VEMP in Diabetes Mellitus

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Abstract

Vestibulo ocular reflex and vestibule spinal reflexes are certain reflexes which are responsible for maintaining the balance and can be assessed by cervical Vestibular Evoked Myogenic potentials (cVEMP) and ocular VEMP (oVEMP) respectively. cVEMP reflects vestibular system activity that is elicited by high intensity sounds and detected as change in muscle potentials in the sternocleidomastoid muscle and oVEMP is a short latency vestibular evoked potential in response to a loud stimulus, recorded from contralateral extra ocular muscles. VEMP and oVEMP were recorded from thirty participants with and without diabetes mellitus. The latency and amplitude measures of cVEMP and oVEMP were studied within and across each group of participants. The findings revealed that the latency, amplitude and amplitude asymmetry ratio of peaks of cVEMP and oVEMP in participants without diabetes were in accordance to the previously published reports. Auditory Brainstem Responses in participants with diabetes mellitus were normal suggesting normal eighth nerve transmission till brainstem level. The duration of diabetes was not found to be a significant factor affecting pure tone average, cVEMP and oVEMP results. The latency of cVEMP and oVEMP peaks were not significantly different between individuals with and without diabetes mellitus but the amplitude of oVEMP and cVEMP responses were reduced in individuals with diabetes mellitus when suggesting a normal nerve conduction but a probable end organ deficit in persons with diabetes. The results also suggested that amplitude measures rather than latency measures were sensitive to vestibular end organ impairments.

Keywords: *cVEMP, oVEMP, Diabetes mellitus, duration of diabetes*

Introduction

Balance is dependent upon integration of signals from the vestibular, visual, and the somatosensory systems to generate the motor responses that maintain upright position and adjust to destabilizing forces. There are certain reflexes which are also responsible for maintaining the balance such as the vestibulo ocular reflex and vestibule spinal reflexes. The vestibular spinal reflexes and vestibule ocular reflexes can be assessed by cervical Vestibular Evoked Myogenic potentials (cVEMP) and ocular VEMP (oVEMP) respectively with similar threshold of elicitation. cVEMP reflects vestibular system activity that is elicited by high intensity sounds and detected as change in muscle potentials within the neck (Colebatch, Halmagyi & Skuse, 1994). oVEMP was first demonstrated by Todd, Rosengren and Colebatch, (2003).They demonstrated a short latency vestibular evoked potential with a negative peak at 10 ms (n10) and a positive peak around 15 ms (p15) in response to a loud 500 Hz bone-conducted stimulus, which could be best recorded from contralateral extra ocular muscles (Rosengren, Todd & Colebatch, 2005). These tests serve as an important tool in the test battery of clinics and medical centers worldwide offering services for patients with balance and vestibular disorders.

Among the many causes of vestibular symptoms diabetes mellitus is one. This systemic disorder alters the normal glucose metabolism leading to glycemia increase beyond physiological levels that causes glucose build up within bodily fluids (hyperglycemia) and changes the osmotic potential and the functioning of all the systems, the vestibular among them (Adriano & Silvia, 2006). Diabetes mellitus is a genetically determined metabolic disorder associated with absolute or relative impairment of insulin and in complete clinical manifestation is characterized by metabolic affections, vascular and neuropathic complications (Maia & Campos, 2005). Individuals with diabetes mellitus may also suffer from central neuropathy, or degeneration of the higher nervous system (Jadzinsky, Faerman & Fox, 1973; Shagan, 1976; Tavormina, Kastner, Slater & Watts, 1976).

Although the prevalence of vestibular deterioration is not well known in persons with diabetes mellitus, recent studies suggest that about 60% to 65% of patients with diabetes mellitus may have vestibular dysfunction, associated with deficits in gaze holding and the vestibular reflex (Jauregui- Renoud, Sanchez, Olmos & Golzalez-Barcena, 2009). In individuals with diabetes, problemsÂ in both the timing and quality of gait have been reported to be absent (Petrofsky,Cuneo, Lee,Johnson & Lohman, 2006; Petrofsky, Lee, Macnider & Navarro, 2005). However, there is dearth of information regarding the other various test findings in individuals with diabetes. Since most of the individuals with diabetes are asymptomatic, the detailed vestibular evaluation has not been done in individuals with diabetes.

This research aimed to study the latency and amplitude measures of cVEMP and oVEMP responses of individuals with diabetes, individuals without diabetes mellitus and compare between these two groups. Attempts were

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made to correlate the findings of cVEMP and oVEMP, VEMP results with hearing threshold, VEMP results with duration of diabetes and VEMP results with the symptomatology presented by the participants.

Method

Participants

Two groups of participants with normal hearing sensitivity or sensorineural hearing loss up to moderate degree were considered for the study. History of conductive pathology or neuromuscular problems especially of that of head and neck region and a history of intake of drugs that lead to vestibulo toxicity were ruled out in all the participants.

