Current Otorhinolaryngology Reports (2022) 10:329–335
https://doi.org/10.1007/s40136-022-00414-5

OTOLOGY: ADVANCES IN OTOLOGY (BD NICHOLAS, SECTION EDITOR)

Update on the Management of Idiopathic Sudden Sensorineural Hearing Loss

Zachary G. Schwam[1,2] · **George B. Wanna**[1,2]

Accepted: 27 June 2022 / Published online: 7 July 2022

Abstract

Purpose of Review To examine the state of the literature as it applies to the treatment options for idiopathic sudden sensorineural hearing loss.

Recent Findings There is an overwhelming amount of data with regard to the management of iSSNHL with a variety of treatment protocols and high spontaneous rates of recovery. Herein, we discuss the data surrounding antivirals, antioxidants, vasoactive substances, systemic and intratympanic steroids, and hyperbaric oxygen therapy in the treatment of this condition.

Summary Heterogeneity of inclusion criteria, patient characteristics, control groups, and treatment regimens render it difficult-to-impossible to generalize as to the efficacy of the below regimens.

Keywords Idiopathic sudden sensorineural hearing loss · Sudden hearing loss · Intratympanic steroids · Hyperbaric oxygen · Review · Treatment

Introduction

Idiopathic sudden sensorineural hearing loss (iSSNHL) is an uncommon condition affecting 5–27 per 100,000 people [1••, 2], with approximately 66,000 new cases each year in the USA [1••]. Numerous etiologies have been posited, namely viral infection, autoimmune or inner ear inflammatory processes, vascular dysfunction causing cochlear hypoxia, and hydrops causing inner ear membrane rupture [3, 4]. While circumstantial evidence of ischemia and viral illness exist as possible etiologies, human temporal bones from patients with iSSNHL do not reflect labyrinthine ossification and no causative viral organism has been successfully targeted or isolated from affected specimens [5–7]. The most commonly used audiometric criteria for iSSNHL is a SNHL of ≥ 30 dB in ≥ 3 consecutive frequencies occurring within a 72-h window; however, in practice, far less rigor is applied to making such a diagnosis [1••].

As the etiology of hearing loss is unknown and the loss of hearing profoundly disconcerting to the patient [8–10], the proverbial kitchen sink has been thrown at this desperate patient population by well-meaning providers seeking to regain every possible decibel. Various steroid preparations, vasoactive substances, vitamins, antioxidants, anticoagulants, and antivirals have all been used, often haphazardly. The small sample sizes and heterogeneity of inclusion criteria, audiometric definitions of SSNHL, definitions of recovery, drug used, dosing, and duration all complicate meaningful comparisons and pooling of data. Furthermore, many studies administer several concomitant therapies, attempt salvage protocols, and have control groups that vary widely [1••, 10–12]. The purpose of this review is not to make recommendations as to treatment but to inform the reader as to the higher-quality data available.

Antiviral Therapy

Stokroos et al. conducted a randomized control trial (RCT) where 44 patients with iSSNHL received 1 week of intravenous prednisolone; half were given additional intravenous acyclovir and the other half placebo; no significant

This article is part of the Topical collection on *OTOLOGY: Advances in Otology*

✉ Zachary G. Schwam
Zachary.schwam@mountsinai.org

George B. Wanna
gwanna@nyee.edu

[1] Icahn School of Medicine at Mount Sinai, Department of Otolaryngology-Head and Neck Surgery, 1 Gustave L. Levy Place, Box 1189, New York, NY 10029, USA

[2] New York Eye and Ear Infirmary of Mount Sinai, Department of Otolaryngology-Head and Neck Surgery, New York, NY, USA

effect on audiometric outcomes was demonstrated by adding acyclovir [13]. Similar results were demonstrated in a RCT conducted by Westerlaken et al. [14] and a Cochrane review of four RCTs by Awad et al. [15].

Carbogen and Other Vasoactive Substances

Using carbogen (a mixture of 95% O_2 and 5% CO_2) to treat iSSNHL is predicated on the theory of vascular compromise causing cochlear hypoxia. In Fisch's study examining perilymph oxygenation in patients with iSSNHL, a stapedotomy was made on anesthetized patients and an oxygen sensor placed; they found that in the early stage of treatment, the perilymph oxygenation level was only 30% that of a normal ear and that inhalation of carbogen nearly doubled the oxygen tension. The group then performed an RCT examining carbogen inhalation versus intravenous papaverine and dextran as a control group. Duration of treatment was not clear. While there was no short-term difference in audiometric outcomes between the two groups, they found significantly better speech-frequency pure tone averages (PTAs) at 1 year (30.0 dB versus 16.6 dB) [4]. In 1997, Kallinen and colleagues performed a trial comparing three groups: anticoagulation (IV heparin followed by warfarin) + betahistine for vasodilation, anticoagulation + carbogen + betahistine, and carbogen + betahistine. The authors found that the anticoagulation arm did best when examining upward sloping audiograms while the carbogen group was best for flat and downward sloping audiograms. Combination treatment had its best results in the 4000–8000 Hz range. While interesting, exact numerical improvements and statistical methods were unclear [3].

