Hyperbaric oxygen therapy in idiopathic sudden sensorineural hearing loss (ISSNHL) in association with combined treatment

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ABSTRACT

The main basic effect of hyperbaric oxygenation (HBO_2) on the human body, in our study, was an increased partial pressure of oxygen resulting from an increased amount of oxygen dissolved in plasma. Thus the plasma can become capable of carrying enough oxygen to meet the needs of the body's tissues. From 1 January 2004 to 31 December 2007, a total of 61 patients (62 ears) received medical treatment at the ENT clinic of the 3rd Faculty of Medicine, Charles University, and at the Central Military Hospital in Prague. Treatment consisted of a combination of vasodilatation infusion treatment and HBO_2 therapy. The results were evaluated in a retrospective study. The overall percentage of patients showing improvement was 59.7%. However, for those patients who started HBO_2 treatment within 10 days of onset, complete recovery, or significant improvement was noted in 65.9%. In contrast, patients who started treatment after 10 days of onset, improvement was noted in only 38.9%. NMR examination revealed that two patients had vestibular schwannoma (also known as acoustic neuroma).

INTRODUCTION

The cause of idiopathic sudden sensorineural hearing loss (ISSNHL) is still not fully understood. There are numerous etiological factors resulting in a variety of theories proposed by otolaryngologists concerning the occurrence of ISSNHL, and each theory is associated with a somewhat different treatment approach.

The vascular theory is based on the hypothesis [1-5] that ISSNHL is likely caused by a partial or total closure of the cochlear vessel channel, while the virus theory suggests that hearing loss is caused by a viral infection. Based on these two theories, Fowler's hypothesis [1-5] claims that partial or complete occlusion of the cochlear vasculature may be caused by sludging (diminished microcirculation).

Viral infections can affect hearing loss in a variety of ways. By damaging erythrocytes, viruses can cause hemagglutination (proven *in vitro*), viremia may result in edema of capillary endothelial cells, and endocellulitis can initiate a state of slight hypercoagulation. These changes probably take place in association with the spiral ligament and in the stria vascularis [1-5].

Although a number of additional factors may be involved in the occurrence of ISSNHL, the relevant observation is that all of these etiologies lead to intra-auricular metabolism failure. In most cases it is assumed that it is the failure of the vascular elements that significantly contribute to the occurrence of hearing loss. Current treatment seeks to positively impact the vascular supply of the inner ear, thereby increasing oxygen delivery to damaged cells. HBO_2 treatment represents a method capable of markedly increasing oxygen supply to the affected areas [6,8-14].

Hyperbaric oxygen therapy works on the assumption that hemoglobin saturation in blood cells reaches a maximum at an arterial oxygen partial pressure (PO_2) of 100 mmHg and cannot be further increased. There is, however, the option of increasing the amount of oxygen dissolved in plasma. While 100 ml of plasma can typically transfer about 0.3 ml oxygen (0.3% vol.), by inhaling pure oxygen with zero overpressure (1 IATA – absolute pressure), the amount of oxygen physically dissolved in the plasma can be increased up to 2% vol. At an overpressure of 2 atmospheres (atm) (3 IATA), the amount of

oxygen physically dissolved in plasma increases to 6.6% vol., which is practically 20 times the normal volume. The effects of HBO_2 include complex changes associated with central hemodynamics, regional blood flow and microcirculation. It also seems to improve local metabolic conditions and acts as an effective therapeutic factor.

MATERIALS AND METHODS

During the review period (2004 - 2007), a total of 61 patients / 62 ears (40 males and 21 females) received medical treatment for ISSNHL with unknown etiology. The average patient age was 48 years and ranged from 19 to 78 years. All patients were treated using vasodilatative infusions containing corticosteroids in combination with HBO_2 therapy. Thirty-eight patients presented with hearing loss in the right ear only, 22 presented with hearing loss in the left ear only, and one patient presented with bilateral hearing loss.

