Quality of life after intratympanic steroid injection for Ménière's disease

Annejet A. Schenck MD1,2 | Claire C. Bommeljé MD, PhD1 | Peter Paul G. van Benthem MD, PhD2 | Henk M. Blom MD, PhD1,2,3

1Department of Otorhinolaryngology, HagaHospital, The Hague, The Netherlands
2Department of Otorhinolaryngology, Leiden University Medical Centre, Leiden, The Netherlands
3Department of Otorhinolaryngology, Antwerp University Hospital, Antwerp, Belgium

Correspondence
Annejet A. Schenck, Els Borst-Eilersplein 275, 2545 AA, The Hague, The Netherlands.
Email: j.schenck@hagaziekenhuis.nl

Abstract
Objective: This study explores how treatment with intratympanic steroid injection affects quality of life, as well as several subjective complaints in patients with Ménière's disease.
Methods: Patients filled in the Ménière's Disease Outcome Questionnaire (MDOQ) and answered questions about subjective complaints. Scores before and after treatment were compared using paired t tests.
Results: Forty-nine patients treated with intratympanic steroid injection were included. Quality of life was improved in 36 (73%) patients, the same in 9 (18%) patients, and lower in 4 (8%) patients. Overall, the mean change in MDOQ was +20.6 points (95% confidence interval +14.5 to +26.7 points, \( p < 0.001 \)). The improvement was seen in the emotional, physical, and mental domain. Most patients experienced less vertigo and instability but did not notice change in subjective hearing, tinnitus, or aural fullness after treatment.
Conclusion: Treatment with intratympanic steroid injection leads to an improvement in quality of life in most patients. Moreover, the procedure is only minimally invasive. Based on the findings in this study, treatment with ITS should be discussed with every patient suffering from vertigo attacks due to active Ménière's disease.
Level of evidence: Level 4

KEYWORDS
intratympanic steroid injection, Ménière's disease, quality of life, vertigo

1 | INTRODUCTION

Ménière's disease (MD) is an inner ear disorder with characteristic bouts of vertigo, accompanied by hearing loss and other aural symptoms. The natural course of the disease seems to be favorable: most patients reach a vertigo-free state within a couple of years after the first vertigo attack, although irreversible damage to the inner ear is common. Because of the debilitating effects of the disease, most patients opt for active treatment. Various treatment modalities have been studied, such as life-style adjustments, drugs, and surgical treatment, both destructive and non-destructive. In recent guidelines, it is recommended to start treatment by administering betahistin. If vertigo attacks still occur, intratympanic injection of steroids is advised.
followed by intratympanic injection of gentamicin if vertigo control is not achieved by the steroid injections. Intratympanic injection with steroids (ITS) is a widely used treatment. It is a relatively simple and quick procedure, with minimal risk. Risk that apply are transient dizziness, a persistent tympanic membrane perforation, and ear infection, occurring in 0.6%–16.9%, 0%–38%, and 0%–7% of the cases, respectively. These adverse events usually resolve spontaneously.

Dexamethasone and methylprednisolone are the most commonly used substrates, delivered into the middle ear through the tympanic membrane. They reach the inner ear by absorption, mainly through the round window membrane. The exact mechanism of action remains unclear, but the immune mediating properties are thought to play a role. Moreover, the drug is not ototoxic and does therefore not carry the risk of causing permanent damage to the inner ear.

Quality of life (QoL) is an important outcome measure for Ménière’s disease, as it is often severely affected by the unpredictable pattern of the attacks. The fear of having an attack hampers everyday life, and therefore, the disease does not only have an impact on physical, but also on emotional health of patients. In this article, the outcomes of ITS in terms of QoL are reported. Furthermore, the evolvement of subjective complaints related to Ménière’s disease after treatment with ITS is assessed.

2 | MATERIALS AND METHODS

2.1 | Study design

This is a retrospective study using questionnaires. The local research committee of the HagaHospital approved of this study. This study was exempt from obtaining approval of the medical ethics research committee.

2.2 | Patients

Patients diagnosed with Ménière’s disease in our outpatient clinic between January 2015 and December 2018, who had been treated with ITS, were asked to participate. If they agreed, they received the questionnaires electronically. Data were captured and analyzed in SPSS (IBM SPSS Statistics version 24). Before analysis of the data, patients’ records were double-checked to assure all patients met the American Academy of Otolaryngology–Head and Neck Surgery criteria for definite Ménière’s disease: all patients had suffered at least two vertigo attacks (each lasting 20 min to 12 h), with audiometrically documented low- to medium-frequency sensorineural hearing loss and fluctuating aural symptoms such as hearing loss, tinnitus, and/or aural fullness in the affected ear. Other diagnoses had been ruled out, either through anamnesis or additional testing.
2.3 | Intratympanic injection with corticosteroids