In a RCT comparing 5 days of treatment with oral (po) prednisone to po placebo, carbogen inhalation, or room air inhalation, Cinamon et al. found no differences in audiometric outcomes in the first month in 41 patients. Regardless of intervention, hearing was found to improve [16].

A Cochrane review from 2009 identified three low-quality RCTs including 189 participants. The studies varied significantly in substance and protocol, thereby not allowing pooling of the results [17]. Ogawa's RCT of IV hydrocortisone + IV prostaglandin E1 versus IV hydrocortisone + placebo yielded no benefit from the prostaglandin [18]. Ni's RCT comparing IV steroid, vitamin B, dextran, salvise miltiorrhiaze, and po vitamin C and E compared to the same regimen with added inhaled carbogen demonstrated a significant benefit in hearing improvement in the carbogen group (76.9% versus 50%) [19]. Poser's RCT included 80 patients receiving dextran with either placebo or naftidrofuryl and found a 70% improvement in the low frequencies in the treatment group compared to 40% in the control group [20].

Antioxidants

Antioxidants have been used in the treatment of iSSNHL under the assumption that superoxide radicals may contribute to inner ear damage [21].

Ahn et al. conducted a RCT of 120 patients undergoing either po steroid, low salt diet, and lipoprostaglandin E1 injections or the same regimen with adjunctive coenzyme Q10 (CoQ) for 2 weeks thereafter. Intratympanic steroids were also done in a salvage setting in both groups. CoQ is a free radical scavenger that inhibits lipid peroxidation and reduces alpha-tocopheroxyl to alpha-tocopherol in the inner ear. The CoQ group did not have an improvement in PTA but was found to have a significantly higher improvement in speech discrimination score (36.9% versus 23.6%) compared to the control group [22].

Joachims et al. conducted an RCT of 66 patients; half the group got treatment consisting of po steroids, IV magnesium, inhaled carbogen, and bedrest, while the other half received the same regimen but with adjunctive vitamin E. A recovery rate of 75% (as defined by the hearing gain divided by the difference in interaural hearing level) was 78.8% in the study group compared to 45.5% in the control group, a significant difference. However, there was no difference in rates of complete recovery between the groups [21].

In a case–control study by Angeli et al., *N*-acetylcysteine (NAC) was used in combination with po + IT steroid, showing a significant improvement in PTA when compared to steroid alone, particularly at 4000 Hz. Patients receiving NAC had higher recovery rates compared to the normal ear in 63% compared to 35% for the steroid group at 6 months [23]. Chen and Young's case control study of 35 patients receiving NAC alone versus 35 matched controls who had received steroids, dextran, and gingko biloba showed a significantly higher mean hearing gain of 43 dB for the NAC group compared to 21 dB for controls and an overall improvement rate of 91% for NAC compared to 57% in controls [24].

These studies are emblematic of many of the problems in the iSSNHL literature with its complicated control groups, multiple temporally spaced interventions, and difficult-to-compare success metrics.

Magnesium

Due to magnesium's role in regulating cellular membrane permeability and its potential protective role in noise-induced hearing loss, Gordin and colleagues performed a RCT of 133 patients inhaling carbogen (control group), or inhaling carbogen while also receiving IV magnesium sulfate. The mean improvement using the Shairashi equation {Improvement rate (%) = 100 [(initial PTA − final PTA) /

(initial PTA – PTA of opposite ear)]} was significantly higher in the adjunctive magnesium group (66.4% versus 49.9%), and recovery was attained in 48% of the magnesium group compared to 31.6% of controls. The authors also found that patients with vestibular symptoms and those treated ≥ 8 days after symptom onset had poorer recovery [25]. In another RCT of 28 patients receiving either po steroid and placebo or po steroid and magnesium aspartate, the magnesium group had significantly higher hearing improvements across all tested frequencies [26].

