Pharmacological, surgical and diagnostic innovations in Meniere’s disease: a review

Alfonso Scarpa
Department of Medicine and Surgery, University of Salerno, Salerno, Italy, alfonzoscarpa@yahoo.it

Follow this and additional works at: https://tmj.unisa.it/journal

Recommended Citation
Scarpa, Alfonso (2020) "Pharmacological, surgical and diagnostic innovations in Meniere’s disease: a review," Translational Medicine @ UniSa: Vol. 23 : Iss. 4 , Article 10.
Available at: https://doi.org/10.37825/2239-9747.1009

This Article is brought to you for free and open access by Translational Medicine @ UniSa. It has been accepted for inclusion in Translational Medicine @ UniSa by an authorized editor of Translational Medicine @ UniSa.
Pharmacological, surgical and diagnostic innovations in Meniere’s disease: a review

Scarpa A\textsuperscript{1}, Ralli M\textsuperscript{2}, De Bonis E\textsuperscript{1}, Troisi D\textsuperscript{1}, Montanino A\textsuperscript{1}, Viola P\textsuperscript{3}, Chiarella G\textsuperscript{3}, Gioacchini FM\textsuperscript{1}, Cavaliere M\textsuperscript{1}, Cassandro E\textsuperscript{1}, Cassandro C\textsuperscript{5}

\textsuperscript{1}Department of Medicine and Surgery, University of Salerno, Salerno, Italy
\textsuperscript{2}Department of Sense Organs, Sapienza University Rome, Rome, Italy; Center for Hearing and Deafness, University at Buffalo, Buffalo, NY 14214, USA.
\textsuperscript{3}Department of Experimental and Clinical Medicine, Unit of Audiology, Regional Centre for Cochlear Implants and ENT Diseases, Magna Graecia University, Catanzaro, Italy
\textsuperscript{4}Ear, Nose, and Throat Unit, Department of Clinical and Molecular Sciences, Polytechnic University of Marche, Ancona, Italy.
\textsuperscript{5}Surgical Sciences Department, University of Turin, Turin, Italy

(Corresponding author: Alfonso Scarpa - mail: alfonsoscarpa@yahoo.it)

\textbf{Abstract}
Meniere’s disease is an inner ear disorder characterized by the presence of endolymphatic hydrops in the inner ear and symptomatology of recurrent and debilitating vertigo attacks, tinnitus, aural fullness, and fluctuating sensorineural hearing loss. Although many therapeutic options for MD have been proposed during years, no consensus has been reached by the scientific community. In the last decade, many therapeutic options have been proposed, as intratympanic steroid, intratympanic gentamicin, and intravenous glycerol. Recently, the role of the antiseretory factor in the diet of MD patients have been investigated. Surgery is recommended for intractable MD; some authors proposed new approaches including transcanal endoscopic infracochlear vestibular neurectomy, new marsupilization technique in sac surgery, and tenotomy of the stapedius and tensor tympani muscles.

\textbf{Keywords:} Meniere’s disease; endolymphatic hydrops; glycerol; intratympanic therapy; diuretics; gentamicin

I. INTRODUCTION
Meniere disease (MD) is an inner ear disorder characterized by the presence of endolymphatic hydrops (EH) in the inner ear and symptomatology of recurrent and debilitating vertigo attacks, tinnitus, aural fullness, and fluctuating sensorineural hearing loss (SNHL)\textsuperscript{1,2,3}. Although hearing loss is mainly sensorineural, low-frequency air-bone gap (ABG) can also be found in the absence of middle ear pathology\textsuperscript{4}, mimicking other conditions such as cerebral vascular anomalies including dural arteriovenous fistula\textsuperscript{5}. MD symptoms can severely affect the quality of life\textsuperscript{6,7}.