After the diagnosis was made, patients were counseled about treatment options. If the disease was quiescent, a “wait and see” policy was advised, and patients were instructed to contact the department if vertigo attacks reoccurred. If the disease was active and patients were suffering vertigo attacks, intratympanic injection was discussed, as this is the standard first treatment option that is offered in our clinic. If patients opted for ITS, the injections were given in our outpatient ear, nose, and throat (ENT) clinic. After inspection to assure that the tympanic membrane was intact, multiple droplets of tetracaine in isopropyl alcohol (15%, produced by the hospital pharmacy) were applied in the external auditory canal for local anesthesia. After 20 min, the tetracaine was removed using suction cleaning. The tympanic membrane was then perforated in the posterosuperior quadrant, to allow escape of air from the middle ear during injection of steroids. Another perforation was then made in the posteroinferior quadrant, through which the steroids were delivered in the middle ear. The used substrates were triamcinolone acetonide (Kenacort 40 mg/ml, Bristol-Myers Squibb, New York City, USA) or dexamethasone (20 mg/ml, Centrafarm B.V., Etten-Leur, the Netherlands). Usually, between 0.4 and 0.8 ml was applied. After injection, patients were instructed to lay still, not talk and minimize swallowing and yawning during 15 minutes. Patients were seen back in our outpatient clinic 6 weeks after the injection in a regular follow-up visit, and the effect of the treatment was evaluated. Note that this is not the evaluation with a questionnaire that is discussed in this article. If patients were still suffering vertigo attacks, another injection was given. If patients were free of complaints, a wait-and-see policy was discussed. Later injections were given when vertigo attacks reoccurred.

2.4 | Outcome measures

QoL was chosen as primary outcome for this study, using the Ménie`re’s Disease Outcome Questionnaire (MDOQ).16 This is a validated, disease-specific tool focusing on Ménie`re’s disease. It includes questions about the emotional, physical, and mental domain. The questionnaire was translated to Dutch by a certified translation agency and cross-validated. The questionnaire results in two scores between 0 and 76 points each; one score for the pretreatment situation and one score for the posttreatment situation.16 One pair of questions was in free-text format for patients to write any additional comments. These two questions did not result in points. Apart from the total scores, the scores per domain were calculated and compared.

Secondary outcome measures are vertigo, tinnitus, hearing loss, instability, and aural fullness. Patients were asked if they had noticed improvement, no change, or worsening of each of these symptoms after treatment with ITS.

Lastly, the risks of intratympanic injections were evaluated by determining the rates of ear infection and persistent tympanic membrane perforation.

3 | RESULTS

3.1 | Patient characteristics

A total of 333 patients were diagnosed with Ménie`re’s disease in our outpatient clinic between January 2015 and December 2018. 133 of these patients were treated with ITS and were asked to participate through phone and email in the period between November 2018 and January 2019. Fifty-five patients agreed and returned the completed questionnaires. Six of these patients did not meet the criteria for definite Ménie`re’s disease and were therefore excluded from the analysis. The other 49 patients were included. A schematic flowchart can be found in Figure 1. Demographic data of the participants can be found in Table 1.

Average time of follow-up, defined as the number of days between first and most recent visit to our clinic, was 787 days. Because of the retrospective nature of this study, patients did not receive the questionnaire at a predefined moment after the IT injection, but questionnaires were sent out in the same period (November 2018–January 2019) to all participants. Therefore, time between the last injection and completing the questionnaire varies among the participants. On average, patients filled in the questionnaires 347 days after the injection.

| TABLE 1 | Characteristics of included patients \( n = 49 \) |
|-----------|-----------|
| **Sex** | |
| Female | 26 (53%) |
| Male | 23 (47%) |
| **Age** | |
| At diagnosis | 50 (±11.8) |
| At first presentation | 56 (±10.8) |
| **Duration of disease**, days | 2780 (range 35–9680) |
| **Side of MD** | |
| Right | 25 (51%) |
| Left | 17 (35%) |
| Both | 7 (14%) |
| **Side of treatment** | |
| Right | 26 (53%) |
| Left | 18 (37%) |
| Both | 5 (10%) |
| **Mean number of ITS** | 3.4 (±2.8) |
| **Mean duration of follow up, days** | 787 (±495) |
| **Mean duration between last ITS and questionnaire, days** | 347 (range 41–988) |

1Minimal duration of disease, as exact as could be extracted from the patients’ records. This was calculated as number of days between the date of diagnosis and the date of last visit to our center.

2In case of bilateral disease, the injections were given at the side of complaints of tinnitus and hearing loss. If patients were unsure, injections were given bilaterally.

