Canadian Audiologist
The Official Publication of the Canadian Academy of Audiology

Treatment of Sensorineural Hearing Loss with Corticosteroids — Some Facts

Published September 7th, 2022

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Editor's Note: This article by Dr. Bob Harrison was initially submitted as his regular contribution as a columnist with CanadianAudiologist. However, we feel that it is of such great importance that it could be used as a primer for this entire area of pharmacological treatment of sensorineural hearing loss and therefore have decided to run this as both an article as well as his regular column.

Audiologists will be familiar with the possible therapeutic value of corticosteroid treatment provided soon after noise induced or sudden hearing loss. However, the clinical and scientific literature on the efficacy of treatment remains controversial. Because of this, there is no firm consensus of opinion by clinicians about treatment (despite "official" practice guidelines), and there is a risk that audiologists may or may not refer patients appropriately. The purpose of this summary is to provide some background information that may be of assistance.

This review is "extensive", so I have provided an "executive summary" is case you just want to get the big picture. This is followed by a short overview of basic laboratory research on the therapeutic action of steroids after inner ear injury, and a then summary of results from clinical trials of steroids for treatment of sensorineural hearing loss. The published literature for both the basic science studies and the clinical trials is vast. For the latter, the most reliable sources are systematic reviews or meta-analyses that have each sampled scores of individual studies. Finally, I have reviewed several published clinical practice guidelines, and have summarized one currently followed by many colleagues in Canada.

Executive summary

- In the context of inner-ear cell damage leading to sensorineural hearing loss, the therapeutic steroid agents most used are dexamethasone and prednisolone. These can be described as anti-inflammatory medications.

- In many body systems, including the inner ear, these agents have been shown to reduce cell damage and cell death when given soon after initial injury, and importantly can prevent inflammatory responses that can limit or reduce a progression of tissue damage.

- The drugs can be given orally (prednisolone) or systemically by IV injection. Local application into the middle ear can be done by intra-tympanic injection. Various combinations of treatment modes have been tested.

- Various timing sequences of steroid therapy have been studied, including: (a) Preventative treatment, i.e., given in advance of possible hearing loss risks (e.g., in military applications). (b) Acute phase treatment given as soon as possible after hearing loss and/or tinnitus onset. (c) Treatment during long-term recovery.

- Steroid treatment has been considered for sensorineural hearing loss (and any resulting tinnitus) caused by acoustic trauma, noise induced hearing loss, sudden hearing loss of unknown cause (idiopathic), hearing loss from viral infection, etc. All these various causes of hearing loss involve some damage to inner-ear tissues that can potentially be reduced by steroid treatments.

- Basic science research shows the potential for corticosteroids to be an effective treatment for noise induced hearing loss. From laboratory research we have some understanding of the mechanisms by which the steroids can have a therapeutic effect on the inner ear after injury.

- The clinical studies of steroid use in patients after acoustic trauma, or sudden hearing loss from other causes are less conclusive than laboratory data. There are published reports that demonstrate a benefit, and some that do not. Systematic reviews or meta-analyses of many studies provide a consensus conclusion that generally indicates useful therapeutic action.

- Many of the clinical trial studies have explored different steroids application modes (e.g., oral vs topical vs, systemic, as well as the timing of steroid treatments after hearing loss (or tinnitus) onset. These studies are the basis for well accepted clinical practice guidelines.

Basic science research

Many laboratory studies have shown the potential for corticosteroids to effectively prevent the severity and progression of hearing loss after injury to the inner ear. There are numerous basic science reports and because they are often well designed laboratory studies the results and conclusions are usually reliable. From such studies, there is a general agreement that corticosteroids can have beneficial effects on prevention of cell damage in the inner ear, and limit the progression of a hearing loss by reducing the spread of cell damage subsequent to an initial injury (e.g. by acoustic trauma, or other causes).

Laboratory studies have also provided us with an understanding of the basic mechanisms of steroid therapeutic action in the prevention or repair of inner ear tissues. Steroids can maintain cells in a

healthy condition (promote cell homeostasis). After cells are damaged, steroids can prevent cell death (apoptosis), and prevent local inflammation caused by the release of chemicals (e.g., cytokines and reactive oxygen species) that can further damage other cells. Steroids can improve local blood flow to areas of tissue damage.

We have yet to understand all the mechanisms by which steroids can improve hearing after inner ear damage. There are corticoid receptors on cells in the inner ear, suggesting that endogenous steroids are involved in cell maintenance such as ionic homeostasis and regulation of protein synthesis. An important action of steroids in treatment for sensorineural hearing loss is to protect cells from harmful chemicals released from damaged cells such as reactive oxygen species (ROS) or inflammatory mediators that are released after injury or infection (e.g., necrosis factors and cytokines). Steroids can increase cochlear blood flow preventing cochlear hypoxia or ischemia. Adequate blood flow in the stria vascularis to maintain the endocochlear potential is essential for hearing function. The stria vascularis may be damaged in sensorineural hearing loss, and steroid therapy may improve strial function and potential recovery from hearing loss.