Although many therapeutic options for MD have been proposed, no consensus has been reached by the scientific community\textsuperscript{8-11}. First-line treatment includes dietary restrictions for salt, caffeine, and alcohol associated to drugs both for acute attacks (dimenhydrinate, benzodiazepines)\textsuperscript{12}, and as prophylactic therapy (betahistine, \(\beta\)-blockers, diuretics)\textsuperscript{13}. When first-line treatment does not offer satisfactory symptom control, intratympanic (IT) administration of gentamicin or corticosteroids can be performed\textsuperscript{14}; however, many studies showed that IT gentamicin may expose the patients to a risk of hearing loss, depending on dosage and intervals between administrations\textsuperscript{15}. Labyrinthectomy or other surgical procedures can be suggested for intractable MD\textsuperscript{16}.

Despite the recent COVID-19 pandemic\textsuperscript{17-20}, scientific research for MD is a growing area in continuous development. This brief review aims to assess the clinical innovations for the therapy of MD.
The main goal of the pharmacological treatment of MD is to reduce the duration and frequency of vertigo attacks, and to prevent hearing loss, which is usually progressive. There’s lack of high-level evidences for efficacy of MD treatment; for this reason, different drugs and different methods of administration have been tested.

IT steroids (dexamethasone, methylprednisolone) treatments have been widely used for MD, especially when first-line treatment does not offer a satisfactory symptoms control; however, there is still lack of evidence that this treatment may have a positive effect in MD. Pradhan et al. evaluated the effects of IT dexamethasone in 30 patients with refractory MD comparing the pre- and post-treatment hearing outcome and dizziness score. They found that 23% of patients were free of vertigo at the end of 24 months after IT steroids, but there was no significant improvement in hearing. These results are in accordance with those from Weckel et al. who retrospectively evaluated 25 patients treated with IT dexamethasone; they reported a satisfactory control of vertigo in 92% of the patients, and this protocol achieved control of vertigo in 70% of patients at 2 years. Harcourt et al. suggested IT methylprednisolone as an effective treatment for the long-term control of vertigo attacks, without he known inner-ear toxicity associated with gentamicin.

Gentamicin, administered at different doses and timing, has been proven as an effective treatment for vertigo control in MD with a potential risk of herring loss; however, discussion about the dosage and the method used is open. Scarpa et al. proposed a low-dose IT gentamicin protocol; they treated 48 patients with 0.5 ml of 10 mg of gentamicin with an interval of 2 weeks between injections. They reported a satisfactory control of vertigo attacks after IT gentamicin, and the effect of this protocol on vestibular system was proved by the reduction in vestibulo-ocular reflex (VOR) gain in the affected side. A meta-analysis from Jian et al. demonstrated that IT gentamicin is superior to IT steroids in reducing the number of vertigo attacks, but both drugs didn’t show hearing improvement. Moreover, Ozturk and Ata proposed an IT mixture of gentamicin and dexamethasone injection for the treatment of intractable MD, even more effective that IT gentamicin, and the effect of this protocol achieved control of vertigo in 92% of patients that are refractory to medical management as a nondestructive option, as the risk to damage hearing is low.

Diuretics have also been recommended to control vertigo attacks in MD, due to their effects in reducing the endolymphatic pressure and volume. As for steroids and gentamicin, there are no high-quality data demonstrating the efficacy of oral diuretic therapy; in addition, a meta-analysis from Rosenbaum and Winter concluded that it is not clear if diuretic lead to a symptomatic improvement of vertigo.

A prospective study from Scarpa et al. evaluated the effectiveness on vertigo control of intravenous (IV) glycerol (an osmotic diuretic), 10% glycerol with 0.9% sodium chloride, 0.5 g/kg once a day for 2 consecutive days every fifteen days for six months; the authors reported an improvement of vertigo attacks and a significant reduction of discomfort generated by tinnitus, raising quality of life.

Recently, some authors suggested a possible action of anti-secretory factor (AF), a protein produced by pituitary gland that plays a role in the innate defense against the inflammatory and secretory components of diarrheal disease. It has been hypothesized that AF can act as a modulator of water and ions and interact with the aquaporins. Viola et al. observed a significant improvement in daily activities in patients treated with specially processed cereals (SPC) compared to those treated with IV glycerol and dexamethasone. The study reported a significant reduction of vertigo spells and a positive effect on tinnitus severity.

