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M. J. R. C Alles · M. A. der Gaag · R. J. Stokroos

Intratympanic steroid therapy for inner ear diseases, a review of the literature

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Abstract To evaluate the value of clinical trials on intratympanic steroid therapy in Ménière's disease (MD), idiopathic sudden sensorineural hearing loss (ISSNHL) and rapidly progressive sensorineural hearing loss (RPSNHL). Medline and Pubmed databases from 1966 to present were searched for clinical studies on intra- or transtympanic (cortico)steroid therapy of MD, ISSNHL and RPSNHL. Results were cross-checked with additional databases to obtain a complete data set. Clinical trials were evaluated on the basis of comparability, internal and external validity. Articles were judged using the following questions: was a randomised double-blind controlled trial performed? Which criteria were used to confirm the diagnosis of MD, ISSNHL, RPSNHL? Which therapy was evaluated? How long was the follow-up? Which criteria were used to evaluate the results? Reliable evidence on the efficiency, optimum dosage and administration schedule of intratympanic steroid therapy in MD, ISSNHL and RPSNHL is lacking, therefore further investigation is required.

Keywords Ménière's disease · Idiopathic sudden sensorineural hearing loss · Rapidly progressive sensorineural hearing loss · Intratympanic steroids · Inner ear · Review

Introduction

Inflammatory processes may play a role in the etiology of various inner ear pathologies of which the pathogenesis is poorly understood, such as Ménière's disease (MD), idiopathic sudden sensorineural hearing loss (ISSNHL) and rapidly progressive sensorineural hearing loss (RPSNHL). Endogenous as well as exogenous triggers may start these inflammatory processes, acting through several immune mechanisms, such as specific or cross reacting autoantibodies, circulating immune-complexes and cell-mediated immune responses, which are thought to contribute to hearing impairment and vestibular function loss [1–5]. In some cases corticosteroids can be effective in improving inner ear function [5, 6]. How steroids affect the inner ear still remains unclear. Steroids may increase labyrinthine circulation [7, 8] or influence the cochlear fluid homeostasis, possibly by attenuating an inflammatory progress [9].

Adverse effects of systemic steroids such as systemic immune suppression, osteoporosis, increase in weight, skin and endocrine changes can be avoided by topical administration of the drug. Animal studies demonstrate that the intratympanic route of administration results in significantly higher inner ear levels of steroids as compared with systemic administration [10, 11]. Other advantages of this route are that costs and complication rate seem to be low. Additionally, this minimally invasive technique is easily to perform, well tolerated by patients and makes it possible to treat only the affected ear [12]. Intratympanic administration of steroids may thus be a promising therapy for several inner ear disorders, but many questions concerning its efficiency, optimum dosage and administration schedule remain. Also, the occurrence of unwanted side effects or adverse effects, of this therapy, for example the occurrence of otomycosis, has to be systematically reviewed befor e such a therapy can be recommended.

We conducted a literature survey on the validity of clinical trials investigating intratympanic steroid therapy. Our aim was to evaluate if there are sufficient evidence-based data on intratympanic steroid treatment to be useful in MD, ISSNHL and RPSNHL and to report the possible occurrence of systematic adverse effects.

M. J. R. C Alles · M. A. der Gaag · R. J. Stokroos (✉)
Department of Otorhinolaryngology, Head and Neck Surgery, University Hospital Maastricht, P. Debyelaan 25, P.O. Box 5800, 6202 AZ Maastricht, The Netherlands
E-mail: RSTO@SKNO.AZM.NL
Tel.: +31-43-3877585
Fax: +31-43-3875580

Materials and methods

We searched Medline and Pubmed databases from 1966 to present for trials concerning clinical evaluation of intratympanic steroid treatment of MD, ISSNHL and RPSNHL. The CINAHL, SUMsearch, and Cochrane library databases were crosschecked with initial search results for possible additional studies. We searched for the following terms: intratympanic, transtympanic (cortico)steroids, dexamethasone, inner ear perfusion, Ménière's disease, ISSHL and RPSNHL. Articles written in the English, German, French and Dutch language were included. The studies were analysed with regard to the requirements of a clinical drug trial:

- Comparability: The results obtained in the group of patients receiving the drug under study have to be compared to those obtained in a reference group of patients, for example receiving no therapy or a placebo.
- Internal validity: The methodology used should allow a good estimate of the therapy-bound effect. The methods used to ensure internal validity are randomisation, double-blinding and imply a prospective study design with a proper follow-up.
- External validity: Generalisation of the results is possible by the strict definition of the disease according to the inclusion and exclusion criteria.