Clinical studies

Because of the positive evidence from basic science research indicating that steroid treatment can be an effective treatment for some types of sensorineural hearing loss, translation of such therapy to patient populations has been made. This has resulted in many clinical trials. The medical/clinical literature on this topic is very extensive. There are hundreds of studies published, but unfortunately relatively few provide high quality evidence. In large part this is because the clinical literature is based on patient populations that are heterogeneous, that is, with subjects having different types of hearing loss, being treated at different times during or after the initial hearing loss (or tinnitus) onset. Most of the clinical reports cannot provide a “high level” of evidence because the studies have small numbers of patients (statistically underpowered), there are no control groups, no randomized design, no double blinded analysis etc. Because of the large number of studies, of different quality, it is better to rely on systematic reviews (or meta-analyses) in which many studies are assessed and a consensus conclusion is reached. In my column today I have focused particularly on systematic reviews, and summarize some of them below.

Systematic reviews of clinical trial literature

The most reliable evidence for the efficacy of corticosteroid treatment in hearing loss comes from systematic reviews or meta-analyses in which many published papers are considered and classified according to the “quality of evidence”. In clinical trials the quality of the results and conclusions depends on how well the trial is designed. The highest level of evidence comes from studies that have large subject numbers, where drug treatment given to some patients on a randomized basis with other patients acting as untreated (placebo) controls. Statistical analysis of results must be appropriate. For many studies these criteria cannot be met and are considered with less weight in a systematic review. I report below on ten relevant systematic reviews. The goal of each study is clearly stated in the title of each publication. I have noted the overall conclusions from each review and added extra comments where appropriate.

It's all about Timing. Early Treatment with Hyperbaric Oxygen Therapy and Corticosteroids Is Essential in Acute Acoustic Trauma. (2021)

Bayoumy AB, Weenink RP, van der Veen EL, Besseling-Hansen FS, Hoedemaeker ADM, de Jong

FJM, van der Laan MH, Swenker R, van Hulst RA, de Ru JA. J Otol. 2021 Oct;16(4):237-241.

Conclusions: The study indicates that best outcomes in patients with acute acoustic trauma are obtained with early initiation of the combination treatment of hyperbaric oxygen and corticosteroids.

Intratympanic Corticosteroids Injections: A Systematic Review of Literature. (2016)

Lavigne P, Lavigne F, Saliba I. Eur Arch Otorhinolaryngol. 2016 Sep;273(9):2271-8.

Conclusions: The objective of the study was to determine the evidence of intratympanic steroids injections for efficacy in the management of tinnitus and noise-induced hearing loss. Of five randomized clinical trials on tinnitus therapy, only one study found better tinnitus control with corticosteroids. The only available trial on noise induced hearing loss showed significant hearing recovery with combination therapy (intra-tympanic and oral steroid therapy).

Effectiveness of Steroid Treatment for Sudden Sensorineural Hearing Loss: A Meta-analysis of Randomized Controlled Trials. (2020) *Li J, Ding L. Ann Pharmacother. 2020 Oct;54(10):949-957.* **Conclusions: This study** was to assess the efficacy of steroids by intratympanic, systemic, and combined therapy routes. Patients treated with combined therapy had significantly improved hearing thresholds compared to those having systemic treatment. Moderate and high dose combined treatment can accelerate hearing improvement.

Hearing Outcomes of Treatment for Acute Noise-induced Hearing Loss: A Systematic Review and Meta-analysis. (2020)

Koochakzadeh S, Gupta A, Nguyen SA, McRackan TR, Kil J, Bhenswala PN, Lambert PR.Otol Neurotol. 2020 Sep;41(8):e971-e981.

Conclusions: Meta-analysis demonstrated significant improvement in mean hearing threshold for patients with high-frequency hearing loss, particularly those treated within 48 hours. Significant heterogeneity was present in experimental design among included studies, and many were of lower levels of evidence.

Noise-Induced Hearing Loss Treatment: Systematic Review and Meta-analysis. (2022) *Ahmed MM, Allard RJ, Esquivel CR. Mil Med. 2022 May 3;187(5-6):e661-e666*

Conclusion: Steroids (with or without hyperbaric oxygen treatment) appear to improve both low and high hearing thresholds following acoustic trauma.

Steroids for Idiopathic Sudden Sensorineural Hearing Loss (2013)

Wei BP, Stathopoulos D, O'Leary S. Steroids for idiopathic sudden sensorineural hearing loss. Cochrane Database Syst Rev. 2013 Jul 2;2013(7):CD003998.

Conclusions: This study investigated oral steroid (prednisolone) treatment. Hundreds of related publications were found in literature search, but most were excluded from the review because the quality of evidence was poor. In the final analysis only three studies were determined to be of high quality. From these it was concluded that there was a small (4-5dB) improvement of hearing in

treated patients.

