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ORIGINAL ARTICLE

Normative and Pathological Ranges of Cervical Vestibular Evoked Myogenic Potentials in Normal Subjects and Patients with Complete Compensated Unilateral Vestibular Loss: A Cross Sectional Study

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Abstract To know the normative ranges of VEMP response metrics in healthy young adults. To know the pathological cutoff of VEMP metrics in unilateral vestibular loss patients. To compare our VEMP metrics with the normative values of other studies from the western world. Prospective cross-sectional study. Tertiary care audiovestibular laboratory. 30 healthy subjects and 15 cases with a unilateral complete compensated loss. Various VEMP parameters-p1 latency, n1 latency, p1-n1 amplitude and Interaural asymmetry ratio (IAR) were entered into databases and analyzed. We compared our parameters with the most cited scientific data on VEMP available in the PubMed database, and we analyzed the results. 90% of controls and 80% of cases got VEMP responses at 95 dB HL threshold, 500 Hz with subject/patient placed in sitting upright with head turned to opposite side position. The normative data of VEMP response metrics in young adults for p1, n1 latencies, p1-n1 amplitude, and IAR are 13 ± 2 ms, 21 ± 2 ms, 91 ± 33 uV, and 9.25 ± 7.3, respectively. As the VEMP test has 100% sensitivity and 100% (95% CI 87–100%) negative predictive value in detecting the saccular dysfunction, we recommend the VEMP test as a mandatory tool in the vestibular test battery. There is no statistically significant difference in various VEMP parameters between the control and normal sides of the case group.

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Introduction

Vestibular-evoked myogenic potential (VEMP) is a test of the integrity of the sacculo-collic reflex. Vestibular afferents with regular spontaneous activity are unresponsive to sound, whereas a sizable fraction of vestibular afferents with irregular activity is acoustically responsive [1]. Sufficiently high-intensity sounds can stimulate Saccule and its afferent fibres. The Saccular afferents project to the lateral portions of vestibular nuclei, which gives vestibulospinal tracts. The reflexive response to such auditory stimuli would be the relaxation of flexor muscles. These transient relaxation potentials recorded in electromyography of a tonically contracted flexor muscle, preferably sternocleidomastoid, are called VEMPs. Because they arise from Saccule, the absence of cervical VEMP can be considered an abnormality in the function of the Saccule and the saccular afferent pathways.

For the last decade, extensive work is being done on VEMP, site of origin, afferent pathways [2–4], spinal and central connections, its role in human vestibular physiology, and clinical importance. Many centres worldwide have performed VEMPs in the normal population [5, 6] with different intensity(thresholds) and duration of auditory stimuli and the patient's position. However, very few scientific papers [7] are available explaining the standard protocol for conducting the test procedure, the normative ranges of latencies, and amplitudes in the Indian population. The present study is undertaken to address grey areas

in the VEMP, standardize the test protocol, and know the normative ranges of various VEMP metrics in normal subjects. We also compared the VEMP metrics between normal subjects and patients with unilateral complete compensated vestibular loss patients.

Objectives

1. To know the normative ranges of VEMP response metrics in healthy young adults.
2. To know the pathological cutoff of VEMP metrics in unilateral vestibular loss patients.
3. To compare our VEMP metrics with the normative values of other studies from the western world.

Materials and Methods

Study Design

Prospective Cross-Sectional study incorporating normal controls and cases with unilateral compensated complete vestibular loss.

Ethical Considerations

Institutional Ethical board approval was obtained with minutes no: IESC/T-308/2011. All subjects had informed consent of the study aims and intent and consented to participation.

Study Site

Tertiary care Academic Otolaryngology and Audiology facility. Institutional vestibular physiology laboratory incorporating Vestibular Evoked Myogenic Potential (VEMP) equipment. (VEMP—NEUROSOFT with audio-neuro.net version 7.0 software).

Participants

Control Group

Thirty healthy young volunteer adults between 20 and 45 years of age with no previous evidence of otologic or neurologic illness, systemic illness, or ototoxic drug intake, and a normal pure tone audiogram. Any subsequent detection of vestibular abnormalities at a comprehensive video-nystagmic-graphic (VNG) evaluation conducted concurrently with otolith function testing was an excluding criteria—but was not noted in any.