Corticosteroids

The American Academy of Otolaryngology-Head and Neck Surgery's (AAO-HNS) 2019 clinical practice guidelines state that clinicians may offer steroids as initial therapy within 2 weeks of onset of symptoms due to the small possibility of hearing improvement despite mixed data. However, they temper their guideline with a grade C recommendation and a medium level of confidence in the available evidence. The guidelines further state that an optimal treatment dose of oral prednisone is 1 mg/kg/day in a single dose (maximum 60 mg) and a treatment duration of 10–14 days (60 mg prednisone is equivalent to 48 mg methylprednisolone and 10 mg IV dexamethasone). In patients with incomplete responses, intratympanic (IT) steroid therapy should be offered between 2 and 6 weeks of symptom onset [1••]. An international consensus document from 2018 builds on the AAO-HNS guidelines and calls attention to the impressive heterogeneity seen across studies, making it difficult or impossible to compare outcomes across trials and reports [10, 27]. In the multitude of reports included below, we recommend reading the primary source with a close eye toward methodology given the heterogeneity of control groups, definitions of hearing recovery, various pure tone averages (PTAs), inclusion criteria, and sample size.

Systemic Steroids Alone

Wilson's 1980 landmark article [28••] set the stage for the use of steroids in iSSNHL. Their overall recovery in the steroid group was 61% compared to 32% in the placebo group, and all their patients had complete recovery in the 4000–8000 Hz range. The authors found that those with profound hearing loss had lower rates of recovery and that the relative odds favoring recovery in the steroid group was 4.39. However, there are a number of methodological issues with the study that should cause significant pause. A total of 67 patients were included (34 controls, 33 placebo), but 52 additional patients who declined to participate were added to the control group for analysis. The intervention group received two different steroid doses thought to be "roughly equivalent," but it is clear that upon examining the dosages administered, there was little-to-no standardization. Additionally, method of randomization and duration of therapy were not discussed. One should interpret the results of this article with caution.

Nosrati-Zarenroe's RCT of adult patients in Sweden examined those getting po prednisolone (8 days of steroid if complete recovery and an additional 22 days of lower-dose steroid if incomplete) and placebo. There was no difference in hearing improvement at day 8 or at 3 months. The investigators did however find that while those with abnormal imaging findings and initial vertigo had worse hearing recovery, those with abnormal lab values had better recoveries [29•].

A Cochrane review by Wei et al. identified 3 trials including 267 patients; all studies were at high risk of bias, and in two-thirds, there was no effect from steroid on hearing recovery. Heterogeneity was considered too great to draw firm conclusions [12].

A retrospective analysis of 318 iSSNHL patients examining steroid treatment in 266 patients within 1 month versus 52 receiving no treatment showed no difference in the mean PTA improvement based on treatment but a higher speech intelligibility score in the treated group. In those with initial PTAs ≥ 60 dB, PTA in the treatment group improved significantly more. The authors used a 15 dB improvement as their definition of recovery, with a 51% success rate compared to 31% of untreated patients spontaneously recovering [5].

Intratympanic Steroids Alone

The rationale for IT as opposed to systemic steroid administration is the higher inner ear concentrations achievable without the systemic effects of po or intravenous steroid administration [2]. While often given in conjunction with systemic steroid or as a salvage treatment after a course of systemic steroid (both of which will be discussed later in this article), there are data regarding its use in isolation. IT injections are relatively low risk, with major adverse effects being transient vertigo, pain, or a residual tympanic membrane perforation rate of < 2.0% [30, 31].

Filipo et al. conducted an RCT examining 50 patients with flat, moderate hearing loss. Half the cohort received three consecutive daily injections of prednisolone compared to a placebo group receiving saline. All patients with incomplete recovery by day 7 were given po prednisolone adjunctively. While there was a huge difference in the complete recovery rate for the steroid group by day 7, by 30 days, the complete recovery rates for both groups were similar and high. However, a substantially higher proportion of the

control group had exhibited no recovery by the final time point (28% versus 4%) [32].

Garavello et al. performed a meta-analysis of 11 RCTs involving nearly 1000 patients, including 4 studies examining primary IT treatment and 7 analyzing IT steroids in the salvage setting. There was statistically significant benefit in the majority of primary and salvage trials; however, there was a lot of heterogeneity in study protocols. Concomitant systemic therapy and a multitude of divergent control groups make it impossible to coherently generalize the results [11].

A small retrospective series of 21 patients receiving weekly IT methylprednisolone found an overall response to treatment of 67%, with treatment initiation < 14 days being the only significant predictor of a positive response [33]. In another retrospective series of 25 patients given IT methylprednisolone or dexamethasone, there was an average PTA and speech discrimination improvement of 27.2 dB and 25.4%, respectively. Treatment within 10 days was found to make a large, significant difference in terms of speech reception thresholds and PTA [34].

