USE OF SKULL VIBRATION-INDUCED NYSTAGMUS DURING FOLLOW-UP IN MÉNIÈRE’S DISEASE PATIENTS TREATED WITH INTRATYMPANIC GENTAMICIN

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USE OF SKULL VIBRATION-INDUCED NYSTAGMUS DURING FOLLOW-UP IN MÉNIÈRE’S DISEASE PATIENTS TREATED WITH INTRATYMPANIC GENTAMICIN
HIGHLIGHTS

1. Among the 18 patients who experienced vertigo attacks again, 15 showed recovery of the gain measured with video head impulse test (vHIT) of the affected ear, while all 18 showed a reduction in the slow-phase velocity (SPV) of the skull vibration-induced nystagmus (SVIN).

2. SPV of SVIN may be better than vHIT for detecting recovery of vestibular function after intratympanic gentamicin (ITG) administration.

3. To the best of our knowledge, this is the first study to describe the association between decreased SPV and the probability of vertigo attacks in patients with MD treated with ITG.
ABSTRACT

Objectives: Ménière’s disease (MD) is an idiopathic disorder that affects patients’ hearing and the inner ear balance. Intratympanic gentamicin (ITG) is also considered an effective treatment for uncontrolled MD characterized by persistent vertigo attacks despite therapy. The video head impulse test (vHIT) and the skull vibration-induced nystagmus (SVIN) are both validated test to assess the vestibular function. A progressive linear relationship has also been described between the slow-phase velocity (SPV) of SVIN with a skull vibrator at 100 Hz and the gain difference (healthy ear/affected ear) measured in vHIT. The objective of this study was to determine whether the SPV of the SVIN was correlated with the restoration of vestibular function after ITG and, consequently, whether the SVIN can predict the appearance of new vertigo attacks in patients with MD treated with ITG.

Methods: A prospective longitudinal case-control study was conducted. We recorded several variables after ITG and during the follow-up and statistical analyses were performed. Two groups were compared, those who presented vertigo attacks 6 months after ITG and those who did not.

Results: Our sample included 88 patients with definite MD who were treated with ITG. Among the 18 patients who experienced vertigo attacks again, 15 showed recovery of the gain of the affected ear, while all 18 showed a reduction in the SPV of the SVIN.

Conclusion: SPV of SVIN may have more sensitivity than vHIT for detecting recovery of vestibular function after intratympanic gentamicin (ITG) administration. To the best of our knowledge, this is the first study to describe the association between decreased SPV and the probability of vertigo attacks in patients with MD treated with ITG.

KEY WORDS:
Skull vibration, nystagmus, vestibular disease, Ménière disease, gentamicins, head impulse test.

INTRODUCTION

Ménière’s disease (MD) is an idiopathic disorder that affects patients’ hearing and the inner ear balance. It is characterized by episodes of vertigo, aural fullness, tinnitus, and fluctuating hearing loss. It is believed to be related to anatomical changes in the inner ear, i.e., an increase in the volume of the endolymph, which fills the membranous labyrinth, and a reduction in the volume of the perilymph, which surrounds the membranous labyrinth and fills the bony labyrinth. This alteration in the fluid dynamics of the inner ear is called endolymphatic hydrops [1]. The most frequently used treatments for MD include dietary measures such as a low-salt diet with limited intake of stimulants such as caffeine and administration of systemic or intratympanic corticosteroids. The prevalence of MD is 39-190 patients per 100,000 inhabitants [2], with 35% and 47% of the cases showing a bilateral presentation over 10 and 20 years, respectively [3].

Intratympanic gentamicin (ITG) is also considered an effective treatment for uncontrolled MD characterized by persistent vertigo attacks despite therapy [4,5]. The primary reasons for using ITG to control these episodes include its vestibulotoxic effect and the fact that it does not damage cochlear function as much as other aminoglycosides [6]. The mechanism of action of ITG is based on the involvement of the peripheral vestibular receptor and a reduction in the gain of the vestibulo-ocular reflex (VOR) for each semicircular canal of the affected ear [7].

