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Diabetes mellitus as a predictor for late recovery of vestibular neuritis

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Abstract

The time course of recovery in vestibular neuritis varies between individuals. The aim of this study was to identify the predictors for the early or late recovery of vestibular neuritis. The inclusion criteria were patients 1) who had an acute onset of vertigo lasting at least 24 hours, 2) with a horizontal-torsional unidirectional spontaneous nystagmus, and 3) with a canal paresis of 20% or more on the bithermal caloric tests. The primary endpoint for this study was an early or late recovery of vestibular neuritis as a dependent variable. A functional level scale was used to define the late recovery (5 or more points) at seven days after the symptom onset. The secondary endpoint was the duration of hospitalization. One hundred twenty eight patients met the inclusion criteria for this study, and among them, 71 patients had an early recovery. Multiple logistic regression analysis showed that diabetes mellitus was the only independent significant variable for the prediction of a late recovery of vestibular neuritis. In addition, the diabetes mellitus was a predicting variable for long duration of hospitalization. Diabetes mellitus was a predictor for a late recovery of vestibular neuritis.

INTRODUCTION

Vestibular neuritis is defined as a sudden unilateral deficit of the peripheral vestibular organ without auditory symptoms and is a common cause of peripheral vertigo.[1,2] It causes a sudden onset of rotational vertigo, nausea, vomiting, gait and postural imbalance with a tendency to fall toward the side of the affected ear and spontaneous nystagmus.[2, 3] Signs and symptoms result from an imbalance of the tonic discharge between the impaired and intact vestibular afferents.[1] The acute stage of severe vertigo lasts for several days to a few weeks in most patients and gradually decreases due to proprioceptive and visual substitution for the unilateral vestibular deficit thereafter combined with a central vestibular compensation of the imbalance in vestibular tone.[1-4] The time course of recovery varies between individuals and almost 50% of patients with vestibular neuritis report sustained dizziness and disequilibrium.[1] In previous study it has been reported that a recovery could be retarded by aging and psychological factors such as anxiety and depression.[3,5]

Diabetes mellitus (DM) is a common metabolic disorder. Its main pathophysiology is a hyperglycemia caused by reduced insulin secretion or insulin resistance.[6] Complications of DM affect many organ systems and the risk of complications increases with the timely duration of DM.[6] Diabetic neuropathy is a common and intractable neurological complication, and is associated with axonal atrophy, demyelination and loss of peripheral nerve fibers. This may result from microvascular injuries with the involvement of nerve supplying small blood vessels.[6] Some reports have been presented about the relationship between a delayed recovery or severity and DM in viral diseases. DM has been associated with an increased disease severity, higher extra-hepatic manifestations and decreased response to antiviral therapy in patients with a chronic HCV infection.[7] In addition, the incidence and severity of herpes zoster increase in patients with DM compared with those without DM.[8] However, there was no study about the effect of DM on recovery of vestibular neuritis yet.

The aim of this study was to follow the recovery during the first one week after the onset of vestibular neuritis, and to identify the predictors for an early recovery of vestibular neuritis. We evaluated the demographic and laboratory

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differences including DM between patients with early and late recovery of vestibular neuritis and assessed the significance of DM for the recovery time of vestibular neuritis.

METHODS

This study was conducted with an approval of the Institutional Review Board at our institution. This case control observational study was performed consecutively in a single tertiary hospital. A total of 220 patients were recruited. The subjects were diagnosed with vestibular neuritis and admitted to the Haeundae Paik Hospital between March 2010 and November 2013. The inclusion criteria were set as followed: First, an acute onset of vertigo lasting at least 24 hours; second, a horizontal-torsional unidirectional spontaneous nystagmus and third, a canal paresis of 20% or more on the bithermal caloric tests. The exclusion criteria were set as followed: First, hearing loss; second, neurologic signs or symptoms suggesting a central lesion; third, a previous history of neuro-otologic disease or fourthly, or fourth, no record about the degree of disturbance in daily activities due to vertigo at seven days. The primary endpoint for this study was an early or late recovery of vestibular neuritis as a dependent variable. Patients were considered as early recovered if they did not have severe vertigo seven days after symptom onset, whereas patients were considered as late recovered if they had a persistent vertigo which was too severe and disturbed the daily life. A functional level scale was used to define the severity which was able to disturb the daily life (5 or more points).[9] Between the patients with an early and a late recovery of vestibular neuritis the demographic and laboratory differences were analyzed such as age, sex, presence of DM, side of affected ear, caloric tests, C-reactive protein (CRP) in blood and duration of hospital stay. Additionally, the second endpoint was the duration of hospitalization. The patients were divided into two groups according to their duration of hospitalization in subjects with short hospitalization or long hospitalization. Therefore, the subjects with a hospital stay < 7 days were defined as short hospitalized and those with a hospitalization ≥ 7 days were defined as long hospitalized. The cutoff values were calculated using areas under receiver operating characteristics curves. The differences of age, DM and canal paresis were analyzed between patients with a short and long hospitalization using multiple logistic regressions. The presence of DM was defined as having medical history of DM and taking anti-diabetic drugs. All of the patients underwent a video-based oculography to record the spontaneous nystagmus and caloric responses. Caloric test was performed for both ears with 27°C cold and 47°C warm air irrigations for 60 seconds. The interval between caloric irrigations was at least five minutes. The asymmetry of vestibular functions was calculated using Jongkee's formula and asymmetry values greater than 20% between the right and left labyrinth were considered pathological in this study. If there were multiple caloric test and CRP done, the first caloric test and CRP were analyzed which were obtained at the same day of admission. The variables were analyzed using Fisher's exact test or Chi-square test for categorical variables and Student's t-test or Mann-Whitney U-test for numerical variables. Also a multiple logistic regression analysis was performed for primary endpoints. All statistical tests were performed using MedCalc®. For all calculations, a *p*-value of less than 0.05 was considered statistically significant. Categorical variables were presented as frequency and percentage. Numerical variables with normal distribution were presented as mean ± standard deviation (SD) and those without normal distribution were described as median with 95% confidence interval and range.

