Hyperbaric oxygen therapy for idiopathic sudden sensorineural hearing loss

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ABSTRACT

Idiopathic sudden sensorineural hearing loss (ISSHL) is the newest indication approved by the Undersea and Hyperbaric Medical Society’s Hyperbaric Oxygen Therapy Committee. Idiopathic sudden sensorineural hearing loss appears to be characterized by hypoxia in the perilymph and therefore the scala tympani and the organ of Corti. A review of the literature reveals more than 100 publications evaluating the use of hyperbaric oxygen (HBO2) for the treatment of ISSHL, including eight randomized controlled trials.

The best and most consistent results are obtained when HBO2 is initiated within two weeks of symptom onset and combined with corticosteroid treatment. The average hearing gain is 19.3 dB for moderate hearing loss and 37.7 dB for severe cases. This improvement brings hearing deficits from the moderate/severe range into the slight/no impairment range. This is a significant gain that can markedly improve a patient’s quality of life, both clinically and functionally.

PROCESS OF ‘NEW INDICATION’ APPROVAL

An individual or group may, after a thorough review of the literature, request a convening of the Undersea and Hyperbaric Medical Society’s Hyperbaric Oxygen Therapy Committee, for consideration of a new indication. If this request is granted, the Committee will ask for, and assign, two presenters. One side presents the “pro” argument and the other the “con” argument.

The “pro” argument is usually presented by the individual or group requesting the review. Presentations are given before the Hyperbaric Oxygen Therapy Committee at the UHMS Annual Scientific Assembly. If a quorum is present, the Committee votes on the proposal following the presentations.

This newest indication, ISSHL, followed this pathway toward acceptance. It was proposed and presented by the LSU Undersea and Hyperbaric Medicine Fellowship. It was favorably voted upon following deliberations at the UHMS Committee Meeting in Fort Worth in June 2011. It was ratified by the UHMS Executive Board in October 2011.

THE ‘PRO’ ARGUMENT

While there is a large body of literature comparing therapeutic interventions for the treatment of idiopathic sudden sensorineural hearing loss (ISSHL), only a small number of controlled studies have been performed. Moreover, there has not been a clear consensus for treatment. More than 60 protocols have been described [1]. However, when the three most prominent and efficacious treatments – corticosteroids, vasodilators and hyperbaric oxygen (HBO2) – were systematically reviewed by meta-analyses from the Cochrane Collaboration, only the use of HBO2 received multiple, positive, objective, critical reviews [2-4]. The Cochrane reviews for the use of HBO2 (2005, 2007 and 2010) were all conservatively favorable. The 2005 review found that “HBO2 did improve hearing” [2]. Both the
2007 and 2010 updates concluded that “For people with acute ISSHL, the application of HBO₂ significantly improved hearing, but the clinical significance remains unclear” [3, 4]. The average hearing gains found to have “unclear clinical significance” are 19.3 dB for moderate loss (hearing aids recommended) and 37.7 dB for severe loss (hearing aids required, lip-reading recommended). Importantly, these gains improve hearing function into the normal range [5].

The World Health Organization lists hearing loss as the number one cause of disability globally, just ahead of refractive errors, and well ahead of depression, cataracts and accidental injuries, which round out the top five [6]. Acquired hearing loss is also the third leading cause of years lost due to disability [6]. It stands to reason that the significant improvements in hearing gains found with adjunctive HBO₂ therapy are functionally important [7]. The reported spontaneous recovery rate for ISSHL is 65% (Mattox and Simmons, 1977) [8]. However, this early work regarding the spontaneous recovery rate is currently contended by most clinical otolaryngologists as an overestimation [9].

Appropriate patient selection is paramount, and the literature suggests that these patients benefit the most from the use of adjunctive HBO₂: those with moderate to profound hearing loss [1, 10-24]; those who receive early HBO₂ therapy [1, 11-17, 19-23, 25-36]; those who receive both corticosteroids and HBO₂ [1, 11-15, 23, 25, 30, 32; and patients younger than 60 years old [13, 32, 34]. While it is conceded that these studies do not have sham controls, and many are unblinded, the treatment of ISSHL with HBO₂ does have eight prospective randomized controlled trials (four in peer-reviewed journals and four in proceedings) and is the only reviewed ISSHL treatment found by the Cochrane Collaboration to be significantly efficacious [2-4].

Multiple controlled studies have demonstrated a clinically and statistically significant degree of hearing improvement when patients receive early concomitant therapy with HBO₂ and oral corticosteroids [1, 10-15, 25]. Additionally, the most recent clinical practice guidelines for sudden hearing loss published by the American Academy of Otolaryngology – Head and Neck Surgery Foundation gave the use of adjunctive HBO₂ a Grade B Level of Evidence (randomized controlled trials; overwhelmingly consistent evidence from observational studies). This is significant, as there was no Grade A Level of Evidence for any other diagnostic tests, treatments, or regimens put forth in these guidelines [9].

**THE ‘CON’ ARGUMENT**

The difficulty of establishing efficacy of any treatment for idiopathic hearing loss is illustrated by a prospective study, in which 65% recovered completely to functional hearing levels spontaneously and independent of any type of medical treatment, with the majority doing so within 14 days [8]. Since then there have been several studies of the efficacy of corticosteroids (which are the preferred treatment by most otolaryngologists) and HBO₂.

Of the studies evaluating HBO₂, only four prospective randomized controlled studies have been published in peer-reviewed journals [13, 16, 17, 37]. In two of these studies, HBO₂ was instituted within 14 days of symptom onset; in the other study, HBO₂ was instituted within two days. These studies showed some benefit of HBO₂. However, no studies of HBO₂ in hearing loss have been appropriately blinded, and there are no prospective studies showing benefit when HBO₂ is initiated more than two weeks after symptom onset.

A recent Cochrane Review concluded that there is limited evidence from methodologically poor studies that HBO₂ improves hearing in patients with ISSHL who present within two weeks of hearing loss, with no evidence that any improvement achieved is functionally important [4]. One major weakness of the available data is that while HBO₂ seems to help some patients, particularly those treated early, there is no useful information to guide patient selection. The perilymph pO₂ measurements are at best suggestive that some cases of ISSHL are associated with lower pO₂. However, there is no definitive evidence to suggest that hypoxia is the cause. What might be interpreted as intriguing preliminary results should provide the impetus for a definitive study.
INTRODUCTION

Idiopathic sudden sensorineural hearing loss (ISSHL) is classically defined as a hearing loss of at least 30 dB occurring within three days over at least three contiguous frequencies [38]. A common clinical presentation involves an individual experiencing a sudden unilateral hearing loss, tinnitus (nearly universal), a sensation of aural fullness, dizziness and vertigo [9, 39].

