ANALYSIS OF RISK FACTORS FOR BENIGN PAROXYSMAL POSITIONAL VERTIGO IN PATIENTS WITH SPONTANEOUS INTRACRANIAL HYPOTENSION

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ABSTRACT

Background: *Few studies analyzed the association of spontaneous intracranial hypotension (SIH) and benign paroxysmal positional vertigo (BPPV), so the risk factors for BPPV in SIH patients remain unclear.*

Materials/methods: *In 2014-2017, we enrolled 29 SIH patients from our hospital who had symptoms of BPPV. Control subjects were selected from the people with no symptoms of BPPV in one year, for a total of 76 SIH patients. We collected clinical data, including age, gender, disease history, symptoms, blood pressure, imaging findings and laboratory examination results.*

Results: *The mean ages of BPPV and non-BPPV cohorts were 45.379 (standard deviation (SD)=11.700) and 40.803 (SD=10.466) years old, respectively. We found that smoking status (P=0.041), time in bed after admission (P=0.003), and a positive venous distension sign (VDS) (P=0.013) were associated with the presence of BPPV. A multiple logistic regression model showed that time in bed after admission (P=0.014) and a positive venous distension sign (P=0.041) were strongly correlated with the presence of BPPV.*

Conclusions: *Our study indicated that long-term bed rest and a positive venous distension sign are potential risk factors for the occurrence of idiopathic BPPV in SIH inpatients. Other potential factors need further investigation.*

Keywords: *Spontaneous intracranial hypotension, benign paroxysmal positional vertigo, positive venous distension sign.*

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Introduction

Spontaneous intracranial hypotension (SIH) is a syndrome characterized by orthostatic headache and low CSF pressure related to CSF leakage[(1)]. The main symptom of benign paroxysmal positional vertigo (BPPV) is vertigo, which is position dependent and transient. BPPV is idiopathic, and only 30% of the patients have known factors associated with a higher prevalence of BPPV[(2-7)]. Clinically, we noted that more than 10% of SIH inpatients suffered from BPPV. Few studies have analyzed the relationship between SIH and BPPV, so the risk factors for BPPV in SIH patients are still unclear. In this study, we retrospectively reviewed records of 269 consecutive SIH patients in our hospital, of whom 29 had BPPV, over 3 years.

Patients and methods

Data for this study were extracted from Sir Run Run Shaw Hospital inpatient electronic medical records. From January 2014 to December 2017, 269 SIH patients were admitted to our hospital. For those SIH patients, initial conservative treatment with bed rest and sufficient fluid intake was applied for at least 1 week. If this failed, after CT myelography or magnetic resonance myelography (MRM), EBP treatment was carried out. Then, following the Clinical Practice Guideline: Benign Paroxysmal Positional Vertigo (3), a diagnosis of BPPV was made based on clinical manifestation and confirmed by observation of a transient nystagmus by Dix-Hallpike and supine roll tests. The 269 SIH patients were divided into two groups: a BPPV group (BPPV+, n=29) and

a non-BPPV group (BPPV-, n=240), according to the manifestations of BPPV. This study was approved by the Ethics Committee of Sir Run Run Shaw Hospital. Signed informed consents were obtained from all participants before the study.

Clinical data

Figure 1 shows the selection procedure of the study participants. We collected 269 SIH patients who were diagnosed in our hospital in 2014-2017. The index date was defined as the date of diagnosis of SIH, and patients who had symptoms of BPPV while in the hospital were assigned to the BPPV group (BPPV+). Control subjects (76 SIH patients) were selected from the population of people with no symptoms of BPPV during their inpatient treatment for SIH. We collected data such as age, gender, disease history, symptoms, blood pressure, imaging findings and laboratory examinations.

For disease history, duration (of symptoms) before admission, smoking, alcohol consumption, hypertension, and diabetes were included. Symptoms included headache, dizziness, neck pain, nausea and vomiting, tinnitus, epilepsy, back pain and visual impairment. Haemoglobin, blood platelet, uric acid, triglycerides and low-density lipoprotein (LDL) levels were included in laboratory work.

