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Analysis of persistent geotropic and apogeotropic positional nystagmus of the lateral canal benign paroxysmal positional vertigo

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ABSTRACT

Objective: This study aims to analyze the clinical characteristics of persistent geotropic and apogeotropic positional nystagmus of LC-BPPV in view of light and heavy cupula discussion. *Material and method:* The study group includes 184 patients with LC BPPV (98 apogeotropic, 86 geotropic type) who have been examined between 2009 and 2020. Ninety-nine females and 85 males, aged between 16 and 92 years were included (Ageotropic 49.32 \pm 14.12, geotropic 44.49 \pm 13.90 years). Average slow phase velocity (SPV) of positional nystagmus was documented and those with persistent direction-changing positional nystagmus lasting more than a minute were grouped separately. Age, gender difference, side of involvement, and recurrence pattern were particularly reviewed. Chi-square and One way ANOVA tests were used to compare the difference between groups. Statistical significance was set at P < 0.05.

Results: Thirty-seven patients with apogeotropic nystagmus (30.7%; 37/98) and 18 patients with geotropic nystagmus (20.9%; 18/86) had persistent nystagmus (p '0.05). Comparison of slow phase velocity (SPV) of persistent and non-persistent geotropic and apogeotropic positional nystagmus of the affected side was significant (p '0.05). Comparison of average age, male to female ratio, side of involvement, and the recurrence rate in patients with persistent and non-persistent geotropic and apogeotropic type positional nystagmus groups were not significant (p = 0.177, p = 0.521, p = 0.891, p = 0.702).

Conclusion: Persistent geotropic and apogeotropic positional nystagmus is mostly correlated with the size, amount, and position of otoconial debris. It is difficult to justify the light cupula as a new geotropic variant of cupular pathology. Patients with persistent positional nystagmus present similar therapeutic outcomes and recurrence rates.

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1. Introduction

Horizontal or lateral semicircular canal canalolithiasis variant of benign paroxysmal positional vertigo with geotropic directionchanging nystagmus (DCN) in supine position was first described in 1985 (McClure, 1985). Another variant of LC BPPV presenting with apogeotropic DCN was reported ten years later by Baloh et al. (1995). It is the second common group of BPPV following posterior canal involvement which is reported to range between 10 and 40.5% (Cakir et al., 2006; Chang et al., 2009). It is characterized by geotropic type nystagmus beating toward the lowermost ear, stronger in the pathologic side, or apogeotropic type nystagmus beating toward the uppermost ear, stronger in the healthy side during head-roll maneuver when the head is turned to either side in the supine position. Geotropic type LC BPPV is associated with canalolithiasis due to otoliths located at the posterior or long arm of the lateral canal. Apogeotropic nystagmus is seen when the otoliths are attached to the canalar or utricle side of the cupula or located at the anterior or short arm of the lateral canal close to the cupula. Therefore, it may be due to cupulolithiasis or canalolithiasis. Geotropic nystagmus usually disappears within 30 s. But apogeotropic type has a higher intensity of vertigo and longer duration with the absence of latency and fatigability. Geotropic type lateral

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canal canalolithiasis accounts for 70% of LC-BPPV cases (Bhattacharyya et al., 2008). Apogeotropic type is relatively less common. The transition from apogeotropic to geotropic nystagmus is possible by head-shaking, maintaining the patient in a prolonged lateral position, or even during supine head roll maneuver in most patients with short-arm canalolithiasis and some of the patients with cupulolithiasis, but with otoconia attached to the canal wall. However, otoconia may attach to the utricular wall of the cupula and there is no clear way to distinguish these two conditions from the way of clinical presentation unless transition has been confirmed.