Surgical Innovations

According to international guidelines, surgical therapy for MD is recommended only for refractory disease, and therefore represents the third (or even the fifth) line of management. Currently, the most popular surgical procedures to control vertigo attacks in MD are also the most aggressive and those that have the most negative impact on auditory function. Besides, there is a lack of evidence suggesting that surgical therapy for MD may provide a significant control of symptoms.

The table below shows the main surgical procedures for MD taking into account of hearing preservation, vestibular injury, surgical difficulty and long-term outcomes (Table 1).

| Procedures                        | Hearing preservation | Vestibular injury | Surgical difficulty | Long-term outcomes |
|-----------------------------------|----------------------|-------------------|---------------------|--------------------|
| Endolymphatic sac surgery         | Yes                  | No                | Medium              | Poor               |
| Grommet insertion                 | Yes                  | No                | Easy                | Poor               |
| Tympanotomy of ear muscles        | Yes                  | No                | Easy                | Few studies        |
| Transmastoid labyrinthectomy      | No                   | Yes               | High                | Good               |
| Vestibular neurectomy             | Yes                  | No                | High                | Good               |
| Triple semicircular canal plugging| Yes                  | Yes               | High                | Good               |

Endolymphatic sac surgery (ESS) can be considered in patients that are refractory to medical management as a nondestructive option, as the risk to damage hearing is low. Xu et al. suggested that ESS with posterior tympanotomy and local steroid treatment could improve hearing and ensure a satisfactory vertigo control in patients with intractable MD. In Gibson et al opinion, ESS can
provide a vertigo control at least as well as IT gentamicin with a lower incidence of audio-vestibular complications. Transmastoid labyrinthectomy alone or in combination with cochlear implantation, grommet insertion, and triple semicircular canal plugging have been proposed as an effective surgical option for the treatment of MD.

New techniques have been recently described. Daneshi et al evaluated the results of a new marsupialization technique in endolymphatic sac decompression surgery, in which the outer layer of the sac was turned around and placed under the anterior bony border. They concluded that this technique can control progressive hearing loss and improve tinnitus, vertigo, and ear fullness among patients with intractable unilateral MD.

Moreover, Trakimas et al proposed a transcanal endoscopic infracochlear vestibular neurectomy on cadaver as a minimally invasive approach to distal vestibular neurectomy. More recently, some authors suggested that tenotomy of the stapedius and tensor tympani muscles (TSTM) may be a potential marker for the diagnosis and evaluation of therapy efficacy, the audio-vestibular test battery has a primary role, and the diagnostic findings are constantly evolving.

Diagnostic Innovations

In the diagnosis and the evaluation of therapy efficacy, the audio-vestibular test battery has a primary role, and the diagnostic findings are constantly evolving. Di Stadio et al proposed head-shaking nystagmus (HSNy) as a useful test in the early stages of MD to predict a new vertigo attack, with a sensitivity of the ipsilesional HSNy of 100% at T0 and 85.7% at T1. Lee et al evaluated the VOR performance during the attacks of MD using video head-impulse tests (video-HITs) according to each ictal phase; the authors suggested that during the vertigo attack, HITs are normal during irritative and recovery phases, but abnormal in 53% of the patients during the paretic phase, reflecting characteristic ictal vestibular discharges. Besides, a common finding in MD is a normal horizontal HIT with an asymmetric caloric function, and this dissociation can be used as a diagnostic marker.

Patients with suspected MD can be examined using magnetic resonance imaging (MRI) to evaluate a possible inner ear disease. The MRI findings in patients with MD are conflicting, due to the MRI sequences used and the inclusion criteria of the patients; also, the early stage of MD and the early symptoms appear too subtle for identification using MRI, making the reproducibility of hydrops MRI scan protocols debatable.