Combination Systemic and IT Steroid

An RCT by Ahn and colleagues dividing 120 patients into getting po methylprednisolone and IT dexamethasone versus po methylprednisolone alone showed similar recovery rates and PTA changes between the two groups. However, upon frequency-specific analysis, adding IT dexamethasone improved hearing at 250 Hz [35]. Battaglia's multicenter RCT of 51 patients had three treatment groups: (A) IT dexamethasone with placebo taper, (B) po prednisone with placebo injection, and (C) combination IT dexamethasone and po prednisone. This last combination group had a 44% increase in speech discrimination and 40 dB improvement in PTA, with significantly higher values than those in group B. Combination therapy was independently associated with better outcomes if hearing was better than profound and had the shortest mean time to recovery [36]. Similarly good results were demonstrated in Gundogan's RCT of 73 patients receiving combination therapy compared to systemic treatment: significantly larger increases in PTA and speech discrimination scores were found in the combination group overall and at severe hearing losses for the entire frequency spectrum [37].

One retrospective series of 37 patients who all received a prednisone taper and a 2-week series of IT dexamethasone injections with two different steroid concentrations (10 versus 24 mg/mL) showed significantly higher recovery rates in the higher concentration group. The authors also found that the probability of significant PTA improvement decreased from a maximum of 0.93 if one started treatment on the day of symptom onset to < 0.05 if one started treatment 3 weeks later [38]. A RCT is necessary to determine the true effect of higher concentration solutions on hearing recovery.

Intratympanic Steroids in the Salvage Setting

IT steroids are often administered in the salvage setting, most often via repeated transtympanic injections, but also through tympanostomy tubes and round window microcatheters. The AAO-HNS recommends IT steroid in the salvage setting within 2–6 weeks of symptom onset [1••].

In a meta analysis by Vlastarakos et al., 525 patients received systemic steroids with effective IT salvage; however, a complete hearing recovery was only reported in a total of 13.4% of these patients. A window of 1–4 weeks from onset of symptoms was identified. Six studies using salvage round window membrane perfusion in 87 patients were also analyzed, with a return to baseline hearing status in 21.3% [39].

In two other meta analyses of RCTs by Li and Ng from 2015, 5 studies were identified with 102 IT salvage patients and 101 controls. In Li's analysis, the mean PTA improvement was 7.43 dB, which was statistically significant [40]. Ng also showed a significant reduction in PTA in the steroid group, and noted better results with IT as opposed to round window catheter. Results with dexamethasone were significantly better than with methylprednisolone [41]. A systematic review by Spear and Schwartz examined 8 randomized studies, with the vast majority showing benefit of salvage IT steroid (mean difference in improvement of 13.3 dB) [42]. A meta-analysis by Crane showed that IT steroids appeared effective in the salvage setting (OR 6.04 for recovery) but cautioned that the observed effect was likely from inadequate randomization and small sample sizes [43].

There are numerous retrospective series examining the administration of IT steroid in the salvage setting. Type and duration of steroid used, initial systemic treatment, and method of IT steroid administration all varied greatly, and their results should be examined with a critical eye. Haynes et al. injected 40 patients with a single dose of IT dexamethasone, and 27.5% showed significant improvement, with better outcomes in those receiving treatment in < 6 weeks from symptom onset. When excluding these late injections, the improvement rate was 39.3% [44]. Choung's case–control series of patients receiving 4 IT dexamethasone injections over 2 weeks compared to those who opted out of treatment showed 39.4% of the treatment group improving their PTA by ≥ 10 dB compared to 6.1% of the control group [45]. Similarly, Dallan administered a single dose of IT steroid, with significant decrease in PTA and 55% with useful improvements in hearing [46]. Using 3 salvage IT triamcinolone treatments, Andrianakis noted a mean hearing improvement of 15.9 dB and a complete or partial recovery in 57.9% [47].

Route of administration has also been examined. In a RCT examining steroid administration via tympanostomy tube versus steroid injection, there were no differences in audiometric outcome. However, patients with the tympanostomy tube had significantly shorter wait times and better overall satisfaction

[48]. When using a Silverstein microcatheter placed in the round window niche, she noted a significantly higher percentage improving and larger PTA improvements in the catheter group. It should be noted that some patients in the treatment group also underwent hyperbaric oxygen and received ribavirin [49]. Chou et al. compared continuous transtympanic therapy to intermittent injections and noted a significantly higher improvement in PTA and speech discrimination scores in the transtympanic group [50]. Vanwijk et al. also showed 31.2% of patients improving their PTA and 54.5% improving speech intelligibility using the microwick [51].