Forced prolonged positioning, head-shaking, barbecue, Semont, Vannucchi-Asprealla, and Gufoni maneuvers have been used to treat patients with LC-BPPV (Oron et al., 2015). However, the success rate is much lower as compared to PC-BPPV. Persistent forms were found more frequently in patients with LC-BPPV as compared to PC-BBPV and more therapeutic maneuver repetitions are required to cure these patients (Choi et al., 2012). On the other hand, the efficacy of any therapeutic maneuver in patients with LC BPPV is probably overestimated since studies focusing on the natural course of BPPV present a better prognosis in favor of LC-BPPV (Shim et al., 2015). The time course of remission in positional vertigo between treated and untreated patients with LC-BPPV has been reported to be significantly shorter than in patients with PC-BPPV (Lee and Kim, 2010). Authors explain this difference based on anatomical orientations of the posterior and lateral canals (Sekine et al., 2006; Imai et al., 2005). The posterior canal is located inferior to the vestibule when the patient is in the sitting position. Debris entering the canal becomes trapped within it and it is hard to get it out without the aid of re-positioning maneuver. Lateral canal slopes slightly up having the cupular end slightly higher. Therefore, debris tends to float back out into the utricle during natural head movement or sometimes simply by lying on the healthy side in bed. On the other hand, LC BPPV has a higher recurrence rate than PC-BPPV (Sakaida et al., 2013). This may be because debris in the utricle can easily re-enter the lateral canal in the same way before dissolving in the vestibule.

Geotropic and apogeotropic forms of LC BPPV may present different clinical outcomes since they may have disparate clinical pictures. However, no specific pathophysiologic difference has been found despite some interesting reports. Nakada et al. have found significantly lower vitamin D serum levels in patients with canalolithiasis of the horizontal canal compared to those with cupulolithiasis (Nakada et al., 2019). Persistent geotropic nystagmus was first described in 2002 (Shigeno et al., 2002). "Light cupula" for persistent geotropic nystagmus and "heavy cupula" for persistent apogeotropic nystagmus, have been used to distinguish these cases from other forms. Endolymphatic density, otoconial load, calcium concentration, etc. could be different (Bisdorff and Debatisse, 2001). The pathophysiological aspect of these cases is the subject of investigation. This study aims to compare the clinical features and long-term follow-up of patients with persistent geotropic and apogeotropic type LC-BPPV to understand the relation between recurrence pattern and the severity and duration of positional nystagmus in view of light and heavy cupula discussion.

2. Material and methods

All procedures were in accordance with the 1964 Helsinki declaration for ethical standards. The study group includes 184 patients with LC BPPV (98 apogeotropic, 86 geotropic type) patients with LC-BPPV who have been examined at the outpatient clinic between 2009 and 2020. Ninety-nine females and 85 males, aged between 16 and 92 years were included (Ageotropic 49.32 \pm 14.12, geotropic 44.49 \pm 13.90 years). Those with a story of ear surgery,

visual disturbance, cervical spine lesions, abnormal eardrum, muscular, ocular, and neurological diagnosis, and those having any anti-vertiginous medication one week before the tests were excluded. Positional nystagmus was recorded by videonystagmography (VNG) (Micromed., Inc, USA) during a supine head-roll maneuver in all patients. Side of involvement was confirmed by lying down positional (straight head hanging) and head bending (bow and lean) tests in patients with lateral canal BPPV. The neutral position where the positional nystagmus stops and the direction changes during slow head rotation in a supine position (ipsilesional for geotropic and contralesional for apogeotropic positional nystagmus) was noted. Average slow phase velocity (SPV) of positional nystagmus was documented in all patients. Those with persistent direction-changing positional nystagmus (geotropic or apogeotropic) lasting more than a minute were grouped separately (video-I and II). Age, gender difference, side of involvement, were particularly reviewed. Patients with geotropic and ageotropic type lateral canal BPPV were treated with barbeque maneuver. Those who still had positional nystagmus at the control visit in a week were treated with Gufoni maneuver and maneuvers were repeated, if necessary. The number of patients with recurrence and recurrence frequency was documented in patients with persistent and non-persistent nystagmus having geotropic or ageotropic type LC BPPV. The Chi-square test was used to statistically compare the significance of percentages of two groups. One way ANOVA test was used to compare the difference between sample groups. Statistical significance was set at P < 0.05(SPSS. Version 26, 2019, IBM, Chicago-USA).