III. CONCLUSION

Despite accumulating evidence for the treatment of MD, there is currently no international consensus on a standardized therapeutic protocol for this condition. Intravenous administration of glycerol, low-dose intratympanic gentamicin, and antisecretory factor are promising innovations. The role of surgery in the treatment of MD is still debated; recent techniques as tenotomy of the stapedius and tensor tympani muscles seems to offer interesting insights, but larger randomized studies are needed to draw conclusions.

REFERENCES

[1] Cassandro C, De Luca P, Ralli M, et al. Recurrence of Non-Hydropic Sensorineural Hearing Loss (SSNHL): a literature review. Translational Medicine UniSA 2019;20:22–7
[2] Gioacchini FM, Albera R, Re M et al. Hyperglycemia and diabetes mellitus are related to vestibular organs dysfunction: truth or suggestion? A literature review. Acata Diabetol. 2018;55(12):1201-1207
[3] Goebel, J.A., 2015 Equilibrium Committee Amendment to the 1995 AAO-HNS Guidelines for the Definition of Meniere's Disease. Otolaryngol Head Neck Surg, 2016. 154(3): p. 403-4
[4] Scarpa A, Ralli M, Cassandro C et al. Inner-Ear Disorders Presenting with Air-Bone Gaps: A Review. J Int Adv Otol. 2020 Apr;16(1):111-116
[5] Cassandro E, Cassandro C, Sequino G et al. Inner Ear Conductive Hearing Loss and Unilateral Pulsatile Tinnitus Associated with a Dural Arteriovenous Fistula: Case Based Review and Analysis of Relationship between Intracranial Vascular Abnormalities and Inner Ear Fluids. Case Rep Otolaryngol. 2015;2015:817313
[6] Lopez-Escamez, J.A., et al., Diagnostic criteria for Meniere's disease. J Vestib Res, 2015. 25(1): p. 1-7
[7] Cavaliere M, De Luca P, Scarpa A et al. SCORE risk scale as a prognostic factor after sudden sensorineural hearing loss. Eur Arch Otorhinolaryngol. 2020 Mar;277(3):953-954
[8] Ciocca, A., et al., Assessment Tools for Use in Patients with Meniere Disease: An Update. Med Sci Monit, 2017. 23: p. 6144-6149
[9] Gurkov, R., et al., What is Meniere's disease? A contemporary re-evaluation of endolymphatic hydrops. J Neurol, 2016. 263 Suppl 1: p. S71-81
[10] Quaranta N, Picciotti P, Porro G et al. Therapeutic strategies in the treatment of Meniere's disease: the Italian experience. Eur Arch Otorhinolaryngol. 2019 Jul;276(7):1943-1950
[11] Scarpa A, Ralli M, De Luca P et al. Letter to Editor concerning the “Therapeutic strategies in the treatment of Meniere's disease: the Italian Experience”. 2020 Jun;277(6):1847-1848
[12] Patel, M., Intratympanic corticosteroids in Meniere's disease: A mini-review. J Otol, 2017. 12(3): p. 117-124
[13] De Luca P, Cassandro C, Ralli M et al. Dietary Restriction for The Treatment of Meniere's Disease. Transl Med UniSa. 2020 May 31;22:5-9.

[14] Schoo, D.P., et al., Intratympanic (IT) Therapies for Meniere's Disease: Some Consensus Among the Confusion. Curr Otorhinolaryngol Rep. 2017. 5(2): p. 132-141.

[15] Naples, J.G., et al., Intratympanic Therapies in Meniere Disease: Evaluation of Outcomes and Early Vertigo Control. Laryngoscope, 2019. 129(1): p. 216-221.

[16] De Luca P, Ralli M, Cassandro C et al. Surgical management of intractable Meniere's disease. Int Tinnitus J. In press.

[17] De Luca P, Petrosinno M, Calvanese M et al. COVID-19 Pandemic and Head and Neck Surgery Residency Program: Proposals for the "Phase 2". Ear Nose Throat J. 2020 Jul 7;145561320940120.