Group 1-Experimental group: 30 participants (60 ears) in the age range of 35 to 55years with diabetes (mean age= 44.1 years) were selected if they had medically confirmed history of type-II diabetes mellitus and if there was no evidence of any retro cochlear pathology confirmed with Auditory Brainstem Response (ABR) results. These participants were screened for uncomfortable loudness level of > 105dB for speech.

Group 2- Control group: 30 participants (60 ears) in the age range of 35 to 55 years without diabetes (mean age= 43.13 years) were selected if they had no history or presence of medically confirmed diabetes mellitus.

A calibrated two channel GSI-61 diagnostic audiometer connected to a TDH-39 headphone and Radio ear 71 bone vibrator was used to find out the air conduction thresholds, bone conduction thresholds and uncomfortable level for speech from all the participants. Calibrated GSI TYMPSTAR immittance meter was used for tympanometry and reflexometry. Intelligent Hearing systems (IHS version 4.3.02) was used for recording auditory brainstem responses and air conducted tone burst evoked cervical VEMP. Calibrated Eartone 3-A insert earphone was used to deliver the stimuli. Biologic navigator ProEP instrument with biologic insert was used for ocular VEMP recordings. The ambient noise levels inside the test room were within permissible limits (ANSI, 1999).

Test Procedure

A detailed case history was taken for each participant prior to testing. It was followed by administration of the five sections of dizziness questionnaire (Maryland Hearing and Balance Centre, 2004) for all the participants. Pure-tone thresholds were obtained for all the participants using modified Hughson and Westlake procedure (Carhart & Jerger, 1959) at octave frequencies between 250 Hz and 8000 Hz for air conduction and between 250 Hz and 4000 Hz for bone conduction. UCL was obtained in both ears for air conducted speech stimuli using ascending method. Immittance evaluation was carried out in both ears using a probe tone frequency of 226 Hz. Tympanometry was done initially and then ipsilateral and contralateral acoustic reflex thresholds were measured for 500, 1000, 2000, and 4000 Hz stimuli. For all the participants ABR were recorded for both the ears to rule out any retrocochlear pathology. ABRs were recorded using an electrode montage of non inverting electrode to the upper forehead, inverting to the ipsilateral (stimulated) ear lobe and ground to lower forehead. The amplifier band pass was 100 Hz to 3000 Hz. Alternating polarity click stimuli were presented monaurally at a rate of 11.1 Hz and 90.1 Hz at 90 dB nHL. Averaged responses to 1500 clicks were collected on each of two runs. Reproducible components were obtained and latencies were measured.

For the cVEMP recordings the sites of electrode placement were prepared using a skin preparation gel. Silver chloride disc electrodes were used for recording. Absolute electrode impedances and inter electrode impedances were maintained below 5000 ohms and 2000 ohms respectively. During the cVEMP recordings the participants were instructed to sit straight and turn their head to the opposite side of the ear in which stimulus was presented, so as to activate ipsilateral sternocleidomastoid muscle, as it gives reliable and greater amplitude. Participants were instructed to maintain the same posture throughout the test run. A visual feedback box in the IHS instrument with green and red LED lights was provided to the participant in order to maintain the tonicity of the sternocleidomastoid muscle within 50microVolt and 100 microvolt. cVEMPs are recorded using 500 Hz tone burst (2 cycles rise, 0 cycles plateau, and 2 cycles fall, Blackman weighting function) in rarefaction polarity which was presented at a rate of 5.1/s. ER - 3A insert ear phone was used to present the stimulus at an intensity of 95 dBnHL to each ear. A pre stimulus period of 10ms and post stimulus duration of 70ms was used to record the stimulus. The amplified responses (X 5000) were band pass filtered between 30 to 1500 Hz. The responses were averaged totally for 200 stimuli. Responses were recorded twice to ensure the replicability of the responses.

Ocular VEMP was recorded for all the participants with upper gaze direction. Participants were instructed to maintain the same upper gaze throughout the test run. The recordings were done from the extraocular muscles contralateral to the ear being stimulated. oVEMPs were recorded for all the participants with upper gaze direction. Participants were instructed to maintain the same upper gaze throughout the test run. Stimuli used to record oVEMPs were identical to stimuli used to record cVEMPs. 500 Hz tone burst (2 cycles rise, 0 cycles plateau, and 2 cycles fall, Blackman weighting function) was presented in rarefaction polarity at a rate of 5.1/s. ER - 3A insert ear phones was used to present the

stimulus at an intensity of 95 dBnHL to each ear. A pre stimulus period of 10ms and post stimulus duration of 60ms was used to record the stimulus. The amplified responses (X 5000) were band pass filtered between 1 to 1000 Hz. The responses were averaged totally for 200 stimuli. oVEMP responses were recorded twice to ensure the replicability of the responses.