Steroids for Treatment of Sudden Sensorineural Hearing Loss: A Meta-Analysis of Randomized Controlled Trials (2015) *Crane RA, Camilon M, Nguyen S, Meyer TA. Laryngoscope. 2015;125(1):209-17*

Conclusions: This meta-analysis of randomized controlled trials does not support the use of steroids over placebo for sudden sensorineural hearing loss. However, steroids for salvage treatment of patients failing traditional therapy appear to have an effect.

Intratympanic vs Systemic Corticosteroids in First-line Treatment of Idiopathic Sudden Sensorineural Hearing Loss: A Systematic Review and Meta-analysis. (2020)

Mirian C, Ovesen T. JAMA Otolaryngol Head Neck Surg. 2020;146(5):421-428.

Conclusions: Corticosteroids delivered intra-tympanically are not more beneficial than with systemic treatment in the case of moderate to severe sudden sensorineural hearing loss. There were no indications that combined treatment was associated with improved hearing outcomes.

Intratympanic Glucocorticosteroid Therapy for Idiopathic Sudden Hearing Loss: Meta-Analysis of Randomized Controlled Trials. (2017)

Lai D, Zhao F, Jalal N, Zheng Y. Medicine (Baltimore). 2017 Dec;96(50):e8955.

Conclusion: Intratympanic and systemic steroid therapies appear to show similar short-term efficacy for restoring hearing in patients with idiopathic sudden SNHL. Intratympanic therapy may reduce systemic side effects associated with steroid use.

Efficacy of Various Corticosteroid Treatment Modalities for the Initial Treatment of Idiopathic Sudden Hearing Loss: A Prospective Randomized Controlled Trial. (2021)

Tong B, Wang Q, Dai Q, Hellstrom S, Duan M. Audiol Neurootol. 2021;26(1):45-52

Conclusion: This study showed that intratympanic injection rendered better treatment efficacy than systemic administration.

Intratympanic Steroids for Sudden Sensorineural Hearing Loss: A Systematic Review. (2011)

Spear SA, Schwartz SR. Otolaryngol Head Neck Surg. 2011 Oct;145(4):534-43.

Conclusion: Intratympanic steroid treatment as primary treatment for sudden sensorineural hearing loss appears equivalent to treatment with high-dose oral prednisone therapy.

Clinical practice guidelines

The theoretical benefits of steroid therapy to reduce cellular injury and reduce further inflammatory reactions have been shown in laboratory studies to be effective in treatment of inner-ear injury causing sensorineural hearing loss. Positive outcomes of some clinical studies have resulted in the establishment of clinical practice guidelines. There are many published “SOPs”, pertaining to steroid treatment of SNHL of various causes, or written and directed to specific

language groups. They all share many common instructions. Below I summarize one important example from the American Academy of Otolaryngology – Head and Neck Surgery; these guidelines are most often followed by our colleagues in Canada and the US.

[1] Clinical Practice Guideline: Sudden Hearing Loss (Update). (2019)

Chandrasekhar SS, Tsai Do BS, Schwartz SR, Bontempo LJ, Faucett EA, Finestone SA, Hollingsworth DB, Kelley DM, Kmucha ST, Moonis G, Poling GL, Roberts JK, Stachler RJ, Zeitler DM, Corrigan MD, Nnacheta LC, Satterfield L. ***Otolaryngol Head Neck Surg. 2019 Aug;161(1_suppl):S1-S45.***

The guideline document is very comprehensive (45 pages) and includes a practice flow chart algorithm.

In brief, the protocol steps are:

1. Evaluate patients with sudden sensorineural hearing loss for retro-cochlear pathology by obtaining magnetic resonance imaging or auditory brainstem response.
2. Clinicians should offer, or refer to a clinician who can offer, intratympanic steroid therapy when patients have incomplete recovery from sudden sensorineural hearing loss 2 to 6 weeks after onset of symptoms.
3. Clinicians should obtain follow-up audiometric evaluation for patients with sudden sensorineural hearing loss at the conclusion of treatment and within 6 months of completion of treatment.
4. Clinicians may offer corticosteroids as initial therapy to patients with sudden sensorineural hearing loss within 2 weeks of symptom onset.
5. Clinicians may offer, or refer to a clinician who can offer, hyperbaric oxygen therapy combined with steroid therapy within 2 weeks of onset of sudden sensorineural hearing loss.
6. Clinicians may offer, or refer to a clinician who can offer, hyperbaric oxygen therapy combined with steroid therapy as salvage therapy within 1 month of onset of sudden sensorineural hearing loss.

Summary

Basic science research shows the potential for corticosteroids to be an effective treatment for noise induced hearing loss. From laboratory studies we have some understanding of the mechanisms by which the steroids can have a therapeutic effect on the inner ear after injury. The clinical studies of steroid use in patients after acoustic trauma, or sudden hearing loss from other causes are less conclusive than laboratory data. There are some published reports that demonstrate a benefit, and others that do not. Systematic reviews or meta-analyses of many studies provide a consensus conclusion that generally indicates a limited therapeutic action. Many of the clinical trial studies have explored different steroids application modes (e.g., oral vs topical vs, systemic, as well as the timing of steroid treatments after hearing onset. These studies are the basis for well-accepted clinical practice guidelines.