Diagnosis and follow-up of patients suffering from vertigo

Ph.D. thesis

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<u>Introduction</u>

Vertigo and dizziness are multisensory syndromes that are often confronted in the daily practice. The manifestation of vestibular disorders is determined by how the vestibular system is functioning, involving the vestibulospinal, the vestibuloocular, and the vestibulocerebellar tracts. Therefore, vertiginous causes may include vestibular and extravestibular systems. The most frequent peripheral vestibular disorder is the benign paroxysmal positional vertigo (BPPV), while Ménière's disease (MD) is a disorder, which strongly affects the patients' life quality. In case of causes not arising from the inner ear, central vestibular disorders (CVD) are often diagnosed in the everyday practice.

The function of the vestibulospinal tract can be examined using the ultrasound-computer-craniocorpography (US-COMP-CCG), and a frequently used test for the vestibuloocular reflex is the caloric vestibular test by electronystagmograpic registration.

The cochlear functions are usually registered using pure tone audiometry (PTA).

Objectives

The first objective of the research was to follow-up a vertiginous population examined at the Emergency Department (ED). We observed the information given to them verbally and in writing after emission and we compared them with the final diagnoses given to the patients after further examinations. Additionally, we investigated the effect of an acute vertigo attack in a person's everyday life and the impact brought upon it.

Second objective aimed the investigation of the capabilities of the US-COMP-CCG, from a simple diagnosis of vestibular disorder to the complete follow-up of a treatment regimen registration possibility, as well as the study of the balance system. Main questions were whether if MD staging can be decided upon imbalance, if intratympanic steroid (ITS) treatment is effective only on the cochleovestibular system or can be beneficial in

the improvement of the gait system. The BPPV possibility to be categorized into idiopathic and secondary based on the findings of US-COMP-CCG and whether if by using registration systems for gait assessment we can objectively estimate the postural imbalance in patients with central vestibular disorders.

Last objective of the research was to evaluate the relationship between the cochlear and vestibular function loss in MD, by the means of PTA and caloric vestibular test (CVT) with involvement of all stages of MD.

Methods

The statistical analysis was performed using IBM SPSS V24 software. Most of the studied parameters did not show normal distribution (Shapiro-Wilk test), therefore non-parametric test were used (Mann-Whitney U test). Categorical analysis was done by Fisher-exact test, Chi-square test and Kappa test. To detect possible correlation between the parameters Pearson and Spearman rank correlations were applied. To determine

sensitivity (TPR) and specificity (TNR) parameters, ROC curves were drawn, and the parameters were calculated based on AUC (area under curve). To investigate the long-term effects of applied therapy on, Kaplan-Meier curves were included, and logistic regression was used as well. The significance level was defined as $p < 0.05$ in all of the cases.

A questionnaire was addressed to 879 patients, who visited the ED in the last 2.5 years, and 308 patients (110 males and 198 females, mean age ± SD, 61.8 years ± 12.31) have answered, and were further analyzed. The questionnaire included questions about different symptoms related to the vestibular system, as well as the Dizziness Handicap Inventory (DHI) attached to it in the Hungarian language.

During the US-COMP-CCG examination the patients complete the standing test (Romberg) and stepping test (Unterberger-Fukuda) for a duration of one minute with closed eyes. The position related to the starting and endpoint is recorded by use of US-COMP-

CCG (ZEBRIS Coordinate Measurement System®, Isny, Germany). The position of markers that are located at the anterior and posterior vertex of the subject's head and left and right shoulder are analyzed with the aid of ultrasound. Main parameters are used for statistical analysis. Standing test includes the longitudinal sway, lateral sway, forehead covering area, and torticollis angle parameters; while stepping test include the longitudinal deviation, lateral sway width, angular deviation, and self spin parameters. In the MD staging, 42 patients (mean age ± SD, 56.3 years ± 9.4) with definite MD participated and 51 patients were included in the control group (mean age ± SD, 55.6 years ± 9.4). In the next investigation, 38 patients suffering from advanced MD and received ITS injection (13 male and 25 female patients, mean age ± SD, 56.3 years ± 10.2) were selected and 82 patients (37 male and 45 female patients, mean age 60.8 years ± 10.6) with advanced MD who had not received ITS were enrolled. The latter group was the control group. In the BPPV investigation 135 patients