The symptoms are often subtle enough, “fullness/blocked,” that they are overlooked by both the patient and the clinician until hearing loss becomes severe. The incidence is estimated at five to 20 cases per 100,000 per year in the United States [40]. This translates into approximately 4,000 new cases annually in the United States [41]. However, the incidence may be higher, as many cases are likely unreported. Additionally, it has been estimated that as many as 65% of cases may resolve spontaneously; however, this number has been recently questioned [8, 9].

The etiologies of ISSHL remain unclear. Several pathophysiological mechanisms have been described including: vascular occlusion, viral infections, labyrinthine membrane breaks, immune associated disease, abnormal cochlear stress response, trauma, abnormal tissue growth, toxins, ototoxic drugs and cochlear membrane damage [1].

Hearing loss imposes a heavy social and economic burden on the individual as well as the community. When hearing loss is in the slight impairment range (26 dB-40 dB), patients are able to hear and repeat spoken words in a normal voice at 1 meter and may only need counseling for treatment. However, when hearing loss is moderate (41 dB-60 dB) or severe (61 dB-80 dB), hearing aids are usually recommended and when not available, lip-reading and signing should be taught [7].

Hyperbaric oxygen therapy has been shown to impart a 37.7 dB improvement in hearing gains to those with a severe hearing deficit and a 19.3 dB improvement in those with moderate hearing deficits. This resolves the impairment toward the normal range, and may dramatically affect quality of life and obviate the need for hearing aids.

COST IMPACT

There are no formal detailed cost analyses for ISSHL in the literature. However, the World Health Organization (WHO) has described the cost impact of hearing loss. Hearing impairment makes it difficult to obtain, perform and keep jobs, and the hearing-impaired are often stigmatized and socially isolated. The cost of special education and lost employment due to hearing impairment imposes a heavy social and economic burden [5]. Adult onset hearing loss is the most common cause of disability globally, and the third leading cause of years lost due to disability. Moreover, adult onset hearing loss is the 15th leading cause of burden of disease, and is projected to move up to seventh by the year 2030 [6].

Hearing aids cost between $1,500 and $3,000 per pair, require replacement every three to five years and they don’t always give the patient fully functional hearing. The cost of 10 hyperbaric treatments at an average outpatient facility ranges between $2,000 and $5,000.

Although additional studies are recommended to further define the pathology and optimize the treatment of ISSHL, based on the current medical evidence, the use of HBO₂ outweighs the risk. Furthermore, significantly improving a patient’s hearing and minimization of the social and economic burden of this disease outweighs treatment costs.

RATIONALE

The use of hyperbaric oxygen therapy in the treatment of ISSHL

The rationale for the use of hyperbaric oxygen to treat ISSHL is supported by an understanding of the high metabolism and paucity of vascularity to the cochlea. The cochlea and the structures within it, particularly the stria vascularis and the organ of Corti (OOC), require a high oxygen supply [42]. The direct vascular supply, particularly to the OOC, is minimal [44]. Tissue oxygenation to the structures within the cochlea occurs via oxygen diffusion from cochlear capillary networks into the perilymph and the cortilymph [43]. The perilymph is the primary oxygen source for these intracochlear structures.

One study investigated perilymph pO₂ in anesthetized humans during surgical exploration of the ear 13 days to 15 years following hearing loss and found that the perilymph pO₂ tended to be lower (8.6 ± 2.8 mm Hg, range 4.0-12.5 mm Hg) in the seven patients with ISSHL than those patients with otosclerosis (mean 11.7 ± 10.0 mm Hg, range 2.2 - 27.3 mm Hg), sudden cochleovestibular loss (mean 10.6 ± 9.1 mm Hg, range 3.3 - 23.1 mm Hg), or rapidly progressive sensorineural hearing loss (16.7 ± 8.2 mm Hg). They observed no correlation between the degree of hearing loss and perilymph pO₂, but commented that these measurements suggest that some cases of ISSHL may be due to ischemia [44]. Later animal studies confirmed that normobaric oxygen
increases perilymph pO₂ 3.4-fold, while HBO₂ increases the perilymph pO₂ 9.4-fold compared to room air [43]. Although normobaric hyperoxygenation increases intracochlear oxygen tensions, only HBO₂ achieves the extremely high arterial perilymphatic oxygen concentration differences [43, 45, 46]. The concept that the efficacy of HBO₂ is related to correction of perilymph hypoxia is only one theory. Other contributory benefits of HBO₂ may be related to its anti-inflammatory effects, as well as the blunting of ischemia reperfusion injury and reduction of edema.

**The use of corticosteroids in the treatment of ISSHL**

Corticosteroids are thought to improve outcomes in ISSHL by decreasing inflammation and edema. Alexiou *et al.* performed a retrospective review that found patients with lower, middle, or pancochlear hearing loss had statistically improved outcomes with the administration of corticosteroids and blood flow-promoting agents [18]. Doyle and colleagues reviewed the literature on intratympanic (IT) corticosteroids versus systemic corticosteroids and found similar outcomes in both groups [47].

Wei *et al.* performed a Cochrane review in 2006, analyzing the only two randomized controlled trials. The results of the trials were conflicting. One showed no difference between groups. The other showed statistically better outcome with corticosteroids [48].

In 2009, Plontke *et al.* performed a Cochrane review on the use of IT corticosteroids for ISSHL. They found the treatments equivalent, but of unclear clinical significance [49]. Two years later, Dispenza and co-workers performed a prospective randomized trial comparing IT corticosteroids to systemic corticosteroids. Both treatments resulted in hearing gain improvements above that which is shown without treatment, but there were no significant differences between groups [50].

In the same year, Alimoglu *et al.* retrospectively reviewed their treatment of 217 ISSHL patients. Hearing gains were most statistically significant for those treated with oral corticosteroids and HBO₂. Moreover, the proportion of those with complete recovery was also highest in those receiving oral corticosteroids and HBO₂. The oral corticosteroid and HBO₂ group also had the highest mean hearing gain among all groups [1].

IT corticosteroids seem to be less efficacious than oral corticosteroids, but may be a reasonable alternative for those patients with contraindications to oral corticosteroid use (e.g., peptic ulcer disease, viral hepatitis and brittle diabetes) [31].

**LITERATURE REVIEW**

**Early investigations**

Hyperbaric oxygen therapy has been investigated as a treatment for hearing loss since the 1970s. Early work began with a comparative study of acoustic trauma patients. De Heyn and Van Opstal (1976) compared acute acoustic trauma (AAT) blast patients treated with vasodilators with or without HBO₂. The addition of HBO₂ improved outcomes, but only if the patients were treated within 10 days of symptom onset [51].

Lamm and co-workers utilized a guinea pig hypoxia cochlea model and found HBO₂ to be protective [52].

