Intratympanic Injections of a Pharmacologic Agent for the Treatment of Meniere’s Disease or Sudden Hearing Loss

Medical Policy

Section: Medicine

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Description

Meniere’s disease, also known as endolymphatic hydrops, is a disorder of the inner ear of unknown cause. It is speculated that Meniere’s disease may be an immune-mediated disorder. Symptoms include tinnitus, vertigo, heightened sensitivity to loud sounds, fluctuating loss of hearing, headache, and aural fullness. In acute phases, nausea, vomiting, and disabling dizziness may occur. Usually, attacks are sudden and may last several hours. The disease commonly lasts a few years and, in most cases, occurs in only one ear. Diagnosis is difficult because its symptoms are often present in other conditions.

Treatment initially consists of diuretics, vasodilators, elimination of nicotine, and a diet low in sodium and without caffeine to reduce fluid retention. Acute exacerbations may be treated with anti-emetics, anti-vertigo medications, and systemic steroids. When these medical and dietary treatments are unsuccessful, other medical and surgical interventions may be considered; these include labyrinthectomy, endolymphatic sac shunt or decompression, vestibular neurectomy, and intratympanic gentamicin (which ablates vestibular function).

Most recently, intratympanic dexamethasone has been used for anti-inflammation and immunosuppression to decrease the incidence of acute attacks in Meniere’s disease. Intratympanic dexamethasone may be considered in patients who wish to avoid destructive surgical procedures and systemic steroid use. Intratympanic dexamethasone injections are made via tympanostomy or myringotomy, with or without placement of ventilation tubes or pressure-equalizing tubes in the tympanic membrane. Disadvantages of intratympanic dexamethasone may include the need for repeated office visits and potential infection.
Intratympanic dexamethasone has also been used for the treatment of sudden sensorineural hearing loss, hearing loss from autoimmune disease (e.g., Cogan syndrome) and other inflammatory inner ear diseases.

Intratympanic latanaprost and ganciclovir is also being studied for the treatment of Meniere’s disease.

See policy number 1.01.23 regarding the treatment of Meniere’s disease with application of transtympanic micropressure.

**Policy**

Intratympanic injections of a pharmacologic agent (e.g., dexamethasone or latanaprost) for the treatment of Meniere’s disease are considered **investigational**.

Intratympanic injections of a pharmacologic agent (e.g., dexamethasone) for the treatment of sensorineural hearing loss, hearing loss from autoimmune disease (e.g., Cogan syndrome), and other inflammatory inner ear diseases are considered **investigational**.

**Policy Guidelines**

Dexamethasone is approved by the U.S. Food and Drug Administration (FDA) for the treatment of a variety of disorders for intravenous, intramuscular, intra-articular, intralesional, and soft tissue injection. Intratympanic dexamethasone injection for the treatment of Meniere’s disease is an off-label use.

**Rationale**

**Meniere’s Disease**

While intratympanic dexamethasone for treatment of Meniere’s has been described in the medical literature since 1991 (1), only 1 published randomized, controlled trial was available when this policy was written. (2) Silverstein and colleagues conducted a prospective, randomized, double-blind, crossover trial of 20 patients with unilateral Meniere’s disease. Patients were randomized to receive either intratympanic dexamethasone (0.2–0.3ml of an 8mg/ml dexamethasone concentration mixed 1:1 with sodium hyaluronate) or placebo injections daily for 3 days via tympanostomy and followed up for 3 weeks. This was followed by the crossover portion of the study, which adhered to the same protocol and follow-up of 3 weeks. A telephone survey of all patients was subsequently conducted 1 month later. The authors
reported finding no statistically significant changes in hearing, electronystamography data, or tinnitus when intratympanic dexamethasone was compared to placebo. Vertigo was not assessed. The authors also noted the potential for a placebo effect with injections since only 5 of 9 patients who were confident they identified the dexamethasone group were correct.