participated, 31 males and 101 females with symptoms of BPPV (mean age ± SD, 56.8 years ± 12.2) and a control group consisting of 140, 43 male and 97 female patients (mean age ± SD, 50.8 years ± 15) were enrolled. The central vestibular disorders investigation was a prospective study, whereas 420 patients were selected in a period of 2 years. Hundred-and-ninety patients (70 male and 120 females, mean age ± SD, 58.9 years ± 15.2) suffering from a central vestibular disorder and 230 healthy control patients (78 male and 152 females, mean age ± SD, 50.9 years ± 15.2) were enrolled in this study.

For the last part of the research, 43 patients (18 males and 25 females, mean age ± SD, 54.8 years ± 13.3) who were diagnosed with definitive MD, were analyzed retrospectively. All participants were evaluated using both CVT and PTA. Audiometric examination was performed using PTA. Extended Fletcher Index was used to calculate hearing loss and to rule out the effects of ageing (i.e. presbycusis) on hearing, the interaural difference of the hearing level (dPTA) was also

calculated. Both tests (PTA and CVT) were performed during the same control.

Results

Based on the ED diagnosis documentation the most usual diagnosis was BPPV, followed by central vestibular disorders and dizziness. It should be noted thought, that in 24% of cases no specific diagnosis was made. The follow-up of this vertiginous population was mostly done with their general practitioner, and later consultation was made in neurology, ear-nose-throat specialization, and internal medicine. Comparing the subsequent diagnosis with the documented diagnosis in the ED, in only 44 patients (14.3%) the diagnosis was agreeing, and in several cases that was of BPPV cause. Total DHI values were compared between three groups based on the duration spent to final diagnosis (days, weeks, months or one year). For the clearance of the final diagnosis, days (28.8%) was reported in the most cases, then weeks (24.2%). According to the results, the

value of deterioration in life quality increases proportionally with time to diagnosis.

Along with sudden vertigo attacks, frequent symptoms included nausea and vomiting. Symptoms which exert a strong impact on everyday life. The predominant duration of the episode was seconds, followed by several of days and hours. By analyzing the DHI answers we made a comparison between the physical (P), functional (F) and emotional (E) question scores, which indicated that the highest values were found in the P score group. Therefore, since this area is affected the most, we could see the deterioration of the other areas increasing simultaneously.

MD is divided into stages according to the severity and frequency of the symptoms. By analyzing the standing test parameters, we found that all of the parameters are pathological. The increasing values showed the deterioration of the vestibular system; the difference in the mean values were of significance. The stepping test parameters showed different results from

each other. Angular deviation and self spin parameters showed statistically significant results (p = 0.013). Whereas, the self spin parameter seemed to be the most sensitive in the objective staging (ROC analysis, AUC: 0.962, TPR: 96.2%).

Before the appliance of the ITS therapy the gait was evaluated as well at 2 weeks after the end of the therapy. In the analysis of standing and stepping tests, the median and mean ± SD values were higher after treatment in some of the cases, but there was no statistically significant difference between the parameters before and after treatment. Based on the analysis it can be stated the ITS therapy has no significant effect on the outcome of neither the standing nor the stepping tests. For the long-term outcomes, Kaplan-Meier curve and logistic regression were used. Based on the analysis, there was no visible difference between the two curves [p = 0.445; Odds ratio: 1.654 (95% CI: 0.166 - 0.197)] and therefore no significant difference between the results of the groups.

Based on the analysis in the case of idiopathic BPPV (i-BPPV) there was no statistically significant difference presented. In the secondary BPPV (s-BPPV) group there was in the case of forehead covering area and self spin parameters. These 2 parameters remark the severe imbalance in s-BPPV clinically and statistically. This could be explained by the fact that patients experiencing it have a more damaged balance system due to the involvement of a primarily affected vestibular disorder, such as a vestibular neuritis, or an advanced MD. By analyzing these parameters further, we compared them based on specificity and sensitivity by using AUC. The forehead covering area parameter showed lower sensitivity (TPR: 29%), but a higher specificity (TNR: 57%). Self spin parameter was highly sensitive (TPR: 67%) and specificity wise was also high (TNR: 76%).