Whereas the majority of patients received outpatient treatment, those patients who did not live in Prague were hospitalized during their treatment program [15-23]. A thorough and targeted patient history was followed by basic biochemical laboratory tests. Additionally, an ECG and internal, neurological, and ophthalmic examinations were performed.

All patients received a complete set of audiological tests including examination of stapedial reflexes and brain stem-evoked response audiometry (BERA) [24-28]. Hearing improvement was evaluated using a pure tone audiogram (PTA) to test:

(i) whether the threshold hearing curve had returned close to the "standard" (the term "standard" is taken to mean that the threshold curve at all frequencies does not exceed 20 dB);

(ii) whether it had significantly improved (*i.e.*, an improvement equal to, or exceeding, 20 dB on at least two impaired frequencies); or

(iii) whether there had been no improvement at all.

Prior to 2006, brain MRI scanning was reserved for patients suspected of having an organic focal lesion in the rear or middle cranial fossa. However, since 2006, all patients undergo MRI scanning without undue delay, ideally on the first day of medical assessment-treatment initiation [17-24,26,32-37].

Initial treatment consists of vasodilatative infusions, which involved application of 20 mg of vinpocetine in 250 ml of physiological solution (10-20 times), or 100 mg of pentoxifylline in 100 ml of physiological solution administered intravenously in combination with methylprednisolone administered intravenously over the first two days at a dose of 80 mg on Day 1 and 40 mg on Day 2. In patients presenting with endolymphatic hydrops, a single injection of furosemide (20 mg) was administered – one vial intravenously on the first day of treatment, followed by amiloride-hydrochlorothiazide p.o. (one tablet per day) for up to two weeks [13-23].

On completion of a basic internal examination, hyperbaric oxygen therapy was started in a hyperbaric chamber located at the Institute of Aviation Medicine. Therapy consisted of 10-20 exposures, administered four times a week. The stay in the hyperbaric pressure chamber, including compression and decompression, took approximately 90 minutes. Patients were in a spacious pressure chamber, inhaling oxygen at a pressure of 0.3 MPa (3 IATA) with one five-minute intermission after 30 minutes of treatment. During the intermission period patients inhaled normal, room air in the pressure chamber. The five-minute intermission from inhalation of 100% oxygen was to avoid the effects of oxygen toxicity. At the conclusion of HBO_2 therapy, patients were immediately administered vasodilatative infusions [5,14-22,29].

RESULTS

Of the 61 patients (62 ears) receiving treatment in combination with HBO_2, an overall improvement in hearing loss following treatment was noted in 37 patients (59.7%). Of these 37 patients, 16 (25.8%) came close to the "standard," and in 21 patients (33.9%) partial hearing improvement was achieved, with hearing improvement exceeding 20 dB in at least two impaired frequencies. In 25 patients (40.3%), there was either minimal or no hearing improvement. The pre- and post-treatment average audiogram is shown in Figure 1 *(facing page)*. Two patients who received partial benefit from HBO_2 treatment were diagnosed [via nuclear magnetic resonance (NMR)] as having vestibular schwannoma [8,30-37].

While vasodilatative infusion therapy was generally started on Day 10 when hypoacusis was present, HBO_2 treatment was often delayed until about Day 19. In 43 patients (44 ears) HBO_2 treatment started on or before Day 10 after onset of hearing loss, while the remaining 18 patients began treatment between Day 11 and Day 90.

In the group of 43 patients (44 ears) who received treatment no later than Day 10, improvement was noted to be 65.9%. Of these 43 (44 ears) patients, 14 patients (31.8%) returned to "standard," 15 patients improved (34.1%), while the remaining 15 patients (34.1%) showed

FIGURE 1

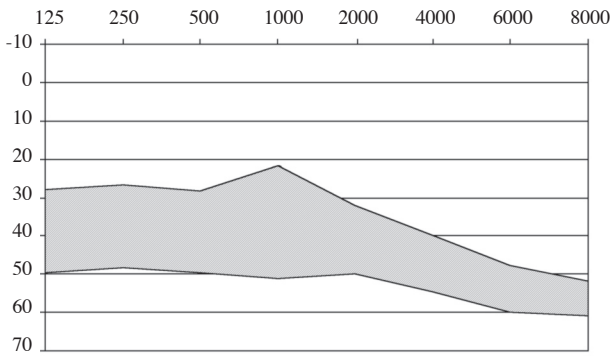

FIGURE 1 – Average pre- and post-treatment audiogram of 61 patients provided with combined HBO_2 and vasodilatative treatment.