The found articles were screened to which extent the above mentioned requirements were judged using the following questions:

- Study design: Was a randomised double-blind controlled trial performed?

I.e. Were intratympanic steroids compared to another or a placebo treatment? Were patients randomly assigned to an intervention group? Was the evaluation carried out double blind?

- Which diagnostic criteria were used to confirm MD, ISSNHL or RPSNHL?

Only patients suffering from MD and meeting the AAO_HNS categories 'definite MD' and 'certain MD' should be reported as having Ménière's disease [13]. ISSHL is usually defined as a non-fluctuating sensorineural hearing impairment of unknown etiology occurring within 24 h and amounts to at least 30 dB or more for three subsequent one octave steps in frequency [14]. For RPSNHL the criteria drawn up by Moscicki et al. [15] are most often applied. These include a bilateral SNHL manifested as a 30 dB threshold or greater at any frequency and audiometric evidence of progression in at least one ear of at least 10 dB threshold shift at any frequency. Audiograms must be less than 3 months apart.

- Which therapy was evaluated?

We examined whether intratympanic steroids were used as a monotherapy, or were combined with systemic steroids. The technique used for inner ear perfusion, and additionally the type of steroid used, its dosage and administration schedule were examined.

- How long was the follow-up?

The AAO-HNS Committee on Hearing and Equilibrium [13] recommends that the period of 6 months before treatment should be compared with the interval between 18 and 24 months after treatment. This enables investigators to make comparisons among studies.

- Which criteria were used to evaluate the results?

The AAO-HNS Committee on Hearing and Equilibrium [13] provides guidelines on the evaluation of hearing, vertigo and functional levels in patients with Ménière's disease. These guidelines on hearing may also be applied for the evaluation of ISSHL and RPSNHL. Hearing changes are considered significant, if there is a change in average hearing level ≥10 dB(HL) or a change in SDS ≥15%, regardless of the underlying clinical presentation of the hearing loss.

Vertigo can be evaluated by dividing the average number of definitive spells per months during the 6 months period after therapy by the number of definitive spells per month during the 6 months before therapy, multiplied by 100. The outcome determines if a patient achieved complete control of the spells (numerical value: 0), substantial (1–40), limited (41–80), insignificant (81–120) or worse (≥120).

It is impossible to measure changes in tinnitus and aural fullness objectively, but by means of validated questionnaires the subjective experience of tinnitus and aural fullness can be evaluated.

Results

Our initial database search showed 58 hits. Of these, 13 clinical studies on intratympanic steroid therapy were found. They are detailed in the Tables 1, 2, 3 and 4. In Table 1 the study set-up is reported. Table 2 reflects the number of patients per study and their diagnosis. Whether the diagnosis meets the disease definition according to the 1995 guidelines of the AAO-HNS, and what kind of medical therapy the patients received before they were assimilated in the study, is also shown in Table 2. In Table 3 the investigated therapy is detailed. Table 4 describes the follow-up period and whether outcome parameters of symptom improvement were met by the criteria mentioned above. In Table 5 we summarize our conclusions with regard to the criteria we used for the evaluation of the literature on intratympanic steroid therapy. The clinical studies are arranged in chronological order.