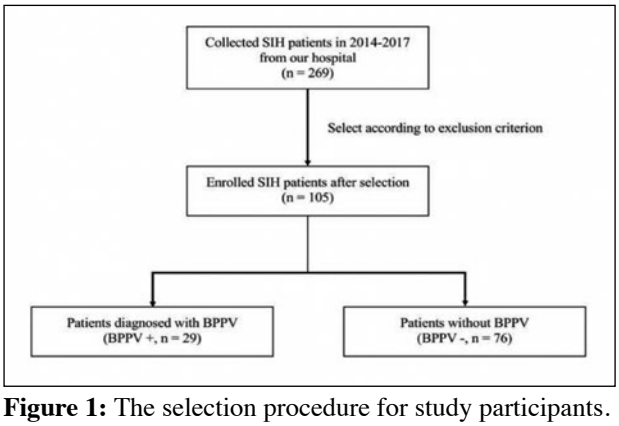

Figure 1: The selection procedure for study participants.

Statistical analysis

Statistical Product and Service Solutions (SPSS) 25.0 software (IBM, Armonk, NY, USA) was employed for statistical analyses. P-values of less than 0.05 were considered statistically significant.

Results

A total of 269 consecutive SIH patients met our inclusion criteria. During their time in the hospital, 29 patients who had symptoms of BPPV were classified into BPPV+ group. In one year, a total of 76 SIH patients who did not have symptoms of BPPV were classified into a BPPV- group. The baseline characteristics and univariate analyses of patients are shown in Table 1.

Variables	BPPV(-) n=76	BPPV(+) n=29	Statistics	*P*
Baseline				
Age (y), Mean ± SD	40.803±10.466	45.379±11.700	t = –1.939	0.055
Gender, n (%)			χ^2 = 0.003	0.957
Female	52 (68.4)	20 (69.0)		
Male	24 (31.6)	9 (31.0)		
Disease History				
Duration before admission (d), Median (IQR)	30.000 (17.500)	30.000 (22.000)	Z = –1.350	0.177
Smoke			χ^2 = 4.194	0.041
Yes	13 (17.1)	0 (0.0)		
No	63 (82.9)	29 (100.0)		
Drinking wine			χ^2 = 0.144	0.705
Yes	6 (7.9)	1 (3.4)		
No	70 (92.1)	28 (96.6)		
Hypertension			χ^2 = 1.601	0.206
Yes	7 (9.2)	6 (20.7)		
No	69 (90.8)	23 (79.3)		
Diabetes			χ^2 = 0.015	0.903
Yes	3 (3.9)	2 (6.9)		
No	73 (96.1)	27 (93.1)		
Clinical Data				
Time in bed after admission (d), Median (IQR)	13.000 (9.500)	17.000 (12.500)	Z = –2.945	0.003
Systolic pressure (mmHg), Median (IQR)	120.500 (17.750)	124.000 (24.500)	Z = –1.029	0.303
Diastolic pressure (mmHg), Mean ± SD	73.026 ± 10.572	75.207 ± 13.484	t = –0.874	0.384
CSF pressure (mmH_2O), Median (IQR)	39.000 (70.000)	25.000 (67.500)	Z = –0.577	0.564
Headache			/	1.000
Yes	75 (98.7)	29 (100.0)		
No	1 (1.3)	0 (0.0)		
Dizziness			χ^2 = 0.035	0.852
Yes	17 (22.4)	6 (20.7)		
No	59 (77.6)	23 (79.3)		
Neck pain			χ^2 = 1.167	0.280
Yes	23 (30.3)	12 (41.4)		
No	53 (69.7)	17 (58.6)		
Nausea and vomiting			χ^2 = 0.006	0.939
Yes	53 (69.7)	20 (69.0)		
No	23 (30.3)	9 (31.0)		
Tinnitus			c^2 = 0.092	0.762
Yes	29 (38.2)	12 (41.4)		
No	47 (61.8)	17 (58.6)		
Epilepsy			/	0.559
Yes	3 (3.9)	0 (0.0)		
No	73 (96.1)	29 (100.0)		
Back Pain			/	0.184
Yes	1 (1.3)	2 (6.9)		
No	75 (98.7)	27 (93.1)		
Visual impairment			χ^2 = 3.003	0.083
Yes	2 (2.6)	4 (13.8)		
No	74 (97.4)	25 (86.2)		
Imaging findings				
Enhancement of the pachymeninges			χ^2 = 0.002	0.961
Yes	65 (85.5)	24 (82.8)		
No	11 (14.5)	5 (17.2)		
Tonsillar herniation			χ^2 = 0.341	0.559
Yes	7 (9.2)	1 (3.4)		
No	69 (90.8)	28 (96.6)		
Subdural effusion or haemorrhage			χ^2 = 2.228	0.136
Yes	14 (18.4)	10 (34.5)		
No	62 (81.6)	19 (65.5)		
Positive venous distension sign			χ^2 = 6.143	0.013
Yes	7 (9.2)	9 (31.0)		
No	69 (90.8)	20 (69.0)		
Cerebral infarction			/	0.478
Yes	1 (1.3)	1 (3.4)		
No	75 (98.7)	28 (96.6)		
Laboratory examinations				
Hemoglobin (g/L), Mean±SD	13.126 ± 1.508	13.110±1.411	t = 0.049	0.961
Blood platelet (10^9/L), Median (IQR)	200.000 (69.750)	186.000 (45.500)	Z = –1.448	0.148
Uric acid (umol/L), Mean±SD	227.540 ± 107.569	237.793 ± 64.194	t = –0.598	0.552
Triglyceride (mmol/L), Median (IQR)	1.450 (1.420)	1.510 (1.870)	Z = –1.180	0.238
LDL (mmol/L), Median (IQR)	2.385 (1.110)	2.220 (1.130)	Z = –0.595	0.552