Response Analysis

The recorded cVEMP and oVEMP responses were analyzed for latency and amplitude measures of the peaks (cVEMP: P13, N23; oVEMP: n1, p1 and n2) for all the participants in the control and experimental groups. The amplitude asymmetry ratio for P13-N23 complex in cVEMP , n1-p1 and p1-n2 complex in oVEMP were calculated using the following formulae.

$$\text{Amplitude asymmetry ratio} = \frac{\text{amplitude of P13-N23 complex in the right ear - amplitude of P13-N23 complex in the left ear}}{\text{amplitude of P13-N23 complex in the right ear + amplitude of P13-N23 complex in thge right ear}} \times 100$$

$$\text{Amplitude asymmetry ratio} = \frac{\text{amplitude of n1-p1 complex in the right ear - amplitude of n1-p1 complex in the left ear}}{\text{amplitude of n1-p1 complex in the right ear + amplitude of n1-p1 complex in thge right ear}} \times 100$$

$$\text{Amplitude asymmetry ratio} = \frac{\text{amplitude of p1-n2 complex in the right ear - amplitude of p1-n2 complex in the left ear}}{\text{amplitude of p1-n2 complex in the right ear + amplitude of p1-n2 complex in thge right ear}} \times 100$$

Note: For the ease of reading the P13 and N23 peaks have been written as P1 and N1 respectively throughout results and discussion.

Results

Results of Control Group

Latency and amplitude of cVEMP and oVEMP in control group: The peaks of cVEMP (P1 & N1) and oVEMP (n1, p1 & n2) were identified and latency, amplitude and amplitude asymmetry ratio was calculated from all the participants in the control group Figure 1 shows a cVEMP and oVEMP recorded from a participant in the control group.

The mean and standard deviation (SD) of latency measures of P1 and N1 peaks, amplitude of P1-N1 complex of cVEMP for right and left ears, similar results of oVEMP and amplitude asymmetry ratio for P1-N1 complex and n1-p1 and p1-n2 complex for participants in the control group is given in Table 1.

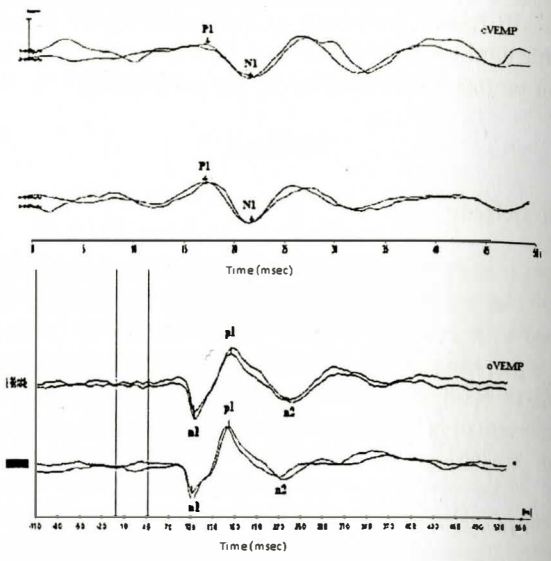

Figure 1: Patterns of cVEMP and oVEMP recorded from a participant in the control group.

From Table 1, the latency of peaks of oVEMP was early compared to the peaks of cVEMP. Also, the amplitude of cVEMP wa higher compared to that of oVEMP. The standard deviation for amplitude of both cVEMP and oVEMP was high in the control group.

Correlation of latency and amplitude measures of cVEMP and oVEMP in control group: Correlation of latency and amplitude measures across cVEMP and oVEMP was studied using Pearson's test of correlation. The cVEMP and oVEMP data from both ears were combined for statistical analysis. There was no significant correlation between the amplitude of P1N1 complex of cVEMP with amplitude of n1p1 complex of oVEMP ($r = -0.045$, $p > 0.05$) and p1n2 complex of oVEMP ($r = 0.084$, $p > 0.05$), P1 latency of cVEMP with n1 latency of oVEMP ($r = 0.211$, $p > 0.05$), P1 latency of cVEMP with p1 latency of oVEMP ($r = 0.195$, $p > 0.05$) and P1 latency of cVEMP with n2 latency of oVEMP ($r = 0.120$, $p > 0.05$). To conclude, there was no correlation between the latencies and amplitude of cVEMP

Table 1: Mean and standard deviation of latency measures, amplitude measures and amplitude asymmetry ratio of P1 & N1 peaks of cVEMP and n1,p1 and n2 peaks of oVEMP

	cVEMP							oVEMP											
	Latency measure (ms)				Amplitude measure (μV)		P1-N1 AmAR (%)	Latency measure (ms)						Amplitude measure (μV)				AmAR(%)	
	P1		N1		P1-N1			n1		p1		n2		n1p1		p1n2		n1p1	p1n2
	Right	Left	Right	Left	Right	Left		Right	Left	Right	Left	Right	Left	Right	Left	Right	Left		
Mean	14.80	14.75	21.37	21.89	38.3	38.64	18.64	11.97	12.16	17.10	17.38	23.13	22.73	5.59	6.21	4.58	5.28	23.28	27.86
SD	1.83	2.47	2.07	2.26	14.34	15.97	12.64	1.87	1.29	1.68	1.57	1.82	1.96	2.99	4.07	2.82	3.38	19.86	18.68

**Note: AmAR= Amplitude Asymmetry Ratio*

with the latencies and amplitude of oVEMP for the control group.