Table 1 Study set-up of 13 clinical studies on intratympanic steroid therapy

Clinical study	Controlled trial	Double blind	Randomised
Itoh and Sakata [18]	Yes[a]	No	No
Shea and Ge [23]	No	No	No
Silverstein et al. [7]	No	No	No
Shea [19]	No	No	No
Arriaga and Goldman [26]	No	No	No
Silverstein et al. [16]	Yes[b]	Yes	Yes
Parnes et al. [11]	No	No	No
Sennaroglu et al. [25]	No	No	No
Hirvonen et al. [20]	No	No	No
Barrs et al. [21]	No	No	No
Chandrasekhar [22]	No	No	No
Gianoli and Li [24]	No	No	No
Sennaroglu et al. [17]	Yes[c]	No	No

[a] Intratympanic dexamethasone versus lidocaine
[b] Intratympanic dexamethasone versus placebo
[c] Intratympanic dexamethasone versus intratympanic gentamicine versus endolymphatic sac decompression

Discussion

Did the authors perform a randomised double-blind controlled trial?

Only the clinical study of Silverstein et al. published in 1998 [16] meets the conditions of a randomised, double-blind, controlled trial. We consider it a demerit, that this study is designed as a cross-over trial. This means that every patient underwent all interventions in a randomised order, thus a carry-over effect may influence the outcome. Sennaroglu et al. [17] and Itoh and Sakata [18] both performed a controlled trial, but compared intratympanic steroid treatment to experimental and non-current therapies. All other studies are uncontrolled. Uncontrolled trials may provide a distorted view of a therapy and are in general more likely to lead to enthusiastic recommendation of a treatment as compared to properly controlled trials.

Which criteria were used to confirm the diagnosis of MD, ISSNHL or RPSNHL?

From Tables 2 and 3 it can be gathered that 10 of the 13 studies investigate the influence of intratympanic steroids on Ménière's disease. Shea [19], Silverstein et al. [16], Hirvonen et al. [20] and Barrs et al. [21], used the definition for Ménière's disease as recommended by the Committee on Hearing and Equilibrium of the AAO-HNS, which renders these studies more valuable than others. The definition of ISSNHL used by Chandrasekhar [22](change in hearing occurring within 12 h to 3 days) is rather general compared to the definition used generally [14].

Patients enrolling in a clinical study, should not receive any previous treatment. In our opinion it is acceptable to include patients suffering MD, whose symptoms did not improve during salt and caffeine restrictions and a diuretic. Patients receiving a treatment with other drugs, especially systemic steroids, should be excluded, since these can interfere with the therapy

Table 2 Number of patients, diagnosis of inner ear pathologies, criteria used for disease definition and previous medical therapy in 13 clinical studies on intratympanic steroid therapy

Clinical study	Diagnosis and number of patients	Criteria used for disease definition according to AAO-HNS	Previous medical therapy
Itoh and Sakata [18]	MD ($N=136$) Other ($N=186$)	Not reported	Unspecified
Shea and Ge [23]	MD ($N=28$)	No[a]	Not reported
Silverstein et al. [7]	MD ($N=22$) ISSNHL ($N=8$) RPSNHL ($N=2$) Other ($N=14$)	Not reported	Unspecified
Shea [19]	MD ($N=48$)	Yes	Not reported
Arriaga and Goldman [26]	MD ($N=15$)	Not reported	Salt-, caffeine restriction, diuretic
Silverstein et al. [16]	MD ($N=20$)	Yes	None
Parnes et al. [11]	ISSNHL ($N=13$) Other ($N=24$)	Not reported	Not reported
Sennaroglu et al. [25]	MD ($N=24$)	Not reported	Salt-, caffeine restriction, vasodilator, diuretic
Hirvonen et al. [20]	MD ($N=17$)	Yes	Salt restriction, diuretic, betahistidine
Barrs et al. [21]	MD ($N=21$)	Yes	Salt-, caffeine restriction, diuretic
Chandrasekhar [22]	ISSHL ($N=10$)	Not applicable[b]	Systemic prednisone, dyazide, valacyclovir, nystatine, ginko biloba
Gianoli and Li [24]	ISSHL ($N=23$)	Not applicable[c]	Systemic steroids
Sennaroglu et al. [17]	MD ($N=65$)	Not reported	Salt-, caffeine restriction, diuretic, vasodilator

[a] Staging according to Shea [30]
[b] Definition ISSHL: change in hearing within 12 h to 3 days
[c] Definition ISSHL: ≥20 dB hearing loss in three or more contiguous frequencies occurring within 3 days