Table 1: Basic characteristics and univariate analysis of patients with spontaneous intracranial hypotension.
Note: BPPV, benign paroxysmal positional vertigo; SD, standard deviation; IQR, interquartile range; CSF, cerebrospinal fluid; LDL, low-density lipoprotein.

The mean ages of BPPV and non-BPPV cohorts were 45.379 (standard deviation (SD)=11.700) and 40.803 (SD=10.466) years old, respectively.

As for the gender, 52 patients (68.4%) were female in BPPV- group, while there were 20 female patients (69.0%) in BPPV+ group. The gender ratios were not significantly different. No significant differences were detected in the disease history, such as drinking wine (χ^2=0.144, P=0.041), hypertension (χ^2=1.601, P=0.206), and diabetes (χ^2=0.015 P=0.903), between two groups.

Univariate analysis showed that not smoking (P=0.041), time in bed after admission (P=0.003), and a positive venous distension sign (VDS) (P=0.013) were related to the presence of BPPV. No significant differences were found in gender, duration before admission, drinking wine, hypertension, diabetes, blood pressure, symptoms and laboratory examinations. A multiple logistic regression model was used to examine the three risk factors of BPPV (Table 2). It showed that time in bed after admission (P=0.014) and a positive venous distension sign (P=0.041) were associated with the presence of BPPV.

Variables	B	Wald	*P*
Smoke	–20.013	0.000	0.999
Time in bed after admission	0.062	6.065	0.014
Positive venous distension sign	1.184	4.163	0.041

Table 2: Logistic regression results examining the risk factors of benign paroxysmal positional vertigo.
Note: B, Coefficient of regression; Wald, Wald test value.

The ROC curve demonstrated that the area under the curve (AUC) for the risk factor model of BPPV was 0.768 (95%CI: 0.676-0.861, P<0.001; Figure 2), indicating this model had a good efficiency of predicting BPPV.

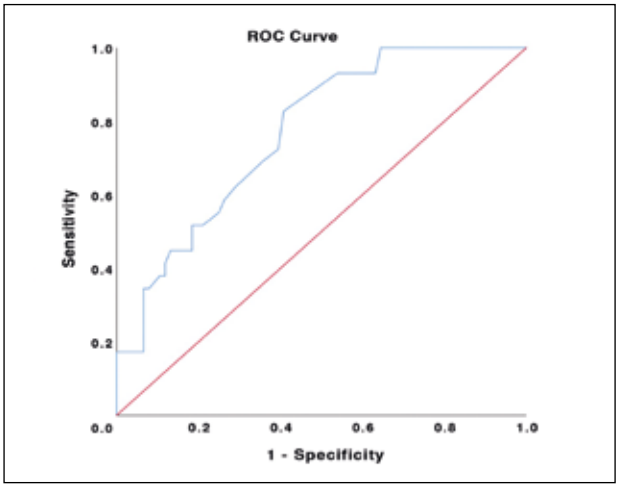

Figure 2: ROC Curve of the risk factor model of BPPV.
Note: The blue line indicates the model.

Discussion

Most BPPV is regarded as idiopathic and benign and considered to be a self-limited vestibular disease. Theoretically, however, any factors that can facilitate the otolith fall off might lead to BPPV. In the current research, we showed that in patients with SIH, the BPPV incidence was significantly higher than in normal people. Therefore, we summarized the past three years of medical records to analyze the correlation and possible risk factors.

To date, no studies have reported the relationship between SIH and BPPV. Muelleman et al.[8] and Nuti et al.[9] showed that BPPV seems to be more common in older adults and women. Whether smoking and drinking have an indirect impact on the incidence of BPPV still lacks relevant research; however, they are not directly associated with the incidence of BPPV[10].