One of the first studies detailing the benefits of hyperoxygenation in those with ISSHL was the Giger study (1979) [53]. It was a prospective, randomized trial in which 55 patients with ISSHL were treated with either 95% oxygen/5% CO₂ (carbogen inhalation) or intravenous (IV) infusion of papaverin and dextran. Immediate differences were not found between groups. However, audiometric testing at one year showed statistically better results in those treated with carbogen. The authors opined that carbogen (O₂-CO₂ mixtures) therapy may improve the spontaneous recovery rate inherent with ISSHL [53].

**Etiopathogenesis of ISSHL**

**Human studies:** It has been proposed that the high metabolism and vascular paucity predispose the cochlea to damage. A number of case reports and series with human patients have been published focusing on possible vascular occlusive etiologies such as vertebrobasilar disease and occlusive carotid disease [54]. However, few studies have been performed.

Nagahara and colleagues examined perilymphatic pO₂ responsiveness to carbogen patients with either ISSHL or slowly progressive sensorineural hearing loss. They found the pO₂ readings were initially low, but responsive to carbogen in those with ISSHL. However, in those with slowly progressive sensorineural hearing loss, the pO₂ was initially normal and unresponsive to carbogen [44]. Wilson’s study reiterated the effectiveness of carbogen in elevating perilymphatic pO₂ [55].

**Animal studies:** There are far more animal studies related to the pathogenesis of ISSHL. Lamm and co-workers utilized a guinea pig model to evaluate the pO₂ in the perilymph and scala tympani under normobaric and hyperbaric conditions via the insertion of oxygen-sensitive microcoaxial electrodes. In all animals, the pO₂ fell 34% during electrode insertions, and increased after
normobaric and hyperbaric O2 [43]. Lamm et al. used this same model to evaluate noise stress. They found the perilymph pO2 of the scala tympani fell 50% to 80% during noise exposure, the compound action potential (CAP) latency times were prolonged, and CMs (a measure of hair cell function) declined by 60% to 70% of original values.

The authors hypothesized that the decline in perilymph pO2 is indicative of cortilymph hypoxia. They surmised that during noise exposure, the oxygen-dependent sodium and potassium pumps of the OOC decompensate, resulting in intracellular sodium accumulation, which causes microstructural damage. This damage is manifested in hair cell-cilia fusion; hair cell-, synaptic- and dendritic swelling; hair cell contraction; and sustained depolarization [56].

Other animal experiments have shown that occlusion of the labyrinthine artery results in severe degenerative changes, fibrosis and new cochlear bone formation. In a similar manner, the human cochlea, deprived of cochlear blood supply, results in progressive ossification of the cochlear spaces, loss of cochlear neurons, labyrinthine fibrosis, new bone formation and endolymphatic hydrops [57].

Lamm and Arnold reported their work on guinea pigs exposed to AAT. They found that AAT induces cochlear hypoxia in an intensity-dependent fashion that correlates with hearing loss and precedes the observed reductions in cochlear blood flow [26].

Kuokkanen et al. evaluated the effect of HBO2 on hair cell preservation using rats exposed to extreme AAT daily for 10 days. The AAT caused permanent damage to the cochlea of all animals, with the most severe lesions in the lower middle coil. In the HBO2-treated group, there was a significantly less hair cell loss in these regions [58].

Pilgramm has shown in guinea pig cochlear experiments that HBO2 leads to an increase in perilymph pO2 and a statistically lower number of damaged inner ear sensory cells 60 hours following AAT [59].

**ISSHL pathogenesis theories:** Belal discusses the role that occlusive arterial disease (thrombotic, embolic or spastic) has in the development of ISSHL and suggests a vascular etiology of ISSHL [60]. This is the reasoning behind the use of vasodilator drugs, stellate ganglion blocks, anticoagulants and rheological agents in the treatment of ISSHL. Gloddek and colleagues remarked upon the differing theories, noting that a viral infection of the stria vascularis, OOC or spiral ganglion is often suggested in the American literature, while European scientists favor a vascular pathology with impaired inner ear perfusion [61].

These authors aimed to meld competing theories by offering a theory based on an immunologically mediated vasculitis resulting in cochlear hypoperfusion. The basis for this theory is that during viral vasculitis, circulating immunoglobulins are deposited perivascularly, associated with local decreases in perfusion and tissue hypoxia [61]. Moreover, in autoimmune disease perivasculitis is common, with the endothelial cells promoting the vasculitis by secreting pro-inflammatory cytokines and adhesion molecules.

The end result of this immunopathological theory is stenosis, atresia and ischemia [61]. At this time, the exact etiologies of ISSHL are uncertain. More than 60 protocols for treatment have been proffered [1]. Among them, the use of systemic corticosteroids in combination with HBO2 has the greatest efficacy.

**Acute acoustic trauma and HBO2**

**Animal studies:** A discussion of acute acoustic trauma (AAT) is appropriate, as a great deal of the early work in sudden hearing loss and the efficacy of HBO2 involved the treatment of these patients. Fakhry et al. assessed AAT in a guinea pig model (extreme exposure of 115 dB bilaterally for 45 minutes). The combination of HBO2 and corticosteroid therapy provided significant protection, especially when started within a day of insult. These results correlate with previous literature, although the hearing loss in this study was considerably greater [62].

Lamm and Arnold used a guinea pig AAT model to compare a placebo control group against various medical treatments, isobaric oxygenation (IBO) and HBO2. The noise-induced cochlear hypoxia was compensated by IBO. However, HBO2 was much more effective (with or without supplements). Other treatments had no sustained effect. The only treatments that showed efficacy were a combination of HBO2 and prednisolone, followed by monotherapy with prednisolone or hydroxyethyl starch [63].

**Human studies:** In human studies, many pharmacological therapies have been used to treat AAT. Pilgramm and Schumann evaluated eight AAT studies (n=400) comparing rheological, vasoactive and metabolically active substances with saline-treated controls. All groups showed superior results, with the rheological agents showing statistically significant improvement above other
agents. Hyperbaric oxygen therapy was found to be beneficial [64].

These same authors conducted a randomized controlled study of 122 soldiers with AAT treated with either betahistine (vasoactive infusion) or HBO₂, following the exclusion of those with spontaneous recovery. Hyperbaric oxygen therapy shortened the recovery of high-pitch dysacusis (both in the acutely and following a week of observation) and reduced the relapse frequency and associated tinnitus that occurs with AAT [65].

Pilgramm reported the results of 10 studies (n=500) with AAT patients who showed no evidence of spontaneous recovery. The combination of low-molecular dextran or hydroxyethyl starch and HBO₂ produced the spontaneous recovery. The best therapeutic outcome with regard to hearing gain and reduction of tinnitus, which was statistically significant [59].