The video head impulse test (vHIT) measures the speed of the eye during high-frequency and high-velocity cephalic impulses on a specific semicircular canal plane and can assess each canal as an independent entity, allowing measurement of the angular VOR (aVOR) within its physiological range. The vHIT also records refixation saccades that were unobserved (covert) or observed (overt) when the aVOR was hypofunctional or do not meet the requirements of head acceleration [8].
The vHIT is a validated test to assess the function of semicircular canals after ITG application [9]. The association between the gain difference in the aVOR of the semicircular canals and the probability of a vertigo attack after ITG treatment has been described previously. Thus, a recovery in the gain of the affected ear and a lower gain difference indicate a higher probability of recurring vertigo attacks and repeated need for ITG [10]. The gain on the affected side is known to worsen during the first four weeks of ITG administration. This gain reduction between 3 and 4 weeks after ITG application may be related to the time required for gentamicin to penetrate from the middle to the inner ear, delayed clearance of the drug, and the temporal progression of cellular damage [11]. We can also analyze the PR score in the vHIT. We have two types of saccades, covert (refixation movements that occur during the head impulse) and overt (when it occurs after the head movement has finished). The saccades indicate vestibular recovery, depending on whether the response is organized or not, that is, the more overt saccades, the less vestibular compensation. The PR score is the result of an algorithm that gives a numerical value to the aggregation of the saccades. It is based on the coefficient of variation that is measured at the peak velocity of the eyes. All present ocular responses to all impulses recorded in the same trial are computed. It gives us a value between 0 and 100, the closer to 0, the less dispersion the saccades have [12].

Assessment of skull vibration-induced nystagmus (SVIN) is another test for measuring vestibular function. It is a reliable, noninvasive test that is easy to perform and indicates the affected side in cases involving vestibular deficits, even in cases with chronic and compensated pathologies. It can reveal vestibular asymmetry and functions as a vestibular Weber test. The optimal stimulation frequency in this test is set at 100 Hz [13]. The SVIN induces a predominantly horizontal nystagmus beating toward the healthy side in patients with a unilateral vestibular
deficit [14]. A progressive linear relationship has also been described between the slow-phase velocity (SPV) of SVIN with a skull vibrator at 100 Hz and the gain difference (healthy ear/affected ear) measured in vHIT [15].

The objective of this study was to determine whether the SPV of the SVIN was correlated with the restoration of vestibular function after ITG and, consequently, whether the SVIN can predict the appearance of new vertigo attacks in patients with MD treated with ITG.

MATERIAL AND METHODS

Patient sample and inclusion criteria

This prospective longitudinal case-control study was conducted on patients with definite MD who were treated with ITG. The following criteria were used to define definite and probable MD, in accordance with the consensus of the Bárány Society [16]:

Definite MD

1. Two or more spontaneous vertigo attacks, each lasting 20 min to 12 h.
2. Audiometrically documented low- to medium-frequency sensorineural hearing loss in one ear, defined as the affected ear, on at least one occasion before, during, or after one of the episodes of vertigo.
3. Fluctuating aural symptoms (hearing, tinnitus, or fullness) in the affected ear.
4. No other suitable vestibular diagnosis.

Probable MD

1. Two or more episodes of vertigo or dizziness lasting 20 min to 24 h.
2. Fluctuating aural symptoms (hearing, tinnitus, or fullness) in the affected ear.
3. No other suitable vestibular diagnosis.
Our sample included patients with definite MD who were treated with ITG at the Department of ENT and Cervicofacial Pathology of the XXXXX. All patients were assessed by the same otoneurology team. Ethical approval for this study was obtained from the institutional review board (IRB) (approval number PI9610/2017A). We included patients who were diagnosed with definite MD, treated with ITG, and did not present with attacks over the first six months after ITG.

The exclusion criteria were as follows: presentation of vertigo attacks within the first six months after administration of ITG and spontaneous nystagmus with SPV > 2°/s (to improve the sensitivity of the test, due to the fact that presenting and spontaneous nystagmus may overly artifact the test measurement if it’s >2°/s. We might not identify the component added to the SPV generated by SVIN if it exists).

Follow-up

Follow-up assessment was performed every month up to six months after injection with ITG, then every three months up to one year and then every six months up to one year more. After that they are seen once a year indefinitely. At each consultation, vHIT and VIN are performed whether or not they have had crises. Duration of follow-up is undefined. All of our patients treated with ITG will not be discharged.

Intratympanic gentamicin

Intratympanic gentamicin (ITG) is considered an effective treatment for uncontrolled MD patients who present persistent vertigo attacks despite treatment. ITG is always injected consistent with the symptoms of the patient, and waiting at least one month between injections [5]. The main goal of using ITG is to control the attacks, due to the vestibulotoxic effect of the drug. ITG compared to other aminoglycosides, induces more damage of cochlear function [6]. We consider the patient controlled vertigo attacks in terms of intensity and duration of the attack, when signs of ototoxicity are noticed or when after five injections no improvement is
achieved [17]. The Cochrane Collaboration concludes that ITG is an effective treatment to control vertigo in MD, recommending its administration at low doses, at distant intervals of time, according to patient’s symptoms [18]. It is spready administered until attacks are controlled, which is why some patients required more than one injection.