Case Group

Fifteen cases with complete unilateral cochleovestibular loss consequent to previous surgery (15 unilateral retrosigmoid vestibular schwannoma excision and one unilateral total labyrinthectomy). The period from surgery to study inclusion ranged from 6 to 24 months. All cases were symptom-free at study inclusion with no significant neurological sequelae (excepting HB Grade II-V lower motor neuron facial palsy in post-surgical vestibular schwannoma patients). The complete cochleovestibular loss was further confirmed by the absence of responses on ipsilateral pure tone audiogram and caloric testing. No subject had any current symptoms relating to vertigo or imbalance, thus indicating complete clinical compensation of the vestibular deficit.

Methodology

In the preparatory phase of this study, we performed a comprehensive vestibular evaluation using VNG and VEMP test in ten young, healthy volunteers between 20 and 45 years. We also took eight patients who underwent complete excision of the vestibular schwannoma by retromastoid suboccipital craniotomy. These patients had unilateral profound hearing loss and absent caloric on the side of surgery. VEMP test is performed in supine with head raised position for a duration of 200 stimuli, 0.1 ms each. As most of the controls and cases were unable to complete the test procedure, we changed the test position to sitting with the head turned to the opposite side.

We have conducted the VEMP test in all 30 controls and 15 cases in the experimental phase with a standard protocol. We compared our testing protocol and VEMP metrics with the most cited scientific papers from PubMed in the last two decades and analyzed the data.

Test Procedure

We took adequate precautions to maintain absolute silence and switch off all the electronic devices that can interfere with the responses. The subject sits in an erect chair and turns their head to the opposite side to contract the sternocleidomastoid being tested. We used appropriate manufacturer software for effective spectral analysis, biofeedback, and noise filtering of the EMG signal (audioneuro.net version 7.0 provided by NEUROSOFT RUSSIA). We placed the positive electrode at the sternal notch; the negative electrode at the upper third of the sternocleidomastoid muscle. The reference electrode is placed on the forehead (Fig. 1). The air conducted alternating 500 Hz Short tone bursts at 95 dB nHL (0.1 ms, 200

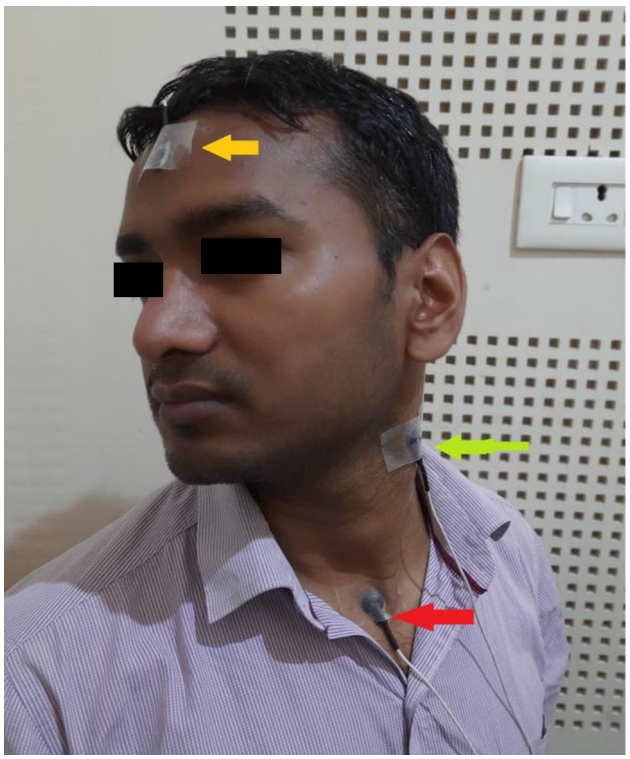

Fig. 1 Placement of electrodes. Yellow – reference electrode; green-negative electrode and red-positive electrode. Note the left Sternomastoid muscle in contracted state and patient in sitting upright position

bursts) were delivered by a snugly fitting headphone and Sternomastoid EMG recorded by surface electrodes.