3. Results

Thirty-seven patients with apogeotropic nystagmus (30.7%; 37/ 98) and eighteen patients with geotropic nystagmus (20.9%; 18/86) had persistent nystagmus. Comparative data are presented in Table 1. Comparison of the incidence of persistent positional nystagmus in patients with geotropic and apogeotropic type LC BPPV was significant (p = 0.013). The duration of positional nystagmus in all patients with geotropic and apogeotropic persistent nystagmus was over a minute. The duration was ranging between 25-47 s and 32-55 s in patients with geotropic and apogeotropic type non-persistent positional nystagmus. Slow phase velocity (SPV) of persistent and non-persistent geotropic positional nystagmus of the affected side was ranging between 5 and $32(9.5 \pm 9.14)$. and $3-21(5.25 \pm 5.77)$ degree/sec, respectively. Comparison of mean SPV of the persistent and non-persistent geotropic positional nystagmus was statistically significant (p = 0.017). Slow phase velocity (SPV) of persistent and nonpersistent apogeotropic positional nystagmus of the affected side was ranging between 3 and 36 (7.97 ± 7.59) and $2-10(2.79 \pm 1.32)$ degree/sec, respectively. Comparison of mean SPV of the persistent and non-persistent apogeotropic positional nystagmus was statistically significant (p = 0.001).

Patients with persistent geotropic positional nystagmus were generally older than those with non-persistent geotropic positional nystagmus. However, comparison of average age in patients with persistent and non-persistent geotropic (48.5 \pm 9.41 and 43.53 \pm 14.67, p = 0.177) and apogeotropic type positional nystagmus groups (49.40 \pm 13.77 and 48.46 \pm 14.56, p = 0.752) was not significant. Comparison of male to female ratio in patients with persistent and non-persistent geotropic (8F/10M v 36F/32M; p = 0.521) and apogeotropic type nystagmus groups (23F/14M v 31F/30M; p = 0.274) was not significant. Right ear involvement was more common in patients with persistent apogeotropic type positional nystagmus (right ear 28, left ear 9). However, comparison of the side of involvement in patients with persistent and

Table	1
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Comparative data are presented (RE; right ear, LE; left ear, SPV; slow phase velocity).

Groups	Geotropic positional persistent nystagmus	Geotropic positional nonpersistent nystagmus	p- Apogeotropic positional value persistent nystagmus	Apogeotropic positional nonpersistent nystagmus	p- value
Frequency of persistent nystagmus	18/86; 20.9%		37/98; 37.7%	-	°0.05
Average SPV (degree/msec)	9.5 ± 9.14	5.25 ± 5.77	*0.05 7.97 ± 7.59	2.79 ± 1.32	°0.05
Age	48.5 ± 9.41	43.53 ± 14.67	0.177 49.40 ± 13.77	48.46 ± 14.56	0.752
Sex (male/female)	8F/10M	36F/32M	0.521 23F/14M	31F/30M	0.274
Affected side (RE/LE)	RE8/LE10	RE29/LE39	0.891 RE28/LE9	RE36/LE25	0.093
Presence of neutral point	88.9% (16/18)		32.4% (12/37)		*0.05
Rate of recurrence	33.3% (6/18)	38.2% (26/68)	0.702 37.8% (14/37)	47.5% (29/61)	0.348
Mean total number of recurrences among recurrent cases	2.17 ± 0.41	2.23 ± 0.59	0.808 2.5 ± 1.16	2.41 ± 0.87	0.792

nonpersistent apogeotropic (RE28/LE9 and RE36/LE25; p = 0.093) and geotropic type nystagmus (RE8/LE10 and RE29/LE39; p = 0.891) was not significant. A null or neutral point was identified in 16 of 18 patients (88.9%; 16/18) with persistent geotropic positional nystagmus. The angle of the neutral point presented a great variability ranging between 25 and 55°. In two patients of whom SPV of positional nystagmus was low, the neutral position was not detected during slow head rotation in a supine position. The neutral position was able to be determined in 12 of 37 (32.4%; 12/37) patients with persistent apogeotropic positional nystagmus. Comparison of the presence of neutral position in patients with persistent geotropic and apogeotropic positional nystagmus was statistically significant (p°0.05).

