



Original Research Article

Are migraine and benign paroxysmal positional vertigo associated diseases? An experience of medical college attached hospital from the western part of India

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ABSTRACT

Objectives : Repeated migraine attacks may cause vestibular dysfunction and dislodge of otoconia from utricle to semicircular canals resulting in benign paroxysmal positional vertigo (BPPV). The aim of the present study was to evaluate risk factors and linkage of migraine in patients of BPPV.

Materials and Methods: This observational case-control study was conducted at Zydus medical college and hospital, Dahod, India from October 2018 to September 2019. Consecutive 18 to 70 years old patients of confirmed BPPV were assigned as the cases. Demographically matched healthy volunteers were assigned as the controls. The cases, as well as the control, were further evaluated for a past or present history and a family history of migraines.

Results : 295 consecutive BPPV cases (250 posterior canals, 45 horizontal canals) and 300 control subjects were studied. In the case group, 55 (18.64%) were having past or present migraine (45 migraines without aura, 8 migraines with aura and 2 vestibular migraines), while in the control group 24 (8.0%) were having migraine (20 migraines without aura, 4 migraines with aura). Among BPPV patients, those associated with migraines were younger and more often females, with many having a history of diabetes mellitus and coronary artery disease and family/past history of migraines. Migraine was 2.3 times higher in cases as compared to the control with significant or Odds Ratio of 2.63 and 2.68 in unadjusted and adjusted analysis respectively.

Conclusion : Migraine was more than two times more common in BPPV patients as compared to the age and sex-matched controls.

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1. Introduction

The BPPV and migraine are among the most commonly reported disorders in general medicine and neurology specialty clinics.¹⁻³ The BPPV carries 2 to 3 % lifetime prevalence in adults and it is the most common cause of vertigo.⁴ This condition is characterized by spinning episodes of surrounding structures or head itself lasting for less than one minute, provoked by the change of head

position in reference to the gravity.⁵ The Otolith particles from macula of the membranous labyrinth are detached due to age-related degeneration, head injury, vitamin D deficiency, estrogen excess, and many unknown reasons. The Free-floating otolith calcium particles or adherence of the particles to the cupula of the semi-circular canals creates gravity directed force in the endolymph and this results in typical crescendo-decrescendo nystagmus with a fast component towards the affected ear and characteristic vertigo symptoms.⁶ The posterior canal BPPV is diagnosed

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by Dix-Hall pike test demonstrating typical vertical with torsional nystagmus with fast component toward the ear facing downward, while lateral canal BPPV by supine roll test showing horizontal nystagmus with a fast component towards the affected ear.⁷

Migraine is a complex disorder with multifactorial pathophysiology, genetic predisposition, and various cephalic and non-cephalic manifestations.^{8,9} Headache is a prominent symptom in migraine of both the varieties, migraine with and without aura; but rarely headache may be absent in some cases of migraines.¹⁰ Auras are transient neurological symptoms like central scotoma, amaurosis fugax, tunnel vision, scintillation or hemianopia; various motor or sensory symptoms; confusion; brain stem symptoms e.g. vertigo or abdominal pain with cyclic vomiting, etc.^{8,10} These symptoms are preceded by or associated with or followed by headache in migraine with aura.^{10,11} Vertigo is one of the common features in migraine and international headache society-3 headache guidelines have included this feature as “atypical migraine with brainstem aura” under subclassification of migraine variants.¹¹ Unexplained vertigo not associated with headache in migraine susceptible patients are also reported as rare migraine variants.¹⁰ BPPV and migraine are common causes of peripheral and central vertigo respectively.^{10,11} So it is interesting to study the association of migraine among BPPV patients. Some researchers have studied linkage of BPPV among migraine sufferers, but the association of migraine among BPPV patients has not been studied to date. Our aim of the present research was to study the association of migraine among BPPV patients.

2. Material and Methods

This prospective observational case-control study was carried out at Zydus Medical College and Hospital, Dahod, India from October 2018 to September 2019. The study protocol was approved by the institutional ethical committee. Human rights of all the participants were taken care as per the Helsinki guidelines and written consent was obtained from all the participants.

All consecutive patients aged 18 to 70 years, presented with BPPV based on a detailed history and clinical examination during the study period were assigned as cases. The controls were selected from age and sex-matched healthy volunteers. All the subjects of the case, as well as the control group, were evaluated for the present, past and family history of migraines by the interviews conducted using standard questionnaires as per the International headache society classification of ICHD-3 guidelines.