Results of Experimental Group

Latency and amplitude of cVEMP and oVEMP: The mean pure tone threshold average (average of thresholds at 500Hz, 1000Hz and 2000Hz) was 19.26 (SD= 4.80) in the right ear and 19.44 (SD= 4.41) in the left ear. From the results of pure tone audiometry done on 60 ears, 45 ears (75%) had a pure tone threshold average above 15dBHL. Further, out of these 45 ears, 7 ears (11.6%) had pure tone threshold average above 25 dBHL (Mild hearing loss) lesser than 30dB. Normal immitance and acoustic reflex was obtained from all the participants in the experimental group. The ABR could be recorded from all the 60 ears and was found to be normal in its latency and amplitude measures.

The VEMP responses were not present in all the participants in experimental group. Out of the 60 ears tested in experimental group (30 participants with diabetes mellitus) for VEMP, cVEMP was absent in 48 ears (80%) and oVEMP was absent in 41 ears (68.33%). This reduced the data corpus for statistical analysis to 12 ears for the cVEMP and 19 ears for oVEMP in the experimental group. Further, in the experimental group, both the cVEMP and oVEMP were absent in 34 ears (56.6%), cVEMP was present and oVEMP was absent in 7 (11.6%) ears, cVEMP was absent but oVEMP was present in 14 (23.33%) ears. Both cVEMP and oVEMP were present only in 5 (8.3%) ears. The latency of P1 and N1 peaks of cVEMP and amplitude complex of P1-N1 peaks were measured for 12 ears. Figure 2 (a) and (b) shows cVEMP recordings from persons with diabetes- one with cVEMP response and another with no cVEMP response respectively. The latency of n1, p1 and n2 peaks of oVEMP was also obtained for 19 ears. Figure 3 (a) and 3 (b) shows the absent and abnormal recordings of oVEMP from persons with diabete. Descriptive analysis was done to find out the mean and standard deviation (SD) of latency and ampltiue measures of peaks of cVEMP in 12 ears and oVEMP in 19 ears of participants with diabetes (Table 2).

Correlation of latency and amplitude measures of cVEMP and oVEMP: Spearmans test of correlation revealed no significant correlation between latency of P1

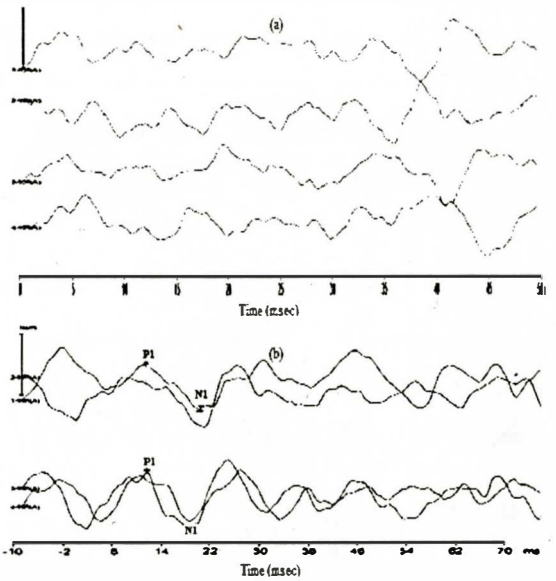

Figure 2: Patterns of cVEMP recorded from individual with diabetes (a) absence of cVEMP and (b) presence of cVEMP.

peak of cVEMP and n1 peak of oVEMP (p=0.370, $p>0.05$), P1 peak of cVEMP and p1 peak of oVEMP (ρ =0.074, $p>0.05$), P1 peak of cVEMP and n2 peak of oVEMP (ρ =0.361, $p>0.05$), N1 peak of cVEMP and n1 peak of oVEMP (ρ =0.353, $p>0.05$), N1 peak of cVEMP and p1 peak of oVEMP (ρ =0.032, $p>0.05$), N1 peak of cVEMP and n2 peak of oVEMP (ρ=0.032, $p > 0.05$) in the participants of experimental group. Similar results were obtained for amplitude measures of cVEMP and oVEMP (P1N1 of cVEMP and n1p1of oVEMP: ρ =-0.126, $p>0.05$, P1N1 complex of cVEMP and p1n2 complex of oVEMP: ρ =0.357, $p >0.05$).