The test was repeated twice on both sides to look for a better superimposition of the waveforms. The latencies of p1, n1 were measured. The amplitude of the waveform obtained by the difference between the p1 and n1 (p1-n1) (Fig. 2). Interaural amplitude asymmetry ratio(IAR) obtained by dividing the difference of the p1-n1 amplitude by the sum of the p1-n1 amplitude of both ears.

Statistical Analysis

The descriptive statistics, quartile coefficient of dispersion of upper and lower limits of various VEMP response metrics, positive and negative predictive values, sensitivity, and specificity were calculated using SPSS software (SPSS Inc., Chicago, USA) version 19.0.0.2. Independent student t-test and Mann Whitney U tests are used to testing the statistical significance between the controls (54 ears) and normal sides of the case group (12 ears) for various VEMP parameters.

Our VEMP response metrics were compared with most cited scientific articles in PubMed.We calculated the Quartile coefficient of dispersion (COD) for mean values of various VEMP metrics from the cited scientific papers and compared it with our study.

Results

The VEMP test is successfully conducted in all thirty subjects and fifteen cases. We got satisfactory waveforms in 27/30 (90%)subjects. There was no significant difference between male–female and right-left ears in controls. In the case group, VEMP responses are absent on the side of ablation in all 15 patients (100%). The VEMP testing of the contralateral (presumably normal) side indicated 3/15 (20%) absent responses. The mean, median of p1, n1 latencies, mean amplitude (p1-n1) and mean interaural amplitude asymmetry ratio (IAR) in both control and case groups were illustrated in Table 1. There is no statistically significant difference between the control and normal sides

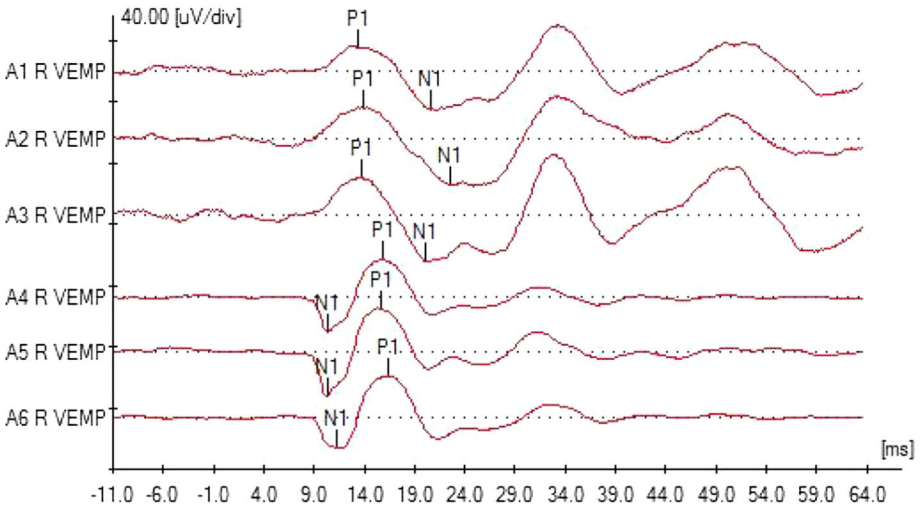

Fig. 2 VEMP response noted in a normal volunteer on right side

Table 1 Indices for calculation of average for p1, n1 latency, p1-n1 amplitude and IAR. As one side responses are absent in the case group, IAR could not be calculated

		Controls	Cases	*P* Value*
p1 latency(ms)	Mean	13.1 ± 2	13.4 ± 1.2	0.271
	Median	13	13.7	
n1 latency(ms)	Mean	21.7 ± 2	21.31 ± 3	0.57
	Median	22	21.4	
Amplitude(p1-n1)(in uv)	Mean	90.8 ± 33	82.6 ± 41	0.46
	Median	89	71.7	
IAR (%)	Mean	9.25 ± 7.3	–	
	Median	6.81	–	

IAR Interaural amplitude Asymmetry Ratio. * *Mann Whitney U test*

Table 2 95% confidence intervals for various parameters

Parameter	Value (in %)	95% CI(in %)
PPV	83.3	58.6–96.4
NPV	100	87–100
Sensitivity	100	78.2–100
Specificity	90	73.5–97.9

PPV Positive predictive value, *NPV* Negative predictive value, *CI* Confidence intervals

of the case group for various VEMP metrics with $p > 0.05$ (Mann Whitney U test, $p < 0.05$ is considered significant).