[18] De Luca P, Colacurcio V, De Bonis E et al. Impact of the COVID-19 Pandemic on Otolaryngology Residency: A Real-Life Experience. Ear Nose Throat J. 2020 May 18;145561320926291.

[19] De Luca P, Scarpa A, Ralli M et al. Nasal, pharyngeal and laryngeal endoscopy procedures during COVID-19 pandemic: available recommendations from national and international societies. Eur Arch Otorhinolaryngol. 2020 Jul;277(7):2151-2153.

[20] De Luca P, Scarpa A, De Bonis E et al. Chloroquine and Hydroxychloroquine Ootoxicity: Potential Implications for SARS-CoV-2 Treatment. A Brief Review of the Literature. Am J Otolaryngol. In press.

[21] Devantier L, Djurhuus BD, Hougaard D et al. Intratympanic steroid for Meniere's Disease. Otol & Neurol. 40(6):806-812.

[22] Pradhan P, Lai P and Sen K. Long Term Outcomes of Intratympanic Dexamethasone in Intractable Unilateral Meniere's Disease, Indian J Otolaryngol Head Neck Surg. 2019 Nov;71(Suppl 2):1369-1373.

[23] Weckel A, Marx M and Esteve-Frayssé MJ. Control of vertigo in Ménière's disease by intratympanic dexamethasone. Eur Ann Otorhinolaryngol Head Neck Dis. 2018 Feb;135(1):7-10.

[24] Harcourt JP, Lambert A, Wong PY et al. Long-Term Follow-Up of Intratympanic Methylprednisolone Versus Gentamicin in Patients With Unilateral Meniere's Disease. Otol Neurotol. 2019 Apr;40(4):491-496.

[25] De Luca P, Ralli M, Scarpa A. Effectiveness of intratympanic administration of gentamicin. Otol Neurotol. 41(8):1066-7.

[26] Scarpa A, Cassandro C, De Luca P et al. Letter to the Editor: Intratympanic gentamicin for Ménière's disease: is there a selective vestibulotoxic effect?. Eur Arch Otorhinolaryngol. 2020 Aug;277(8):2399-2400.

[27] Scarpa A, Ralli M, Cassandro C et al. Low-dose intratympanic gentamicin administration for unilateral Meniere's disease using a method based on clinical symptomatology: Preliminary results. Am J Otolaryngol. Nov-Dec 2019;40(6):102289.

[28] Jian M, Zhang Z and Zhao C. What is the efficacy of gentamicin on the incidence of vertigo attacks and hearing in patients with Meniere's disease compared with steroids? A meta-analysis. J Neurol. 2020 Jun 25. doi: 10.1007/s00415-020-10011-5.

[29] Ozturk K and Ata N. Intratympanic mixture gentamicin and dexamethasone versus dexamethasone for unilateral Meniere's disease. Am J Otolaryngol. Sep-Oct 2019;40(5):711-714.

[30] Shavit SS and Lalwani AK. Are diuretics useful in the treatment of meniere disease? Laryngoscope. 2019 Oct;129(10):2206-2207.

[31] Rosenbaum A and Winter M. Are diuretics effective for Meniere’s disease? Mewave. 2018 Mar 28;18(2):27188.

[32] Scarpa A, Cassandro C, De Luca P et al. Therapeutic role of intravenous glycerol for Meniere's disease. Preliminary results. Am J Otolaryngol. Jul-Aug 2020;41(4):102498.

[33] Scarpa A, Ralli M, Viola P et al. Food-induced stimulation of the antisecretory factor to improve symptoms in Meniere's disease: our results. Eur Arch Otorhinolaryngol. 2020 Jan;277(1):77-83.

[34] Viola P, Pisani D, Scarpa A et al. The role of endogenous Antisecretory Factor (AF) in the treatment of Ménière's Disease: A two-year follow-up study. Preliminary results. Am J Otolaryngol. 2020 Aug 11;41(6):102673.