Other prospective studies have reported mixed results. (3-6) Barrs and colleagues reported on 21 patients with Meniere’s disease treated with 0.3–0.5 ml of 4mg/ml dexamethasone injected intratympanically through a pressure equalizing tube placed after myringotomy. (3) Patients received dexamethasone twice on day 1, once on day 2, and weekly for 3 weeks thereafter. Follow-up at 3 and 6 months demonstrated complete relief of vertigo at 52% and 43%, respectively. However, patients lost an average of 2.7 dB in hearing and 1 patient lost a significant 35 dB in pure-tone average. Sennaroglu et al reported on 24 Meniere’s disease patients who received 0.25 mg instillations of dexamethasone intratympanically at the time of placement of a ventilation tube and by the patient every other day for 3 months thereafter. (4,5) The authors reported vertigo control in 63% of patients in the first month and in 25% of patients in the second month of treatment. Hearing improved in 17% of patients, although 37% reported a pure-tone average decrease. In another report, Sennaroglu et al compared these same 24 patients to 16 patients who received intratympanic gentamicin and 25 patients who had endolymphatic sac decompression (ESD) during different time periods. The gentamicin group achieved complete vertigo control in 50% of patients, whereas the ESD group only achieved 28% complete control of vertigo. There were no significant differences among the 3 treatment approaches when complete and substantial control of vertigo were considered. Comparisons of hearing in the 3 groups of intratympanic dexamethasone, intratympanic gentamicin, and ESD showed no change in hearing levels of 46%, 38%, and 72%, and hearing loss of 38%, 13%, and 10%, respectively. Finally, Shea and Ge reported hearing improvements in 67.9% (19 of 28) of patients followed up for 1 year after treatment with intratympanic, intravenous, and oral dexamethasone. (6) However, the effects of intratympanic dexamethasone cannot be isolated in this uncontrolled study, since 3 routes of administration of dexamethasone were used, thereby confounding results.

As of 2005, there was not sufficient published medical evidence available to adequately assess the health outcomes of intratympanic dexamethasone for the treatment of Meniere’s disease. Further randomized controlled trials (RCTs) are needed to determine health outcomes over the natural course of this fluctuating illness, along with long-term health outcomes and adverse effects, especially in the area of hearing loss. In addition, any incremental effects over placebo and comparative effectiveness studies would be useful.

In a literature review update, 2 randomized controlled trials were identified. In a prospective, double-blind, randomized trial of intratympanic injections of dexamethasone versus placebo in 22 patients, Garduno-Anaya and colleagues (7) found statistically significant improvements at 2-year follow-up in vertigo and dizziness but not in tinnitus or hearing loss. However, this is a small study that is not sized sufficiently to address the natural progression of this disease, and 4 patients were removed from the control group and offered other treatments in violation of intention to treat analysis. In a randomized, single-blind study of 36 patients with severe, disabling tinnitus, Araujo et al (8) found that intratympanic injections of dexamethasone produced no significantly better outcomes than saline intratympanic injections. Like the Silverstein (2) study, a placebo effect was noted in patients receiving only saline injections.

Only 1 small published, randomized controlled trial using intratympanic injection of latanoprost for treatment of Meniere’s disease was identified (9). In this placebo-controlled, crossover study,
patients (n=10) received either latanaprost or placebo intratympanic injections once per day for 3 days then crossed over to the other treatment group after 2 months. Patients experienced statistically significant decreases in reports of vertigo or disequilibrium and increases in speech discrimination but not in pure tone average or visual analog scale assessments of tinnitus and hearing. Therefore, it is uncertain whether latanaprost intratympanic injections are useful in the treatment of Meniere’s disease and additional studies are needed. Guyot and colleagues conducted a placebo-controlled, randomized, double-blind trial of intratympanic administration of the antiviral agent ganciclovir in 29 patients who had failed medical therapy for Meniere’s disease. (10) The ganciclovir and placebo groups showed similar improvements in the intensity of vertigo, which lasted up to 90 days after treatment. Surgery was postponed in 22 (81%) patients, and required in 3 patients from each group. As concluded by the investigators, the similar improvements in the active and control treatment groups raise questions about the contribution of middle ear ventilation alone. These results also reinforce the need for placebo-controlled randomized trials in the evaluation of other intratympanic treatments for Meniere’s disease.