The sensitivity (95% CI) and specificity (95% CI) of VEMP testing in detecting saccular dysfunction is noted at 100% (78.2% -100%) and 90% (73.5%-97.9%) respectively. Table 2 enlists the 95% Confidence intervals for PPV (positive predictive value), NPV (negative predictive value), sensitivity and specificity for VEMP test.

Our VEMP response metrics were compared with most cited scientific articles in PubMed (Table 3). Figures 3,4,5 and 6 depict the comparisons of p1,n1 latencies, p1-n1 interpeak amplitudes, and interaural amplitude asymmetry ratios(IAR). The quartile co-efficient of dispersion for upper and lower limits of all VEMP response metrics were calculated and shown in Table 4.

Discussion

One can test the human vestibular function by examination of vestibulo-ocular, vestibulospinal, and vestibulocollic reflexes. The vestibulocollic reflex helps stabilize the head's position during movements of the body [8]. Sacculocollic reflex depends on the inhibitory projections of the Saccule to the spinal accessory nucleus, thereby to ipsilateral sternomastoid muscles via inhibitory neurons and medial vestibulospinal tract [9]. The influence of other areas and projections in the brainstem and other higher centres on sacculocollic reflex is poorly understood. However, some animal models have proven the projections of vestibular nuclei to the cerebellum, external cuneate nucleus, cochlear nucleus, and interstitial nucleus of the eighth nerve [2].

The present study is undertaken to know the normative ranges in healthy young adults (27 ± 2.5 years) without any prior history of vestibular dysfunction. We also checked the VEMP responses in patients (mean age of 30 ± 3.2 years) with the unilateral complete compensated vestibular loss on the normal and lesioned sides.

Ergonomics Related to the Testing Procedure

Maintaining the optimal contraction of sternomastoid muscle throughout the test procedure is paramount important for obtaining good responses. In the present study's preparatory phase, 4/10 controls and 8/8 cases could not complete the procedure supine with head raised in pitch plane (Fig. 7). Hence, as an alternate method to neck flexion, we attempted to do the test sitting upright with the head turned to the opposite side. Though many workers suggested VEMP in sitting position [6, 10–13], other centres also adopted supine with head rise with consistent results[14, 15]. Kim et al. [16], Isaradisaikul et al. [10] recommended head turned to the opposite side in a seated position as the best test position due to good compliance and consistent level of sternomastoid contraction.

We recommend the positive/active/noninverting electrode placement on the sternal notch. Negative/inverting electrode placement on the upper one-third of the sternomastoid muscle showed a larger amplitude than any other part of the muscle [17]. Placing the electrode at a constant location on the muscle yielded more consistent responses between the sides and also between the subjects [10].

Table 3 Various VEMP test positions and settings followed at various centres across the world. SCM-Sternomastoid Muscle, NA- not available

