

Ménière's disease and quality of life: the diagnosis and complex therapy

Ph.D. thesis

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Introduction

Ménière's disease (MD) is clinically characterized by episodes of vertigo, sensorineural hearing loss (SNHL), tinnitus and vegetative symptoms. The management of MD exists of more symptomatic management. The diagnosis is based on the symptoms and pure tone audiometry (PTA), although, the vestibular system can be examined objectively, based on the vestibuloocular reflex (VOR), using caloric and video-head-impulse tests (vHIT).

According to the international guidelines, conservative management of MD involves lifestyle changes, diuretics and betahistine. In the later stages of MD, intratympanic steroid (ITS) and intratympanic gentamicin (ITG) as local conservative and destructive treatment can be applied. As a complication of ITG treatment, SNHL can be monitored using PTA, before and after application of it.

The two main methods for registration of the VOR are the caloric and vHIT tests. Using them, hypofunction of the horizontal semicircular canals and/or the vestibular nerve can be registered.

Common comorbidities, just like hypertension and diabetes mellitus can influence the occurrence of the symptoms and the effectiveness of the therapy.

Objectives

In case of the conservative therapy, the main aim was to analyze the effectiveness of the different treatment options, including betahistine, nootropics and ITS.

It was also an objective to register the possible SNHL caused by the ITG therapy. In this case, the effectiveness of the treatment on the vertigo attacks was also investigated.

Our study also aimed to investigate the typical characteristics of the MD symptoms.

Due to their influence, the possible effects of diabetes and hypertension were also analyzed, both on the symptoms and effectiveness of the therapy.

We also aimed to contrast the results of the caloric and vHIT tests, in different peripheral vestibular disorders (i.e., MD, benign paroxysmal positional vertigo – BPPV and vestibular neuritis – VN).

Methods

105 definite MD patients (31 male, 74 female patients, mean age \pm SD, 57.38 years \pm 11.07 SD) were enrolled in the retrospective part of the investigation. These patients were diagnosed as having MD based on the diagnostic criteria of the Bárány Society. Medical records and vertigo diaries were collected from each patient, giving the possibility of long-term follow up (mean follow-up time: 47.6 months \pm 33.8 SD). The reports gained from the medical documentation, especially those related to the attacks were contrasted with the characteristics of medications used since the previous check-up.

Intratympanic therapies were carried out using injections, under a microscope through the anteroinferior parts of the tympanic membrane, after local anesthesia. ITS therapy consisted of daily injections for 5 days using 4 mg/mL dexamethasone-phosphate. ITG therapy was based on the intratympanic application of 8 mg gentamicin-sulphate, for 2-4 days, until the symptoms of acute vestibular hypofunction occurred. In both cases, before and after application, PTA was carried out, and

results were contrasted based on the modified Fletcher-index.

The last part of the research was a prospective case-control study, including 177 patients (47 male, 130 female patients, mean age \pm SD, 55.8 years \pm 14.07 SD) suffering from different peripheral vestibular disorders as follows: BPPV (n = 68), MD (n = 26), VN (n = 27). 56 subjects with normal vestibular system were also enrolled. Bithermal caloric test was performed using a CHARTR Air Caloric Stimulator NCA-200, and vHIT applying the ICS Impulse System (Otometrics 1085).

Statistical analysis was carried out using IBM SPSS V24 software. Mann-Whitney U and Kruskal-Wallis tests were used, and qualitative analysis was based on Chi square and Fisher tests. Correlation was determined applying Spearman, Pearson and Kappa tests. Logistic regression was used as well, and Kaplan-Meier curves were included too. For each diagnostic tests, sensitivity and specificity parameters were also calculated.

Results

Betahistine, one of the first-line treatments in the symptomatic control for MD, was effective in the management of vertigo attacks. Using betahistine, about 70% of the patients can be in symptom-free period. Based on long-term follow-up, statistically significant difference was detected in case of frequency of dizziness ($p = 0.00031^*$) and vertigo ($p < 0.0001^*$) as well, also was successful in the reduction of duration of them ($p = 0.000098^*$), although, in the mean intensity of them it was not ($p = 0.0887$). P values were determined based on One-Way ANOVA test. The mean dose in the symptomatic management was determined as $87.5 \text{ mg} \pm 27.2 \text{ SD}$ per day, however, there was no statistically significant correlation detected between the dose of betahistine and the effectiveness of symptomatic management. Therefore, it is important to use individual daily doses for all MD patients. Based on the Kaplan-Meier curve and logistic regression, in case of the frequency of vertigo attacks, there was a significant difference detected between the control group and those treated with betahistine [$p = 0.01^*$; Odds ratio: 2.75 (95% CI: 1.068 – 4.442)].

Effectiveness of the dual therapy (betahistine+piracetame) was examined as well, and by using it, vertigo episodes appeared significantly less often [$p = 0.018^*$; Odds ratio: 4.9 (95% CI: 1.2 – 20.2)], contrasted to the monotherapy.