Table 3 Applied intratympanic steroid therapy in 13 clinical studies on intratympanic steroid therapy

Clinical study	Drug	Administration route	Dosage	Schedule
Itoh and Sakata [18]	DEX[a]	IT[c]-Injection	2 mg (0.5 ml)	4–5 injections; interval 1–2 weeks
Shea and Ge [23]	DEX[a] in hyaluronan	IT[c]-Injection	16 mg/ml (0.5 ml)	3 consecutive days
	plus DEX[a]	IV[c]	16 mg	3 consecutive days
	plus DEX[a]	Oral	0.25 mg/day	1 month
Silverstein et al. [7]	Depo-medrol or	IT[c]-Injection	80 mg/cc (0.2–0.3 ml)	Most pts ≥ 2 injections
	Decadron ophthalmic solution or	Wick or instillation	1 mg/cc	2 drops 2×/day,
	Depo-Medrol + Decadron ophthalmic solution or	Injection + Wick or instillation	80 mg/cc, 1 mg/cc	Unspecified frequency and 2 drops 2×/day
	DEX[a]	IT[c]-Injection onto Gelfoam	4 mg/cc (0.2–0.3 ml)	3×/week for 3–4 weeks
Shea [19]	DEX[a] in hyaluronan	IT[c]-Injection	16 mg/ml (0.5 ml)	3 consecutive days
	plus DEX[a]	IV[d]	16 mg	3 consecutive days
	plus DEX[a]	Oral	0.25 mg	30–90 days
Arriaga and Goldman [26]	DEX[a] in hyaluronan	IT-Injection onto Gelfoam	8 mg	Single application
Silverstein et al. [16]	DEX[a] in sodium hyaluronate or	IT[c]-Injection	8 mg/ml (0.2–0.3 ml)	3 consecutive days, after a 3–week interval start of the cross-over therapy (also 3 consecutive days)
	Placebo	IT[c]-Injection	1:1 mixture	
Parnes et al. [11]	DEX[a] or	IT[c]-Injection	Unspecified	Unspecified
	MPRED[b]	IT[c]-injection	Unspecified	Unspecified
Sennaroglu et al. [25]	DEX[a]	IT[c]-instillation	0.25 mg/cc (5 drops)	5 drops/day for 3 months
Hirvonen et al. [20]	DEX[a] in hyaluronan	IT[c]-Injection	16 mg/ml (0.2–0.4 ml)	Day 1,4 and 8
	Plus DEX[a]	IM[e]	15 mg	Single application
Barrs et al. [21]	DEX[a]	IT[c]-Injection	4 mg/ml (0.3–0.5 ml)	2 consecutive days and weekly thereafter for 3 weeks
Chandrasekhar [22]	1: DEX[a] in normal saline or	IT[c]-Injection	1: 4 mg/ml (0.25 ml) + saline (0.25 ml)	1: based on audiogram
	2: DEX[a]	IT[c]-Injection	2: 4 mg/ml (0.5 ml)	2: based on audiogram
Gianoli and Li [24]	DEX[a] or	IT[c]-Injection	25 mg/ml (0.4–0.6 ml)	4 injections in 10–14 days
	MPRED[b]	IT[c]-Injection	125 mg/2 ml (0.4–0.6 ml)	4 injections in 10–14 days
Sennaroglu et al. [17]	DEX[a]	IT[c] instillation	1 mg/ml (each instillation 0.25 mg)	5 drops/day for 3 months

[a] dexamethasone
[b] methylprednisone
[c] intratympanic
[d] intravenous
[e] intramuscular

tested. Silverstein et al. [16] included patients, who had not used any previous medication. This is preferable as no interference is possible. The other authors [17, 20, 21, 25, 26] included patients whose symptoms did not improve on conservative treatment (salt and caffeine restriction and a diuretic), sometimes in combination with a vasodilator or betahistidine, and thus minimized possible bias from systemic acting anti-inflammatory drugs as much as possible.