Study	Test position	Position of electrodes	Type of Stimulus	Stimulus intensity	No.of stimuli
Present study	Sitting with head rotated to opposite side	Positive- sternal notch Reference- upper 1/3 rd SCM Ground- forehead	500 Hz STB	95 dB nHL	200
Brantberg [24]	Supine, head raised	Positive- SCM Reference-midpoint of clavicle Ground-sternum	rarefaction clicks	100 dB nHL	128
Ochi [12]	Sitting, head turned	Positive- upper SCM Reference- sternal notch Ground-forehead	rarefaction clicks	95 Db	50
Basta [6]	Head turned	Positive-midpoint of SCM Reference-sternum Ground-forehead	500 Hz STB	115 dB SPL	NA
Kelsh [15]	Supine, head raised	Positive- midpoint of SCM Reference- upper sternum Ground- contralateral Neck	clicks	90 dB nHL	150
Wu [14]	Supine, head raised	Positive- upper SCM Reference-sternal notch Ground-forehead	500 Hz rarefaction clicks	90dBnHL	200
Isaradisaikul [23]	Recumbent,head raised and turned	Positive- sternum Reference-midpoint of SCM Ground-forehead	500 Hz STB	110dBnHL	100
Maes [13]	Sitting,head turned	Positive- midpoint of SCM Reference-sternoclavicular junction Ground-forehead	500 Hz STB	95dBnHL	256
Janky [11]	Sitting,head turned	Positive- SCM Reference- sternum Ground-forehead	500 Hz STB	80dBnHL	200
Isaradisaikul [10]	Sitting,head turned	Positive- midpoint of SCM Reference-sternal notch Ground-forehead	500 Hz STB	98dBnHL	200

VEMP Settings

The recommended protocol that yielded more consistent results in this study was using air conduction short tone bursts of 500 Hz, 95 nHL stimulation intensity,0.1 ms, 200 stimuli monaurally when the subject was sitting upright with the neck rotated to the opposite side to contract the ipsilateral sternomastoid muscle. Table 3 depicts various other protocols with a difference in the test position, type of stimulus, intensity threshold. Because acoustically responsive vestibular fibres are more responsive between 500 and 1000 Hz [1], optimal stimulus frequencies for VEMP testing were in this range. However, Todd et al. [18] noticed a maximum response at 300–350 Hz. In the present study's preparatory phase, authors found the use of rarefaction clicks had yielded a scattered response, and poor compliance in both controls and patients as the stimulation intensity required for rarefaction clicks was higher than with STBs, as was noticed by other authors [6, 19]. We recommend Tone bursts at 500 Hz with a stimulation intensity of 95dBnHL (115dBSPL) as an ideal setting for obtaining VEMP responses [20, 21].

VEMP Response Metrics

In the present study, the VEMP response rate for the control and case group is 90% (27/30) and 80% (12/15) (the contralateral normal side in the case group)

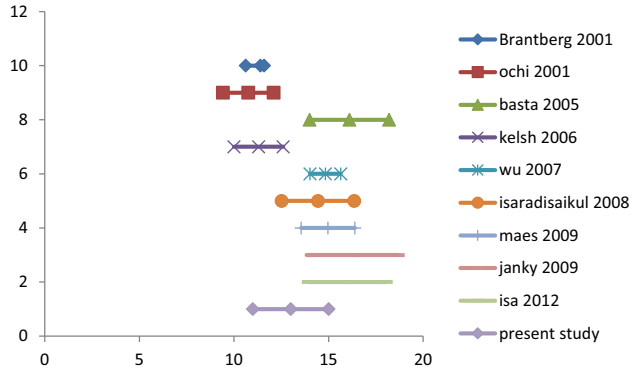

Fig. 3 Mean ± 2SD of p1 latencies given in the literature. The quartile coefficient of dispersion(COD) for the upper and lower limit of p1 latencies is 0.18 and 0.14; respectively, it suggests a good consistency across the studies

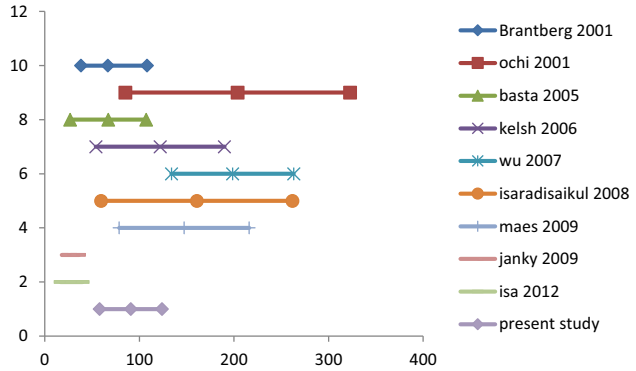

Fig. 4 Mean ± SD of n1 latencies shown in the literature is consistent with our results. The quartile coefficient of dispersion(COD) for upper and lower limits of n1 latency is 0.08 and 0.11, respectively