Control of vertigo attacks is due to partial ablation of the vestibular organ. The toxic effect is produced by destruction of hair cells, producing an alteration of the integrity of the plasmatic membrane and preventing the formation of inositol triphosphate IP3, acting intrinsically in the cell releasing free radicals [19].

As we said, we included patients who were diagnosed with definite MD, treated with ITG, and did not present with attacks over the first six months after ITG. This six-month interval was chosen because the response to ITG is considered to stabilize after this period [12]. The dose of ITG used per injection was 0.4-0.5 mL (drug concentration 27mg/ml).

**SVIN**

To perform SVIN, the patient was placed in a seated position with videonystagmoscopy and without makeup. Patients were required to avoid blinking. A skull vibrator with a cylindrical contact at 100 Hz was placed on the mastoid apophysis on either side or perpendicular to the cranial vertex, with a pressure of 10 N for approximately 10 s. The tester held the patient’s head with the other hand and measured the SPV of the induced nystagmus [20] using a handheld vibrator VVIB 100 (Synapsys, France). The SPV was recorded over 10 s using VNG software (Ulmer, France). The SPV of the SVIN for both mastoids was obtained for each patient.

**vHIT**

The vHIT was performed using Otometrics ICS Impulse. The patient was seated with goggles secured to the head and fitted with a video camera, sensor, and mirror that reflected the pupil. The device was calibrated for each patient before testing. The patient was asked to stare at a point 1.5 m away. The doctor held the patient’s head and horizontally rotated it in
different directions randomly. The pupil was calibrated to cephalic impulses of 10-20° and 100-200°/s. The data recorded met all the necessary quality criteria and included evaluations of speed, consistency, time, groupings, and saccade direction. Gain was also measured (normal: 0.8-1.2; VOR gain = eye velocity/head velocity) [21]. At least 20 impulses were applied to each side, which was sufficient to perform the test according to the literature, and the records were reviewed and maintained manually to prevent artifacts. The most common artifacts in this test include the head overshoot, which is associated with a significantly higher velocity, longer duration, and lower impulse amplitude and consequently leads to a higher saccade latency and lower saccade amplitude; eye blinking, which is associated with a higher number of saccades; and overshoot, which increases the probability of an impulse being located in the atypical gain and velocity ranges [22]. Other common artifacts include those caused by poor calibration of the device, lack of differentiation between refixation saccades and spontaneous nystagmus, manual movements of the goggles or loose goggle straps, head movements when the jaw is being held, head bouncing after the impulse ends, impulses that are not bell-shaped, alterations in pupil tracking that may be affected by light or the corneal reflex, malformations, and ptosis of the eyelid [23].

Because the calculation method for each vHIT device is different, instead of using the vHIT asymmetry criterion to compare the records, we measured the gain difference, since this approach yielded test results that were comparable across all vHIT devices.

**Statistical analysis**

The following variables were recorded: sex, age, and affected side. The duration of the disease prior to ITG administration, the number of previous intratympanic corticosteroid injections, and the number of Tumarkin crises and number of ITG injections were also registered. We measured the following variables 6 months after administration of gentamicin and during the follow-up period and compared them: average gain measured with vHIT on the affected and
healthy sides, gain difference between the two sides, presence of spontaneous nystagmus, the SPV of the SVIN on the affected and healthy sides, and the modification of the SPV (that is the difference measured in % between the SPV 6 months after ITG and during follow-up), and PR score of the affected side (horizontal canals) [24]. We also recorded new vertigo attacks appearing six months after ITG and the interval between administration of gentamicin and the attack. The follow-up protocol included visits every six months, while cases showing a new crisis were followed-up in the unit within a week. The follow-up period varied between patients because at the time of data collection, some patients had been monitored for longer periods than others.

Statistical analyses were performed using SPSS 21.0. Two groups were compared, those who presented vertigo attacks after the six-month interval from ITG, and those who did not. A descriptive study of the sample was conducted and was followed by an analytical study. The chi-squared test was used for assessment of qualitative variables; Student’s t-test was used for assessment of qualitative and quantitative variables; and linear regression, Pearson coefficient, and correlation analyses were used for evaluation of quantitative variables. Logistic regression analysis was used to establish the relationship between the qualitative and quantitative variables. Statistical significance was defined as p < 0.05.