Six patients with persistent geotropic positional nystagmus and 14 patients with persistent apogeotropic positional nystagmus had recurrence during the follow-up period. Comparative analysis of recurrence rate in patients with persistent and nonpersistent apogeotropic (14/37 v 29/62; p = 0.348) and geotropic type positional nystagmus (6/18 v 26/68; p = 0.702) was not significant. When the mean total number of recurrences detected through the follow-up period in recurrent cases were compared in patients with persistent and nonpersistent positional nystagmus, it was not statistically significant in both groups (apogeotropic; p = 0.792, geotropic type; p = 0.808).

4. Discussion

In a common type of LC BPPV, following a short latency period in supine head roll position, the intensity of positional nystagmus reaches a maximal point and then slowly disappears in less than a minute. Persistent positional nystagmus is not observed very often and it could be associated with a variety of central or peripheral lesions like intracranial space-occupying lesions, migraine, Meniere's disease, etc. (Lechner et al., 2014). In some of the patients with LC BPPV, geotropic or apogeotropic nystagmus lasts for a very long time. These forms have been described as heavy or light cupula to distinguish them from common forms (Kim et al., 2014). The proposed mechanism indicates a cupular pathology for both types rather than traveling debris (Ichijo, 2012a; Bergenius and Tomanovic, 2006) Hypothetically, it is the result of the change in density of the cupulo-endolymphatic system (Hiruma and Numata, 2004). However, theories to explain the light (light cupular debris less dense than endolymph) or heavy cupula (expansion of attached cupula, labyrinthine hemorrhage, inner ear hypoperfusion, plasma protein leak to the inner ear due to impaired blood-labyrinthine break following inflammatory reaction) remain to be clarified. No underlying pathogenesis; macular abnormality, alteration of biochemical composition, homeostasis abnormality of inner ear fluid is currently available. Baloh et al. (1995) reported three patients with persistent apogeotropic positional nystagmus and suggested that the condition is the result of otoliths adhering to the utricle side of the LC cupula. The incidence of conversion of apogeotropic nystagmus to geotropic form is quite low in patients with persistent direction-changing nystagmus (Sekine et al., 2006b; Koo et al., 2006). However, how this finding is related with location of the otoconia on the cupular wall and what is the true incidence of cupulolithiasis of the utricle side is unknown since the nystagmus pattern is the same regardless of the side.

Identification of neutral point has been reported to be an important sign to make a clear distinction between peripheral and central disease and also to determine the involved side (lateralization) (Koo et al., 2006; Kim et al., 2014). During slight rotation of the head to one side in a supine position, there is a moment when the nystagmus disappears beyond which the direction of nystagmus changes (Bisdorff and Debatisse, 2001). For those who credit the cupular pathology for the occurrence of the neutral point, they claim that the neutral position is always located in the direction opposite to that of the more intense nystagmus (ipsilesional in light cupula and contralesional in heavy cupula). It is not clear whether it is due to cupular pathology or because of the reversal of the otoconial movement. They state that the neutral point corresponds to a position where the cupula of the ipsilateral lateral canal would be placed on the sagittal plane, and presumably, no longer will be subject to gravitational vector (Hiruma and Numata, 2004). Some authors reported that patients with light cupula always have a null point and can be considered as a reliable sign to support the cupular pathology (Kim et al., 2014). However, the reliability of null point to determine the side of involvement is unclear. In a review of 27 patients with persistent positional nystagmus of the lateral canal, Seo et al. (2016) have reported that the affected side was determined on the same side as the neutral position in 18, on the opposite side in 4 and was not clear in the remaining 5 cases. The slow phase velocity of persistent nystagmus was usually strong on both sides during head roll maneuver particularly in geotropic form and furthermore, it is our observation that it is a difficult task to achieve the detection of neutral point even on VNG recordings when SPV of positional nystagmus is lower than 10°/sec. Comparison of the presence of neutral position in persistent geotropic and apogeotropic groups was significant in our study. Patients with apogeotropic nystagmus usually had nystagmus with a smaller amplitude than that of geotropic type. In a mathematical model, it was proposed that the nystagmus mechanism in canalolithiasis is more powerful than cupulolithiasis in deflecting cupula. A bigger amount of debris is needed to produce the same nystagmus intensity in cupulolithiasis (Hain et al., 2005). The angle of null point in the current study presented a great variability ranging between 25 and 55° which may be related to mass effect of the otoconial quantity moving back.