Shea and Ge [23], Shea [19] and Parnes et al. [11] did not mention if their patients received previous treatment. Seven of 10 patients included in Chandrasekhar's study [22] received also systemic steroids or other drug treatment. Gianoli and Li [24] investigated whether patients, who failed to respond to or are not able to tolerate systemic steroid treatment benefit from intratympanic steroids, therefore most of the patients included had received systemic steroids previously.

Which therapy was evaluated?

There are several techniques to administer steroids intratympanicaly [12]. The technique most authors applied is a transtympanic injection under local anaesthesia [7, 11, 16, 18–24]. Usually the steroid is injected into the middle ear over the round window. An second paracentesis, to allow the escape of air, was made by some [19, 20, 22, 23]. The round window niche can be obstructed by extraneous membranes or by fibrous plugs. A temporal bone study [27] demonstrated this in 33% of the examined ears. Several authors [7, 16, 19, 23, 24, 26] examined the round window niche endoscopically and eventually removed any adhesions blocking access to the round window membrane. After injection the patient remains with the treated ear upwards for 15–60 min. Dissolving steroids in hyaluronic acid, as was done in the clinical trials done by Shea [19, 23],

Table 4 Follow-up in 13 clinical studies on intratympanic steroid therapy

Clinical study	Duration of follow-up	Evaluated symptom	Outcome criteria
Itoh and Sakata [18]	Not reported	Vertigo	AAOO 1972, AAO-HNS 1985, Sakata's criteria 1987
		Tinnitus	Unspecified
Shea and Ge [23]	1 year	Vertigo	Unspecified
		Tinnitus	Unspecified
		Aural fullness	Unspecified
Silverstein et al. [7]	3, 6 and 12 months	Hearing	AAO-HNS 1995
		Tinnitus	Questionnaire
Shea [19]	≥2 years	Vertigo	AAO-HNS 1995
		Hearing	AAO-HNS 1995
		Functional level	AAO-HNS 1995
Arriaga and Goldman [26]	≥1 month	Hearing	AAO-HNS 1995
Silverstein et al. [16]	Up to 13 weeks	Hearing	AAO-HNS 1995
		Tinnitus	3 Questionnaires
		Vertigo	ENG
Parnes et al. [11]	Not reported	Hearing	Unspecified
		Vertigo	Unspecified
Sennaroglu et al. [25]	3 months	Vertigo	AAO-HNS 1985
Hirvonen et al. [20]	2 weeks, 3 months and 1 year	Hearing	AAO-HNS 1995
		Aural fullness	Questionnaire
		Tinnitus	Questionnaire
		Vertigo	Questionnaire
Barrs et al. [21]	3, 6 and partly at 12 months	Hearing	AAO-HNS 1995
		Vertigo	AAO-HNS 1995
Chandrasekhar [22]	3 weeks–4 years	Hearing	Unspecified
Gianoli and Li [24]	1–2 weeks	Hearing	Comparable to AAO-HNS 1995
Sennaroglu et al. [17]	18 months	Vertigo	AAO-HNS 1985
		Hearing	AAO-HNS 1995
		Tinnitus	Questionnaire
		Aural fullness	Questionnaire

Arriaga and Goldman [26] and Silverstein et al. [16], to prolongs the presence of the drug in the tympanic cavity [28] and facilitate transport across the round window membrane [26]. A second technique is injection onto absorbing material in the round window niche, as applied by Arriaga and Goldman [26] and Silverstein et al. [7]. As a third technique inner ear medication delivery devices like the Round Window Microcatheter and the Silverstein MicroWick can be used. Both claim to provide a direct and near-continuous perfusion of the inner ear [12]. A fourth technique is instillation through a ventilation tube in the tympanic membrane. An advantage of this technique is that the patient can use the medication himself and is not dependent on a medical team [25], but it is uncertain how much of the applied quantity of steroid solution will be able to perfuse to the inner ear fluids. In both trials by Sennaroglu et al. [17, 25] the steroids were administrated by this

Table 5 Requirements of a clinical drug trial applied to 13 clinical trials on intratympanic steroid therapy

