Intratympanic Dexamethasone in the Treatment of Meniere's Disease: A Retrospective Review

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Abstract

Objectives: This study sought to understand the effect of intratympanic dexamethasone (IT Dex) on vertigo control in unilateral Meniere's disease, and to document hearing progression during IT Dex therapy.
Study Design: Retrospective case series review from a tertiary neurotology clinic.
Methods: One hundred and twenty-five consecutive adult patients with definite unilateral Meniere's disease who had failed medical management were studied for an average of 1061 days. None had prior ablative treatment. IT Dex was injected, and repeated for unchanged/worsened symptoms. The main outcome measures were requirement for subsequent ablative therapy in the form of intratympanic gentamicin injection. Hearing outcomes were measured using standard audiometry.
Results: The number of IT Dex injections per patient ranged from 1 to 29 (median = 4). Survival analysis with the Kaplan-Meier method demonstrated that the predicted survival (patients not requiring intratympanic gentamicin ablation) at two and four years following initial treatment was 84.3% and 79.9%, respectively. In patients only treated with IT Dex, most recent pure-tone averages (0.5, 1, 2, and 3kHz) had declined compared to pre-treatment values (p=0.000002).
Conclusions: The majority of Meniere's patients appear to have control of vertigo with IT Dex, though this must be measured against the disease natural history. Hearing mildly declined over the treatment course, which may represent natural disease progression or treatment effect. Our results support a modest benefit of IT Dex. A large multi-center double-blinded randomized placebo controlled trial is needed to further evaluate this treatment modality.

Introduction

The use of intratympanic corticosteroid injection is common in the management algorithms of otologists for Meniere's disease. Compared with systemic administration of steroids, intratympanic injection achieves higher inner ear drug concentrations, and avoid systemic side effects[1]. Entry is gained to the inner ear through passive diffusion through the round window into the perilymph[2]. While many patients report subjective improvement in the severity and frequency of their vertigo spells, there is conflicting evidence. Phillips and Westerberg[3] performed a Cochrane review of intratympanic steroids for Meniere's disease. Only one randomized placebo-controlled study was found that met their selection criteria[4]. Following 5 consecutive daily IT Dex injections (4mg/mL) or placebo, vertigo control at the 2-year follow up was class A in 82% of dexamethasone treated patients, and class A in only 57% of placebo patients[4]. Phillips and Westerberg[3] concluded that the results of a single trial only provide limited evidence to support intratympanic steroid effectiveness. A further confounding variable is the range of IT Dex concentrations used at different centres (4-24mg/mL), which may theoretically impact symptom control results.

Given the variability of vertigo control reported in the literature with IT Dex, we critically reviewed our outcomes to document those with poor vertigo control who proceeded to IT Gent or labyrinthectomy, and to evaluate changes in hearing during IT Dex treatment.

Methods and Materials

This study was approved by the University of Western Ontario Health Sciences Research Ethics Board (Protocol #16930E). The charts of one hundred and twenty-five consecutive patients with active definite unilateral Meniere's disease (1995 AAO-HNS criteria) were retrospectively reviewed. IT Dex therapy (10mg/mL) was administered following failure of medical therapy. Two injection protocols were used, based on the protocol of the respective senior author. LSP performed one initial IT Dex injection, and repeated future single injections if the patient had poor vertigo control. SKA performed an initial series of four injections of IT Dex over a four week period, and repeated future single or series of injections if the patient had poor vertigo control. After one or more IT Dex injections, the patient could decide their vertigo frequency/severity was sufficiently problematic that an escalation of therapy, in the form of IT Gent or labyrinthectomy, was required. Survival analysis was performed using the Kaplan Meier method.

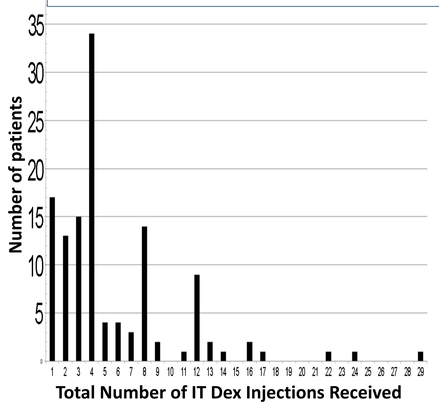

Figure 1. Distribution of total number of IT Dexamethasone Injections per patient.

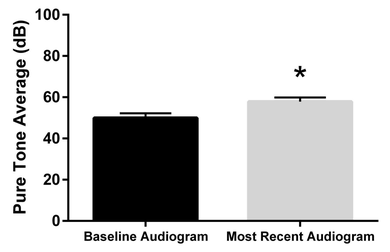

Figure 2. Comparison of baseline and most recent pure tone averages (mean +/- SEM) for patients who received only IT Dex injection(s) (n=89). *p<0.01

Results

The range of number of injections of IT Dex was 1 to 29 (Figure 1). For patients who received only IT Dex injections during the course of the study, PTA scores worsened during the study (p<0.01) (Figure 2). Based on Kaplan-Meier survival analysis (Figure 3), survival at 1, 2, 3, 4, and 5 years was 86.3%, 84.3%, 83.2%, 79.9%, and 77.5%, respectively. Subgroup survival analysis comparing patients treated with repeated single injections (n=63) and those treated with repeated series of injections (n=62) (Figure 4) did not reveal a significant difference (p=0.3804).