3Duration of follow up was calculated as the number of days between the first and the last visit to our center.
The mean MDOQ score before treatment was 29.9 (±13.6). The mean change in score was +20.6 points (95% confidence interval +14.5 to +26.7 points, \(p < .001\)) after treatment. When calculated per domain, a significant improvement was seen in each domain.

The majority of patients (73%, \(n = 36\)) experienced an increase in QoL after treatment with ITS. Among the patients who experienced better QoL after treatment, the mean increase in MDOQ score was

### TABLE 2  MDOQ scores before and after treatment

| Pretreatment score | Post-treatment score | Difference | \(p\) |
|--------------------|----------------------|------------|-------|
| Total (\(n = 49\)) | 29.9                 | 50.5       | +20.6 | < .001|
| Social well-being  | 37.9                 | 58.4       | +20.5 | < .001|
| Physical well-being| 24.5                 | 46.2       | +21.8 | < .001|
| Mental well-being  | 35.8                 | 50.8       | +15.0 | < .001|

### TABLE 3  Changes in MDOQ scores, grouped per possible outcome (i.e., better, same of worse quality of life)

| Pretreatment score | Post-treatment score | Difference | \(p\) |
|--------------------|----------------------|------------|-------|
| Decreased QoL (\(n = 4\)) | 33.2              | 30.6       | -2.6  | .142 |
| No difference in QoL (\(n = 9\)) | 33.5              | 33.5       | 0.0   | NA   |
| Increased QoL (\(n = 36\)) | 28.6              | 56.9       | +28.3 | < .001|

### FIGURE 2  Evolution of subjective complaints after treatment with ITS. In green, the proportion of patients suffering less from this complaint after ITS is depicted. In orange, the proportion of patients who did not notice change in this complaint after ITS and in red, the proportion of patients who had more of the specific complaints after treatment with ITS.

#### 3.2  Quality of life

The mean MDOQ score before treatment was 29.9 (±13.6). The mean change in score was +20.6 points (95% confidence interval +14.5 to +26.7 points, \(p < .001\)) after treatment. When calculated per domain, a significant improvement was seen in each domain.

The majority of patients (73%, \(n = 36\)) experienced an increase in QoL after treatment with ITS. Among the patients who experienced better QoL after treatment, the mean increase in MDOQ score was
28.3 points. Nine (18%) patients did not experience improvement or decline. Four (8%) patients had a decrease in QoL, with a mean decline of 2.6 points.

All results can be found in Tables 2 and 3.

3.3 Secondary outcomes

Most patients had less complaints of vertigo and instability after ITS. In most patients, treatment had no effect on (subjective) hearing loss, tinnitus, and aural fullness. The results for the secondary outcomes can be found in Figure 2.

Ear infection or persistent tympanic membrane perforation were not seen among our patients.

4 DISCUSSION

Intratympanic injection with steroids is a widely used method to control Ménière’s disease attacks. Although its efficacy is debated, most patients seem to benefit from treatment with ITS.\(^4^,17^–^19\) Success rates range from 24% to 91%, with a median of around 70%.\(^4^,13^,20^–^22\)

Reportedly, the most important factor for success is administration “as-needed.”\(^13\)

As recommended by the Committee on Hearing and Equilibrium, most papers report outcomes of treatment in terms of “class of vertigo control,” which compares the number of vertigo attacks before and after treatment.\(^23\) Standardizing the outcome measure is a useful tool to assimilate results and therefore facilitate comparison among studies. However, using only the number of vertigo spells to evaluate treatment results may disregard personal and emotional experience of the individual patient. The imminence of another attack and the unpredictable pattern of the disease are factors that disrupt everyday life and lead to severe loss of QoL,\(^8\) but may be missed by counting merely the number of attacks. Moreover, bouts of vertigo are usually not objectified, and therefore, reporting of vertigo attacks inevitably carries a risk of recall bias. The guidelines acknowledge these limitations and suggest to also use the “functional level scale” (FLS) to assess the effect of MD on daily life. This 6-point scale (ranging from “no effect on daily life” to “disabled from over 1 year”) gives insight into the patient’s burden of disease, albeit limited.

A more extensive way of measuring QoL is the MDQQ.\(^16\) It allows evaluation of overall QoL after treatment, and especially surgery, for Ménière’s disease. It consists of 20 pairs of questions focused on three domains: the physical, mental, and social well-being. In the paper of Kato et al., where the MDQQ is introduced, results of endolymphatic sac decapsulation in 159 patients were evaluated using the new questionnaire.\(^16\)

On average, the overall score improved with +26.8 points. Furthermore, the scores increased in every domain. In our results, we found that treatment with ITS achieves improvement of QoL in the majority of patients, endorsing previous findings. The mean improvement in score of +20.6 points is fairly similar to the finding of Kato et al.\(^16\)

Moreover, we also found improvement in each of the separate domains, although the improvement in the mental domain was slightly higher in our study, and the improvement in the social domain was lower than in Kato’s study.