	Comparability	Internal validity					External validity		Total
	C[a]	DB[b]	R[c]	PM[d]	IT[e]	OP[f]	IC[g]	FU[h]	
Itoh and Sakata [18]	+	–	–	–	+	+	–	–	3/8
Shea and Ge [23]	–	–	–	–	–	–	+	+	2/8
Silverstein et al. [7]	–	–	–	–	+	+	–	+	3/8
Shea [19]	–	–	–	–	–	+	+	+	3/8
Arriaga and Goldman [26]	–	–	–	+	+	+	–	+	4/8
Silverstein et al. [16]	+	+	+	+	+	+	+	+	8/8
Parnes et al. [11]	–	–	–	–	+	–	–	–	1/8
Sennaroglu et al. [25]	–	–	–	+	+	+	–	+	4/8
Hirvonen et al. [20]	–	–	–	+	–	+	+	+	4/8
Barrs et al. [21]	–	–	–	+	+	+	+	+	5/8
Chandrasekhar [22]	–	–	–	–	+	–	–	–	1/8
Gianoli and Li [24]	–	–	–	+	+	+	+	+	4/8
Sennaroglu et al. [17]	+	–	–	+	+	+	–	+	4/8

[a] Controlled trial
[b] Double blind
[c] Randomized
[d] Previous medication
[e] Intratympanic administration
[f] Outcome criteria
[g] Inclusion criteria
[h] Duration of follow-up

instillation technique. Silverstein et al. [7] compared four groups of Ménière's disease patients and applied several of the described techniques with different kinds of corticosteroid drugs (Table 4). Whether one of the different used methods is more effective remains still unclear.

To evaluate the influence of intratympanic steroids on inner ear disorders objectively, these should not be combined with systemic steroids. Shea and Ge [23] administrated intravenous dexamethasone at the time the patient received the intratympanic injections. After intratympanic administration the patient took oral dexamethasone for the duration of 1 month. In his study published in 1997 Shea [19] again evaluated the combination of intratympanic and intravenous dexamethasone. The patients included in the study of Hirvonen et al. [20] initially received an intramuscular injection of 15 mg of dexamethasone. Therefore no clear picture about the effects of intratympanic administration can be drawn in these trials. In the other trials only intratympanic steroids were administrated.

The used steroid varies among the evaluated trials (Table 3), though dexamethasone was applied most frequently. Parnes et al. [11] evaluated intratympanic dexamethasone, hydrocortisone and methylprednisolone in guinea pigs. Of the tested drugs, methylprednisolone achieved the highest concentration for the longest duration in both endolymph and perilymph. But on clinical application some patients did not tolerate the burning discomfort in ear or throat associated with methylprednisolone. To relieve these complaints methylprednisone was given together with lidocaine, but because of possible interference of lidocaine, this is not a preferred option in our opinion. Parnes et al. [11] and Gianoli and Li [24] used methylprednisone as well as dexamethasone. Because a tissue esterase was needed to activate long acting methylprednisone, Silverstein et al. [7] switched over to dexamethasone during the study.

All authors, with the exception of Parnes et al. [11], described very accurately which dosage and administration schedule they exerted. Chandrasekhar [22] adjusted the frequency of administration to the audiologic results, although details about the administration schedule and by what audiologic findings an injection was repeated, were not described.

How long was the follow-up?

The Committee on Hearing and Equilibrium of the AAO-HNS recommends comparing the 6 months period before treatment to the period between 18 and 24 months after treatment. None of the authors followed this advice. Silverstein et al. [16] were interested in the immediate effects of therapy and therefore chose a limited duration of follow-up. Some studies did not report follow-up length [11, 18] and in others [22, 26] the follow-up period differed among patients. This complicates drawing comparisons between individual patients and hinders the interpretation of results. Shea [19] and Sennaroglu et al. [17] observed patients longer than 18 months. The follow-up periods of the other trials were 1 year at most [7, 16, 20, 21, 24–26, 29].

Which criteria were used to evaluate the results?

After intratympanic steroid therapy hearing was evaluated in 10 out of 13 studies, vertigo in 8, tinnitus in 6 and aural fullness in only 3 studies. Changes in hearing were mostly [7, 16, 17, 19–21, 26] evaluated according to or similar to the 1995 AAO-HNS guidelines [13]. Some studies didn't describe didn't describe according to which criteria their outcome was evaluated [11, 22] whilst others [20] used added a questionnaire to judge subjective changes in hearing.

