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Hyperbaric Oxygen Therapy for Patients With Sudden Sensorineural Hearing Loss
A Systematic Review and Meta-analysis

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IMPORTANCE Sudden sensorineural hearing loss (SSNHL) is an acute, usually unilateral deficit. Systemic and intratympanic steroids are accepted treatments. Although evidence suggests that hyperbaric oxygen therapy (HBOT) may be beneficial, it is not widely offered.

OBJECTIVES To review and evaluate recent evidence of the association of HBOT with hearing outcomes in SSNHL and to determine if HBOT should be a single or part of a combination treatment regimen.

DATA SOURCES Cochrane Central Register of Controlled Trials, PubMed, EMBASE, CINAHL, Web of Science, CAB, ICTRP, Google Scholar, Clinicaltrials.gov, and ISRCTN databases were searched for randomized controlled trials (RCTs) published in English from January 1, 2000, and April 30, 2020.

STUDY SELECTION Prospective RCTs involving only adult participants (≥18 years) with SSNHL and comparing HBOT, as a single or combination therapy, with control therapies, such as steroids and/or placebo. Only RCTs that used the American Academy of Otolaryngology–Head and Neck Surgery's diagnostic criteria for SSNHL were included.

DATA EXTRACTION AND SYNTHESIS Data were extracted independently by 2 researchers. A fixed-effects model was used for analysis and performed from November 30, 2020, to May 20, 2021.

MAIN OUTCOMES AND MEASURES The mean difference in absolute hearing gain recorded by pure-tone audiometric (PTA) thresholds averaged across 4 low (0.5, 1, 2, and 3 or 4 kHz) or 3 high (3 or 4, 6, and 8 kHz) frequencies was the primary outcome. The secondary outcomes were the odds ratio of hearing recovery defined as a hearing gain of ≥10 decibels (dB) in PTA average and treatment-related adverse effects.

RESULTS Of the 826 records initially identified, 358 duplicates and 451 articles were excluded based on article type, title, and abstract. The full texts of 17 articles were reviewed, of which 14 were excluded because they were either not prospective RCTs (11 articles), the participants were less than 18 years old (2 articles), or the PTA was not reported at frequencies of interest (1 article). Three prospective RCTs with a total of 88 participants who received HBOT in the intervention groups and 62 participants who received only medical therapy in the control groups were studied. The intergroup difference in mean absolute hearing gain (mean difference, 10.3 dB; 95% CI, 6.5-14.1 dB; I^2 = 0%) and the odds ratio of hearing recovery (4.3; 95% CI, 1.6-11.7; I^2 = 0%) favored HBOT over the control therapy.

CONCLUSIONS AND RELEVANCE In this systematic review and meta-analysis, HBOT as part of a combination treatment was significantly associated with improved hearing outcomes in patients with SSNHL over control treatments.

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Sudden sensorineural hearing loss (SSNHL) is defined as a hearing loss of at least 30 decibels (dB) affecting 3 or more contiguous frequencies and occurring during 3 days without a known cause.[1] Usually SSNHL is attributed to inner ear hair cell damage; however, many patients demonstrate partial or complete hearing recovery.[2,3] Factors believed to affect the rate of hearing recovery in patients with SSNHL include initial hearing loss severity, duration, time to starting treatment, age at presentation, and coexisting vertigo or tinnitus.[4,5]

Corticosteroids are commonly used to treat SSNHL and can be given systemically (ie, oral, intravenous [IV], and intratympanic [IT]).[1,6] Some clinicians favor IT steroids over systemic administration because the IT route can achieve a higher concentration of steroids at the site of damage and may avoid systemic absorption.[7] Hyperbaric oxygen therapy (HBOT) is another treatment that may be used to improve outcomes in patients with SSNHL in conjunction with steroids or as salvage therapy.[6] Decreased oxygenation in the tissues of the cochlea is one suggested mechanism for SSNHL; therefore, by increasing oxygen supply to the cochlea, HBOT improves hearing.[8,9]

A systematic review including 392 patients by Bennett and colleagues[10] identified that HBOT increased the chance of any hearing improvement and achieved an absolute improvement in average pure-tone audiometric (PTA) thresholds but questioned the clinical significance. A more recent systematic review including 2401 patients by Rhee and colleagues[11] similarly reported that complete hearing recovery, absolute hearing gain, and any hearing recovery were significantly greater in the HBOT plus medical therapy group compared with the group that received only medical therapy. Rhee and colleagues[11] concluded that HBOT was of greatest benefit when offered to patients presenting with an average hearing loss of 70 dB or greater, as salvage therapy, and when HBOT continued for at least 20 hours; however, they admitted that their conclusions were of low statistical power, and they called for further studies.