The BPPV cases having severe cervical spine disease, significant carotid artery stenosis, Meniere's disease, and active cerebrovascular disease were excluded from the study. Rest of the cases were subjected for provocative

positional tests (PPT) like Dix Hallpike followed by supine roll tests of both the sides. The cases having positive tests were included in the study. Subjects who were not willing to sign written consent or migraine feedback form were also excluded from the study in both the groups.

2.1. Statistics

The latest SPSS software was used to analyse the data and they were noted as the mean value for continuous variables and percentage/numbers for discrete variables. The sample size was calculated for assuming 80% power and alpha level of 0.05 before commencing the study. Demographic and clinical features were compared with student t-test on continuous and chi-square test for categorical variables between the case and the control. Unadjusted and adjusted odds ratio (OR) was calculated for case versus control by using a logistic regression test.

3. Results

305 subjects were enrolled in the case as well as the control group. In the case group, 6 patients were not subjected for PPTs as per the exclusion criteria and 4 patients refused to participate in the study. Five participants were excluded in the control group as they were not ready for written consent. 295 consecutive BPPV cases were further tested by PPTs and among them, 250 were positive for posterior canals and 45 for horizontal canals (40 geotropic and 5 a pogotropic) BPPV. The mean age was 42.32 ± 11.45 years in cases and 44.15 ± 12.30 years in the control group. Out of the total subjects, females were outnumbered as compared to the males in both the groups. Table 1

In the case group, 55 (18.64%) were having past or present migraine in form of 45 as migraines without aura (MOA), 8 as migraines with aura (MA) and 2 with vestibular migraine. While in the control group, 24 (8.0%) were having migraine in the form of 20 as MOA, and 4 as MA. However, 5/45 (9%) of MOA and 2/8 (25%) of MA patients were having active migraine at the time of presentation in the case group, while none of the controls were having a migraine at the time of interview. Table 2

Among the BPPV patients, those associated with the migraine were quite younger and more often females, with many having a history of diabetes mellitus, coronary artery disease and a positive family history of migraine. Table 2 The Migraine was 2.3 times higher in cases as compared to the control (OR 2.63, 95% C.I. 1.58-4.39, $p=0.0002$) in unadjusted analysis. These results were persisted even after multidiscipline adjustment of variables like the history of diabetes mellitus, coronary artery disease and positive family history of migraine (OR 2.68, 95% C.I., 1.62 - 4.43). Table 3

Table 1: Demographic and clinical features in BPPV and control group

	BPPV n= 295 (%)	Control n=300 (%)	p- value
Mean age (Years)	42.32 ±11.45	44.15±12.30	0.75
Female	200 (67.80)	198 (66.00)	0.64
Hypertension	25 (08.47)	23 (07.66)	0.62
Diabetes mellitus	28 (09.49)	19 (06.33)	0.02
Chronic kidney injury	04 (01.35)	04 (01.33)	0.72
Coronary artery disease	26 (08.81)	17 (05.66)	0.02
Migraine	32 (10.85)	15 (05.00)	0.01

Table 2: Comparison of migraine and No-migraine patients of BPPV (case) group

	Migraine n= 55 (%)	No-migraine n=240 (%)	p- value
Mean age (Years)	34.13 ±08.45	45.70±13.24	0.02
Female	47 (85.45)	153 (63.75)	0.02
Hypertension	04 (07.27)	17 (07.08)	0.56
Diabetes mellitus	06 (10.91)	15 (06.25)	0.03
Chronic kidney injury	01 (01.82)	04 (01.66)	0.69
Coronary artery disease	07 (12.73)	16 (06.66)	0.03
Family/Past H/O migraine	07 (12.73)	12 (05.00)	0.01

Table 3: Logistic regression results of variables between cases versus control

	Unadjusted OR (95% CI) (p-value)	Adjusted OR (95% CI)
Female Gender	1.08 (0.77 – 1.53) (0.64)	Insignificant
Hypertension	1.11 (0.62 - 2.13) (0.71)	Insignificant
Diabetes mellitus	1.55 (0.85 – 2.84) (0.15)	1.87 (0.71 – 5.04)
Chronic kidney injury	1.01 (0.25 – 4.11) (0.98)	Insignificant
Coronary artery disease	1.60 (0.85 – 3.03) (0.14)	1.98 (0.93 -5.39)
Migraine	2.63 (1.58 – 4.39) (<0.01)	2.68 (1.62 - 4.43)