Winiarski et al. evaluated various pharmacological agents and HBO₂ in AAT patients. The HBO₂ group showed statistically significant gains in pure tone audiometry (PTA) compared to pharmacological therapy when continued over 10 days (p<0.00001) and if started within five days (p<0.000001) [66].

In 2008, Ylikoski and colleagues also observed an enhanced recovery rate from AAT with the use of HBO₂ compared to normobaric oxygen treatment (p<0.01) [27].

Medical therapies vs. primary HBO₂ therapy
To date, HBO₂ is generally used as an adjunctive agent that is most efficacious with systemic corticosteroids. There is a paucity of literature using HBO₂ as a primary therapy for ISSHL.

In 2001, Fatorri and co-workers reported a prospectively controlled study of patients who presented to their ENT offices within 48 hours of symptom onset and were randomly assigned treatment with either HBO₂ or buflomedil. The HBO₂ group experienced a significantly greater response to treatment than the vasodilator group (73% vs. 55%, respectively). Those with pantonal hypoacusis responded significantly better than those with a milder presentation [16].

In 2007, Dundar et al. prospectively compared ISSHL patients treated with HBO₂ versus those treated with medical therapy. The patients receiving HBO₂ had statistically significant hearing gains across all frequencies, with tinnitus patients showing the greatest hearing improvement [19]. In 2009, Cekin and colleagues conducted a randomized, prospective and controlled study evaluating ISSHL patients treated with medical therapy (including corticosteroids) with or without HBO₂. Both groups had success rates above 70% (79.0% HBO₂ vs. 71.3% control). However, there was no statistical difference between groups [37].

The following year, Ohno and colleagues compared ISSHL patients who had failed four weeks of medical treatment (and then given HBO₂) with ISSHL patients (controls) treated with medical treatment alone. The mean hearing gains were not different between groups. However, hearing gains were significantly higher in those with profound hearing loss than in other patients [20].

Use of HBO₂ following medical failures
Two of the difficulties in evaluating the efficacies of ISSHL treatments are the reportedly high rate of spontaneous improvement and the various pharmacological therapies employed. Recently, the often-quoted spontaneous recovery rate of 65% has been questioned [8, 9]. Lamm et al. reported a rate of between 25% - 68% for spontaneous full remissions and 47% - 89% for spontaneous partial remissions [67]. Most authors agree, however, that a significant number (35% - 39%) of patients do not respond to medical or placebo therapies.

In 1998, Lamm and colleagues performed a literature analysis of more than 50 studies utilizing HBO₂ as an adjunctive therapy for ISSHL, acoustic trauma, noise-induced hearing loss and tinnitus. Corticosteroid therapy was significantly more effective than placebo or NSAID treatment [67].

They also analyzed the 35% - 39% of patients in these studies who failed to respond to any medical therapies. In evaluating these 4,109 refractory patients, they found that if HBO₂ was started between two to six weeks, 50% showed marked hearing gain (at least 3 frequencies of > 20 dB); 33% showed moderate improvement (10 dB - 20 dB); and 13% had no improvement [67]. If adjunctive HBO₂ was not started within six weeks but within three months, 13% showed definite improvement in hearing, 25% moderate improvement, and 62% had no improvement [67].

In 2000, Marchesi et al. retrospectively studied 95 patients, 80% of whom had previous, ineffective medical treatment, then treated with HBO₂ (2.2 atm abs for 75 minutes). The mean age was 45 years and the mean hearing loss was 76.4 ± 25 dB. Within the HBO₂ group, 78.9% had a mean improvement of 38.3 ± 8.3 dB and 41% gained > 20 dB. Complete recovery occurred in 11.6%. HBO₂ was effective in those patients treated within 14 days [68].
Also in 2000, Murakawa and colleagues reviewed 522 cases of ISSHL occurring over a 10-year period in patients unresponsive to medical therapies. The patients were treated at 2.5 atm abs for 80 minutes (10 to 15 sessions). Complete recovery occurred in 19.7%, with significant improvement in 34.9% and slight improvement in 23.2%. Delay in treatment of more than 14 days, advanced age and vertigo were associated with poorer outcomes [34].

In 2010, Muzzi and co-workers treated 19 ISSHL patients who had failed medical therapy with HBO2 (2.5 atm abs for 90 minutes for 30 sessions). Salvage HBO2 improved PTAs, particularly at the low frequencies. Positive results were more likely in those with reduced delay in receiving HBO2, but also in older patients [35].

More recently, the clinical practice guidelines for sudden hearing loss published by the American Academy of Otolaryngology – Head and Neck Surgery Foundation have recommended that HBO2 may be considered for use within three months of diagnosis [9].

**Chronic hearing loss and HBO2**

The strength of evidence for use of HBO2 to treat chronic hearing loss is far less robust than for the treatment of acute ISSHL. However, there is some evidence it may be useful. Those patients who have had hearing loss for longer than three months prior to the initiation of therapy are the least likely to improve.

In 1990, Schumann and co-workers evaluated 557 patients with chronic hearing loss treated with 10 sessions of HBO2 and found an improvement of > 10 dB in 27.8% of cases [69].

In 1997, Kau et al. analyzed 359 patients with refractory hearing loss. Of the patients who had had hearing loss for more than one month but less than three months, noticeable improvement or complete recovery was seen in 13% (20 dB in at least three test frequencies); 25.2% showed an improvement between 10 dB to 20 dB. Patients with hearing loss for longer than three months had markedly less benefit from HBO2. Overall, 30% had an improvement of > 10 dB, but only 2% regained normal hearing function [70]. Similar results were found by Lamm et al. [67].

The efficacy of HBO2 for chronic hearing loss shows some promise for these patients who have not responded to other treatments and have chronic loss. However, further randomized, controlled studies are required before its use can be routinely recommended.

**Medical and HBO2 combination therapies**

The effectiveness of HBO2 with various medical and procedural therapies has been extensively investigated. These therapies include: vitamins, corticosteroids (reduction of edema and inflammation), vasodilatory agents (vasoactive agents and stellate ganglion blocks), antiviral agents (herpes virus may be a causative agent for a subset of ISSHL), agents that reduce hematocrit and improve blood flow (volume expanders, rheological agents and normovolemic hemodilution), antibiotics, diuretics, osmotic agents, anticoagulants and carbogen. The results of the most important retrospective, case-controlled and randomized controlled trials are discussed below.

**ISSHL retrospective and prospective studies**

**HBO2 and medical therapies:** One of the earliest studies compared medical therapy, stellate ganglion block (SGB) and HBO2 [25]. Researchers found that 100% of the patients treated with SGB and HBO2 achieved > 10 dB PTA improvement. Moreover, 40% of these patients recovered to within 20 dB of their normal hearing levels [25].

The French conducted several studies evaluating the effectiveness of HBO2 in combination with various medical therapies. Both studies found HBO2 a useful synergistic adjunct, with twice-daily sessions reducing the length of treatment [28, 29].