RESULTS

Of the 220 patients admitted to the hospital with vestibular neuritis, 128 patients met the inclusion criteria for this study. Sixty three patients were men and 65 patients were women. The mean age was 54.2±14.2 years. Seventeen patients had DM. Sixty six patients presented their affected ear on the right side, whereas 62 patients presented their affected ear on the left side. All patients underwent a caloric test and a CRP test within 3 days of onset of symptoms. The caloric test showed a presence of median canal paresis with 62.5% (95% CI 55.0-74.6%, range 21-100%). The median CRP was 0.09 mg/dL (95% CI 0.07-0.11 mg/dL, range 0.01-1.6 mg/dL) and the median duration of hospitalization was 4 days (95% CI 3-5 days, range 1-19 days). All patients were treated with vestibular sedatives such as antihistamine agents during admission. However, no rehabilitation therapy or other agents such as corticosteroid or antiviral agents were administered.

Among the 128 patients, 71 patients showed an early recovery and 57 patients revealed a late recovery. Table 1 shows a comparison of demographic and laboratory profiles between

Table 1: A comparison of demographic and laboratory profiles between patients with early and late recovery of vestibular neuritis

Parameter	Early recovery (n = 71)	Late recovery (n = 57)	*p*-value
Men, n (%)	37.0 (52.1)	26.0 (45.6)	0.5802
Age, years (±SD)	53.1(±16.1)	55.5(±11.5)	0.3502
DM, n (%)	2.0 (2.8)	15.0 (26.3)	<0.0001
Right side, n (%)	35.0 (49.3)	31.0 (54.4)	0.6930
Canal paresis, % (range)	60.0 (21.0-100.0)	69.0 (22.0-100.0)	0.2134
CRP, mg/dL (range)	0.1 (0.0-1.6)	0.1 (0.0-1.0)	0.8055
Duration of hospitalization, days (range)	3.0 (1.0-16.0)	5.0 (2.0-19.0)	0.0012

DM, diabetes mellitus; CRP, C-reactive protein

patients with early and late recovery of vestibular neuritis. In the univariate analysis patients with an early recovery suffered less from DM and presented a shorter duration of hospitalization than those with a late recovery (p<0.0001, *p*=0.0012, respectively). In the multiple logistic regression analysis, only DM was shown as an independent significant variable as a late recovery predictor of vestibular neuritis (OR=13.0, 95% CI=2.75-61.56, *p*=0.0012) (Table 2). However, there were no significant differences shown between age, sex, affected side, caloric tests, and CRP in patients with early and late recovery of vestibular neuritis. Among the 128 patients, 100 patients had a short hospitalization. DM was also a significant variable for predicting long duration of hospitalization (OR=3.1, CI=1.02-9.62, *p*=0.0461) (Table 3).

DISCUSSION

This was a first study to evaluate the association between the symptom recovery of vestibular neuritis and DM. The major finding of this study was that patients with DM present a more slowly recovery of vestibular neuritis than those without DM. As primary endpoint for this study the rotational vertigo was used instead of dizziness. Dizziness is a general term for a sensation presenting as a feeling of imbalance, unsteadiness or light-headedness and is usually non-directional, whereas vertigo means a more directional and often more severe perception of an erroneous motion of either the own body or the surrounding space.[10] Although dizziness may develop from a vestibular disorder, it can be also a symptom of mental disorders, especially anxiety disorder such as agoraphobia or panic disorder and can be related with depression.[3,10] Thus, vertigo may be more appropriate than dizziness to evaluate the dysfunction of the vestibular organ. However, because of its subjective nature the measurement of vertigo is difficult. Thus, a six-point functional level scale was used to support an objective assessment of the vertigo effect on daily activities. Despite its usual use in the Meniere's disease, this scale was used to evaluate the severity of vertigo because it is simple and reflects the functional impairment and disability.[9] In addition, it was demonstrated that DM was a predicting variable for longer hospitalization. Most patients stayed at the hospital due to the effect of vertigo on their daily life, although the duration of hospitalization may be affected by other factors, such as patient's economic state, co-morbid diseases or the propensity of physician.