Systemic Versus IT Steroid

Numerous trials, series, and meta-analyses have compared systemic to IT steroid administration, with many trials showing essentially equivalent audiometric results using a variety of regimens [2, 43, 52–56]. Select trials have shown a distinct benefit at the higher frequencies in favor of the systemic steroid group [52]. In contrast, Kosyakov's trial of 73 patients getting either IT steroid through a tympanostomy tube over 6 months, 15 days of IV steroids and multiple other medications, or 15 days of IV steroids, there was a significant advantage in hearing recovery at all frequencies for the IT group at 6 months [57].

In the various trials, systemic steroids had a more severe adverse effect profile, including changes in mood, sleep, appetite, weight, and glucose regulation, compared to significant injection site pain and vertigo and rare systemic effects for IT steroid [2]. From a cost perspective, 2 weeks of po steroid is < $10, while 4 IT injections present significant monetary costs in addition to the societal costs of going to appointments and not working [2].

Hyperbaric Oxygen Therapy

Hyperbaric oxygen therapy (HBOT) is used in the treatment of iSSNHL with the goal of increasing cochlear oxygen tension. The 2019 AAO guidelines do not recommend HBOT but make it available as an option when combined with primary treatment within 2 weeks of symptom onset or in the salvage setting within 4 weeks of symptom onset [1••]. HBOT is often costly and not routinely covered by insurance companies.

In a series of 102 patients receiving either IV steroid with or without adjunctive HBOT, those receiving adjunctive HBOT had significantly larger hearing improvements in the lower frequencies after 10 days. This effect was particularly true for those with severe-to-profound initial losses [58]. In an RCT of 136 cases receiving either medical treatment (systemic steroid, several vitamins, anticoagulants, and nerve growth factors) with or without HBOT, the success rate (≥ 15 dB PTA improvement) was significantly higher for the HBOT group compared to the medical therapy alone group (60.6% versus 42.9%) [59].

In a meta-analysis comparing HBOT to IT steroid in the salvage setting, there were no significant differences between the proportion exhibiting hearing improvement and there was no difference in changes of PTA [60].

A recent meta-analysis by Joshua et al. examined three RCTs with a total of 88 patients receiving HBOT in addition to medical therapy while 62 patients received only medical therapy. The HBOT group had an additional hearing gain of 10.3 dB and an odds ratio of 4.3 for hearing recovery. However, the regimens of medical therapy as well as frequency and duration of HBOT varied widely. All studies had concerns for bias and were rather heterogeneous [61]. Rhee and colleagues also a performed a meta-analysis including 3 RCTs and 16 non-randomized studies analyzing the effect of adjunctive HBOT in 2401 patients. Pooled odds ratios of 1.61 and 1.43 were calculated for complete and partial hearing recovery with HBOT, respectively. The weighted mean difference in absolute hearing gain was 8.74 dB in the HBOT group. The authors also noted that HBOT was most effective in severe-to-profound hearing loss and if administered at least 20 h [62]. Another large systematic review identified a number of trials in which adjunctive HBOT had utility in the severe-to-profound setting when combined with systemic steroids [63]. Regimens were again quite heterogeneous and make generalization difficult [62, 63].

Conclusions

There is an overwhelming amount of data with regard to the management of iSSNHL with a variety of treatment protocols and high spontaneous rates of recovery. We recommend that readers critically examine individual studies for methodology and engage the patient in shared decision making to chart the most reasonable course forward. We call on the broader otolaryngology community to collaborate on large, multicenter, randomized control trials with rigid treatment protocols to obtain the highest quality data possible to inform decision making.

Acknowledgements None.

Declarations

Conflict of Interest None.

Human and Animal Rights and Informed Consent This article did not involve research on human or animal subjects.

References

Papers of particular interest, published recently, have been highlighted as:
• Of importance
•• Of major importance

