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RESEARCH

ASSESSMENT OF VESTIBULAR SYSTEM AND BALANCE FUNCTION IN PATIENTS WITH PSEUDOEXFOLIATION SYNDROME

Abstract

Introduction: This study aims to evaluate the balance and vestibular system of patients with pseudoexfoliation syndrome.

Materials and Method: A prospective case–control study was performed in a university hospital. The study population consisted of 37 patients (16 patient group, 21 control group). The Modified Clinical Test of Sensory Interaction Balance was performed in four conditions: 1) eyes open, firm surface; 2) eyes closed, firm surface; 3) eyes closed, foam surface; and 4) eyes open, foam surface. The Equilibrium Score, Anteroposterior Stability Index, Mediolateral Stability Index were employed for all conditions in both groups. Scores were compared between and within groups. Additionally, the physical activity of the patients with pseudoexfoliation syndrome was assessed using questionnaires based on the Turkish versions of the Modified Falls Efficacy Scale and the Physical Activity Scale for the Elderly.

Results: There were no significant differences in terms of stability index and equilibrium scores with eyes open or closed conditions between the two groups; the only difference was in the mean mediolateral stability index score in the eyes open, firm surface condition with low scores in the pseudoexfoliation group (p=0.01). In the group analysis, patients with pseudoexfoliation had a significant increase in the equilibrium scores when their eyes were closed in the firm and foam surface conditions (p=0.001 for both).

Conclusion: The central nervous system redistributes its dependence on sensory information when vision is compromised in patients with pseudoexfoliation syndrome. Their somatosensory input might deteriorate in some way but not the vestibular system.

Keywords: Dizziness; Glaucoma; Aged.

INTRODUCTION

Pseudoexfoliation syndrome (PES) is characterized by deposition of microfibrillar material mainly in the anterior segment of the eye. Gradual accumulation of this material in the outflow pathways may cause a common and severe type of chronic open-angle glaucoma (1). Exfoliative material can also be found in the connective tissue of blood vessels and internal organs, such as the lungs, kidneys, liver, and inner ear (2). The prevalence of PES varies by country: 4% in England, 4.7% in Germany, 6.3% in Norway, 7.2% in Turkey, 9.6% in Iran, 12% in Russia, 16.1% in Greece, 22% in Finland, and 29% in Iceland (3). In Scandinavia, 20–25% of those over the age of 60 and 40% of those over the age of 80 are affected by PES (4). Both population-based and pedigree-based studies have shown that genetic factors contribute to the pathogenesis of PES (1).

Although PES is a systemic disease, the initial diagnosis is often made by an ophthalmologist (5). Several studies demonstrated the presence and accumulation of pseudoexfoliative material in the inner ear using electron microscopy and immunohistochemical methods, suggesting a connection between vestibular end-organ damage and PES (5-7). However, there are few studies demonstrating the involvement of the vestibular system in terms of postural balance (3,8).

Balance is maintained by complex interactions among visual, vestibular, and somatosensory inputs, and its impairment can have a substantial impact on an individual's ability to perform daily activities. Although studies suggest that balance relies greatly on visual input, which is connected to musculoskeletal coordination, proprioceptive function, and neural information integration (9), the vestibular end organs also have a similar significant effect on balance. It is possible that the vestibular part of the inner ear is involved in PES and the balance system may be affected by the accumulation of pseudoexfoliative material in the end organs.

Therefore, in this study, we evaluated the vestibular system with the Modified Clinical Test of Sensory Interaction Balance (M-CTSIB) in patients with PES. The M-CTSIB is a modified version of the original clinical test of sensory interaction balance that evaluates the contribution of the visual, somatosensory, and vestibular systems to postural control (10). The Equilibrium Score (ES), Anteriorposterior Stability Index (APSI), and Mediolateral Stability Index (MLSI) were also employed. The ES indicates the overall coordination of the visual system, vestibular system, and proprioceptive sensations for maintaining standing posture. APSI and MLSI scores relate to more biomechanical aspects of postural stability; like weight and ankle moment, than the ES and are also subunits of the ES (11). To our knowledge, this is the first study using the M-CTSIB for the evaluation of the vestibular system in patients with PES. Additionally, we aimed to assess the physical activity of patients with PES using questionnaires based on the Turkish versions of the Modified Falls Efficacy Scale (MFES) (12) and the Physical Activity Scale for the Elderly (PASE) (13) since physical activity is connected with postural stability and balance.

MATERIALS AND METHOD

This study was reviewed and approved by the institutional review board of the Baskent University Ethics Committee. The tenets of the Helsinki Declaration were followed throughout the study. Informed consent was obtained from each participant before all procedures.

