)	5.1	1.1	8.0–12.3	1.1–15.0
	1000	20.8	21.5	13.0–30.0 (17.0)	9.7	2.0	16.7–24.9	2.1–30.0
	2000	30.3	34.0	28.0–39.2 (11.2)	9.9	2.0	27.1–35.4	2.9–40.0
	4000	13.5	14.9	12.4–15.0 (2.7)	4.5	0.9	11.6–15.4	5.0–27.0
	Sum	75.7	73.9	62.5–99.2 (36.7)	22.9	4.7	66.0–85.4	11.1–100.0
After treatment	500	5.2	3.8	1.10–9.5 (8.4)	5.0	1.0	3.1–7.3	0.2–15.0
	1000	11.5	10.2	3.8–18.6 (14.9)	9.9	2.0	7.3–15.7	0.3–30.0
	2000	16.7	12.5	7.3–29.1 (21.8)	13.0	2.7	11.2–22.2	0.4–39.2
	4000	7.9	8.0	2.7–13.5 (10.8)	5.7	1.1	5.6–10.3	0.1–15.0
	Suma	41.3	44.6	19.2–63.4 (44.2)	28.9	5.9	29.1–53.5	1.0–95.8
Absolute improvement		34.3	35.5	12.0–50.3 (38.3)	24.8	5.1	23.9–44.8	2.5–94.1
Relative improvement		48.1	50.6	17.5–76.5 (60.0)	31.9	6.5	34.6–61.5	4.1–99.0

M – mean, Me – median, Q_1–Q_3 (IQR) – interquartile range, SD – standard deviation, SE – standard error, 95%CI – confidence interval, min–max – minimum–maximum. **Level of statistical significance (p–value) <0.001**

Table 5. Descriptive statistics of the evoked potentials (mV) by inter-peak latency before *versus* after treatment for group I

Stage of the study	Lead	Statistical parameter						
		M	Me	$Q_1 – Q_3$ (IQR)	SD	SE	95% CI	Min. – max.
Before treatment	I	1.9	1.9	1.7–2.0 (0.3)	0.3	0.1	1.7–2.0	1.2–2.4
	III	4.2	4.1	3.8–4.5 (0.7)	0.3	0.1	4.0–4.3	3.7–4.6
	V	6.2	6.1	5.9–6.3 (0.4)	0.3	0.1	6.0–6.3	5.8–6.9
	Interval I–V	4.3	4.2	3.9–4.7 (0.8)	0.5	0.1	4.1–4.6	3.7–5.3
After treatment	I	1.8	1.8	1.5–1.9 (0.4)	0.3	0.1	1.6–1.9	1.3–2.5
	III	4.0	4.0	3.8–4.3 (0.5)	0.4	0.1	3.8–4.9	3.3–4.7
	V	6,0	6,0	5.7–6.1 (0.4)	0.3	0.1	5.8–6.1	5.5–6.5
	Interval I–V	4.2	4.1	3.9–4.6 (0.7)	0.4	0.1	4.0–4.4	3.6–5.1

M – mean, Me – median, Q_1–Q_3 (IQR) – interquartile range, SD – standard deviation, SE – standard error, 95%CI – confidence interval, min–max – minimum–maximum. **Level of statistical significance (p–value) <0.001**

scale (NRS) (0–10) up to 10 points, which showed subjective improvement in hearing compared with the onset of sudden hearing loss (Table 6). No adverse effects were observed in patients treated in a hyperbaric chamber.

DISCUSSION/CONCLUSION

In the research on ISSHL, there have been many attempts to find effective treatment, which consider the mixed etiology of this disease. Heuschkel et al. in a population-based study on healthcare draw attention to the fact that inpatient treatment of ISSNHL is variable in clinical practice and still no effective treatment can be stated. Their study conducted on 490 inpatients showed that 51% of the patients reached a ΔPTAabs (median absolute hearing gain) of ≥10 dB. About 2 out of 5 patients recovered to a ΔPTArel contral (median relative hearing gain in relation to the contralateral side) ≥50% or reached ≤10 dB of the contralateral ear. They found no association between prior outpatient prednisolone treatment and better recovery after hospital therapy [5]. According to Tsounis et al., no statistically significant differences were found in treatment with the systemic, intratympanic and combined steroid administration in the primary treatment of idiopathic sudden hearing loss [20]. On the other hand, de Sousa et al. in a systematic review of research data on 611 patients stated that the vasodilators are not a good therapeutic option in ISSHL, but there is evidence that combination of vasodilators with steroid treatment may be effective [2]. HBO is the only known method that increases partial pressure of oxygen in the inner ear. Lamm et al., in experimental studies, showed that there is an increase in the cochlear microphonics in guinea pigs after postmortem HBO treatment. They also found a 204% increase in the partial pressure of O_2 in the cochlea, when a pure oxygen atmosphere was used. However, when the pressure was increased to about 1.6 B, the partial pressure of oxygen increased by 563% compared to the initial values. It was also observed that the increased O_2 partial pressure maintained after the therapy in the hyperbaric cham-