1.•• Chandrasekhar SS, Tsai Do BS, Schwartz SR, et al. Clinical practice guideline: sudden hearing loss (Update). Otolaryngol Head Neck Surg. 2019;161:S1–S45. **This practice guideline is considered the authority on options for workup and management of iSSNHL and incorporates high quality data into its recommendations**.
2. Rauch SD, Halpin CF, Antonelli PJ, et al. Oral vs intratympanic corticosteroid therapy for idiopathic sudden sensorineural hearing loss: a randomized trial. JAMA. 2011;305:2071–9.
3. Kallinen J, Laurikainen E, Laippala P, et al. Sudden deafness: a comparison of anticoagulant therapy and carbogen inhalation therapy. Ann Otol Rhinol Laryngol. 1997;106:22–6.
4. Fisch U. Management of sudden deafness. Otolaryngol Head Neck Surg. 1983;91:3–8.
5. Chen CY, Halpin C, Rauch SD. Oral steroid treatment of sudden sensorineural hearing loss: a ten year retrospective analysis. Otol Neurotol. 2003;24:728–33.
6. Schuknecht HF, Kimura RS, Naufal PM. The pathology of sudden deafness. Acta Otolaryngol. 1973;76:75–97.
7. Schuknecht HF, Donovan ED. The pathology of idiopathic sudden sensorineural hearing loss. Arch Otorhinolaryngol. 1986;243:1–15.
8. Carlsson PI, Hall M, Lind KJ, Danermark B. Quality of life, psychosocial consequences, and audiological rehabilitation after sudden sensorineural hearing loss. Int J Audiol. 2011;50:139–44.
9. Chen J, Liang J, Ou J, Cai W. Mental health in adults with sudden sensorineural hearing loss: an assessment of depressive symptoms and its correlates. J Psychosom Res. 2013;75:72–4.
10. O'Connell BP, Hunter JB, Haynes DS. Current concepts in the management of idiopathic sudden sensorineural hearing loss. Curr Opin Otolaryngol Head Neck Surg. 2016;24:413–9.
11. Garavello W, Galluzzi F, Gaini RM, Zanetti D. Intratympanic steroid treatment for sudden deafness: a meta-analysis of randomized controlled trials. Otol Neurotol. 2012;33:724–9.
12. Wei BP, Stathopoulos D, O'Leary S. Steroids for idiopathic sudden sensorineural hearing loss. Cochrane Database Syst Rev. 2013;7:CD003998.
13. Stokroos RJ, Albers FW, Tenvergert EM. Antiviral treatment of idiopathic sudden sensorineural hearing loss: a prospective, randomized, double-blind clinical trial. Acta Otolaryngol. 1998;118:488–95.
14. Westerlaken BO, Stokroos RJ, Dhooge IJ, Wit HP, Albers FW. Treatment of idiopathic sudden sensorineural hearing loss with antiviral therapy: a prospective, randomized, double-blind clinical trial. Ann Otol Rhinol Laryngol. 2003;112:993–1000.
15. Awad Z, Huins C, Pothier DD. Antivirals for idiopathic sudden sensorineural hearing loss. Cochrane Database Syst Rev. 2012;8:CD006987.
16. Fisch U, Bendet E, Kronenberg J. Steroids, carbogen or placebo for sudden hearing loss: a prospective double-blind study. Eur Arch Otorhinolaryngol. 2001;258:477–80.
17. Agarwal L, Pothier DD. Vasodilators and vasoactive substances for idiopathic sudden sensorineural hearing loss. Cochrane Database Syst Rev. 2009;4:CD003422.
18. Ogawa K, Takei S, Inoue Y, Kanzaki J. Effect of prostaglandin E1 on idiopathic sudden sensorineural hearing loss: a double-blinded clinical study. Otol Neurotol. 2002;23:665–8.
19. Ni Y, Zhao X. Carbogen combined with drugs in the treatment of sudden deafness. J Clin Otorhinolaryngol. 2004;18:414–5.
20. Poser R, Hirche H. A randomized, double-blind study for the treatment of sudden deafness: low-molecular weight dextran and naftidrofuryl versus low-molecular weight dextran and placebo. HNO. 1992;40:396–9.