To assess changes in vertigo most authors used the guidelines of the AAO-HNS published in 1985 [17, 18, 25] or 1995 [19, 21]. Some didn't mention which criteria they used [11, 23].

As no objective tests to assess tinnitus and aural fullness exist, these symptoms can only be evaluated by means of questionnaires. Silverstein et al. [16] used three validated questionnaires regarding tinnitus. In other studies [7, 17, 20] the patients were asked if their tinnitus changed. In two studies [18, 23] it is unclear how tinnitus was evaluated. Sennaroglu et al. [17] and Hirvonen et al. [20] evaluated aural fullness by means of a questionnaire.

After intratympanic therapy a complete control of vertigo in MD was reported in 43–96.4% [21, 29]. Tinnitus improved in 45–82.1% [7, 29]. In the studies of Hirvonen [20] and Silverstein [16] vertigo and tinnitus remained unchanged. Aural fullness improved slightly in Hirvonen's study [20], and in 89% in the study by Shea and Ge [29]. Changes in hearing after intratympanic steroid treatment in MD differ widely. Improvement in hearing varied between 16 [17] and 67.9% [29], deterioration between 3.6 [29] and 38% [17] or the level of hearing remained unchanged [16, 20, 21]. In ISSNHL Gianoli [24] found hearing improvement in 44% and the hearing level remained the same in 52%. Parnes [11] found no significant changes in hearing after intratympanic steroid therapy in ISSNHL. Only Silverstein [7] included two patients with RPSSNHL, but the outcome of these two specific patients was not described. No studies report any adverse effects of intratympanic corticosteroids, so it seems to be a safe treatment.

Conclusions

In conclusion, we can establish that none of the evaluated studies on intratympanic steroid therapy completely meets the requirements of a clinical drug trial. Results are therefore difficult to interpret. Several factors, such as differences in study set-up, relatively small population sizes and differences in inclusion- and exclusion criteria have their negative effects on internal

and external validity. Because reliable clinical evidence on intratympanic steroids is lacking, it remains unclear how efficacious this therapy is and what the optimum dosage and administration schedule would be. Therefore further investigation by means of controlled, randomised, double-blind trials is required.