4. Discussion

In our study females were more affected by both the migraine as well as the BPPV. However, a significantly much higher number of females were having an association of migraine among BPPV patients as compared to the general population. Previous studies from other researchers also reported female preponderance in the BPPV as well as the migraines patients as compared to the male gender.¹²⁻¹⁴ In our study patients suffering from diabetes mellitus and coronary artery disease (CAD) and those having past/family history of migraines were having a statistically high association with BPPV and migraine. The BPPV and the migraine diseases were also individually reported higher among diabetics and CAD patients by other studies and it matches our study.^{2,4,14}

The Migraine affects the young population, while the BPPV is a disease of the middle and old age people.^{4,13} In our study, BPPV patients with associated migraine were one decade younger as compared to those BPPV patients who were not having the migraine and many of the BPPV patients were suffering from active migraines during BPPV episodes. The Migraine association was also more than two

times more common among BPPV patients as compared to the controls. These facts support migraine as a risk factor of BPPV. Studies have shown that BPPV is highly associated with migraines and that subjects suffering from the migraines have three times more possibility to develop BPPV as compared to their counterparts who have not suffered migraines.^{12,14}

No direct common pathophysiological pathway between the BPPV and the migraine has yet been established.¹⁵ Baloh had hypothesised that neuro-otological symptoms in migraine patients may originate from either vasospasm or some ion channel abnormalities.¹⁶ Ishiyama et al postulated that patients with migraines suffered recurrent labyrinthitis because of either vasospasm or due to some unknown mechanism, which predisposes them to BPPV.^{17,18} Therefore, it could be concluded that repetitive vasospasms or disturbance of inner ear capillaries might play a role in vestibule-cochlear inflammation, causing dislodge of the otoconia from utricular macula into the semicircular canal, and thus give rise to BPPV in migraine sufferers. The same facts are applicable vice versa also. The same postulation may also explain the correlation between migraine and other inner ear pathologies like Meniere's

disease that had been largely reported.^{19,20} It should also be noted that inflammation in the labyrinth has been reported in experimental migraine animal models.^{21,22}

Many chemical mediators like nitric oxide, serotonin, calcitonin, and prostanoids have been found to play a role in the pathophysiology of a typical migraine attack and it is characterized by altered blood flow changes in the brainstem and inner ear.^{18,23,24} Diabetes is considered as CAD risk equivalent.^{25,26} In our study, CAD and diabetes were associated with an increased risk of migraine in BPPV patients. Other studies also reported the same observations of higher migraine and BPPV among the patients of CAD and Diabetes.^{12,27,28} These facts could possibly explain the assumption that atherosclerosis and the consequent vascular events occurring intracranially as well as in the inner ear may explain the relationship between migraine and BPPV to some extent. However, further large scale randomized trials would be required to understand the underlying pathophysiology for the link between BPPV and migraine.

Our study has many clinical and therapeutic implications. Physicians must be vigilant to BPPV patients who are not responding to repetitive rehabilitation treatment, especially in females, with associated diabetes and CAD or who had family/past history of migraine, since they are more likely to have underlying migrainous vertigo as the underlying cause of resistant BPPV. Early recognition and prompt management of migraine are important for the alleviation of patients' symptoms. Finally, all BPPV patients should be routinely inquired about past and family history of migraines. Detail evaluation of migraine history can be used to differentiate whether vertigo symptoms are due to BPPV or migraine itself and it could have further directions for management plan or prognosis.

Our study has certain limitations. First, The BPPV and migraine diagnosis are clinical and there is some extent of overlap between the BPPV and the atypical migraine with brainstem aura. A major differential diagnosis is central positional vertigo due to a lesion in the cerebellum and its vestibular connection, and in addition, positional nystagmus can sometimes be seen during vestibular migraine attacks. However, in this study, we tried to achieve high validity by confirming the diagnosis by a neurologist or senior physicians. Therefore, we believe this considerably improved the error of diagnosis. The second limitation is the small size study sample, although we have studied statistically enough sample size as per statistician's advice before commencing the study. The small sample size of the western part India might have contributed to failure in showing migraines as a significant risk factor in the analyses. Strong part of our study is, we have included only PPT positive BPPV cases and excluded those cases who were contraindicated to perform the PPT.

5. Conclusions

In conclusion, our study demonstrated that patients with BPPV had a 2.3-fold greater risk of associated migraines compared to age and sex-matched control. Although migraine is a common condition, persistent vertigo symptoms in BPPV patients should alert physicians to the possibility of associated migraine, especially those who are females, have comorbid diabetes or CAD, or who have family/past history of migraine.

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7. Conflict of Interest

None

8. Source of Funding

None

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