Correlation of pure tone average and the results of cVEMP and oVEMP: The findings obtained for the cVEMP and oVEMP for participants in the experimental group were classified into three categories: normal, abnormal and absent. A Pearson test of correlation was done to study the correlation of pure tone average (average of hearing thresholds at 500 Hz, 1000 Hz and 2000 Hz tones) and the results of cVEMP and oVEMP in the participants of the experimental group. There was no significant correlation between pure tone average of right ear with cVEMP results in the right ear (r=-0.61, p >0.05), pure tone average of right ear with oVEMP

Table 2: Mean and standard deviation of latency and amplitude measures of cVEMP and oVEMP in participants of experimental group

	cVEMP			oVEMP				
	Latency measures (ms)		Amplitude measures (μV)	Latency measures (ms)			Amplitude measures (μV)	
	P1	N1	P1-N1	n1	p1	n2	n1-p1	p1-n2
Mean	14.91	20.93	26.31	11.85	17.50	22.95	3.82	4.08
SD	1.74	2.053	5.47	1.36	1.90	2.53	3.93	4.72

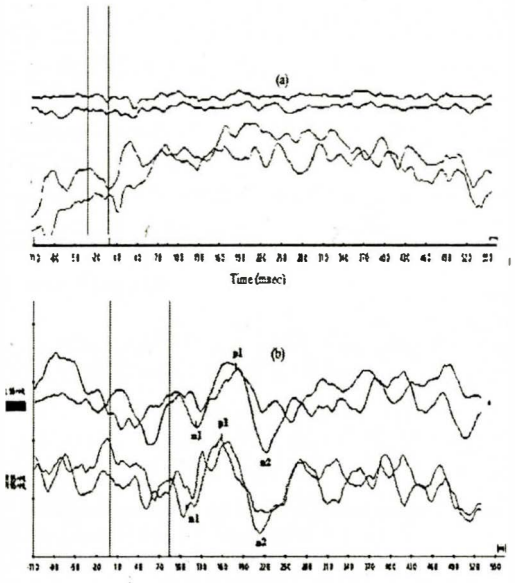

Figure 3: Patterns of oVEMP recorded from participants in the experimental group. (a). absence of oVEMP, and (b) Presence of oVEMP.

results in the right ear (r=-0.16, p >0.05), pure tone average of left ear with cVEMP results in the left ear (r=-0.13, p >0.05), pure tone average of left ear with oVEMP results in the left ear (r=-0.12, p >0.05).

Correlation of duration of diabetes mellitus and latency and amplitude measures of cVEMP and oVEMP: The mean duration of diabetes mellitus in the participants of experimental group was calculated and was found to be 12.53 ± 8.10 months. Spearmans test of correlation was run to study the correlation of duration of diabetes mellitus with latency and amplitude measures of cVEMP and oVEMP in experimental group of participants. No significant correlation was found between the duration of diabetes mellitus and latency of cVEMP (P1: ρ=0.35, p>0.05; N1: ρ =0.62 , *p*>0.05) and oVEMP (n1: ρ =-0.16, p>0.05; p1: ρ =0.08, p>0.05; n2: ρ =0.05, , p>0.05). There was no significant correlation of amplitude of cVEMP (P1-N1: ρ =0, p>0.05) and oVEMP (n1p1: ρ =-0.13, p>0.05, p1n2: ρ =-0.10, p>0.05) with the duration of diabetes.

Comparison between Control and Experimental Group

Results of cVEMP

The mean latency of P1 and N1 peak for control and experimental group is shown in Figure 4. From Figure 4, the latencies of P1 for both the control and the experimental group were similar whereas, the latency of N1 peak for experimental group was lesser compared to the control group. To statistically understand these measures, a non parametric Mann Whitney U test was carried out and it revealed no significant difference in the latency of P1 peaks (Z= -.378, *p* > 0.05) and N1

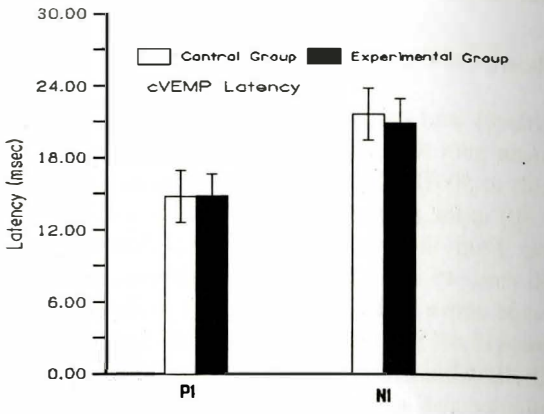

Figure 4: Mean and standard deviation of latency (in ms) of P1 and N1 peaks of cervical VEMP in control and experimental group.

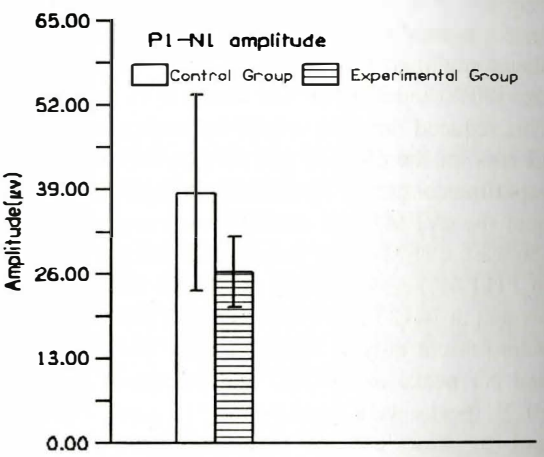

Figure 5: Mean and standard deviation of amplitude (in μV) of P1-N1 complex of cervical VEMP in control and experimental group.

peaks (Z= -1.649, *p* > 0.05) across control and experimental groups.