Aslan and co-workers published a study of patients treated with medical therapy combined with either SGB or HBO2 [14]. A significant increase in hearing gain was found with the addition of HBO2.

Racic et al. compared HBO2 with pentoxifylline infusions. The HBO2 group showed statistically significant improvement in overall hearing gains, attainment of physiological hearing values and moderate hearing gains [21].

Narozny and colleagues reviewed two historical groups of ISSHL patients treated with combinations of medical therapy, corticosteroids and HBO2 [12]. Hearing gains were statistically superior for the HBO2 group over all frequencies and in four ranges of frequencies for both relative and absolute values [12]. Moreover, the combination of high-dose corticosteroids and HBO2 resulted in statistically improved clinical outcomes [12]. Delay to treatment and flat hearing loss were found to be predictors of poor clinical outcome. Narozny and co-workers also performed linear regression analyses of their work to identify
prognostic factors related to hearing improvement as measured by objective change of gain, PTA, high-tone average and pure middle-tone average. They identified two favorable prognostic factors for ISSHL: treatment with high-dose corticosteroids and HBO₂, and early treatment (within 10 days). A poor prognosis was found with delayed treatment, labyrinth responsiveness disorders, and decreased TSH levels [30].

Fujimura et al. reported their work with 130 consecutive ISSHL inpatients treated with corticosteroids (with or without HBO₂) [11]. The HBO₂ group showed a statistically superior rate of recovery [11]. Additionally, a subset analysis of those with severe hearing loss (> 80 dB) showed that the HBO₂ group had a statistically superior rate of hearing improvement.

Dundar et al. prospectively compared patients treated with HBO₂ or medical therapy. The HBO₂ group had statistically significant hearing gains across all frequencies [19].

Suzuki and colleagues analyzed 196 consecutive ISSHL patients, comparing corticosteroid or IV PGE₁ combined with HBO₂ [31]. There were no differences noted, implying that PGE₁ and corticosteroid therapy are equally effective when combined with HBO₂ therapy, and that PGE₁ is a potential alternative in the corticosteroid-intolerant patient (diabetes, peptic ulcer disease, or viral hepatitis) [31].

Suzuki and co-workers have also compared patients treated with IV PGE₁ or SGB combined with HBO₂. In those with less severe hearing loss (< 80 dB) the outcomes were similar. However, for those with hearing loss > 80 dB, the hearing rate was statistically superior in the patients treated with SGB and HBO₂ [22].

Ohno and colleagues reported patients treated with medical therapy or HBO₂ and found that while overall mean hearing gains were not different between groups, those with profound hearing loss had significantly better outcomes with the use of HBO₂ than other groups [20].

Körpinar and co-workers reviewed the treatment of patients treated with medical therapy and HBO₂ to identify factors that affect treatment outcomes. The gains were significant for those with early HBO₂; a higher number of HBO₂ treatments; the use of corticosteroids; low frequency-ascending and total audiogram configuration; and profound hearing loss [23]. The most important favorable prognosis was found with corticosteroid therapy [23].

Liu et al. reported on patients treated within two weeks with medical therapy with or without HBO₂ [24]. The overall effectiveness was clinically and statistically superior for those treated with HBO₂, with the difference being significant and most profound for those with moderate to severe deafness and those with descending and flat types of audiograms [24].

Suzuki and colleagues also performed simple and multiple regression analyses on 174 consecutive ISSHL patients treated with hydrocortisone and HBO₂. Their aim was to develop a regression model for predicting hearing outcome in ISSHL patients. They found significant inverse correlations between hearing improvement rate and days from onset to treatment, patient age and presence of vertigo [32].

Alimoglu and co-workers reviewed the treatment of patients receiving various combinations of oral or IT corticosteroids and HBO₂ [1]. Mean hearing gains and the proportion of patients with complete recovery were statistically superior for those treated with oral corticosteroids and HBO₂.

Hóly and colleagues treated patients with IV vasodilation therapy and HBO₂ [33]. Improvement was seen in 59.7% of patients. However, if HBO₂ was started within 10 days, significant or complete recovery was noted in 65.9% of patients. In those patients treated with HBO₂ after 10 days, improvement was noted in only 38.9% [33].

Liu and co-workers reported their work on patients treated with either corticosteroids, corticosteroids plus dextran, or corticosteroids, dextran and HBO₂ [10]. The addition of HBO₂ was found beneficial in those with initial profound hearing loss. However, the addition of dextran to corticosteroid therapy was not associated with improved outcomes [10]. These studies are compared in Table 1 (Pages 786-787).

**ISSHL prospective randomized controlled trials**

**HBO₂ and medical therapies:** The earliest randomized controlled trial was the 1985 study of Pilgramm et al., studying patients treated with medical therapy with or without HBO₂. The HBO₂ group had statistically superior outcomes [17].

Ten years later, Hoffman and colleagues performed a similar study on patients refractory to previous medical therapy. In this study as well, the HBO₂ group had statistically significant improvement [15]. Hoffman and his co-workers published a second study in the same year, this time evaluating patients with symptoms occurring longer than six months. They found no differences between the HBO₂ group and the air control group. However, in this study, all patients had chronic symptomatology [71].
Cavallazzi and colleagues reported a study the following year that also compared medical patients (controls) treated with or without HBO2. Again, no differences were found between groups; however, the trend favored the HBO2 group [72].

In 1998, Schwab et al. reported on patients treated with either medical therapy or HBO2. They found clinical and statistical improvement with the use of HBO2 [36].

In 2001, Fatorri et al. studied patients treated within two days and randomly assigned to treatment with either bufomedil (vasodilator) or HBO2. The HBO2 group experienced a significantly greater response to treatment [16]. In 2004, Topuz and colleagues conducted a study involving patients undergoing dietary and medical treatment with or without HBO2 [13]. The HBO2 group had statistically significant improvement in hearing gains over all frequency ranges except 2,000 Hz, and significant hearing gains in those with initial hearing losses > 60 dB when compared to lesser hearing losses. Within the HBO2 group, the mean hearing gains for those older than 50 years was greater than for those younger than 50 years [13].

Most recently, Cekin and colleagues evaluated patients treated with prednisolone with or without HBO2. Both groups had success rates above 70%, with no statistical difference between groups [37]. These studies are compared in Table 2 (Page 788).

**ISSHL meta-analyses of treatments**

Five treatment modalities for ISSHL have been reviewed by the Cochrane Collaboration: HBO2 therapy, corticosteroids, vasodilators / vasoactive substances, antivirals and IT corticosteroids. There are three Cochrane meta-analyses involving the use of HBO2, one reviewing the use of oral corticosteroids, one reviewing IT corticosteroids and one reviewing the use of vasodilators and vasoactive substances [2-4, 48, 49, 73]. The antiviral review has yet to be completed. The IT corticosteroid treatment was found equivalent to systemic corticosteroids and of unclear clinical significance [49].