Table 2: Results of multivariate analysis of variables in patients with early and late recovery of vestibular neuritis

Independent variable	Adjusted odds ratio	95% confidence interval	*p*-value
Age	1.0	1.00-1.03	0.9483
DM	13.0	2.75-61.56	0.0012
Canal paresis	1.0	1.00-1.03	0.1677

DM, diabetes mellitus

Table 3: Results of multivariate analysis of variables in patients with short hospitalization and long hospitalization

Independent variable	Adjusted odds ratio	95% confidence interval	*p*-value
Age	1.0	1.00-1.03	0.8276
DM	3.1	1.02-9.62	0.0461
Canal paresis	1.0	1.00-1.02	0.7288

DM, diabetes mellitus

This finding means that subjects with DM showed a longer duration of severe symptoms which affected the daily life and in consequence a longer hospital stay as those subjects without DM. Both of the subjective symptom like vertigo and objective factor like duration of hospitalization suggested that patients with DM present a more slowly recovery of vestibular neuritis than those without DM. This result may be useful not only for clinical practice, but also for patient counseling.

The exact mechanism for the delayed recovery of vestibular neuritis in patients with DM is still unknown. However, these study findings can be explained by two assumptions originated from the etiology of vestibular neuritis. The etiology of vestibular neuritis is thought to be a result from a viral inflammation of the vestibular nerve and ganglions, though in rare cases, the cause may be a labyrinthine ischemia.[11] The first assumption is related with inflammation. DM is associated with a state of chronic low-level inflammation. An Elevation of inflammatory markers such as CRP, tumor necrosis factor-α and interleukin-6 has been well demonstrated in patients with DM.[12] Thus, these inflammatory conditions in patients could delay the relaxation of inflammation in vestibular neuritis and produce the delayed recovery of vestibular neuritis in patients with DM. Another plausible explanation may be the effect of a pre-existing nerve injury caused by ischemia. Diabetic neuropathy is a common complication and the prevalence is generally estimated as 30% to 50% in patients with DM.[13,14] However, the prevalence of diabetic neuropathy is higher than expected, since subclinical or asymptomatic diabetic neuropathy exists.[15] A diabetic neuropathy is a nerve damage associated with microvascular injuries and a reduced nerve blood flow and results in chronic nerve ischemia in patients with DM. Hyperglycemia, increased oxidative stress and mitochondrial dysfunction are mainly associated with the nerve dysfunction and the diminished regenerative capacity, although various pathogenic components contribute to the development and progression of diabetic neuropathy.[12] Thus, a pre-existing nerve injury caused by ischemia in subjects with DM could delay the recovery of vestibular neuritis.

No significant differences were found regarding the age between patients with early and late recovery of vestibular neuritis. In a previous study it was reported that patients with an old age were associated with higher ratings of perceived vertigo.[5] This may be the result of a less complete vestibular compensation due to age changes in the central nervous system.[5] No statistical significance could be found due to the small sample size in the present study although there was a tendency that patients with a late recovery were older than those with an early recovery. Interestingly, a mild canal paresis was not a predictor for an early recovery in this study. The caloric test is the traditional way for the evaluation of the vestibular function and a more severe canal paresis may reflect a higher dysfunction of the vestibular system. However, the vestibular impairment, derived from the results of bedside and laboratory tests, usually does not correlate with the severity of symptoms, thus the caloric test does not reflect the subjective clinical complaints.[16,17] In addition, the caloric test did not reflect the tempo of recovery, but revealed the severity of initial dysfunction of vestibular system only. The study also revealed no relationship between CRP and recovery time. CRP is a characteristic inflammation marker.[18] However, the inflammation in the vestibular nerve produced by vestibular neuritis is too focal to affect the level of CRP. Thus, the CRP does not reflect the inflammation in the vestibular nerve, and it may be not related with the recovery time of a vestibular neuritis.

Our study had several limitations. First, otolith function tests were not accounted such as ocular torsion, subjective visual vertical and vestibular evoked myogenic potential as well as other canal function tests such as head thrust test and head shaking nystagmus, which could be associated with the symptom recovery.[19-21]

Second, the effect of DM control on the recovery time of vestibular neuritis could not be analyzed because a few study patients only underwent a laboratory test reflecting the degree of DM control such as glycated hemoglobin. Therefore a further prospective study with large sample size where these factors may be included will help to clarify this issue.

In conclusions, we demonstrated that DM was a predictor for late recovery of vestibular neuritis.

DISCLOSURE

Conflict of Interests: None

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