References

1. Ryan AF, Harris JP, Keithley EM (2002) Immune-mediated hearing loss: basic mechanisms and options for therapy. Acta Otolaryngol (Stockh) 548(Suppl):38–43
2. Derebery MJ (1996) Allergic and immunologic aspects of Ménière's disease. Otolaryngol Head Neck Surg 114(3):360–365
3. Yoo TJ, Kwon SS (2002) Molecular mechanism of autoimmune hearing loss. Acta Otolaryngol (Stockh) 548(Suppl):3–9
4. Fuse T, Hayashi T, Oota N et al (2003) Immunological responses in acute low-tone sensorineural hearing loss and Ménière's disease. Acta Otolaryngol (Stockh) 123:26–31
5. McCabe BF (1979) Autoimmune sensorineural hearing loss. Ann Otol Rhinol Laryngol 88:585–589
6. Moskowitz D, Lee KJ, Smith HW (1984) Steroid use in sudden sensorineural hearing loss. Laryngoscope 94:664–666
7. Silverstein H, Choo D, Rosenberg S, Kuhn J, Seidman MD, Stein I (1996) Intratympanic steroid treatment of inner ear disease and tinnitus (preliminary report). Ear Nose Throat J 75(8):468–471
8. Shirwany NA, Seidman MD, Tang W (1998) Effect of transtympanic injection of steroids on cochlear blood flow, auditory sensitivity, and histology in the guinea pig. Am J Otol 19(2):230–235
9. Fukushima M, Kitahara T, Uno Y, Fuse Y, Doi K, Kubo T (2002) Effects of intratympanic injection of steroids on changes in rat inner ear aquaporin expression. Acta Otolaryngol (Stockh) 122:600–606
10. Chandrasekhar S, Rubinstein R, Kwartler J et al (2000) Dexamethasone pharmacokinetics in the inner ear: comparison of route of administration and use of facilitating agents. Otolaryngol Head Neck Surg 122(4):521–528
11. Parnes LS, Sun AH, Freeman DJ (1999) Corticosteroid Pharmacokinetics in the inner ear fluids: an animal study followed by clinical application. Laryngoscope 109(Suppl 91):1–17
12. Jackson LE, Silverstein H (2002) Chemical perfusion of the inner ear. Otolaryngol Clin North Am 35:639–653
13. Committee on Hearing and Equilibrium AAO-HNS (1995) Committee on hearing and equilibrium guidelines for the diagnosis and the evaluation of therapy in Ménière's disease. Otolaryngol Head Neck Surg 113(3):181–185
14. Stokroos RJ, Albers F (1996) The etiology of idiopathic sudden sensorineural hearing loss. A review of the literature. Acta Oto-rhino-laryngol Belg 50:69–76
15. Moscicki R, San Martin J, Quintera C (1994) Serum antibody to inner ear proteins in patients with progressive hearing loss. Correlation with disease activity and reponse to corticosteroid treatment. JAMA 272(8):611–616
16. Silverstein H, Isaacson J, Olds M, Rowan P, Rosenberg S (1998) Dexamethasone inner ear perfusion for the treatment of Ménière's disease: a prospective, randomized, double-blind, crossover trial. Am J Otol 19(2):196–201
17. Sennaroglu L, Sennaroglu G, Gursel B, Dini FM (2001) Intratympanic dexamethasone, intratympanic gentamicin, and endolymphatic sac surgery for intractable vertigo in Ménière's disease. Otolaryngol Head Neck Surg 125(5):537–43
18. Itoh A, Sakata E (1991) Treatment of vestibular disorders. Acta Otolaryngol (Stockh) Suppl 481:617–623
19. sShea JJ (1997) The role of dexamethasone or streptomycin perfusion in the treatment of Meniere's disease. Otolaryngol Clin North Am 30(6):1051–1059
20. Hirvonen T, Peltomaa M, Ylikoski J (2000) Intratympanic and systemic dexamethasone for Ménière's disease. ORL J Otorhinolaryngol Relat Spec 62(3):117–120
21. Barrs D, Keyser J, Stallworth C, McElveen JJ (2001) Intratympanic steroid injections for intractable Ménière's disease. Laryngoscope 111(12):2100–2104
22. Chandrasekhar S (2001) Intratympanic dexamethasone for sudden sensorineural hearing loss: clinical and laboratory evaluation. Otol Neurotol 22(1):18–23
23. Shea JJJ, Xianxi G (1996) Dexamethasone perfusion of the labyrinth plus intravenous dexamethasone for meniere's disease. Otolaryngol Clin North Am 29(2):353–358
24. Gianoli GJ, Li JC (2001) Transtympanic steroids for treatment of sudden hearing loss. Otolaryngol Head Neck Surg 125(3):142–146
25. Sennaroglu L, Dini FM, Sennaroglu G, Gursel B, Ozkan S (1999) Transtympanic dexamethasone application in Ménière's disease: an alternative treatment for intractable vertigo. J Larngol Otol 113:217–21
26. Arriaga M, Goldman S (1998) Hearing results of intratympanic steroid treatment of endolymphatic hydrops. Laryngoscope 108(11 Pt 1):1682–1685
27. Alzamil KS, Linthicum FHJ (2000) Extraneous round window membranes and plugs: possible effect on intratympanic therapy. Ann Otol Rhinol Laryngol 109(1):30–32
28. Plontke S, Zenner HP (2002) Pharmacokinetic considerations in intratympanic drug delivery to the inner ear. Acta Oto-rhino-laryngol Belg 56:369–370
29. Shea JJ Jr, Ge X (1996) Dexamethasone perfusion of the labyrinth plus intravenous dexamethasone for Ménière's disease. Otolaryngol Clin North Am 29(2):353–358
30. Shea JJ Jr (1993) Classification of Ménière's disease. Am J Otol 14:224–229