[35] Devantier L, Schmidt JD, Djurhuus BD et al. Current state of evidence for endolymphatic sac surgery in Meniere's disease: a systematic review. Acta Otolaryngol. 2019 Nov;139(11):953-958.

[36] Cooper MW and Kaylie DM. Is Endolymphatic Sac Surgery Beneficial For Meniere's Disease?. Laryngoscope. 2020 Apr 3.

[37] Xu J, Yi H, Li X et al. Effects of endolymphatic sac decompression combined with posterior tympanotomy with local steroids for intractable Meniere's disease. Acta Otolaryngol. 2020 Apr;140(4):258-261.

[38] Gibson AW, Moon IJ, Golub JS et al. A comparison of endolymphatic shunt surgery and intratympanic gentamicin for meniere's disease. Laryngoscope. 2019 Dec 6.

[39] Viola P, Scarpa A, Pisani D et al. Sub-Clinical Effects of Chronic Noise Exposure on Vestibular System. Transl Med UniSa. 2020 May 31;22:19-23.

[40] Bergmark RW, Semco RS, Abdul-Aziz D et al. Transmastoid Labyrinthectomy for Menièrde's Disease: Experience and Outcomes. Otol Neurotol. 2020 Aug 17.

[41] Skykapetrides V, Giannuzzi AL, Lauda L et al. Surgical Labyrinthectomy and Cochlear Implantation in Menière's Disease, Otol Neurotol. 2020 Jul;41(6):e775-781.

[42] Kanegaonkar RG, Najuko-Mafemera A, Hone R et al. Menière's disease treated by grommet insertion. Ann R Coll Surg Engl. 2019 Nov;101(8):602-605.

[43] Zhang D, Lv Y, Han Y et al. Long-term outcomes of triple semicircular canal plugging for the treatment of
intractable Meniere’s disease: A single center experience of 361 cases. J Vestib Res. 2019;29(6):315-322

[44] Daneshi A, Hosseinzadeh F, Mohebbi S et al. New marsupialization technique in endolymphatic sac surgery. laryngoscope Invest Otolaryngol. 2020 May 26;5(3):546-551

[45] Trakimas DR, Kempfle JS, Reinschagen K et al. Transcanal endoscopic infracochlear vestibular neurectomy: A pilot cadaveric study. Am J Otolaryngol. Nov-Dec 2018;39(6):731-736

[46] Albu S, Babighian G, Amadori M et al. Endolymphatic sac surgery versus tenotomy of the stapedius and tensor tympani muscles in the management of patients with unilateral definite Meniere’s disease. Eur Arch Otorhinolaryngol. 2015 Dec;272(12):3645-50

[47] Di Stadio A, Ricci G, Ralli M et al. Head-Shaking Nystagmus in the Early Stage of Unilateral Meniere’s Disease. J Int Adv Otol. 2019 Dec;15(3):425-430

[48] Lee SU, Kim HJ, Choi JY et al. Evolution in the Findings of Head-Impulse Tests During the Attacks of Menière’s Disease. Otol Neurotol. 2020 Jul;41(6):e744-e750

[49] Hannigan IP, Welgampola MS and Watson SRD. Dissociation of caloric and head impulse tests: a marker of Meniere’s disease. J Neurol. 2019 Jun 20

[50] Lopez-Escamez JA and Attye A. Systematic review of magnetic resonance imaging for diagnosis of Meniere disease. J Vestib Res. 2019;29(2-3):121-129

[1] National committee of Bioethics. I Criteri di Accertamento della Morte. (Criteria for the Declaration of Death) [Internet] 2010 [cited 2012 Jul 18]. Available from: http://www.governo.it/bioetica/pareri_abstract/criteri_accertamento_morte24062010.pdf (Italian)

Examples for a reference to a book:
[1] Jenkins PF. Making Sense of the Chest x-ray: a Hands-on guide. New York: Oxford University Pree; 2005. 194 p.