The present systematic review and meta-analysis evaluated the recent literature and focused exclusively on prospective randomized controlled studies, while Rhee and colleagues[11] included nonrandomized studies. Although HBOT has been shown to significantly improve hearing recovery, its clinical significance remains unclear, specifically whether HBOT should only be offered as salvage therapy to a subgroup of patients who have SSNHL with severe to profound hearing loss. Our null hypothesis was that patients who received HBOT alone or in addition to other treatments had the same hearing outcomes and treatment-associated adverse effects as patients who received comparator treatments with steroids and/or placebo.

The purpose of this study was to evaluate the current literature on the effectiveness of HBOT in patients with SSNHL, assessed by the mean PTA change averaged across 4 low (0.5, 1, 2, and 3 or 4 kHz) or 3 high (3 or 4, 6, and 8 kHz) frequencies, with the odds ratio (OR) for hearing recovery defined as a hearing gain of 10 dB or greater in PTA average.

Key Points

Question What is the prospective randomized controlled trial evidence for using hyperbaric oxygen therapy (HBOT) as a single or combination therapy for improving hearing outcomes for patients with sudden sensorineural hearing loss (SSNHL) compared with control treatments?

Findings This systematic review and meta-analysis included 3 prospective randomized controlled trials with a total of 88 participants who received HBOT in intervention groups and 62 participants who received routine treatment in the control groups. The meta-analysis found a significant mean difference in absolute hearing gain and odds ratio for hearing recovery following HBOT, favoring the intervention.

Meaning The findings of this systematic review and meta-analysis suggest that clinicians treating patients with SSNHL should consider including HBOT as part of a combination treatment regimen.

Methods

This systematic review and meta-analysis was reviewed and approved by the institutional review board of University of British Columbia (Canada). Informed consent was waived because the data were available and legally accessible to the public and appropriately protected by law. This study followed the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) reporting guideline.

Search Strategy

The CAB Abstracts, Cumulative Index to Nursing and Allied Health Literature, ClinicalTrials.gov, Cochrane Central Register of Controlled Trials, Embase, Google Scholar, International Clinical Trials Registry Platform, International Standard Randomised Controlled Trial Number, PubMed, and Web of Science databases were searched using the MeSH terms "hyperbaric oxygenation," "hearing loss, sudden," "hearing loss, sensorineural," and related acronyms (ie, HBOT, HBO, SSNHL, SSHL). The Boolean operator AND was added between search terms for a more focused search. For databases that did not use MeSH keywords, we added "sudden deafness" and "hyperbaric." The reference lists of selected articles were also searched for additional articles.

Study Selection

We included prospective randomized controlled trials (RCTs) involving adult (≥18 years) participants, published in English from January 1, 2000, to April 30, 2020, and using the diagnostic criteria outlined by the American Academy of Otolaryngology–Head and Neck Surgery in its *Clinical Practice Guideline: Sudden Hearing Loss*.[1] The search was restricted to the past 20 years to increase the likelihood of finding articles that used comparable HBOT treatment protocols and similar diagnostic criteria, thus decreasing interstudy heterogeneity. Articles comparing HBOT, as single therapy or as part of a combination treatment protocol, with other treatments (eg, oral steroids, IT steroids, IV steroids, or placebo) in a single therapy

or as part of a combination treatment protocol were included. Articles with insufficient PTA data were excluded.