Figure 5 depicts the mean amplitude measures of P1N1 complex. The amplitude of P1N1 complex for the experimental group was lesser compared to the control group. Mann Whitney U test revealed significant difference in the mean amplitude of P1N1 complex across groups (Z= -2.856, p < 0.05).

Results of oVEMP

The latency of n1, p1 and n2 peaks of oVEMP was calculated for both the control and the experimental groups (Figure 6). From the figure, the difference between control and experimental group in terms of latencies of oVEMP was not evident. Statistically significant differences in latency measures across the groups were studied with non parametric Mann Whitney U test and

Table 3: Percentage of individuals reported with various vestibular symptoms and their cVEMP results

	cVEMP right				cVEMP left			
	A	N	Ab	Total %	A	N	Ab	Total %
Light headedness or swimming sensation in the ear	0	2(50%)	2(50%)	4(13.3%)	3(75%)	1(25%)	0	4(13.3%)
Blacking out or loss of consciousness	0	1(100%)	0	1(3.3%)	0	1(100%)	0	1(3.3%)
Tendency to fall	10(83.3%)	0	2(16.6%)	12(40%)	13(92.8%)	0	1(7%)	14(46.6%)
Objects spinning or turning around you	7(100%)	0	0	7(23.3%)	8 (100%)	0	0	8(26.6%)
Sensation that you are turning or spinning inside	0	0	1(100%)	1(3.3%)	0	1(100%)	0	1(3.3%)
Loss of balance when walking	5(100%)	0	0	5(16.6%)	2(100%)	0	0	2(6.6%)
Total	22(73.3%)	3(10%)	5(16.6%)	30(100%)	26(86.6%)	3(10%)	1(3.3%)	30(100%)

Note: cVEMP= Cervical Vestibular Evoked Myogenic Potential; A= Absent, N= Normal, Ab= Abnormal

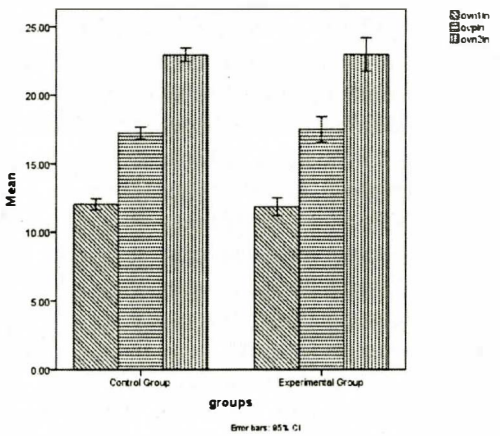

Figure 6: Mean and standard deviation of latency (in ms) of n1, p1 and n2 peaks of oVEMP in participants of control and experimental groups.

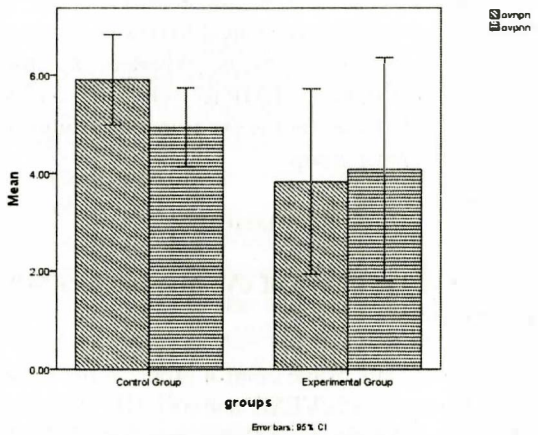

Figure 7: Mean and standard deviation of amplitude (in μV) of n1p1 and p1n2 complexes of ocular VEMP in participants of control and experimental groups.

there was no significant difference between the groups in terms of p1 (Z= -0.574, $p > 0.05$), n1 (Z= -0.034, $p > 0.05$) and n2 (Z= -0.488, $p > 0.05$) latency measures.

Figure 7 depicts the amplitude of n1p1 complex and p1n2 complex for both the control and experimental group. The amplitude of both the n1p1 complex and p1n2 complex was lesser for the experimental group compared to the control group. Mann Whitney U test revealed a statistically significant difference in amplitude of n1p1 complex (Z= -2.862, $p < 0.05$) and also p1n2 complex (Z= -2.478, $p < 0.05$). This implies that the participants with diabetes mellitus had a significantly lesser amplitude for both the cVEMP as well oVEMP. However, there was no significant difference in terms of latencies of the various peaks of cVEMP or oVEMP. Standard deviation in the experimental group was higher compared to the control group for both the n1p1 and p1n2 complex.