In recent years, some studies suggested BPPV had a relationship with vascular risk factors, such as hypertension and diabetes. The study also suggested these conditions can cause damage to the inner ear blood vessels, resulting in loss of the otolith, and might be involved in the pathogenesis of BPPV[11]. Kim et al.[12] found that dyslipidemia and serum uric acid levels also correlated with BPPV. Celikbilek et al.[13] found that a rise of the platelet index is also part of the pathogenesis of BPPV, due to the average platelet volume and platelet distribution values, resulting in recurrent spasm and ischemia of blood vessels, with the otolith repeatedly shedding as a cause of BPPV. We did not find any differences in gender, duration before admission, drinking habits, hypertension, diabetes, blood pressure, symptoms and laboratory examinations, including haemoglobin, blood platelet, uric acid, triglyceride, and LDL levels in all the SIH patients studied. P-values were greater than 0.05.

For these SIH patients, an initial conservative treatment, including bed rest and sufficient fluid intake, was applied for at least 1 week. If that treatment failed, a targeted EBP was taken. Previous studies found that BPPV occurred with greater than usual frequency after prolonged bed rest necessitated by other diseases, or after surgery[14], because bed rest may cause loosening of the otoconia[15]. However, whether this applies to SIH patients remains unknown, and studies on the correlation between BPPV and SIH are still lacking. Through this study, we found that time in bed after admission (P=0.003) was associated with the presence of BPPV. A mul-

tiple logistic regression model showed that time in bed after admission (P=0.014) was still strongly correlated with the presence of BPPV. We also found that a positive venous distension sign (P=0.041) was also strongly correlated with the presence of BPPV.

Three mechanisms have been proposed for BPPV in SIH patients: First, in SIH patients, initial management often involves bed rest, oral hydration, oral caffeine, abdominal binders or simple analgesia. Patients need to stay in bed to reduce the symptoms. Hoseinabadi[16] suggested that any damage to the otolith of the utricle can be a predisposing cause of BPPV because the cupula of the PSC is located just below the utricle. It is conceivable that, when BPPV is in its latent period due to damage of the utricle, long-term bed rest may facilitate the deposition of degenerated otolithic material on the posterior canal cupula, inducing cupulolithiasis. Cakir et al.[17] revealed that habitual lateral head-positioning during bed rest could be a major factor leading to the development of BPPV in the ipsilateral ear. The longer the bed rest, the higher the incidence of BPPV. Therefore, patients with SIH are prone to develop BPPV because of reduced daily activities due to the positional headache.

Second, in SIH patients, venous engorgement becomes evident when dural venous sinuses or large cerebral veins are involved. Previous studies reported that irritation of the vestibular and cochlear nerves by venous engorgement in the internal acoustic canal might be another mechanism for tinnitus and vertigo[18]. However, no research has yet found a direct link between BPPV and SIH. We suggest that this outcome results from the abnormal CSF pressure and brain structure. When intracranial pressure is lower, according to the Monro-Kellie hypothesis, peripheral blood pressure and the intracranial arterial blood flow is decreased, resulting in an insufficient supply of the inner ear artery. Additionally, the venous sinus compensatory expansion and venous blood stasis aggravate oedema and ischemia of the inner ear. This oedema and ischemia result in damage to the inner ear hair cells. Erythrocyte epidermis damage and hemolysis cause micro-bleeding, resulting in otolith fragments falling off.

Third, another hypothesis is the result of the abnormal CSF pressure and brain structure. Xia et al.[19] showed that the presence of BPPV was associated with lower CSF pressure, but not SDH or drooping of the brain. They speculated that water-soluble endolymph current-induced damage to the small intestinal macula and mechanical brush promoted the removal of loose earwax from the fundus. This process may be the cause of BPPV development in SIH patients. However, our results demonstrated no significant difference in CSF pressure between the BPPV and non-BPPV groups.

One possible reason is that the CSF pressure was only measured 1-2 times in the whole process and even then, the pressure was not the same CSF pressure when the BPPV incident occurred. Therefore, CSF pressure did not show dynamic changes during the entire hospitalization process.

This study had some limitations. First, this was a retrospective analysis and single-centre experience. Second, the blood pressure and laboratory examination data were not unique and constant in all cases. We selected the raw data on the first admission. Third, the sample size of BPPV in this study was small. Future studies with larger samples and more in-depth analyses are needed.

Conclusions

This study confirms that patients with SIH are more likely to develop BPPV than the general population. Prolonged bed rest and positive venous dilatation are potential risk factors for idiopathic BPPV in SIH inpatients.

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