The 2006 Cochrane review on the use of oral corticosteroids for the treatment of ISSHL evaluated only two studies. One showed significant improvement in hearing in 61% of patients who received corticosteroids compared to only 32% of controls. The other study showed a lack of effect of corticosteroids on hearing improvement. The authors’ conclusions were that “the value of corticosteroids in the treatment of ISSHL remains unclear” [48].

The 2009 Cochrane review on the use of vasodilators and vasoactive substances for the treatment of ISSHL evaluated three trials (n=189) and found that “the effectiveness of vasodilators in the treatment of ISSHL remains unproven” [73]. Both the use of corticosteroids and vasoactive treatments were found to have “no good evidence to suggest the effectiveness or lack thereof” in the treatment of ISSHL [48, 73].

The only reviews that show benefit of therapy are the HBO2 meta-analyses [2-4]. In the 2005 review, six trials (n=304) were analyzed and it was reported that “HBO2 did improve hearing” [2]. The 2007 update by the same authors analyzed six trials (n=308), and confirmed again that “For people with early presentation of ISSHL, the application of HBO2 significantly improved hearing loss” [3]. Additionally, this update defined that the number of needed to treat (NNT) for one extra good outcome was 5.3. This correlates well with the NNT for diabetic foot wounds and HBO2 (NNT=4) reported in the 2009 Cochrane review on the use of HBO2 for chronic wounds [74].

The latest update (2010) for the use of HBO2 for ISSHL analyzed seven trials (n=392) and reported the same objective, conservatively positive conclusions as the 2007 update [74].

**LITERATURE CONCLUSIONS**

- **Treatment of ISSHL with Adjunctive HBO2**

Many prospective and retrospective studies have shown significant efficacy utilizing HBO2 as an adjunct to medical therapy [1, 10-12, 14, 19, 20, 21, 24, 25, 31]. Nine of these 11 studies showed statistically positive results. These studies are compared in Table 1.

There are also eight randomized, controlled prospective studies (Table 2) [13, 15-17, 36, 37, 71, 72]. Four of these studies were published in peer-reviewed journal and four in Proceedings. Five of these eight trials were positive. Of the remaining studies, one favored the HBO2 group, and two studies (one of which enrolled chronic hearing loss patients) found no statistical differences between treatment groups [37, 71, 72]. The best and most consistent outcomes occur with the use of oral corticosteroids and HBO2, especially in those with profound hearing loss treated within two weeks from symptom onset. The use of HBO2 for the treatment of ISSHL is Class IIa (AHA Evidence-Based Scoring System) with an “A” Level of Evidence (data derived from multiple randomized clinical trials).
<table>
<thead>
<tr>
<th>Study</th>
<th>Patient groups</th>
<th>HBO2 treatments</th>
<th>Concomitant therapies</th>
<th>Hearing gains</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alimoglu¹ 2011</td>
<td>n = 219</td>
<td>2.5 atm abs</td>
<td>oral and intratympanic</td>
<td>86.9% POS/HBO₂</td>
</tr>
<tr>
<td></td>
<td>HBO2 (n = 57)</td>
<td>120 minutes</td>
<td>corticosteroids as</td>
<td>63.8% POS</td>
</tr>
<tr>
<td></td>
<td>POS (n = 58)</td>
<td>20 sessions</td>
<td>controls and combined</td>
<td>46.5% IT</td>
</tr>
<tr>
<td></td>
<td>POS + HBO2 (n = 61)</td>
<td></td>
<td>with HBO₂</td>
<td>43.9% HBO₂</td>
</tr>
<tr>
<td>Liu¹⁰ 2011</td>
<td>n = 465</td>
<td>2.5 atm abs</td>
<td>IV and PO corticosteroids, Dextran-40</td>
<td>HBO₂ is beneficial with profound initial hearing loss</td>
</tr>
<tr>
<td></td>
<td>HBO2 (n = 112)</td>
<td>60 minutes</td>
<td>type(s) unknown</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Corticosteroids (n = 77)</td>
<td>10-20 sessions</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Corticosteroids + HBO2 (n = 277)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Liu²⁴ 2010</td>
<td>n = 120</td>
<td>2.0 atm abs</td>
<td>MT as control type(s) unknown</td>
<td>Overall Effectiveness</td>
</tr>
<tr>
<td></td>
<td>treated &lt; 14 d</td>
<td>60 minutes</td>
<td>MT only (n = 60)</td>
<td>83.3% HBO₂*</td>
</tr>
<tr>
<td></td>
<td>MT + HBO2 (n = 60)</td>
<td></td>
<td></td>
<td>60% MT</td>
</tr>
<tr>
<td>Ohno²⁰ 2010</td>
<td>n = 92</td>
<td>2.0 atm abs</td>
<td>corticosteroids, vitamins and adenosine triphosphate</td>
<td>mean hearing gains not different between groups; hearing gains for those with profound loss significantly higher than other groups*</td>
</tr>
<tr>
<td></td>
<td>HBO2 (n = 48)</td>
<td>60 minutes</td>
<td>type(s) unknown</td>
<td></td>
</tr>
<tr>
<td></td>
<td>MT only (n = 44)</td>
<td>10 sessions</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Suzuki³¹ 2008</td>
<td>n = 196</td>
<td>2.5 atm abs</td>
<td>PO corticosteroids, PGE1</td>
<td>No Difference; PGE1 as an alternative for corticosteroid-intolerant</td>
</tr>
<tr>
<td></td>
<td>loss &gt; 40 dB for &lt; 30 d unaffected ears served as controls</td>
<td>60 minutes</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>POS + HBO2 (n = 101)</td>
<td>10 sessions</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>PEG1 &amp; HBO2 (n = 95)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dundar¹⁹ 2007</td>
<td>n = 80</td>
<td>unavailable</td>
<td>none; unaffected ears served as controls</td>
<td>HBO₂ Gains Across All Frequencies*</td>
</tr>
<tr>
<td></td>
<td>hearing loss &gt; 40 dB for &lt; 30 days HBO₂ (n = 55)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>controls (n = 25)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fujimura¹¹ 2007</td>
<td>n = 130</td>
<td>unavailable</td>
<td>PO corticosteroids; unaffected ears served as controls Hearing Rate Improvement</td>
<td></td>
</tr>
<tr>
<td></td>
<td>hearing loss &gt; 40 dB for &lt; 30 days POS + HBO2 (n = 67)</td>
<td></td>
<td>51.1% HBO₂*</td>
<td></td>
</tr>
<tr>
<td></td>
<td>POS only (n = 63)</td>
<td></td>
<td>27.1% controls</td>
<td></td>
</tr>
<tr>
<td></td>
<td>hearing loss &gt; 40 dB for &lt; 30 days POS + HBO2 (n = 67)</td>
<td></td>
<td>Rate of Recovery – Severe loss (&gt; 80 db)</td>
<td>59.7% HBO₂*</td>
</tr>
<tr>
<td></td>
<td>POS only (n = 63)</td>
<td></td>
<td>39.7% controls</td>
<td></td>
</tr>
</tbody>
</table>