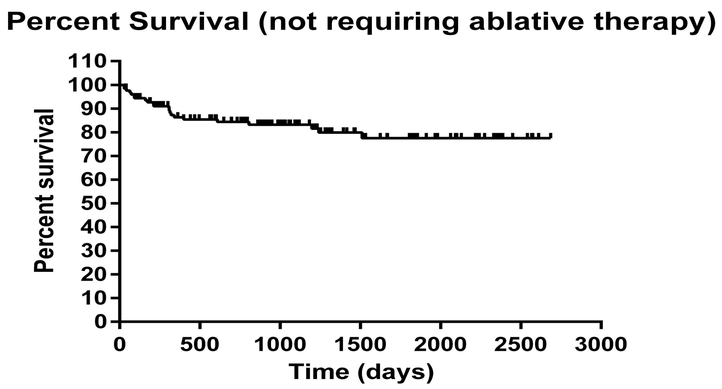

Figure 3. Kaplan Meier survival analysis (n=125) of percent of patients not requiring ablative therapy.

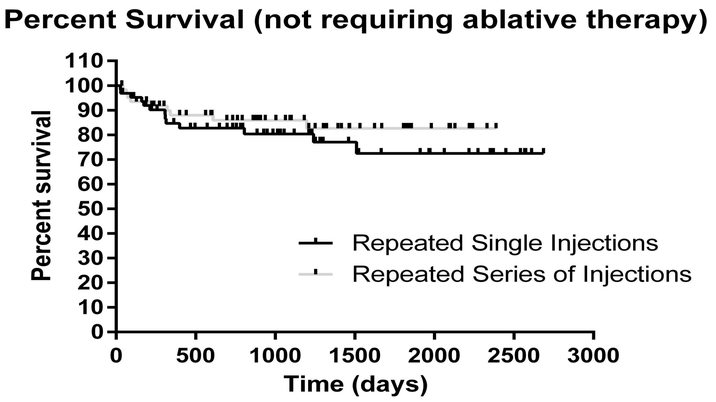

Figure 4. Kaplan Meier subgroup survival analysis comparing patients treated with repeated single injections of IT Dex (n=63) and those treated with repeated series of injections of IT Dex (n=62) (p=0.3804).

Discussion

Silverstein et al.[5] found that of fifty patients who declined surgery for Meniere's disease, 57% had complete vertigo control at 2 years, 73% had improvement at 2 years, and 71% had complete control after an average of 8.3 years. These numbers are typical of the spontaneous improvement rates reported for Meniere's, which are 60-80% over two to eight years[6]. Any therapy targeted at control of vertigo spells, including IT Dex, must be measured against this relatively high spontaneous improvement rate. The rate of 84.3% control of symptoms at 2 years with IT Dex treatment is improved compared to the natural history. However, the rate dropped to 79.9% at four years, which is at the upper end of the spontaneous improvement rate for Meniere's. These results indicate that IT Dex may provide improved symptom control in the shorter term, but it may not alter the long-term control of vertigo symptoms in patients with Meniere's disease.

Comparable results were achieved by Boleas-Aguirre et al.[7]. They reported a 91% survival at 2 years, compared with 84.3% in the current study. This small difference may reflect the heterogeneity of symptom control in patients with Meniere's disease.

Taken together, although IT Dex is a safe and promising treatment for Meniere's disease based on the present study, its clinical efficacy requires further clarification. .

Conclusions

The results of this study support a **modest** short-term benefit of IT Dex in the management of vertigo episodes in Meniere's disease. Repeated single injections of Dex and repeated series of injections of Dex have statistically comparable results, although there is a trend to better vertigo control in patients treated with repeated series of injections. Hearing, although only mildly worsened over the course of IT Dex therapy, did demonstrate a significant decline. A large, multi-centered double-blinded randomized placebo controlled trial of IT Dex is needed to conclusively determine if there is a therapeutic benefit in Meniere's disease, both in the short and the long term.

Contact

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References

1. Banerjee A, Parnes LS. Intratympanic corticosteroids for sudden idiopathic sensorineural hearing loss. Otol Neurotol. 2005;26:878-81.
2. Plontke SK, Biegner T, Kammerer B, Delabar U, Salt AN. Dexamethasone concentration gradients along scala tympani after application to the round window membrane. Otol Neurotol. 2008;29:401-6.
3. Phillips JS, Westerberg B. Intratympanic steroids for Ménière's disease or syndrome. Cochrane Database Syst Rev. 2011;CD008514.
4. Garduño-Anaya MA, Couthino De Toledo H, Hinojosa-González R, Pane-Pianese C, Ríos-Castañeda LC. Dexamethasone inner ear perfusion by intratympanic injection in unilateral Ménière's disease: a two-year prospective, placebo-controlled, double-blind, randomized trial. Otolaryngol Head Neck Surg. 2005;133:285-94.
5. Silverstein H, Smouha E, Jones R. Natural history vs. surgery for Menière's disease. Otolaryngol Head Neck Surg. 1989;100:6-16.
6. Pullens B, Verschuur HP, van Benthem PP. Surgery for Ménière's disease. Cochrane Database Syst Rev. 2013;2:CD005395.
7. Boleas-Aguirre MS, Lin FR, Della Santina CC, Minor LB, Carey JP. Longitudinal results with intratympanic dexamethasone in the treatment of Ménière's disease. Otol Neurotol. 2008;29:33-8.