Data Extraction

Two investigators (T.G.J. and A.A.) independently screened the articles and extracted data from the included studies using a standard data extraction form. For each study, the year of publication; authors; study design; sample sizes; participants' age and sex distribution; severity of hearing loss; number and duration of HBOT sessions; additional treatment details (ie, medication types, delivery methods, dosages, and treatment onset); PTA threshold averages before and after treatment; proportion of patients showing hearing recovery; and treatment-related adverse effects were recorded.

Outcomes

The primary outcome was the absolute change in PTA threshold averages among participants in the HBOT groups compared with the control therapy groups. The secondary outcomes were the proportion of patients showing a hearing gain of 10 dB or greater in PTA average following treatment and the adverse effects of treatment adverse.

Assessment of Risk of Bias

The risk of bias was assessed by 3 investigators (T.G.J., A.A., and D.A.N.) independently using the Cochrane Risk of Bias tool.[12] The overall risk of bias was denoted as low concern, some concerns, or high risk based on the majority opinion. A high-quality study was defined to have low risk of bias in all the assessed domains. The reviewers were not blinded to study details.

Statistical Analysis

A meta-analysis was conducted from November 30, 2020, to May 20, 2021, using Review Manager, version 5.3 (Cochrane Collaboration). Data extracted from the included studies were used to calculate mean differences, odds ratios (OR), and 95% CIs. Depending on heterogeneity, either the fixed-effects or the random-effects model was applied to obtain pooled effect size estimates, 95% CIs, and *P* values using the inverse variance and Mantel-Haenszel methods. Intertrial statistical heterogeneity was determined using the I^2 test.[13] A statistically significant ($P < .05$) I^2 value (>50%) was taken as indicative of heterogeneity.

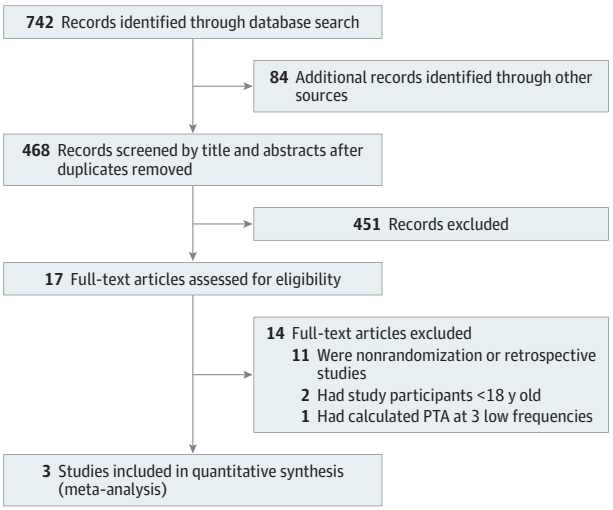
A fixed-effects model was used if no heterogeneity was identified, and a random-effects model was applied if heterogeneity was present. Correlation coefficients and SDs for absolute hearing gain were imputed from a retrospective chart review study[14] when not reported.[15] The PTA threshold averaged across 4 low frequencies was labeled PTA_4. In addition, if SD imputation was adopted, the posttreatment PTA_4 threshold means were compared, as recommended by Higgins and colleagues.[15]

Results

Search Yield

Initially, 826 records were identified, which included 358 duplicates. Another 451 articles were excluded based on title and abstract screening, leaving 17 full-text articles that were reviewed. Of these,14 articles were excluded because of absence of randomization (n = 11), participants being older than 18 years (n = 2), and PTA threshold averaged across 3 frequencies (n = 1). The remaining 3 articles met all of the inclusion criteria and assessed a total of 150 patients with SSNHL in 2018(**Figure 1**).[16-18]

Figure 1. PRISMA Flow Diagram



PTA denotes pure-tone audiometric average.

Study Characteristics

The characteristics of the included studies are summarized in the **Table**. Cho and colleagues[16] included patients with SSNHL who had severe to profound hearing loss (≥70 dB). Krajčovičová and colleagues[17] included patients with SSNHL who had moderate hearing loss (41-60 dB). Khater and colleagues[18] did not report recruiting patients with a specific degree of hearing loss; however, the mean initial PTA_4 (SD) for the HBOT and control groups was 72.86 (1.43) and 71.94 (2.1) dB, respectively. In all 3 included studies, HBOT was an adjuvant therapy in the intervention groups.