MT = Medical Therapy  
ITS = Intratympanic Corticosteroids  
SGB = Stellate Ganglion Block  
POS = PO Corticosteroids  

* (p < 0.05)  
** (p < 0.01)
**TABLE 1 – Retrospective and Prospective Case-Controlled Studies of ISSHL and HBO₂**

<table>
<thead>
<tr>
<th>Study</th>
<th>Patient groups</th>
<th>HBO₂ treatments</th>
<th>Concomitant therapies</th>
<th>Hearing gains</th>
</tr>
</thead>
<tbody>
<tr>
<td>Narozny¹² 2004</td>
<td>n = 133</td>
<td>2.5 atm abs 60 minutes</td>
<td>MT + HBO₂ group = vasodilators, high-dose corticosteroids, vitamins and histamine analog</td>
<td>Hearing Gain Over All Frequencies* (HBO₂)</td>
</tr>
<tr>
<td></td>
<td>MT + HBO₂ (n = 52)</td>
<td></td>
<td></td>
<td>% Hearing Gain in All Frequencies* (HBO₂ Group)</td>
</tr>
<tr>
<td></td>
<td>MT only (n = 81)</td>
<td></td>
<td></td>
<td>MT only = vasodilators, low-dose corticosteroids and vitamins</td>
</tr>
<tr>
<td>Racic²¹ 2003</td>
<td>n = 115</td>
<td>2.8 atm abs</td>
<td>MT = pentoxifylline infusion as control group</td>
<td>Hearing Improvement</td>
</tr>
<tr>
<td></td>
<td>HBO₂ (n = 51)</td>
<td></td>
<td></td>
<td>46.4 dB HBO₂*</td>
</tr>
<tr>
<td></td>
<td>MT (n = 64)</td>
<td></td>
<td></td>
<td>21.5 dB MT</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Recovery of Physiologic Hearing</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>47.1 dB HBO₂*</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>6.2% MT</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Moderate Hearing Gains</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>41.2% HBO₂*</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>12.5% MT</td>
</tr>
<tr>
<td>Aslan¹⁴ 2002</td>
<td>n = 50</td>
<td>2.4 atm abs BID 90 minutes 20 sessions</td>
<td>MT = betahistine hydrochloride, prednisone, SGB</td>
<td>37.9 dB HBO₂*</td>
</tr>
<tr>
<td></td>
<td>MT + HBO₂ (n = 25)</td>
<td></td>
<td></td>
<td>20 dB MT</td>
</tr>
<tr>
<td></td>
<td>MT only (n = 25)</td>
<td></td>
<td></td>
<td>effective if treated within 60 d</td>
</tr>
<tr>
<td>Goto²⁵ 1979</td>
<td>n = 91</td>
<td>2.4 atm abs 90 minutes 20 sessions</td>
<td>Group 1 vasodilators, corticosteroids, vitamins</td>
<td>Treated &lt; 7 d</td>
</tr>
<tr>
<td></td>
<td>Group 1 (n = 22)</td>
<td></td>
<td></td>
<td>PTA &gt; 10 dB</td>
</tr>
<tr>
<td></td>
<td>Group 2 (n = 49)</td>
<td></td>
<td></td>
<td>69% Group 1</td>
</tr>
<tr>
<td></td>
<td>Group 3 (n = 20)</td>
<td></td>
<td></td>
<td>83% Group 2</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>100% Group 3</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Treated &lt; 14 d</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>PTA &gt; 10 dB</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>33% Group 1</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>69% Group 2</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>100% Group 3**</td>
</tr>
</tbody>
</table>

MT = Medical Therapy  
SGB = Stellate Ganglion Block  
POS = PO Corticosteroids  
*(p < 0.05)  
***(p < 0.01)

**Continued from previous page**

- **Acute Acoustic Trauma:** Two animal studies utilizing HBO₂ and corticosteroids were positive [62,63]. One meta-analysis (10 studies) and two more recent human studies comparing HBO₂ with medical therapies were positive [27,65,66]. HBO₂ may be beneficial for the treatment of AAT. However, this will need to be confirmed in appropriately randomized and controlled studies before the use of for AAT can be routinely recommended.