Table 6. Descriptive statistics of the subjective scale for the hearing improvement (NRS) in group I

Investigated trait	Statistical parameter						
	M	Me	$Q_1 – Q_3$ (IQR)	SD	SE	95% CI	Min. – max.
NRS (pts.)	6.0	5	3–10 (7)	3.6	0.7	4.5–7.5	0–10

M – mean, Me – median, Q_1–Q_3 (IQR) – interquartile range, SD – standard deviation, SE – standard error, 95%CI – confidence interval, min–max – minimum–maximum.

ber [10]. It is known that the arterial partial oxygen saturation and the oxygen tension of the inner ear affect the hearing process in patients with idiopathic sudden sensorineural hearing loss who have had the oxygen tension of the perilymphatic fluid reduced [13]. The results of our investigations show that the combination of pharmacotherapy and hyperbaric oxygen treatment causes a significant improvement in hearing. The use of monotherapy may seem to be useful to assess a particular treatment. However, this is not possible due to the multifactorial background of sensorineural hearing loss and unknown aetiology. Attention should be drawn to the fact that the important factor of therapeutic success is the time of implementation. Similarly to the results from studies by Jadczak et al., our results confirm that the time of implementation of pharmacotherapy influences the final result of the therapy. According to our results, the long duration of hearing loss before the treatment with pharmacotherapy or hyperbaric oxygen had a negative effect at high frequencies. It seems vital to start therapy as soon as possible, even before hospitalization [6]. A quick diagnosis, referral to a specialist and implementation of treatment seem to be decisive for future prognosis. Many authors emphasize HBO as a valuable complement to existing methods of treatment of sudden hearing loss [14, 21]. The usefulness of combined therapies with HBO is confirmed by Pezzoli at al.'s research on patients who have experience deafness for a period of 4 weeks and who failed primary corticosteroid treatment. According to the authors, the patients with SSHL treated by means of HBO showed significant improvement in pure tone hearing thresholds with the mean improvement of 15.6 dB (SD ± 15.3) as compared to untreated patients, who exhibited a spontaneous mean improvement of 5.0 dB (SD ± 11.4) [14]. Particularly interesting are Yong at al.'s investigations, which used combined ITS and HBO as salvage treatment in patients with SSNHL after failure of systemic therapy. They found significantly larger hearing gains in PTA and better word recognition after combined therapy [21]. Our combined therapy allowed us to achieve improvement in NRS (0-10) up to 10 points in 33.3% of the patients, which gave subjective improvement in hearing compared with the onset of sudden hearing loss. The use of high doses of steroids and their continuous oral therapy should be controlled because of their side effects. Contraindications for the use of systemic steroids include Cushing's syndrome, diverticulitis, peptic ulcer disease and bleeding ulcers, diabetes, heart failure, myasthenia gravis, osteoporosis, psychosis, and renal disease [4]. On the other hand, it is known that increased oxygen pressure may be beneficial for instant diabetic leg ulcers and diabetic retinopathy. However, there are also reports regarding the side effects of hyperbaric oxygen therapy in the form of ocular complications. Although the changes are of a short-lived nature, antioxidant dietary supplementation should be used, especially in older patients. Special care is indicated in cataract or age-related macular degeneration and keratoconus [12]. In the long term, we did not observe adverse reactions of treatment in a hyperbaric chamber in connection with combined pharmacotherapy, which indicates that the method seems to be safe.

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STATEMENT OF ETHICS

The study protocol has been approved by the Medical University of Lodz Bioethics Committee No: RNN/69/19/KE.

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