Sensorineural Hearing Loss, Hearing Loss from Autoimmune Disease (e.g., Cogan’s syndrome), and Other Inflammatory Inner Ear Diseases.

A review of the literature on MEDLINE through June 2008 identified 2 randomized controlled trials (RCTs) and 2 non-randomized controlled trials of intratympanic dexamethasone for patients with severe or profound sudden sensorineural hearing loss. (11) In an RCT by Ho and colleagues, 29 patients who did not respond with a hearing improvement of more than 30 dB after standard 10-day treatment with oral steroid and other facilitating agents were randomized to either a group receiving intratympanic dexamethasone once per week for a total of 3 weeks or a control group of further standard treatment. In the intratympanic dexamethasone group, 8 of 15 (53.3%) patients experienced hearing improvement versus only 1 of 14 (7.1%) patients in the control group. After a minimum follow-up of 1 month, hearing thresholds decreased an average of 28.4 dB in the intratympanic dexamethasone group versus 13.2 dB for the control group. Another study randomized 37 patients who had failed intravenous prednisolone into treatment with intratympanic dexamethasone or no treatment controls. (12) Nine (47%) of 19 treated patients showed an improvement in pure tone average of >10 dB, compared with none of the controls at 1.5 months after the last treatment. A non-randomized controlled study compared outcomes from 10 consecutive patients who received initial treatment of intratympanic dexamethasone with 21 consecutive patients who were treated with intravenous dexamethasone. (13) All 10 patients (100%) treated with intratympanic steroids were reported to have improved more than 10 dB, with an average improvement of 41 dB. Fourteen (67%) patients in the intravenous treatment group showed improvement of >10 dB with a mean change of 25 dB. Another non-randomized study compared 33 prospectively treated patients who were refractory to a course of oral steroid therapy with historical age- and sex-matched controls (assessed 4 and 8 weeks following oral steroids). (14) Thirteen (39%) of the patients treated with intratympanic dexamethasone (4 times over 2 weeks) showed an improvement of more than 10 dB in pure-tone average compared with 2 (6%) patients in the control group. Of note, for 20 patients who had no objective change of hearing after intratympanic dexamethasone, 16 reported subjective improvements in either hearing or tinnitus. Because of variable recovery rates and a high rate of spontaneous recovery, additional placebo-controlled double-blinded trials are needed to establish the efficacy of intratympanic steroid treatment for sudden hearing loss.

Two randomized controlled trials were published in 2008 on the combined use of intratympanic dexamethasone and systemic steroids in patients with sudden hearing loss. Ahn and colleagues
randomized 120 patients with either intratympanic dexamethasone on 3 days plus methylprednisolone (14 days), or methylprednisolone alone. (15) Although there was mean improvement in hearing threshold at 250 Hz with the combined treatment, the percentage of patients showing improvement in hearing was found to be similar for the 2 groups. For the combined treatment and control groups (respectively), complete recovery was observed in 15%-16% of patients, partial recovery in 9% (both groups), slight improvement in 16%-18%, and no improvement in 16%-18%. Another study randomized 60 patients to combined treatment with intratympanic injection of dexamethasone (once per week for 3 weeks) and 14 days of systemic prednisone, intratympanic injection with systemic placebo, or intratympanic placebo with systemic prednisone. (16) All 3 groups were reported to show improvement over time, with probability of hearing recovery being greater in the combined treatment group (44% average improvement) than in the control groups (36% for intratympanic and 20% for systemic alone). Although the report states that there was no significant difference in baseline measurements between the groups, the mean number of days between onset and treatment was 4 days in the combined treatment group in comparison with 11 and 7 days for the individual treatment groups. In addition, the mean pretreatment discrimination was 41% for the combined treatment group, 24% for intratympanic alone, and 34% for systemic treatment alone. This study is also limited by the small number of subjects (16-18 per group at study completion). Overall, results from these studies are inconsistent and inconclusive. Thus, while intratympanic dexamethasone for the treatment of sudden or profound sensorineural hearing loss may appear promising, the available evidence is insufficient to draw conclusions concerning the effect of this procedure on health outcomes.

References:


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**Type of Service**: Medical

**Place of Service**: Inpatient, Outpatient

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