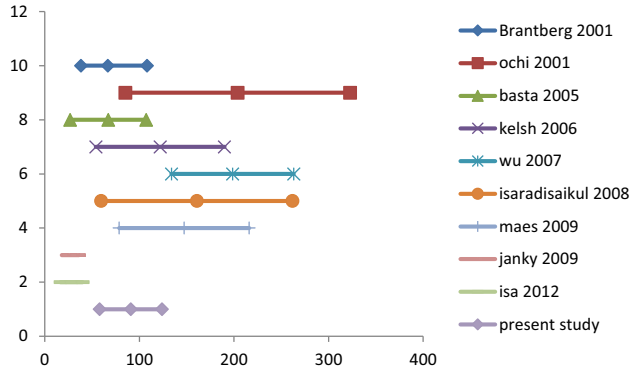

Fig. 5 Means of amplitude shown in various studies with COD for upper and lower limits is 0.49 and 0.53, respectively

respectively at the stimulus threshold of 95dBnHL at 500 Hz. Increasing the threshold to 100dBnHL has not evoked responses in the rest of the controls and cases. (3 controls and 3 cases). The response rates of 97%(at 115dbSPL) [11] and 100%(at 113dBSPL) [13] were

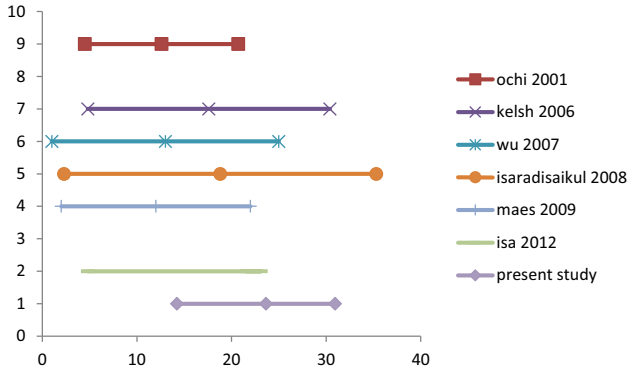

Fig. 6 Means of IAR from various studies with COD for upper and lower limits is 0.19 and 0.42, respectively

reported using short tone bursts. There were reports with 95 dBnHL click stimulation, the response rates of 90% (in older people) and 97% (in younger people) [22]. Some studies have considered VEMP thresholds as the only clinically important parameter [5]. But the variation in the thresholds between the studies is more, and thresholds depend on the test position and muscle contractility [10]. We opine VEMP thresholds alone should not be considered in interpreting the results. In the present study, the authors noted that absent responses in the control group are probably thinner sternomastoid, bulky neck [7], and repeated attempts in performing the procedure, which could cause fatigue of the muscle. All 15 patients in our study have absent responses on the side of vestibular ablation (sensitivity 100% in detecting the saccular dysfunction). Three of the fifteen cases had no appreciable responses on the normal side (intact vestibular function) in our study. The reason for the absence of responses on the normal side is not known. Poor compliance, inability to complete the test procedure by keeping the muscle in contracted state throughout was the noted cause in the case group. Studies have noted the absent responses on the normal side of early Meniere's disease were pointed to binaural interactions of otolith-cervical reflex arc [21]. The saccular central connections need to be elaborately studied to know the exact reason for absent responses on the normal sides in the case group.