In the study by Cho and colleagues,[16] all patients received oral methylprednisolone (0.8 mg/kg/d) plus IT dexamethasone 0.4 to 0.8 mL (4 mg/mL) for 7 days; the dose of methylprednisolone was then tapered for the next 5 days. The study's intervention group had daily 60-minute HBOT sessions for 10 days at 2.5 atmospheres absolute (ATA).

In the study by Khater and colleagues,[18] all patients received oral prednisolone (1 mg/kg) for 10 days plus an initial dose of IT methylprednisolone 0.4 to 0.6 mL (40 mg/mL); the dose of prednisolone was then tapered during the next 10 days. Patients received an additional dose of IT steroids 1 week later if there had not been any or only partial hearing improvement. All of the patients also received antiviral therapy (acyclovir, 500 mg, 3 times daily) for 1 week.[18] The intervention group underwent 60-minute daily HBOT sessions for 20 days at 2 ATA.[18]

In the study by Krajčovičová and colleagues,[17] all patients received IV methylprednisolone (250 mg daily) for 2 days; the dose was then tapered during 3 days. This was reportedly

Table. Characteristics of the Prospective Randomized Controlled Trials Included in the Study of PTA_4 Before and After Treatment

Trial	Study group	Treatment	No. of patients treated	Patient age, mean (SD), y	Sex (male: female)	PTA_4, mean (SD), dB	
						Before treatment	After treatment [time to follow-up]
Cho et al,[16] 2018	Intervention	HBOT + oral and IT steroids	30[a]	53.8 (13.1)	17:13	90.07 (11.06)	51.95 (22.55) [1 mo]
	Control	Oral + IT steroids	30	56.1 (13.6)	11:19	92.36 (14.79)	61.98 (31.21) [1 mo]
Khater et al,[18] 2018	Intervention	HBOT + oral and IT steroids + antiviral drugs	11	45.9 (6.9)	5:06	72.86 (1.43)	18.1 (2.2) [1 mo]
	Control	Oral + IT steroids + antiviral drugs	11	45.8 (7.14)	7:04	71.94 (2.1)	28.1 (8.7) [1 mo]
Krajčovičová et al,[17] 2018	Intervention	HBOT + oral and IV steroids + hemorheologic therapy	47	50 (14)	33:35:00	46.55 (26.19)	28.35 (24.35) [~1 mo]
	Control	Oral + IV steroids + hemorheologic therapy	21			40.9 (23.34)	32.1 (21.24) [~1 mo]

Abbreviations: dB, decibel; HBOT, hyperbaric oxygen therapy; IT, intratympanic; IV, intravenous; PTA_4, pure-tone audiometric thresholds averaged across 4 low frequencies (0.5, 1, 2, and 4 kHz).

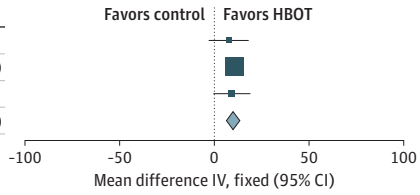
[a] Two lost to follow-up at 2 and 3 months.

Figure 2. Forest Plot of Mean Difference in PTA_4 Change Following Treatment in the HBOT vs Control Groups

A Fixed-effects model

Study or subgroup	HBOT group Mean	SD	Total	Control group Mean	SD	Total	Weight, %	Mean difference IV, fixed (95% CI)
Cho et al,[16] 2018	38.12	17.22	30	30.38	23.96	30	13.1	7.74 (-2.82 to 18.30)
Khater et al,[18] 2018	54.76	1.63	11	43.84	7.46	11	71.6	10.92 (6.41 to 15.43)
Krajčovičová et al,[17] 1998	18.20	20.60	47	8.8	18.2	21	15.3	9.40 (-0.36 to 19.16)
Total (95% CI)			**88**			**62**	**100.0**	**10.27 (6.45 to 14.09)**