RESULTS

Group comparison

This descriptive frequency study included a study population of 88 patients with definite MD who were treated with ITG. The average age of the patients with vertigo attacks (group A) was 55 years, and that of patients without crises (group B) was 59 years (table 1).

The statistical analyses showed no significant association between groups in the following variables: sex, age, affected side, prior use of intratympanic corticoids, number of ITG injections and Tumarkin crises.
vHIT

A statistically significant association (p < 0.05) was observed between the gain on the affected side and the gain difference between the healthy and the affected sides and PR score after 6 months and during follow-up (Table 1).

The difference between the gains in the healthy and affected ears at six months was 0.59 ± 0.05 (mean ± standard deviation) in group A and 0.52 ± 0.08 in group B. After follow-up assessments, the gain difference in group A was 0.16 ± 0.6 and that in group B was 0.34 ± 0.6. Among the 18 patients of group A, 15 showed recovery of the gain of the affected ear, and among the 70 patients of group B, none showed a recovery in the gain of the affected ear (Figure 1).

SVIN

A statistically significant association (p < 0.05) was observed the SPV of the affected and healthy sides, and the changes in SPV after 6 months and during follow-up (Table 1).

The SPV of the affected side in group A had changed by 37% ± 12% and that in group B had changed by 0.8% ± 5%; at six months, the SPV of the affected side was 9°/s ± 2°/s in group A and 9.6°/s ± 3°/s in group B.

In group A, all 18 patients showed a reduction in the SPV of the SVIN (Figure 1).

vHIT vs VIN

We observe a positive correlation between the modification of the SPV of the affected side during follow-up and the gain on the affected side (Pearson correlation coefficient = 0.6; p-value = 0.000). Statistical significance was observed between the gain difference during follow-up and the modification of the SPV (p-value = 0.000; Pearson correlation coefficient = 0.7). A linear
regression model using these variables showed a positive linear relationship. A progressive linear relationship with a Pearson correlation coefficient of 0.6 (p-value = 0.000) was observed between SPV and its modification with PR. The linear regression model between the changes in SPV and the difference in gains during follow-up showed a linear relationship. (Figure 2).

A logistic regression model was used to observe the relationship between the presence of vertigo crises after ITG administration and the following variables: SPV on the affected side, changes in SPV, gain on the affected side, and differences between gains. A statistically significant association (p < 0.01) was found between these variables and the presence of crises after ITG administration.

**DISCUSSION**

Assessment of the SVIN is an easy to perform clinical test in which the application of a vibrator at a frequency of 100 Hz and a moderate intensity (about the strength of a body massager) to either mastoid of a patient with a total unilateral vestibular loss elicits a nystagmus, primarily horizontal, with clinically evident rapid phases moving away from the affected side [13]. The nystagmus ceases as soon as the vibration is displaced, with no subsequent nystagmus. Video recordings show that the nystagmus is composed of SPV deviations away from the healthy ear, interspersed with fast return phases directed in the opposite direction away from the affected ear [25]. The fast phases are easily detectable by the clinician at the bedside by using Frenzel glasses; however, quantification of SPV requires three-dimensional recordings. With SVIN, the surprising result is that the direction of nystagmus is the same on stimulation of either mastoid. However, the same procedure in healthy subjects does not cause such consistent nystagmus with an SPV greater than 2.5°/s [13].
The clinical interpretation of these findings can be summarized as follows: an SVIN at 100 Hz with the same direction when both mastoids are stimulated indicates an asymmetry in the function of the semicircular canals between the two labyrinths. The fast phase indicates the labyrinth with the lower function [26]. Tridimensional recordings [13] showed that when mastoid vibration was induced in patients with a unilateral vestibular deficit, the SVIN showed a horizontal and torsional component toward the side of the healthy ear, and evidence shows that mastoid vibration activates all semicircular canals and otoliths simultaneously [27].

Vestibular afferent recordings in guinea pigs have shown that vibration at 100 Hz is an effective stimulus that activates semicircular canals and otolithic organs with irregular resting discharges. These discharges are considered "irregular" because in these neurons, the interval between action potentials in the absence of stimulation, i.e., the resting discharge, is variable. These irregular afferents innervate amphora-shaped type I receptors in the crista crest or striola of otolithic maculae [28]. However, gentamicin has a preference for ototoxicity in type 1 hair cells [29].