A prospective case–control study was conducted at our university hospital. The study population consisted of 37 patients (18 male, 19 female), 16 of whom were diagnosed with PES. The PES group included patients over the age of 65 diagnosed with PES without any glaucomatous optic nerve or visual field changes within the previous year and with best-corrected visual acuity of 20/40 or more in the Snellen chart. The control group included patients over the age of 65 with best-corrected visual acuity of 20/40 or more in the Snellen chart. Exclusion criteria for both groups were any ocular pathology other than cataracts and previous ocular surgery other than cataract surgery in the proposed study eye, diseases of the ear (acoustic neuroma, Meniere's disease, chronic otitis media, ototoxic or vestibulotoxic medication history, cholesteatoma, and any ear surgery) except presbycusis, any neurological disease that can cause central vertigo, and any disease or surgery that can affect the lower extremities.

All subjects underwent a complete ophthalmic examination, including best-corrected visual acuity, applanation tonometry, slit-lamp biomicroscopy, indirect ophthalmoscopy under dilated pupil conditions, and Humphrey Swedish Interactive Thresholding Algorithm SITA Standard 24-2 visual field testing. PES was identified based on modest changes on the lens surface and pupil margin, as well as poor pupillary dilation and pigment-related symptoms, such as pigment dispersion and pupillary atrophy. After the complete ophthalmic evaluation, patients eligible for the study were referred to the otorhinolaryngology clinic for the application of the Turkish versions of the MFES and PASE questionnaires followed by the M-CTSIB, which was conducted under the following four conditions:

1. Standing on firm surface with eyes open; three balance systems (visual, somatosensory, and vestibular) are fully engaged to evaluate baseline condition.
2. Standing on firm surface with eyes closed; visual input is eliminated to evaluate vestibular and somatosensory systems.
3. Standing on foam surface with eyes open; somatosensory input is purposely eliminated with the compliant surface.
4. Standing on foam surface with eyes closed; both somatosensory and visuals systems are purposely eliminated.

During the test conditions, the patients kept their arms at their sides. If the patients opened or closed their eyes, lifted their arms away from their bodies, or lost their balance during the 30-second test, the timer was stopped. If numerous trials were required, the trial times were averaged to calculate the score.

Three trials were performed in each condition, and the mean of the three trials was taken as the final measurement. M-CTSIB measurements included the ES, which quantifies the center of postural stability under each condition, as well as APSI, MLSI, and Overall Stability Index (OSI) scores, which are derived from the summation of the degrees of tilt calculated in the anteroposterior and mediolateral axis. The mean scores of the three trials were analyzed.

Statistical Analysis

The SPSS 25.0 (IBM SPSS Statistics for Windows, Version 25.0) package program was used for the statistical analysis of the data. Categorical measurements were summarized as numbers and percentages, and continuous measurements were presented as means and standard deviations (as median and minimum–maximum when required). Chi-square or Fisher test statistics were used to compare categorical variables. In comparing continuous measurements between the groups, the distributions were controlled, and the student's t-test was used for the parameters that showed normal distribution according to the number of variables. The Mann-Whitney U test was used for the parameters that did not show normal distribution. When the expected frequencies were below 20%, to include these frequencies in the analyses, the Monte Carlo Simulation Method was used. The statistical significance level was taken as $p<0.05$ and $p<0.01$ in all tests.

RESULTS

A total of 16 PES patients (9 male, 7 female) and 21 healthy volunteers (9 male, 12 female) were included in the study (Table1). There were no statistically significant differences between these two groups in terms of age, Body Mass Index, and MFES and PASE scores (p>0.05 for all).

There were no significant differences between the groups in terms of the mean values of the APSI, MLSI, OSI, and ES measurements in the foam surface condition, regardless of whether their eyes were open or closed. However, in the firm surface condition, there was a significant decrease in the mean MLSI in the eyes open condition in the PES group when compared to the control group (p=0.01) (Table 2). There were no significant differences between male and female participants in both groups with respect to the stability indexes and ES.

In the group analysis, PES patients had a significant increase in the ES when their eyes were closed in the firm and foam surface conditions (p=0.001 for both) (Table 3). There were no significant

Table 1. Demographic distribution of patients

		Control	PES	Total
Male	n	9	9	18
	%	50.0%	50.0%	100.0%
Female	n	12	7	19
	%	63.2%	36.8%	100.0%
Total	n	21	16	37
	%	56.8%	43.2%	100.0%

Table 2. Mean values of Mediolateral stability index (MLSI) scores according to the surface and eyes condition.