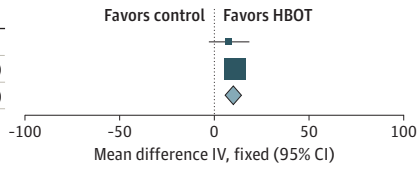
Heterogeneity: $\chi^2 = .33$; $df = 2$ ($P = .85$); $I^2 = 0\%$
Test for overall effect: $z = 5.27$ ($P < .001$)



B Subgroup analysis

Study or subgroup	HBOT group Mean	SD	Total	Control group Mean	SD	Total	Weight, %	Mean difference IV, fixed (95% CI)
Cho et al,[16] 2018	38.12	17.22	30	30.38	23.96	30	15.4	7.74 (-2.82 to 18.30)
Khater et al,[18] 2018	54.76	1.63	11	43.84	7.46	11	84.6	10.92 (6.41 to 15.43)
Total (95% CI)			41			41	**100.0**	**10.43 (6.28 to 14.58)**

Heterogeneity: $\chi^2 = .29$; $df = 1$ ($P = .59$); $I^2 = 0\%$
Test for overall effect: $z = 4.93$ ($P < .001$)



A, All 3 RCTs included were subjected to meta-analysis using a fixed-effects model. B, Subgroup meta-analysis excluding the study by Krajčovičová and colleagues.[17] HBOT denotes hyperbaric oxygen therapy; IV, weighted mean difference; PTA_4, pure-tone audiometric thresholds averaged across 4 low frequencies (0.5, 1, 2, and 4 kHz); and RCTs, randomized controlled trials.

followed by oral prednisone (400 mg daily, likely typographical error that should have been 40 mg daily) for 5 days and then 20 mg daily for 5 days.[17] Pentoxifylline (100 mg, twice daily) and betahistin (16 mg, 3 times daily) were also given to all patients.[17] The intervention group underwent 90-minute daily HBOT sessions for 10 days at 2 ATA.[17]

Absolute Hearing Gain Following Treatment

In all, the 3 studies had a total of 88 patients in the HBOT intervention groups and 62 patients in the control groups. Absolute hearing gain following treatment significantly favored HBOT therapy over control therapy (mean difference, 10.3 dB; 95% CI, 6.5-14.1 dB; $I^2 = 0\%$; **Figure 2**A). Krajčovičová and colleagues[17] did not specify when posttreatment audiograms were recorded; thus, to conduct a sensitivity analysis, we excluded their data, which left 41 patients in both the HBOT and control groups. The sensitivity analysis showed that the absolute hearing gain still significantly favored HBOT over control therapy (mean difference, 10.4 dB; 95% CI, 6.3-14.6; Figure 2B). Furthermore, because Cho and colleagues[16] and Khater and colleagues[18] studied patients with SSNHL with severe to profound hearing loss (≥70 dB), the finding in favor of HBOT applies to the subgroup of patients presenting with severe to profound hearing losses.

PTA_4 Following Treatment

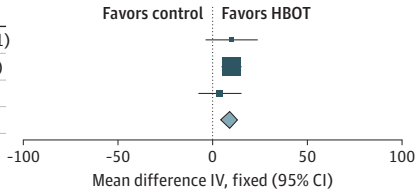
The SD values were imputed to calculate the intergroup mean difference in absolute PTA_4 change following treatment. Therefore, we also conducted a meta-analysis comparing the intergroup posttreatment mean PTA_4 (**Figure 3**A). The HBOT group showed an improvement (mean difference, 9 dB; 95% CI,

Figure 3. Forest Plot of Mean Difference in After Treatment PTA_4 Between the HBOT vs Control Groups

A Fixed-effects model

Study or subgroup	Control group Mean	SD	Total	HBOT group Mean	SD	Total	Weight, %	Mean difference IV, fixed (95% CI)
Cho et al,[16] 2018	61.98	31.21	30	51.95	22.55	30	10.9	10.03 (-3.75 to 23.81)
Khater et al,[18] 2018	28.10	8.70	11	18.10	2.20	11	73.4	10.00 (4.70 to 15.30)
Krajčovičová et al,[17] 2018	32.10	21.24	21	28.35	24.35	47	15.8	3.75 (-7.69 to 15.19)
Total (95% CI)			62			88	100.0	9.02 (4.48 to 13.56)