Another interesting finding is that the score change in patients with decreased QoL \((n = 9)\) is only \(-2.6\) points, compared to a mean increase of \(+28.3\) among patients with a better QoL after treatment \((n = 36)\). Apart from being not statistically significant, the clinical relevance of this decrease can be disputed. On the contrary, the found increase is statistically significant and seems to reflect a convincing increase in QoL.

Considering the subjective outcome measures, most patients in our cohort experienced less vertigo and instability after treatment. ITS did not seem to influence complaints of tinnitus, aural fullness, and subjective hearing. In a study of Garduño-Anaya et al.\(^20\) among 22 patients, patients were asked for subjective improvement of complaints from 0 (no improvement) to 10 (100% improvement). Most patients in the active treatment group (consisting of IT injection of dexamethasone) experienced less vertigo, but did not notice difference in subjective hearing or tinnitus, which is very similar to our results.

In the current literature, the effectiveness of ITS is debated. A recent systematic review questions the effect based on four randomized controlled trials, although “a beneficial effect linked to this treatment modality cannot be ruled out.”\(^17\) A randomized, double-blind trial reports an average of 91% decrease in number of vertigo attacks among patients treated with ITS, but a control group treated with a placebo is lacking.\(^21\) When reading these papers, it is important to note that the main focus is on the quantitative outcomes such as number of attacks. This article hopes to bring the importance of patients’ perception to the attention of clinicians. In the case of Ménière’s disease, QoL may improve after treatment with ITS, even if attacks still occur. In our study, this is illustrated by the fact that only 51% of the patients report less vertigo complaints, but over 70% of our population reported higher QoL after ITS. This may indicate that other factors, such as emotional aspects, play an important role, and that treatment with ITS has an impact on these factors as well.

Moreover, ITS is a simple procedure with minimal risks. In literature, rates of 0%–7% and 0%–38% for ear infection and persistent tympanic membrane perforation, respectively, are reported. However, in our cohort neither of these adverse events were seen. The authors therefore find that the benefits of ITS outweigh the risks of the procedure.

Regarding alternative treatment options, betahistin lacks both evidence of effectiveness\(^7\) and does not prove to increase QoL.\(^24\)

Intratympanic injection of gentamicin has proven to be as effective as steroids in a randomized, double-blind trial\(^21\) and leads to an increase in QoL\(^25\) but carries the risk of irreversible hearing loss.\(^26\)

Although these results of ITS treatment are encouraging, several alternative explanations should be taken into account. Firstly, an important consideration for any intervention for Ménière’s disease, is the natural course of the disease. Usually, vertigo attacks diminish with time.\(^1\) When determining treatment effect, one should always realize that patients might experience a decrease in disease activity instead of response to treatment. Especially because on average nearly a year had passed between treatment and the questionnaire,
this factor should be taken into account. Secondly, the placebo effect is known to play a role in any treatment for Ménière’s disease, and as there is no placebo arm in this study, it cannot be determined. Moreover, the subjective outcome measures leave space for individual perception of symptoms, but may distort reliability of outcomes. For example, the complaint “vertigo” may be interpreted by participants as the spinning sensation that was meant, but also as unsteadiness or instability. In our results, it is interesting to see that the same proportion of patients experienced improvement of vertigo and instability. It is likely that patients define one sensation as both “vertigo” and “instability.” Fourthly, there is a risk of selection bias, as our center is specialized in Ménière’s disease. This is reflected by the fact that the mean age of first presentation is higher than the age at which patients were diagnosed with MD. Other limitations are the risk of recall bias, the absence of a control group treated with a placebo and the risk of regression toward the mean. Patients are treated with ITS at the moment they have many complaints, and therefore, it is likely that a later measurement will be less extreme, regardless of therapy. Lastly, the retrospective design of the study limits several aspects. For example, the time between the last attack and administration of the injection could not be determined. A prospective study could overcome some of these limitations.

5 | CONCLUSION

In conclusion, we recommend offering treatment with ITS to every patient suffering vertigo attacks due to Ménière’s disease, based on the findings of this study. Additionally, extensive measurement of QoL should be part of future research, as the (FLS) may be too limited in its ability to assess patients’ perception of complaints. The MDOQ is a validated tool that could be useful for this purpose.

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CONFLICT OF INTEREST

The authors have no conflict of interest to declare.

ORCID

Annejet A. Schenck https://orcid.org/0000-0002-3093-175X
Claire C. Bonmelij https://orcid.org/0000-0001-7227-6629
Peter Paul G. van Benthem https://orcid.org/0000-0002-7946-1912
Henk M. Blom https://orcid.org/0000-0002-6075-9647

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