Biomechanical effects can change the intensity of nystagmus. The density and viscosity of the endolymph are as important as gravitational force (Hain et al., 2005). Sudden change in volume or density of endolymphatic environment may cause positional nystagmus and mimic sudden onset characteristic of BPPV as seen after alcohol or glycerol intake (Lee et al., 2013; Reitz et al., 1987). But this particular example can not be applied to other subtypes of LC BPPV. Canal dynamics are not probably the same in all patients (Sekine et al., 2004a). The size, amount, and weight of otoconia, particle to particle and wall interactions, location and the distance to the cupula, anatomy may affect cupular displacement, Rabbitt (2019) has demonstrated that large otoconial aggregate settles faster than small group leading to a very short latency as seen in light cupula cases and small particles also settle slowly with less intensity but with a prolonged response. On the other hand, the location of the otoconia inside the canal may also change the response since particles in the center of the canal have a greater effect than those moving near the walls (Squires et al., 2004). Previous reports agree that persistent nystagmus of the light or heavy cupula of the LC BPPV occurs mainly under influence of gravity during head roll maneuver.

Previous reports indicate a low incidence of the light cupula. The reason is unclear as to its pathogenesis. Kim et al. (2014) have reported light cupula in 14.2% of patients with geotropic LC BPPV. We have documented a slightly higher incidence (20.9%) in the current study which may be related to the review of patients in a longer period of over 10 years. Age, gender ratio, and the affected side were not different in patients with persistent and nonpersistent geotropic or apogeotropic positional nystagmus in the current study.Ichijo (2020c)has reviewed the recurrence pattern of subtypes of LC BPPV and has found that it is much higher in the light cupula group than in the other subgroups. According to this author, spontaneous remission is related to the absorption of small debris by the cupula and the light/heavy cupula is the final result of the distortion of absorption capability. Seo et al. (2016) have reported similar recurrence rates. Comparative analysis of recurrence rate and the mean number of recurrences detected through the followup period in patients with persistent and nonpersistent apogeotropic and geotropic type positional nystagmus was not significant in the current study. It is difficult to assert persistent geotropic positional nystagmus as a distinct pathology. Caloric testing of patients with persistent and nonpersistent geotropic or apogeotropic positional nystagmus is far from showing different results (Ichijo, 2016b).

In conclusion, it is important to exclude vestibular migraine and central lesions in case of persistent positional nystagmus which may mimic LC BPPV. In a group of patients with lateral canal BPPV, positional nystagmus may persist for more than a minute. In these patients, the severity and duration of geotropic and apogeotropic positional nystagmus are mostly correlated with the characteristics, that is, size, amount, position, and the quality of otoconial debris. It is difficult to describe the light cupula as a new geotropic variant of cupular pathology. Understanding the concept of unilateral cupular pathology and the underlying mechanism proposed for light cupula is difficult and the question of why cupular pathology exists in only one canal and one labyrinth remains unsolved. The neutral position phenomenon is likely to be due to the reversal of otoconial movement within the canal rather than cupular pathology. Positional nystagmus in canalolithiasis of the lateral canal can be without latency, of low intensity, and long duration. In clinical practice, patients with persistent geotropic positional nystagmus respond well to barbeque or Gufoni maneuver. The proposed pathophysiological mechanism of cupular pathology due to attachment of light debris in patients with light cupula remains to be proved in the light of similar therapeutic outcomes and similar recurrence rates with the regular geotropic LC BPPV. No evidence is provided that light cupula belongs to a distinct subtype of LC BPPV.

Declaration of competing interest

We hereby declare that we don't have any conflicts of interest in the manuscript, including financial, consultant, institutional and other relationships that might lead to bias or a conflict of interest. This study has no grant or funding.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.joto.2022.01.002.

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