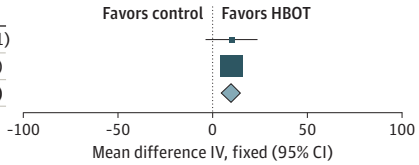
Heterogeneity: $\chi^2 = .97$; $df = 2$ ($P = .62$); $I^2 = 0\%$
Test for overall effect: $z = 3.89$ ($P < .001$)



B Subgroup analysis

Study or subgroup	Control group Mean	SD	Total	HBOT group Mean	SD	Total	Weight, %	Mean difference IV, fixed (95% CI)
Cho et al,[16] 2018	61.98	31.21	30	51.95	22.55	30	12.9	10.03 (-3.75 to 23.81)
Khater et al,[18] 2018	28.10	8.70	11	18.10	2.20	11	87.1	10.00 (4.70 to 15.30)
Total (95% CI)			41			41		10.00 (5.05 to 14.95)

Heterogeneity: $\chi^2 = .00$; $df = 1$ ($P > .99$); $I^2 = 0\%$
Test for overall effect: $z = 3.96$ ($P < .001$)



A, Meta-analysis of all 3 RCTs included using a fixed-effects model. B, Subgroup analysis excluding the study by Krajčovičová et al.[17] HBOT denotes hyperbaric oxygen therapy; IV, weighted mean difference; PTA_4, pure-tone audiometric thresholds averaged across 4 low frequencies (0.5, 1, 2, and 4 kHz), and RCTs, randomized controlled trials.

4.5-13.6 dB; I^2 = 0%) in mean posttreatment PTA_4 over that achieved with control therapy. The sensitivity analysis excluding Krajčovičová and colleagues[17] (Figure 3B) still showed a statistically significant improvement (mean difference, 10 dB; 95% CI, 5.1-15.0 dB) in mean posttreatment PTA_4 among patients in the HBOT vs the control therapy.

Proportion of Patients Demonstrating Hearing Recovery

Two of the 3 studies, Cho and colleagues[16] and Krajčovičová and colleagues,[17] were included in the analysis of patients showing a PTA_4 of 10 dB or greater in hearing gain following treatment (**Figure 4**). The study by Khater and colleagues was excluded because the proportion of patients showing hearing recovery as defined for the current analysis was not reported. Of patients in the HBOT groups, 74.7% (56 of 75 patients) showed hearing recovery, as did 60.8% (31 of 51 patients) in the control group. The odds of hearing recovery was 4.3 times greater (95% CI, 1.6-11.7; I^2 = 0%) in patients with SSNHL who received HBOT compared with those who underwent the control treatment.

Adverse Effects of Treatment

Cho and colleagues[16] described 2 patients who reported mild otalgia at the initiation of HBOT. The other studies did not comment on the adverse effects of treatment; therefore, no statistical analysis of the such effects could be conducted.

Risk of Bias

For Cho and colleagues[16] and Khater and colleagues,[18] the risk of bias was assessed as presenting some concerns. Krajčovičová and colleagues[17] was assessed as being at high risk of bias. Therefore, all of the participants in the present analyses were included in studies that had at least some concerns for risk of bias. Only articles published in the English were included; therefore, there was a high risk of publication language bias.

Heterogeneity

Statistical Heterogeneity

All studies reported PTA_4, indicating that outcome measurements were made on the same scale. Two studies (Cho and colleagues[16] and Krajčovičová and colleagues[17]) defined hearing recovery as 10 dB or greater in absolute hearing gain. Intertrial statistical heterogeneity was 0% on I^2 tests for all meta-analyses conducted; therefore, a fixed-effect model was used.[13]

Clinical Heterogeneity

The 3 included studies recruited patients with differing severities of hearing loss; therefore, they were clinically heterogeneous based on presenting audiograms. Cho and colleagues[16] recruited patients with severe to profound SSNHL. Krajčovičová and colleagues[17] recruited patients with moderate hearing loss. Khater and colleagues[18] did not specify any audiometric recruitment criteria.