	CONTROL (n=21)	PES (n=16)	p-value
Eyes Open Firm Surface MLSI	0.56±0.27	0.43±0.15	**0.010**
Eyes Closed Firm Surface MLSI	0.49±0.3	0.42±0.18	0.390

Table 3. Mean values of ES according to the surface and eyes condition. ES: Equilibrium Score

	CONTROL (n=21)	PES (n=16)
Eyes Open Firm Surface ES	53±12.47	50.14±17.24
Eyes Closed Firm Surface ES	61.93±13.17	59.3±12.04
p-value	0.078	**0.001**
Eyes Open Foam Surface ES	45.4±17.34	44.95±17.85
Eyes Closed Foam Surface ES	42.08±18.92	48.86±22.19
p-value	0.615	**0.001**

differences in the ES regardless of whether the eyes were open or closed in the control group. There were no statistically significant differences in the stability index scores in both groups.

DISCUSSION

According to our findings, when visual input is eliminated, PES patients showed a higher ES in firm and foam surface conditions within the group analyses. When compared to the control group, they showed worse MLSI scores on a firm surface, indicating that their somatosensorial systems, but not the vestibular system, deteriorated in some way.

The advantage of the M-CTSIB is that it is designed to assess the level of use of each sensory input when more than one sensory system is affected in older individuals. When standing on a foam surface, the somatosensorial system is disabled and balance control is maintained with information from the visual and vestibular systems. However, when attempting to maintain balance on a firm surface, the somatosensory system is activated. To our knowledge, this is the first study to use the M-CTSIB for the evaluation of the vestibular system in individuals with PES (PubMed search terms: "pseudoexfoliation, balance, M-CTSIB" on 01/10/2022.) Several research studies have revealed that the accumulation of pseudoexfoliation material in the cochlea causes sensorineural hearing loss (14-17). However, few investigations assessed the involvement of the vestibular system, which is another component of the inner ear. Bilgec et al. observed pathological findings in the vestibular system, including in the saccule, vestibular nerve, and semicircular canal; however, they did not observe balance problems (8). Turgut et al. obtained similar results, revealing that the visual and proprioceptive systems compensate for balance even when vestibular function is impaired (3). The aforementioned studies relied mostly on the bithermal caloric, Romberg, Unterberger, Dix-Hallpike, and Vestibular evoked myogenic potential (VEMP) tests to assess vestibular function. These tests are helpful before performing more objective tests but are not as precise as the M-CTSIB. We could have used a combination of the caloric test and M-CTSIB, which would have been more helpful for the evaluation of the vestibular system; however, it would have been very disturbing and exhausting for the study participants since they were presented only for the eye exam and the caloric test would have caused a real spinning sensation. Interestingly, the mean age in both studies was under 65. Since PES incidence increases markedly with age (4), and the mean age in our study group was 74, the increasing amount of elastic fiber components accumulation may have a time-dependent impact on the balance system.

In our study, stability index scores (mediolateral, eyes open) on a firm surface were different for the PES and control groups, suggesting that visual input is less likely to increase the vestibular and somatosensory contribution to postural stability. Shabana et al. demonstrated that glaucoma patients aged 40-66 years exhibited greater somatosensory contributions to postural stability to maintain a steady stance when compared with controls (18). However, Black et al. found a significant association between glaucomatous visual impairment and postural sway in older adults (19). While our results are comparable with those of Black et al., our study group consisted of individuals with PES and not glaucoma.

Our study also found that vision is not contributing to balance in older persons with PES because there were significant differences in the ES regardless of surface condition. Kotecha et al. showed that during silent standing conditions on firm surfaces, patients with a visual impairment might make better use of nonvisual inputs to maintain balance (20). Our study confirms their results. The central nervous system redistributes its dependence on sensory data when available information is compromised, even in older people (19, 21).

In one study, the combination of PES and glaucoma resulted in poor balance on foam and firm surfaces, demonstrating that glaucomatous visual field loss contributes to balance limitations that cannot be compensated for by the somatosensory and vestibular systems (22). Another study reported that balance was worse in glaucoma patients with greater visual field damage under foam surface and firm surface conditions (23).

Our results showed that individuals with PES have the same physical activity and the same fear of falling scores as their peers. Previous studies have shown that patients with glaucoma had worse scores on the fear of falling questionnaires compared to control subjects (20,21). Ramulu et al. (22) and De Luna et al. (23) revealed that fear of falling mediates the relationship between vision loss and physical activity restrictions.

The main limitation of our study was the low patient number. Also, we did not run the full vestibular test battery due to time constraints and patient intolerance. The addition of VEMP tests and video head impulse test (vHIT) could have added more specific information to improve our understanding of the difference in MLSI and APSI scores for the PES and control groups on a firm surface and supplied more information about the location of fibrillar deposition in the vestibular system.

In conclusion, PES patients demonstrated a high ES in firm and foam surface conditions when visual input was removed. Since the ES was high, we may conclude that the central nervous system redistributes its dependence on sensory information when vision is compromised in patients with PES. This suggests that balance control is not compromised in this patient group. They displayed lower MLSI scores on hard surfaces compared to those in the control group but not in the other stability index scores in any other condition, which suggests that their somatosensory input might deteriorate in some way but not the vestibular system.

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