FIGURE 2

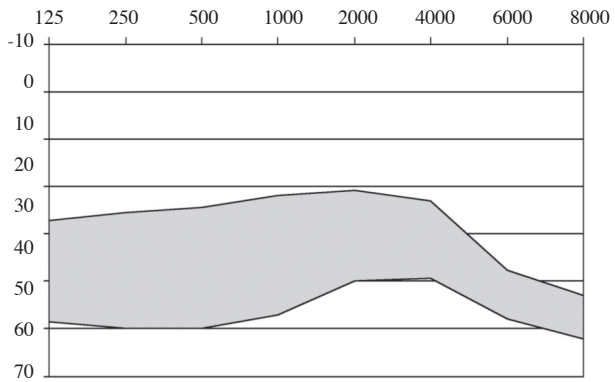

FIGURE 2 – Hearing improvement following HBO_2 treatment. Pre- and post- treatment average audiogram of seven patients provided with treatment after vasodilatative infusions had proven ineffective.

no improvement. In the group of 18 patients (18 ears) who started treatment between Day 11 and Day 90, an overall improvement was noted in 38.9% of the cases (seven of 18 patients). Two patients (two of 18) (11.1%) returned to "standard," and an overall improvement was observed in five (five of 18) patients (27.8%), while 11 (11 of 18) patients (61%) showed no sign of improvment *(Figure 1)*.

Among the 61 patients (62 ears receiving treatment) there was a group of seven patients (seven ears) who were initially treated without success; vasodilatative infusion treatment for those patients started about Day 15 (average = 14.7 days). Because of the minimum effect of the vasodilatative medications, the patients were subsequently treated with HBO_2 therapy. However, HBO_2 therapy started between Day 30 and Day 60 (average = Day 44). Improvement to "standard" occurred in two patients, while significant improvement was noted in five other patients. At the respective frequencies, average improvements were noted as follows *(Figure 2, above, right)*:

- 125 Hz / 21.4 dB;
- 250 Hz / 24.3 dB;
- 500 Hz / 25.7 dB;
- 1,000 Hz / 25 dB;
- 2,000 Hz / 19.3 dB;
- 4,000 Hz / 16.4 dB;
- 6,000 Hz / 10 dB; and
- 8,000 Hz / 9.2 dB.

Within this set of HBO_2-treated patients, a significant impairment at frequencies of 1,000 Hz and 2,000 Hz was apparent – *i.e.*, a drop in the audiometric curve to 50.9 dB and 49.8 dB at 1 kHz and 2 kHz frequencies, respectively. After treatment, a 29.2-dB and 17.9-dB improvement (up to 21.7 dB and 31.9 dB at 1,000 Hz and 2000 Hz frequencies, respectively) was achieved *(Table 1, right)*.

TABLE 1

Treatment success rate on 1000 Hz and 2000 Hz frequencies

	Average losses prior to treatment (dB)		**Average losses after treatment (dB)**		**Improvement (dB)**	
	1000	2000	1000	2000	1000	2000
After treatment with HBO_2	50.9	49.8	21.7	31.9	29.2	17.9

It has been statistically evaluated and established that improvement in hearing depends, from a statistical point of view (with the significance level 0.05), on the elapsed time between diagnosis and initiation of HBO_2 treatment. There was significantly more improvement in patients when the treatment was commenced in a timely fashion – *i.e.*, within 10 days *(Table 2, below)*.