Methodological Heterogeneity

Sources of methodological heterogeneity include the time to treatment initiation, timing of posttreatment audiograms, and differences in intervention and control therapies. Khater and colleagues[18] and Krajčovičová and colleagues[17] began treatment within 7 days of the onset of hearing loss symptoms. It is unclear when Cho and colleagues[16] began treatment in relation to symptom onset; however, they excluded patients presenting 10 days or more after onset of hearing loss.

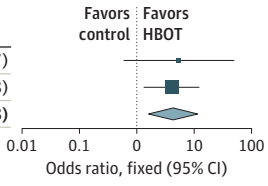
Cho and colleagues[16] and Khater and colleagues[18] recorded audiograms 1 month after treatment. In addition, Cho and colleagues[16] assessed hearing recovery 3 months after treatment. Krajčovičová and colleagues[17] did not specify when posttreatment audiograms were measured.

The HBOT treatment protocols differed among the 3 studies. Cho and colleagues[16] conducted 10 sessions with a duration of 60 minutes; Krajčovičová and colleagues[17] con-

Figure 4. Forest Plot of Proportion of Patients Showing a 10-Point or Greater Audiometric Gain in the HBOT vs Control Groups

Study or subgroup	HBOT group Events	HBOT group Total	Control group Events	Control group Total	Weight, %	Odds ratio, fixed (95% CI)
Cho et al,[16] 2018	27	28	25	30	21.3	5.40 (0.59-49.47)
Krajčovičová et al,[17] 2018	29	47	6	21	78.7	4.03 (1.32-12.28)
Total (95% CI)	**56**	**75**	**31**	**51**	**100.0**	**4.32 (1.60-11.68)**

Heterogeneity: $\chi^2 = .05$; $df = 1$ ($P = .82$); $I^2 = 0\%$
Test for overall effect: $z = 2.88$ ($P = .004$)



A fixed-effects model was used for meta-analysis. dB denotes decibels and HBOT, hyperbaric oxygen therapy.

ducted 10 sessions of 90 minutes; and Khater and colleagues[18] conducted 20 sessions of 60 minutes. Control therapies also differed by dosages, routes of steroid administration, and additional medications used.

Discussion

This systematic review and meta-analysis analyzed data from 3 prospective RCTs published in 2018 with a total of 88 participants assigned to the HBOT groups and 62 patients to the control therapy. Included RCTs had adopted the SSNHL diagnostic criteria outlined in the *Clinical Practice Guideline: Sudden Hearing Loss*[1] and reported mean differences in PTA thresholds (averaged across 4 frequencies: 0.5, 1, 2, and 4 kHz) before and after treatment. The uniformity of SSNHL diagnostic criteria, RCT study design, and outcome measures contributed to the I^2 equal to 0% interstudy statistical heterogeneity.[13] This is an improvement over the statistical heterogeneity of more than 79% for the meta-analyses of the HBOT literature by Rhee and colleagues,[11] which included more diverse studies; and the Cochrane review by Bennett and colleagues,[10]which reported on a cohort of RCTs published earlier. We reject the null hypothesis that patients who received HBOT alone or in addition to other treatments had the same hearing outcomes as patients who received comparator treatments with steroids and/or placebo.

The 9- to 10.4-dB increase in hearing gain following HBOT in the current review is within the effect size range of 6.3 to 14.6 dB reported for HBOT by other reviews.[10,11] The present study's findings strongly support an absolute HBOT effect within the 6.3 to 14.6 dB range, as has been consistently identified by a wide range of studies.[10,11,16-18] Only the study by Topuz and colleagues[19] was common to the reviews of both Rhee and colleagues[11] and Bennett and colleagues,[10] and there was no overlap with the studies assessed by the present review, which emphasizes that the effect and its size have been repeatedly observed.