Vestibular Symptoms Presented by Individuals with diabetes and their cVEMP and oVEMP Results

The percentage of individuals reporting with each symptom and their cVEMP and oVEMP results were tabulated (Table 3 and Table 4 respectively) for participants in the experimental group.

To summarize the results, the cVEMP and oVEMP could be recorded in all the participants of the control group whereas, cVEMP for the experimental group could be recorded only from 12 ears and oVEMP could be recorded for only 19 ears. Further, there was no correlation between the cVEMP and oVEMP results in both the control as well as the experimental group. Also, there was no correlation between the duration

Table 4: Percentage of individuals reported with various vestibular symptoms and their oVEMP results

	cVEMP right				cVEMP left			
	A	N	Ab	Total %	A	N	Ab	Total %
Light headedness or swimming sensation in the ear	3(50%)	2(66.6%)	1(33.3)	6(20%)	2(33.3%)	2(33.3%)	2(33.3%)	6(20%)
Blacking out or loss of consciousness	1(50%)	1(50%)	0	2(6.7%)	2	0	2(100%)	2(6.7%)
Tendency to fall	9(90%)	1(10%)	0	10(33.3%)	10(100%)	0	0	10(33.3%)
Objects spinning or turning around you	5(71.4%)	0	2(28.5%)	7(23.3%)	3(42.8%)	1(14.2%)	1(42.8%)	7(23.3%)
Sensation that you are turning or spinning inside	1(100%)	0	0	1(3.3%)	1(100%)	0	0	1(3.3%)
Loss of balance when walking	2(50%)	2(50%)	0	4(13.3%)	2(50%)	2(50%)	0	4(13.3%)
Total	21(70 %)	6(20 %)	3(10%)	30	20(60%)	5(16.6%)	5(23.3%)	30

(Note: oVEMP= Ocular Vestibular Evoked Myogenic Potential; A= Absent, N= Normal, Ab= Abnormal)

of the diabetes and puretone average with the cVEMP and oVEMP results. Latency of neither cVEMP nor the oVEMP showed significant differences across the control and experimental groups. Whereas, the amplitude values of both the cVEMP as well as the oVEMP was significantly lesser for the experimental group compared to the control group.

Discussion

Latency and Amplitude of cVEMP and oVEMP in Control Group

All the participants of the control group in the present study had presence of cVEMP and oVEMP. The latency of P1, N1 and amplitude of P1N1 complex of cVEMP and latency of n1, p1 and amplitude of n1p1 complex obtained in the present study was similar to the studies reported in the literature earlier (**Akin & Murnane** 2001; **Akin, Murnane & Medley** 2003; Bohra, Sanju & Sinha, 2012; Colebatch et al., 1994; Chiarovano, Zamith, Vidal & de Waele, 2011; Murnane, Akin, Kelly & Byrd, 2011; Smulders et al., 2009; **Welgampola & Colebatch,** 2001).

During the oVEMP recording an additional negative peak n2 was identified which occurred immediately after the p1 peak. The 'n2' peak of oVEMP was present in all the participants of the control group at a latency of 22 to 23 ms. The presence of 'n2' peak in oVEMP has not been reported earlier in any of the studies. It is hypothesized that the generators of the 'n2' peak also might be confined in the same anatomical structures from where the 'n1' and 'p1' peak is generated.

The first peak of the oVEMP in the present study was recorded around a mean latency of 11.97 ms and 12.16 ms for right and left ear respectively, whereas first peak of cVEMP was recorded with a mean latency of 14.89 ms and 14.75 ms for right and left ear respectively. Thus, the latency measures indicate that the latency for the oVEMP is shorter compared to that of cVEMP. The differences in latencies between cVEMPs and oVEMPs might be due to the differences in length and nerve conduction velocity between vestibular ocular (Broussard & Lisberger, 1992) and vestibulo spinal pathways (Uchino et al., 2005) as shown in animal studies. cVEMPs and oVEMPs responses obtained by air conduction stimulation are generated from different anatomical pathways (Chiarovano et al., 2011) and follows a different pathway before the muscle potential (Sternocleidomastoid and Contralateral extraocular muscle) is recorded (Halmagyi & Curthoys, 1999; Rosengren, Welgampola & Colebatch, 2010). The pathway for the oVEMP is relatively shorter compared to that of cVEMP (Rosengren et al., 2010) and hence the latency differences were obtained in the present study.