TABLE 2

		Improvement		**Total**
		No	Yes	
Commenced	within 10 days	15	29	44
	11 and more	11	7	18
Total		26	36	62

Tested by the chi-square test p=0.05

Because of medical, legal and ethical restrictions in the Czech Republic regarding the use of placebo, we are unable to provide comparison results with a group of patients with untreated ISSNHL.

DISCUSSION

The importance of a sufficient oxygen supply to inner ear structures has been experimentally demonstrated many times. Oxygen insufficiency causes a drop of the positive endo-cochlear potential which affects [1-6] the transport of ions from the perilymph via Reissner's membrane [1-6]. It also affects the activity/function of the stria vascularis, which is assumed to act as an ion pump, maintaining a high concentration of potassium and a low concentration of sodium in the endolymph. It is the function of the latter that requires the greatest amount of oxygen [1,4,5,7].

Under normal circumstances, the most important method of oxygen transfer to tissues is oxygen released from hemoglobin. With 100 ml of blood averaging about 15 g of hemoglobin, and given that 1 g Hb is capable of transferring 1.34 ml oxygen, then 100 ml of blood can chemically bind 20.1 ml of oxygen. Compared to that amount, the proportion of oxygen physically dissolved in plasma is physiologically negligible since 100 ml of plasma can carry only 0.3 ml of oxygen (0.3% vol.) [1,4,6].

When inhaling pure oxygen with zero overpressure (1 IATA) the amount of oxygen, physically dissolved in plasma increases to 2% vol. However, at 1 atm overpressure (2 IATA) the amount of oxygen physically dissolved in plasma reaches 4.3% vol., and at 2 atm pressure (3 IATA) the volume of dissolved oxygen reaches a level of 6.6% vol., which is approximately 20 times the volume at normal PO_2. This increase in the amount of oxygen physically dissolved in plasma is able to meet the oxygen requirements of tissues almost entirely, because under basal conditions the arteriovenous differential tends to range between 5-6% vol. of oxygen.

In addition to the extra oxygen dissolved in plasma, there is also an increase in the amount of oxygen physically dissolved in the interstitial fluid and cellular cytoplasm [1,4,6,14]. In some cases, blood cell clusters are formed, these prevent red blood cells and the oxygen carried by hemoglobin from further penetration into the vascular network; however, these clusters do not prevent the flow of oxygen-enriched blood plasma. By increasing the proportion of oxygen physically dissolved in plasma we are able to compensate for the lack of oxygen delivered by hemoglobin [1,5,14,15,17,19,20,22].

In our set of patients, there was an apparent difference in the success of HBO_2 treatment based on when treatment was initiated, *i.e.,* sooner than 10 days after hearing loss onset or longer than 10 days after onset. In patients receiving timely HBO_2 treatment, the success rate was 65.9% versus 38.9% for those who received delayed treatment. Overall, the treatment success rate in patients receiving HBO_2 treatment was 59.7%. Japanese authors Fujimura *et al.* had the same results, 59.7% [17], Kawamata *et al.* showed 64.8% success from HBO_2 therapy [38], and Croatian authors Racic *et al.* reported a success rate of 47.1% [39].

CONCLUSION

With the etiology of sudden sensorineural hearing loss still unclear, idiopathic sudden sensorineural hearing loss (ISSNHL) represents a major health problem, with an uncertain prognosis. For patients, who have seen the significant accomplishments offered during this age of scientific and medical advances, failure to restore their hearing, or even offer a straightforward explanation for the impairment, is hard for them to understand.

Based on our experience, we believe that timely HBO_2 treatment started during the first 10 days following onset of hearing loss is more effective than treatment delayed, even if delayed by only a few weeks. It is also significant that in seven patients in our study who were initially but unsuccessfully treated with infused medication, hearing quality was still markedly improved following HBO_2 treatment, despite treatment beginning well after, what we consider, to be the optimal time period. This observation gives further credence to the impact and potential of HBO_2 treatment in ISSNHL. Expertise gained from extensive experience in our ENT department appears to indicate that a combination of treatment with medication and HBO_2, especially when administered in a timely fashion, clearly improves the state of hearing and is therefore, fully indicated.

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