ITS therapy was effective in the treatment of SNHL in MD. In most cases (70.4%), stagnation in the hearing was detected, although there was a smaller group (13.5%), which demonstrated significant improvement. All patients from this group were treated with ITS, therefore, logistic regression indicated strong correlation between hearing improvement and ITS therapy [$p < 0.001^*$; Odds ratio: 2.75 (95% CI: 1.068 – 4.442)]. Regarding the effectiveness of ITS in the management of vertigo attacks, the occurrence of the attacks in case of dual therapy (ITS+betahistine) and monotherapy (betahistine only) were contrasted. Logistic regression did not identify differences between the groups [$p = 0.972$; Odds ratio: 1.051 (95% CI: 0.065 – 16.89)], indicating no benefits of ITS therapy in the management of vertigo attacks.

Nine patients were treated using ITG, and it was concluded that the therapy was effective in all cases, as the vertigo attacks completely resolved. Although, there was no statistically significant difference detected between the PTA results after and pre administration. When the occurrence of hearing loss was contrasted based on logistic regression [$p = 0.001^*$; Odds ratio: 0.141 (95% CI: 0.064 – 0.313)], a significant difference was detected, and according to the Kaplan-Meier curve, hearing loss was more common in the control group (MD patients, who were not treated with ITG). When PTA stages between the control and treated groups were contrasted, no significant difference was detected ($p = 0.84$, Mann-Whitney U test), either.

Based on the vertigo diaries collected from the MD patients, vertigo attacks were determined as the most tormenting symptom (5.38 ± 2.06 SD), tinnitus was the second one (4.54 ± 2.81 SD), followed by headache (2.77 ± 3.1 SD), measured on a scale of 1 to 10. When vertigo attacks with and without headache were contrasted, statistically significant difference was detected ($p = 0.001^*$, Mann-Whitney U test), indicating that headache

had influence on the intensity of vertigo attacks. In case of vegetative symptoms, the difference was even stronger ($p < 0.01^*$, Mann-Whitney U test).

In the examined population, 44.8% of the patients were diagnosed as having hypertension and 15.2% as having diabetes mellitus. 12 patients had both comorbidities. Based on logistic regression, hypertension had no significant [$p = 0.02$; Odds ratio: 2.05 (95% CI: 1.1-3.7)] effect on the occurrence of vertigo attacks, although, according to the Kaplan-Meier curve, a tendency was shown (i.e., in case of hypertension vertigo attacks occurred more common, contrasted to the normotensive group). The influence of hypertension was also strengthened by the higher daily doses of betahistine and the more frequent use of nootropic infusions, contrasted to the normotensive group. On the other hand, hypertension had significant effects on the appearance of tinnitus ($p = 0.013^*$, Chi square test). In case of hearing loss, higher stages of hearing loss were detected in the group with diabetes, and there was a worse reply detected to the ITS therapy in case of hypertension.

The results of vHIT and caloric test were analyzed in MD, BPPV and VN patients. In MD, CP% (Canal Paresis) was abnormal in 88.5% and GA% (Gain Asymmetry) in 65.3%. Although, GA (Gain) parameter was not often in pathologic range (only one of the cases). Both CP% ($p = 0.046^*$) and GA% ($p = 0.029^*$) parameters were statistically significantly different between MD and control groups. On the other hand, no linear and non-linear correlation was shown between CP% and GA% parameters, which was also confirmed by Kappa test ($\kappa = -0.311$). In case of BPPV CP% was not often pathologic, but GA% was in abnormal range in 63.2%, and GA was normal in all cases. Correlation tests did not show correspondence between the parameters. Moderate correlation was only identified in VN ($\kappa = 0.412$), in which case CP% was abnormal in 96%, GA% in 80, and GA also 52%. Based on ROC analysis, caloric test was more sensitive, while vHIT more specific in all disorders.

Conclusion

Based on the vertigo diaries, vertigo is the most tormenting symptoms, although the management of the accompanied symptoms (especially of headache and vegetative symptoms) are also of great importance. Comorbidities, just like hypertension have considerable effects on both the symptoms and effectiveness of the therapy. Therefore, the management of comorbidities is also important due to the effect of them on the patients' quality of life.

Betahistine was effective in the conservative management of vertigo attacks, using it in 70% of the patients vertigo attacks have been resolved. Although, it is important to set up the daily dose of betahistine for every patient individually. The benefits of dual therapy were also confirmed.

ITS was defined as a potent agent to prevent SNHL in MD, all patients, who presented improvement in hearing stages were treated with ITS. Although, in case of vertigo attacks, the effects of ITS therapy were not significantly better than those of conservative therapy.

Using ITG, vertigo attacks have been completely resolved in all cases. On the other hand, there was no higher risk for hearing loss than in case of spontaneous progression of the disorder.

Based on the results of the vHIT examination, besides GA value, GA% should be taken into consideration as well. Due to the poor correlation between the outcome of vHIT and caloric tests, it can be stated that the methods give complementary examinations. None of the examinations can be used as a screening tool alone.

Publications related to the PhD thesis

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