21. Joachims HZ, Segal J, Golz A, Netzer A, Goldenberg D. Antioxidants in treatment of idiopathic sudden hearing loss. Otol Neurotol. 2003;24:572–5.
22. Ahn JH, Yoo MH, Lee HJ, Chung JW, Yoon TH. Coenzyme Q10 in combination with steroid therapy for treatment of sudden sensorineural hearing loss: a controlled prospective study. Clin Otolaryngol. 2010;35:486–9.
23. Angeli SI, Abi-Hachem RN, Vivero RJ, Telischi FT, Machado JJ. L-N-Acetylcysteine treatment is associated with improved hearing outcome in sudden idiopathic sensorineural hearing loss. Acta Otolaryngol. 2012;132:369–76.
24. Chen CH, Young YH. N-acetylcysteine as a single therapy for sudden deafness. Acta Otolaryngol. 2017;137:58–62.
25. Gordin A, Goldenberg D, Golz A, Netzer A, Joachims HZ. Magnesium: a new therapy for idiopathic sudden sensorineural hearing loss. Otol Neurotol. 2002;23:447.
26. Nageris BI, Ulanovski D, Attias J. Magnesium treatment for sudden hearing loss. Ann Otol Rhinol Laryngol. 2004;113:672–5.
27. Marx M, Younes E, Chandrasekhar SS, Ito J, Plontke S, O'Leary S, Sterkers O. International consensus (ICON) on treatment of sudden sensorineural hearing loss. Eur Ann Otorhinolaryngol Head Neck Dis. 2018;135:S23–8.
28.•• Wilson WR, Byl FM, Laird N. The efficacy of steroids in the treatment of idiopathic sudden hearing loss: a double-blind clinical study. Arch Otolaryngol. 1980;106:772–76. **This landmark article has provided many providers throughout the years with the justification for administering steroids to patients with iSSNHL. However, its methods deserve critical review**.
29.• Nosrati-Zarenoe R, Hultcrantz E. Corticosteroid treatment of idiopathic sudden sensorineural hearing loss: randomized triple-blind placebo-controlled trial. Otol Neurotol. 2012;33:523–31. **This is one of a few high quality, true placebo controlled trials examining the use of steroids in iSSNHL and shows no significant audiometric benefit of steroid using their regimen**.
30. Simani L, Shilo S, Oron Y, Eta RA, Handzel O, Muhanna N, Warshavsky A, Horowitz G, Ungar OJ. Residual perforation risk assessment of intratympanic steroids via tympanostomy tube versus transtympanic injections. Laryngoscope. 2021;131:E2583–91.
31. Topf MC, Hsu DW, Adams DR, Zhan T, Pelosi S, Willcox TO, McGettigan B, Fisher KW. Rate of tympanic membrane perforation after intratympanic steroid injection. Am J Otolaryngol. 2017;38:21–5.
32. Filipo R, Attanasio G, Russo FY, et al. Intratympanic steroid therapy in moderate sudden hearing loss: a randomized, triple-blind, placebo-controlled trial. Laryngoscope. 2013;123:774–8.
33. Fitzgerald DC, McGuire JF. Intratympanic steroids for idiopathic sudden sensorineural hearing loss. Ann Otol Rhinol Laryngol. 2007;116:253–6.
34. Banerjee A, Parnes LS. Intratympanic corticosteroids for sudden idiopathic sensorineural hearing loss. Otol Neurotol. 2005;26:878–81.
35. Ahn JH, Yoo MH, Yoon TH, Chung JW. Can intratympanic dexamethasone added to systemic steroids improve hearing outcome in patients with sudden deafness? Laryngoscope. 2008;118:279–82.
36. Battaglia A, Burchette R, Cueva R. Combination therapy (intratympanic dexamethasone + high-dose prednisone taper) for the treatment of idiopathic sudden sensorineural hearing loss. Otol Neurotol. 2008;29:453–60.