- **Medical Therapies Versus Primary HBO₂ Therapy:** Four studies have prospectively compared medical vs. HBO₂ therapies; three studies were positive, and one found both treatments resulted in outcomes greater than that found with spontaneous recovery, but without statistical differences between groups [16,19,20,37]. Although HBO₂ has been found more beneficial than medical therapies in three of these studies, it is not currently recommended as a primary therapy. There are a greater number of studies showing the beneficial effects of adjunctive HBO₂ therapy.
<table>
<thead>
<tr>
<th>Study</th>
<th>Patient groups</th>
<th>HBO2 treatments</th>
<th>Concomitant therapies</th>
<th>Hearing gains</th>
<th>Study flaws</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cekin37 2009</td>
<td>n = 57</td>
<td>2.5 atm abs</td>
<td>MT = prednisolone, famotidine</td>
<td>79.0% HBO2* 71.3% Controls</td>
<td>unblinded no sham controls no intention-to-treat analysis</td>
</tr>
<tr>
<td></td>
<td>Presenting &lt; 10 d HBO2 + MT (n = 36) MT alone (n = 21)</td>
<td>90 minutes 10 sessions</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Topuz13 2004</td>
<td>n = 51</td>
<td>2.5 atm abs</td>
<td>MT = prednisone, diazepam, rheomacrodex and pentoxiphylline</td>
<td>Mild Loss no difference</td>
<td>unblinded no sham controls randomization unclear</td>
</tr>
<tr>
<td></td>
<td>treated within 14 d HBO2 + MT (n = 30) controls (MT) (n = 21)</td>
<td>90 minutes 25 sessions</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>no prior therapy</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fattori16 2001</td>
<td>n = 50</td>
<td>2.2 atm abs</td>
<td>vasodilator group received IV buflomedil only</td>
<td>Improvement 61.3 dB HBO2* 24 dB controls</td>
<td>unblinded no sham controls randomization unclear</td>
</tr>
<tr>
<td></td>
<td>treated within 2 d HBO2 Group (n = 30) Vasodilator Grp (n = 20)</td>
<td>90 minutes 10 sessions</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Schwab36 1998</td>
<td>n = 75</td>
<td>1.5 atm abs</td>
<td>None</td>
<td>15.6 dB HBO2* 10.7 dB controls</td>
<td>unblinded no sham controls randomization unclear Proceedings publication</td>
</tr>
<tr>
<td></td>
<td>treated within 14 d HBO2 (n = 37) controls (n = 38)</td>
<td>45 minutes 10 - 20 sessions</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cavallazzi72 1996</td>
<td>n = 62</td>
<td>2.5 atm abs</td>
<td>MT = heparin, flunarzine, dextran, betamethasone, vitamins, nicotinic acid, citidinephosphocholine, antivirals, phosphocholine and neurotropic and antiviral agents</td>
<td>Favored HBO2 Group (95% vs. 71%) Improvement in those with downward configured audiograms (80% vs. 33%)</td>
<td>unblinded no sham controls randomization unclear Proceedings publication</td>
</tr>
<tr>
<td></td>
<td>time unknown HBO2 + MT (n = 32) controls (MT) (n = 30)</td>
<td>90 minutes 15 sessions</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hoffman71 1995</td>
<td>n = 44</td>
<td>1.5 atm abs</td>
<td>None</td>
<td>Favored Control Group</td>
<td>no sham controls randomization unclear Proceedings publication Chronic hearing loss</td>
</tr>
<tr>
<td></td>
<td>symptoms for &gt; 6 months HBO2 (n = 22) controls (n = 22)</td>
<td>HBO2 (100% O2) 45 minutes 15 sessions</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hoffman13 1995</td>
<td>n = 20</td>
<td>1.5 atm abs</td>
<td>previous MT = hydroxyethyl starch pentoxifylline and cortisone</td>
<td>Acute Hearing Loss 7.5 dB HBO2* 0.7 dB controls</td>
<td>unblinded no sham controls randomization unclear Proceedings publication</td>
</tr>
<tr>
<td></td>
<td>refractory x 14 d following MT HBO2 (n = 10) Controls (n = 10)</td>
<td>45 minutes 10-20 sessions</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pilgramm 1985</td>
<td>n = 37</td>
<td>2.5 atm abs</td>
<td>MT =10% dextran 40, 5% sorbitol, vitamin B, and naphthidrofuryl hydrogenalate</td>
<td>Acute Loss 29.2 dB HBO2* 20.2 controls</td>
<td>unblinded no sham controls</td>
</tr>
<tr>
<td></td>
<td>hearing loss &lt; 14 d HBO2 + MT (n = 18) controls (MT) (n = 19)</td>
<td>60 minutes 10 sessions</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* p < 0.05; MT = Medical Therapy
HBO$_2$ Following Medical Failures: One literature analysis of more than 50 studies ($n = 4,109$) found that if HBO$_2$ was started two to six weeks following medical failure, 50% of patients showed marked hearing gains and 33% showed moderate improvement [67]. Two other studies were positive. One ($n = 95$) showed that 78.9% of patients had a mean improvement of 38.3 dB and 41% gained $> 20$ dB. The other study ($n = 522$) showed significant improvement in 34.9%, slight improvement in 23.2% and complete recovery in 19.7% [34, 68]. Recent otolaryngologist clinical guidelines recommend HBO$_2$ be considered as a therapy within three months of diagnosis [9]. HBO$_2$ may be beneficial for the treatment of refractory ISSHL. However, further studies are needed.

Chronic Hearing Loss: Three studies have shown improvements of between 10-20 dB in 27.8% to 30% of patients [67, 69, 70]. The use of HBO$_2$ for chronic hearing loss may have some benefit in these recalcitrant patients; however, further studies are required.

TREATMENT GUIDELINES

Patient selection criteria

Patients with moderate to profound ISSHL ($\geq 40$ dB) who present within 14 days of symptom onset should be considered for HBO$_2$. While patients presenting after this time may experience improvement when treated with HBO$_2$, the medical literature suggests that early intervention is associated with improved outcomes. The American Academy of Otolaryngology recommends that HBO$_2$ be considered an option for treatment up to three months after symptom onset [9]. However, the best evidence supports the use of HBO$_2$ within two weeks of symptom onset.

Clinical management

Patients who present with ISSHL should undergo a complete evaluation by an otolaryngologist and audiologist, inclusive of appropriate audiological and imaging studies, to determine the degree and potential etiology of disease.

Initial management: The clinical practice guidelines published by the American Academy of Otolaryngology in March of 2012 strongly recommend the following:

1. Distinguish sensorineural hearing loss from conductive hearing loss in a patient;
2. Educate patients with ISSHL about the natural history of the condition, the benefits and risks of medical interventions, and the limitations of existing evidence regarding efficacy; and
3. Counsel patients with incomplete recovery of hearing about the possible benefits of amplification and hearing-assistive technology and other supportive measures.

The panel made recommendations that clinicians should:

1. Assess patients with presumptive SSNHL for bilateral disease, recurrent episodes of SSNHL, or focal neurologic findings;
2. Diagnose presumptive ISSHL if audiometry confirms a 30-dB hearing loss at 3 consecutive frequencies and an underlying condition cannot be identified by history and physical examination;
3. Evaluate patients with ISSHL for retrocochlear pathology by obtaining magnetic resonance imaging, auditory brainstem response, or audiometric follow-up;
4. Offer intratympanic corticosteroid perfusion when patients have incomplete recovery from ISSHL after failure of initial management; and
5. Obtain follow-up audiometric evaluation within six months of diagnosis for patients with ISSHL [9]. They also recommended that treatment with corticosteroids and hyperbaric oxygen therapy be considered an option [9].

Corticosteroid therapy: Patients with no known contra-indications to corticosteroid therapy should also be treated with oral corticosteroids. Several dosing regimens have been proffered. It is reasonable to begin with an initial dose of 1 mg/kg/d and taper over two to three weeks. Intratympanic corticosteroids may be a reasonable alternative in patients with contraindications to oral corticosteroids.

Hyperbaric oxygen therapy: Patients determined to have ISSHL and meet the selection criteria may benefit from HBO$_2$. The recommended treatment profile consists of 100% O$_2$ at 2.0 to 2.5 atmospheres absolute for 90 minutes daily for 10 to 20 treatments.

Specialty follow-up: Continued consultation and follow-up with an otolaryngologist is recommended. Additional medical therapies may be used at the discretion of the otolaryngologist, and the patient should continue to be followed by an otolaryngology specialist during and following HBO$_2$. The American Academy of Otolaryngology recommends against the routine use of antivirals, thrombolytics, vasodilators, vasoactive substances or antioxidants to patients with ISSHL [9].
Utilization review

The optimal number of HBO₂ treatments will vary, depending on the severity and duration of symptomatology and the response to treatment. Utilization review is recommended after 20 treatments since there is no data to suggest benefit beyond the 10-20 treatment range.

REFERENCES