The correlation between the SPV values of the SVIN and the difference between the gains (healthy side-affected side) measured in the vHIT has been previously described [15]. In patients with a unilateral vestibular deficit, the sensitivity of the test is 98%, which is negative in patients with hypoexcitability of the healthy side measured by the caloric test [30].

The results obtained in the present study corroborate the reduction in gains measured in the vHIT once gentamicin was injected as well as the relationship between the recovery of the gain and increase of the PR score on the affected side and the recurrence of vertigo attacks. The PR score increases when patients have ungrouped saccades indicating vestibular decompensation in the group that has vertigo attacks again, while in the other group this score decreases, showing vestibular compensation and less probability of recurrence of vertigo attacks [12]. According to previous studies, the frequency of recurrent crises is significantly lower if the
VOR gain had been reduced by less than 33% from baseline after the first application of ITG [31] indicating the importance of monitoring changes in the VOR in patients treated with ITG. The vHIT is a useful and simple tool for this purpose.

In contrast, several studies have confirmed the existence of spontaneous vestibular regeneration after ototoxic damage in mammals [32] and histological studies have demonstrated spontaneous hair cell regeneration after ITG [33].

The findings of our study are consistent with those described previously, but we also found that monitoring SPV in VIN can be as useful as measurement of VOR gains with vHIT, because patients with MD treated with ITG who experienced new vertigo crises had recovered the gain in the affected ear in 15/18 cases, while the SPV of the VIN had decreased prior to the crisis in all 18 cases, which could indicate that VIN has more sensitivity and is quite valuable for its use on expecting recurrence of vertigo attack in Meniere’s disease after treated with ITG.

The fact that the SPV of the VIN may have more sensitivity than vHIT for vertigo crises in these patients may be explained by the fact that gentamicin has a predilection for type 1 hair cells, which are the ones stimulated by SVIN [23].

It’s been demonstrated that, if VOR gain difference of horizontal canal is relatively low after initial ITG, the patient might have poor vertigo control [10].

Qian et al, [26] combined in vivo two antibody markers and demonstrated that through all subdivisions of the utricular macule, hair cells type I (HC-I) exhibited greater capacity for gentamicin uptake than hair cells type II (HC-II). That observation is in accordance with previous findings that HC-I are the primary target of gentamicin and that it is more vulnerable to gentamicin than hair cells type II [7].

There are several explanations for the higher in vivo gentamicin accumulation in HC-I compared to HC-II. First, HC-I development precedes type II [34]. Thus, the mechanisms for
gentamicin uptake are likely present in HC-I before they develop in HC-II. Second, gentamicin can enter hair cells through the MET channel on the stereocilia [35] or via apical endocytosis [36]. As hair bundles from HC-I are more voluminous, they provide greater numbers of MET channels resulting in a larger transduction current [37]. Third, HC-I of the crista of the semicircular canals have higher negative resting potentials than HC-IIs [38] leading to a greater electrochemical gradient across the apical membrane, which would be expected to provide an electromotive force for gentamicin entry into the HC [35]. On the other way, the utricular maculae is anatomically divided into striolar and extrastriolar regions based on the density and morphology of HC, In the striola, HC are less densely packed with proportionally more HC-I, while the number of both types of HC are equivalent in the extrastriola [39].

Other analysis [26] showed a nearly total loss of type I hair cells at 94% for the crista ampullaris of the LSC and 86% for the utricular macula with negligible loss of type II hair cells at 4% for the crista ampullaris of the LSC and 6% for the utricular macula. Hirvonen et al, [40] adopted a chinchilla model and filled with ITG the tympanic cavity until it was full. It resulted in a 57% reduction in overall hair cell density with a 99% removal of type I hair cells and 36% removal of type II hair cells.

On the other hand, recordings from single vestibular afferents in guinea pigs have shown that low frequency skull vibration (100 Hz) is an effective stimulus activating those semicircular canal and otolith neurons with irregular resting discharge. These afferents are called “irregular” because in these neurons the interval between action potentials in the absence of stimulation (the resting discharge) is variable and thus termed “irregular”. These irregular afferents innervate the amphora shaped type I receptors at the crest of the crista or at the striola of the otolithic maculae [9,10] and these afferents are activated with high sensitivity by 100 Hz vibration. In contrast other afferent neurons, synapsing predominantly on type II receptors on
the slopes of the crista or in the extrastriolar area of the otolithic maculae, show a regular resting discharge but have a very poor or absent response to vibration at clinically safe intensities [4].