Additionally, HBOT protocols differed in the 3 included studies.[16-18] The total duration of HBOT ranged from 600 to 1200 minutes. Rhee and colleagues[11] concluded that a significant HBOT effect was only evident at treatment durations of 1200 minutes or more. The more recent RCTs in this review demonstrate a clear benefit for HBOT protocols of half that duration. It is difficult to be certain about the optimal HBOT protocol based on the articles reviewed; however, 2.0 ATA protocols were used in both studies that demonstrated an HBOT effect.[17,18] Furthermore, these 2 studies suggest that 10 sessions of 90 minutes achieve a similar therapeutic effect as 20 sessions of 60 minutes. Hence, we recommend a minimum of 900 minutes of 2.0 ATA HBOT delivered either by 10 sessions of 90 minutes or 15 sessions of 60 minutes for the treatment of patients with SSNHL.

Only 1 trial reported treatment-related adverse effects, ie, transient otalgia in 2 patients during the first week of treatment.[16] There was no report that these patients required myringotomy and ventilation tube placement to complete their course of treatment.[16] All included studies[16-18] started HBOT within 7 to 10 days of hearing loss; therefore, it is safe to conclude that the benefit of HBOT applies when it is adopted within 10 days of hearing loss onset.

Rhee and colleagues[11] concluded that the benefit of HBOT was greater in patients with severe to profound hearing loss at baseline; a forest plot of their subgroup analyses by severity of hearing loss showed only "any hearing improvement" in that group. The RCTs in this review[16-18] recruited patients with differing severities of hearing loss, ranging from moderate to profound SSNHL. In addition, the forest plot of patients showing a 10 dB or greater hearing gain demonstrates a clear benefit among patients with moderate hearing loss in the study by Krajčovičová and colleagues[17] (Figure 3). Therefore, until there is more definitive evidence of a difference in benefit based on the severity of hearing loss, we recommend offering HBOT to patients with SSNHL with any degree of hearing loss at presentation.

Limitations

The main limitations of this review were the small number of studies that fulfilled the inclusion criteria (n = 3) and the overall risk of bias in the included studies. The risk of bias was ascertained to be of some concern in the studies by Khater colleagues[18] and Cho colleauges[16] and of high risk in the study by Krajčovičová and colleagues.[17] However, the patients allocated to the intervention and control groups were similar in age, sex, and the severity of hearing loss across the studies. It is likely that the conclusions that arose from the studies with some concerns of bias are reliable. Therefore, because the meta-analysis that excluded the study by Krajčovičová and colleagues[17] (Figure 2B) identified a greater hearing gain of 10.4 dB associated with HBOT, the risks of bias do not detract from the interpretation of this review's findings. The secondary outcome (adverse effect of treatment) could not be assessed. Future studies should assess and report on the adverse effects of treatment. Extending the search criteria to include non-English language publications would address the language bias and could yield a higher number of eligible studies.

Conclusions

This systematic review and meta-analysis suggests the therapeutic usefulness of HBOT in adult patients with SSNHL. In 3 RCTs, the mean PTA_4 change following treatment, final PTA_4, and hearing recovery were all associated with significant improvements in patients assigned to the HBOT intervention (a combination treatment regimen) compared with control therapy alone. Further research is required to determine the optimal HBOT protocol.

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Invited Commentary

Is It Time to Encourage Hyperbaric Oxygen Therapy in Combination With Medical Treatment for Sudden Sensorineural Hearing Loss?

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The treatment of idiopathic sudden sensorineural hearing loss (SSNHL) continues to be a substantial clinical challenge, in part because of the heterogeneity of the patient population and in part because of the difficulty of studying a disorder with no known causes and no defined, proven, or widely accepted course of clinical intervention. We read with interest the systematic review and meta-analysis by Joshua and colleagues[1] on hyperbaric oxygen therapy (HBOT) for patients with SSNHL. Rhee and colleagues published a review of the same topic in 2019[2]; however, their conclusions were criticized for significant heterogeneity of the pooled studies, which introduced potentially unsurmountable bias.[3]

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Joshua and colleagues,[1] however, performed a broad systematic review of recent literature and maintained strict criteria for inclusion in the meta-analysis. They specifically selected prospective randomized clinical trials published in the past 20 years whose diagnostic criteria was based on the American Academy of Otolaryngology–Head and Neck Surgery's *Clini-*