To determine which parameter of US-COMP-CCG could be specific for central vestibular disorders based on the gait dysfunctions, mean ± SD parameters

were calculated for each test of the control group and of those involved in central vestibular disorder. Postural sway was detected in the patients suffering of central disorders, and according to the US-COMP-CCG analysis the objective registration of instability was successful. ROC curves specificity and sensitivity parameters for each test were determined, where standing test parameters showed to be more sensitive, while parameters of stepping test showed to be more specific. This fact indicates the necessity to combine the two examinations.

For the comparison of vestibular and cochlear function in MD, the patients were divided based on their staging. According to PTA, most patients were in stage C, and caloric weakness was found in 29 patients. For each MD stage the relationship of the PTA and responses of the CVT were examined and showed that the average thresholds were increasing with the stage, however, such a correlation in case of canal paresis (CP%) was not unequivocal. Linear ($R^2 = 0.06$) and non-linear

correlation tests (rho = 0.245, p = 0.113) between CP% and dPTA showed no correlation, as well was between CP% and PTA analysis (R^2 = 0.007, rho = 0.11, p = 0.481). As per the categorical analysis, no correlation was detected between the groups either (kappa = 0.174, 95%, CI: 0.431 - 0.0883).

Conclusion

Proper diagnosis and information to the patient is often missing in the population visiting the ED with acute vertigo complain, leading to increased anxiety and deterioration of the quality of life, since proper guidance is missing. Therefore, substantial investigation and detailed vestibular examination is essential, but the latter should take place in justified cases.

For the management of dizzy population self-reported measures are unique parts of the information. According to the DHI results, patients with acute dizziness and with a clinical diagnosis of vestibular disorder indeed present with decreased life quality.

Therefore, in order to avoid this remarkable alteration, we have noticed that a proper examination of the symptoms is necessary combined with questionnaires in the everyday clinical practice. For typical peripheral vestibular disorders, the neurotological examination is necessary, and further examination is recommended also for patients whose DHI score is above 16, indicating mild deterioration in life quality.

The worsening results of the parameters of US-COMP-CCG run parallel with the progression of MD, and this is measured objectively regardless of what the patient says about the frequency of the episodes. The deterioration of the stages is not only measured by the impairment of hearing but also with the deterioration of balance. US-COMP-CCG is capable of evaluating the severe imbalance of these patients efficiently. Alone though, it is not capable for the diagnosis of the disease.

While ITS treatment can improve hearing impairment, as well as it decreases the vertigo attacks occurrence, it appears to have no effect on postural

control. According to our results there are no changes detected on vestibular function based on US-COMP-CCG post-administration of ITS injection. Based on the literature, the effectiveness of ITS therapy is very variable, and using objective vestibular tests, no significant change was detected, so further studies are necessary to investigate the potential benefits of the therapy.

The distinction between idiopathic and secondary cases of BPPV is important. Secondary cases, unlike idiopathic cases, cannot be treated solely by repositioning maneuver, but also require treatment of the underlying disease. Based on the US-COMP-CCG result analysis, s-BPPV was detectable. US-COMP-CCG indicates imbalance in late stage MD combined with BPPV, indicates imbalance in migraine, shows uncertainty in unilateral dysfunction in vestibular neuritis and post-neuritis BPPV, whereas normal in i-BPPV.

In the central vestibular disorder study, we reinforced the recommendation to perform vestibular tests in daily clinical practice for the investigation of postural instability in patients suffering from central vestibular disorder. Patients with imbalance were objectively registered and based on the gait analysis severe imbalance was shown. Therefore, appropriate counselling should be discussed with the patients as well as vestibular rehabilitation planning.

Our study showed that audiometric changes do not directly correlate with vestibular changes, therefore, no specific correlation exists between cochlear and vestibular function loss in MD. Consequently, for therapy planning and the diagnosis of the disorder, both tests are necessary. The caloric test can identify the function of the affected lateral canal, and audiometry indicates the severity of the existing hearing loss in MD patients.

Publications related to the PhD thesis

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