37. Gundogan O, Pinar E, Imre A, Ozturkcan S, Cokmez O, Yigiter AC. Therapeutic efficacy of the combination of intratympanic methylprednisolone and oral steroid for idiopathic sudden deafness. Otolaryngol Head Neck Surg Off J Am Acad Otolaryngol Head Neck Surg. 2013;149:753.
38. Alexander TH, Harris JP, Nguyen QT, Vorasubin N. Dose effect of intratympanic dexamethasone for idiopathic sudden sensorineural hearing loss: 24 mg/mL is superior to 10 mg/mL. Otol Neurotol. 2015;36:1321–7.
39. Vlastarakos PV, Papacharalampous G, Maragoudakis P, Kampessis G, Maroudias N, Candiloros D, Nikolopoulos TP. Are intratympanically administered steroids effective in patients with sudden deafness? Implications for current clinical practice. Eur Arch Otorhinolaryngol. 2012;269:363–80.
40. Li H, Feng G, Wang H, Feng Y. Intratympanic steroid therapy as a salvage treatment for sudden sensorineural hearing loss after failure of conventional therapy: a meta-analysis of randomized, controlled trials. Clin Ther. 2015;37:178–87.
41. Ng JH, Ho RC, Cheong CS, et al. Intratympanic steroids as a salvage treatment for sudden sensorineural hearing loss? A meta-analysis Eur Arch Otorhinolaryngol. 2015;272:2777–82.
42. Spear SA, Schwartz SR. Intratympanic steroids for sudden sensorineural hearing loss: a systematic review. Otolaryngol Head Neck Surg. 2011;145:534–43.
43. Crane RA, Camilon M, Nguyen S, Meyer TA. Steroids for treatment of sudden sensorineural hearing loss: a meta-analysis of randomized controlled trials. Laryngoscope. 2015;125:209–17.
44. Haynes DS, O'Malley M, Cohen S, Watford K, Labadie RF. Intratympanic dexamethasone for sudden sensorineural hearing loss after failure of systemic therapy. Laryngoscope. 2007;117:3–15.
45. Choung YH, Park K, Shin YR, Cho MJ. Intratympanic dexamethasone injection for refractory sudden sensorineural hearing loss. Laryngoscope. 2006;116:747–52.
46. Dallan I, De Vito A, Fattori B, et al. Intratympanic methylprednisolone in refractory sudden hearing loss: a 27-patient case series with univariate and multivariate analysis. Otol Neurotol. 2010;31:25–30.
47. Andrianakis A, Moser U, Wolf A, Kiss P, Holzmeister C, Tomazic PV, Graupp M. Intratympanic triamcinolone acetonide as a salvage treatment for idiopathic sudden sensorineural hearing loss. Audiol Neurootol. 2021;26:425–34.
48. Chang WT, Zee B, Lee HSH, Tong MCF. Dexamethasone eardrop with grommet placement vs intratympanic steroid injection for sudden sensorineural hearing loss: a randomized prospective clinical trial. Am J Otolaryngol. 2020;41: 102515.
49. She W, Dai Y, Du X, Yu C, Chen F, Wang J, Qin X. Hearing evaluation of intratympanic methylprednisolone perfusion for refractory sudden sensorineural hearing loss. Otolaryngol Head Neck Surg. 2010;142:266–71.
50. Chou YF, Chen PR, Kuo IJ, Yu SH, Wen YH, Wu HP. Comparison of intermittent intratympanic steroid injection and near-continual transtympanic steroid perfusion as salvage treatments for sudden sensorineural hearing loss. Laryngoscope. 2013;123:2264–9.
51. Vanwijck F, Rogister F, Pierre Barriat S, Camby S, Lefebvre P. Intratympanic steroid therapy for refractory sudden sensory hearing loss: a 12-year experience with the Silverstein catheter. Acta Otolaryngol. 2019;139:111–6.
52. Hong SM, Park CH, Lee JH. Hearing outcomes of daily intratympanic dexamethasone alone as a primary treatment modality for ISSHL. Otolaryngol Head Neck Surg. 2009;141:579–83.
53. Lim HJ, Kim YT, Choi SJ, et al. Efficacy of 3 different steroid treatments for sudden sensorineural hearing loss: a prospective, randomized trial. Otolaryngol Head Neck Surg. 2013;148:121–7.
54. Tsounis M, Psillas G, Tsalighopoulos M, Vital V, Maroudias N, Markou K. Systemic, intratympanic and combined administration of steroids for sudden hearing loss. A prospective randomized multicenter trial. Eur Arch Otorhinolaryngol. 2018;275:103–10.
55. Dispenza F, Amodio E, Stefano A, et al. Treatment of sudden sensorineural hearing loss with transtympanic injection of steroids as single therapy: a randomized clinical study. Eur Arch Otorhinolaryngol. 2011;268:1273.
56. Ermutlu G, Suslu N, Yilmaz T, Sarac S. Sudden hearing loss: an effectivity comparison of intratympanic and systemic steroid treatments. Eur Arch Otorhinolaryngol. 2017;274:3585–91.
57. Kosyakov S, Atanesyan A, Gunenkov A, Ashkhatunyan E, Kurlova A. Intratympanic steroids for sudden sensorineural hearing loss. J Int Adv Otol. 2011;7(3):323.
58. Huang C, Tan G, Xiao J, Wang G. Efficacy of hyperbaric oxygen on idiopathic sudden sensorineural hearing loss and its correlation with treatment course: prospective clinical research. Audiol Neurootol. 2021;26:479–86.
59. Tong B, Niu K, Ku W, Xie W, Dai Q, Hellström S, Duan M. Comparison of therapeutic results with/without additional hyperbaric oxygen therapy in idiopathic sudden sensorineural hearing loss: a randomized prospective study. Audiol Neurootol. 2021;26:11–6.
60. Lei X, Feng Y, Xia L, Sun C. Hyperbaric oxygen therapy versus intratympanic steroid for salvage treatment of sudden sensorineural hearing loss: a systematic review and meta-analysis. Otol Neurotol. 2021;42:980–6.
61. Joshua TG, Ayub A, Wijesinghe P, Nunez DA. Hyperbaric oxygen therapy for patients with sudden sensorineural hearing loss: a systematic review and meta-analysis. JAMA Otolaryngol Head Neck Surg. 2022;148:5–11.
62. Rhee TM, Hwang D, Lee JS, Park J, Lee JM. Addition of hyperbaric oxygen therapy vs medical therapy alone for idiopathic sudden sensorineural hearing loss: a systematic review and meta-analysis. JAMA Otolaryngol Head Neck Surg. 2018;144:1153–61.
63. Eryigit B, Ziylan F, Yaz F, Thomeer H. The effectiveness of hyperbaric oxygen in patients with idiopathic sudden sensorineural hearing loss: a systematic review. Eur Arch Otorhinolaryngol. 2018;275:2893–904.