To the best of our knowledge, this is the first study to describe the association between decreased SPV and the probability of vertigo attacks in patients with MD treated with ITG.

CONCLUSIONS

Recovery in gain and a reduction in the SPV of SVIN are good predictors of new vertigo attacks after ITG administration.

The fact that gentamicin shows a preference for type 1 cells and that SVIN primarily stimulates type 1 cells is probably the reason why the SPV of SVIN might be better than vHIT for detecting recovery of vestibular function after intratympanic gentamicin (ITG) administration and further studies are needed to confirm it.

CONFLICTS OF INTEREST

The authors have no conflicts of interest to declare. All co-authors have seen and agree with the contents of the manuscript and there is no financial interest to report. We certify that the submission is original work and is not under review at any other publication.

REFERENCES


Figure 1: Box and whisker plots: We can observe that in the group which did not present vertigo attacks after ITG (“No”, group B, green), the gain on the affected side was not modified along the time (graph A), nor was the SPV (B) and the SPV modification percentage was near to 0% (C). However, in the group that presented attacks again (“Yes”, group A, blue), the SPV decreased by 37% (C), the gain on the affected side recovered (A), and the SPV decreased (B). In all the patients of group A the gain difference decreased because in all of them the gain in the affected side recovered. The SPV also decreased in all the patients of group A.

Figure 2: The blue dots represent the patients who presented vertigo attacks after ITG (“Yes”, group A) and the green dots represent those who do not (“No”, group B).
A: We can observe that as the gain in the diseased ear increases, the SPV decreases (lower right quadrant, mainly occupied by blue dots), showing correlation between the SPV of the affected side and the gain on the affected side during follow-up (after ITG). Pearson correlation coefficient = 0.6; p-value = 0.000.
B: In the blue group, as the gain in the diseased ear recovered and therefore the difference between gains between both sides became smaller, the SPV presented a higher percentage of modification, i.e., it became slower with respect to the pre-crisis SPV. In the green group, the SPV was not modified. Pearson correlation coefficient = 0.7; p-value = 0.000.

Table 1: Results are described in mean ± standard deviation. M=male. F=female.
R=right. L=left. Variables followed by “6m” represent the measurement six months after ITG.
<table>
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<th>Vertigo attack after ITG</th>
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<td><strong>YES</strong> (n=18)</td>
<td><strong>NO</strong> (n=70)</td>
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<td>(Group A)</td>
<td>(Group B)</td>
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<td>Gain healthy side follow up</td>
<td><strong>,8739±0,02</strong></td>
<td><strong>,8589±0,04</strong></td>
<td><strong>0,13</strong></td>
</tr>
<tr>
<td>Gain difference follow up</td>
<td><strong>,1583±0,06</strong></td>
<td><strong>,3443±0,06</strong></td>
<td><strong>0,00</strong></td>
</tr>
<tr>
<td>Variable</td>
<td>Follow-up</td>
<td>Modification</td>
<td></td>
</tr>
<tr>
<td>----------------------------------------------</td>
<td>-----------</td>
<td>--------------</td>
<td></td>
</tr>
<tr>
<td>Spontaneous nystagmus follow up</td>
<td>0.4778±0.5</td>
<td>0.3157±0.4</td>
<td></td>
</tr>
<tr>
<td>SPV VIN Affected side follow up</td>
<td>5.5000±1.7</td>
<td>9.6043±3.1</td>
<td></td>
</tr>
<tr>
<td>SPV VIN Healthy side follow up</td>
<td>4.5889±1.5</td>
<td>8.1429±2.9</td>
<td></td>
</tr>
<tr>
<td>SPV affected side Modification (%)</td>
<td>37.9020±12</td>
<td>-8.183±5</td>
<td></td>
</tr>
<tr>
<td>SPV modifications healthy side (%)</td>
<td>38.9884±13</td>
<td>-1.2645±9</td>
<td></td>
</tr>
<tr>
<td>PR 6m</td>
<td>41.7222±10</td>
<td>54.7429±11</td>
<td></td>
</tr>
<tr>
<td>PR follow up</td>
<td>68.7778±8</td>
<td>41.6571±9</td>
<td></td>
</tr>
</tbody>
</table>

Table 1: Results are described in mean ± standard deviation. M= male. F= female. R= right. L= left. Variables followed by “6m” represent the measurement six months after ITG.
Figure 2

A

B

Vertigo attacks after gentamicin

Yes

No

p-value 0.00