There was no statistically significant difference between the p1,n1 latencies,p1-n1 amplitudes between the normal sides of controls and cases (Table 1). There was no correlation between p1 and n1 latencies in our study; however, few workers noted the more prolonged the p1 latency, the longer n1 latency was noted in some studies [10, 23]. The quartile coefficient of dispersion of the upper and lower limits of p1, n1 latencies across the literature was less variable than p1-n1 amplitudes and IAR. As p1-n1 amplitude depends on the muscle's contractility, its negative correlation with age [6, 24], and as the range of amplitude

Table 4 Co-efficient of dispersion(COD) of both upper and lower limit of various VEMP response metrics mentioned across the literature

VEMP metric		Coefficient of dispersion(COD)
p1 latency	Upper limit	0.18
	Lower limit	0.14
n1 latency	Upper limit	0.08
	Lower limit	0.11
p1-n1 amplitude	Upper limit	0.49
	Lower limit	0.53
IAR	Upper limit	0.19
	Lower limit	0.42

Upper and lower limits of p1 and n1 latencies are less variable compared to p1-n1 amplitude and IAR

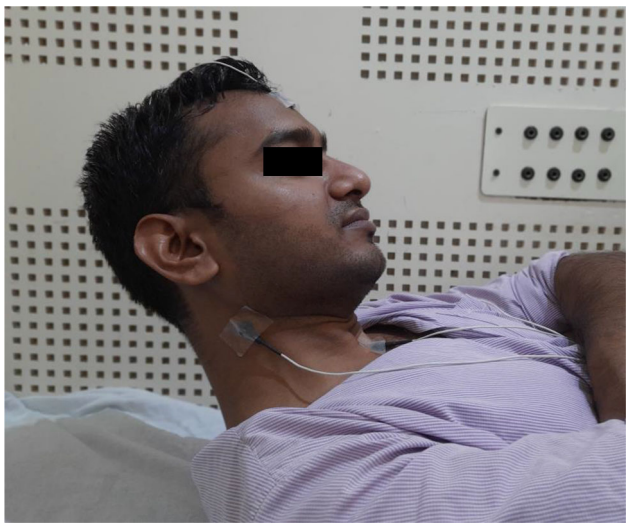

Fig. 7 Testing VEMP in supine with head elevation in the preparatory phase. This position is reported as being uncomfortable by most of the controls and cases

is wide across the literature, its clinical significance is questionable. Our study's mean IAR was 9.25 ± 7.3, consistent with the literature (Table 3). Some authors consider IAR more than 33% as abnormal. IAR may increase when subjects are old or very young and when the test procedure time is delayed due to muscle fatigue [7]. The clinical application of the VEMP in the literature helps diagnose vestibular neuritis, Meniere's disease, Vestibular Migraine, the nerve of origin of vestibular schwannomas, monitoring the efficacy of intratympanic gentamycin therapy, superior canal dehiscence [25]. However, no particular VEMP parameter reliably guides us towards the diagnosis of any of these pathologies. Sequential testing in a specific patient may nevertheless help assess the response to treatment.

The VEMP parameters studied in the present study are p1, n1 latency, p1-n1 interpeak amplitude in both control and case groups. Interaural asymmetry ratio (IAR) in the control group only as one side responses are absent in the case group. Though various studies quote the usefulness of VEMP in peripheral and central vestibular pathologies, the VEMP test as a single stand-alone diagnostic test should not be considered.

Conclusions

The normative data of VEMP response metrics in young adults for p1, n1 latencies, p1-n1 amplitude, and IAR are 13 ± 2 ms, 21 ± 2 ms, 91 ± 33 uV, and 9.25 ± 7.3, respectively. VEMP test's sensitivity in detecting the saccular dysfunction in the present study is 100% (95% CI 78.2- 100%). The normal sides of patients with unilateral complete compensated vestibular loss showed a similar range of VEMP response metrics as controls ($p > 0.05$). One has to customize the protocols to evoke VEMP responses in individual clinic and case scenario. The subject sitting upright with the neck turned to the opposite side has given the best evoked responses in the present study. The authors support using VEMP in standard vestibular test battery and not as a replacement for conventional testing. As the sensitivity of VEMP in diagnosing saccular dysfunction is 100%, when performed along with another strip of vestibular investigation, it could point us towards pathologies of otolith (saccular) origin or pathologies involving otolith organs. The absence of VEMP responses on the intact vestibular function in the case group is unknown and cannot be explained by current knowledge. Further studies are required to know the higher saccular connections and binaural interactions.

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Declaration

Conflicts of interest The authors declared that they have no conflict of interest.

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