Also, the amplitude obtained for the P1N1 complex was higher compared to the oVEMP in the present study. The differences in amplitude between cVEMP and oVEMP may be due to the differences in the muscle unit content between SCM and extraocular muscles (Park et al., 2010). The muscle thickness is reported to be more at the SCM compared to the extraoccular muscles and hence the tonic activation is more for the SCM comared to the extraoccular muscles (Park et al., 2010).

cVEMP and oVEMP Results in the Experimental Group

The results indicate a normal functioning of the cochlear nerve since the auditory brainstem responses are normal. Since cochlear and the vestibular nerves are the part of the same 8^{th} cranial nerve, it can hypothesised that the vestibular nerve functions are also normal in diabetic individuals. The primary site of lesion in the individuals with diabetes might be confined to the end

organs specifically in the utricle or the saccule.

Myers, Ross, Jokelainen, Graham and McClatchey (1985) have demonstrated vestibular end-organ pathological changes, such as increased capillary diameter of the small blood cells of the utricle and saccule and accumulation of lipid droplets in subneuroepithelial connective tissue cells of these vestibular organs. It is common for capillaries within a capillary bed to vary in size but it is noteworthy that over 25 % of the control capillaries in persons with diabetes were under 4 μm in diameter (Myers et al., 1985). The higher viscosity of diabetic blood (Schmid-Schonbein & Volger, 1976) and the decreased deformability of diabetic red blood cells (McMillan, Utterback & La Puma, 1978; McMillan & Gion, 1981; Otsuji, Baba & Kamada 1981) are likely to cause impaired blood flow through such narrow channels. Under these conditions, either the passage of red blood cells would be slowed down reducing oxygen delivery to the tissues, or the mechanical force exerted on the capillary wall would be increased. The latter situation is considered a strong candidate in the development of diabetic microangiopathy (McMillan, 1983) and could explain the increased capillary diameters in the saccules and utricles of the diabetic subjects.

The increased density of capillaries in the saccules and utricles of the diabetic subjects indicates vascular proliferation induced by the presence of diabetes and that this proliferation occurs within the first three months of diabetes (Myers et al., 1985). A vascular proliferation such as this would be expected to be a reflection of either an increased oxygen demand by the tissue or alternatively, by a decreased efficiency of oxygen delivery by the capillary bed. No evidence is available to support the former possibility. The latter case is supported by studies which have shown that the glycosylation of hemoglobin in diabetic blood increases the oxygen affinity of the hemoglobin thereby impairing the release of oxygen to the tissues (Ditzel, 1976; Bunn, Gabbay & Gallop, 1978).Reduced oxygen delivery by diabetic blood has been challenged (Bunn et al.,1978)however, on the grounds that other physiological variables in the blood which influence oxygen release would negate the affect of the increased oxygen affinity of glycosylated hemoglobin. If this is the case, then the possibility of a reduced flow rate, mentioned earlier with regard to elevated blood viscosity, could be an alternative cause of a relative hypoxia of the saccule and utricle leading to a damage of the saccule and utricle and hence absence of cVEMP and oVEMP.

There was no difference in the latency of P13 peaks or N23 peaks among the control versus experimental groups. Various studies have reported that latency parameter of VEMP is relatively less subject to undergo changes than amplitude and threshold of VEMP response (Faith et al., 2004). Also, the latency parameters were insensitive to stimulus characteristics (Faith et al., 2004).

Other studies which involved the study of degeneration process of the sacculocollic pathways and other pathological conditions have also reported no significant change in the latency parameters compared to the amplitude parameters (Kumar et al., 2007; Murofushi, Matsuzaki & Takegoshi 2001; Sun Kyu Lee, et al., 2007; Welgampola & Colebatch, 2001; Young, Huang & Cheng, 2003). However, in older population a prolongation in the latency of VEMP has been reported (Lee et al., 2008; Kumar, Sinha & Bhat, 2011), indicating that the latency parameters might be sensitive only in the nerve pathology rather than the end organ pathologies. In end organ pathologies the amplitude parameter seem to be more sensitive in detecting the pathology. Thus, no difference in the latency of cVEMP and oVEMP between the persons with and without diabetes mellitus is an indication that pathology could be restricted to the otolith organs of the diabetic subjects and not the vestibular nerves.

The results of the present study also indicate that in most of the participants, both the saccule as well as the utricle was involved bilaterally. The presence of cVEMP in the absence of oVEMP indicates a possible involvement of the utricle alone whereas, the absence of cVEMP in the presence of oVEMP indicates involvement of the saccule alone. Overall, the saccule was more involved compared to the utricle in individuals with diabetes mellitus suggesting a higher susceptibility of saccular end organ to the deoxygenation caused by diabetes compared to the utricle.

Correlation of Latency and Amplitude Measures of cVEMP and oVEMP in Control and Experimental Group

No correlation was obtained for the latency or amplitude measures of cVEMP and oVEMP for control group as well as the experimental group. There is dearth of information regarding the correlation between the cVEMP and oVEMP measures in normal healthy subjects. However, there are studies which have reported a poor correlation between the cVEMP and oVEMP in individuals with Meniere's disease (Chiarovano et al., 2011; Murofushi, Nakahara, Yoshimura & Tsuda, 2011). Murofushi etal., (2011) reported poor correlation of cVEMP and oVEMP, while oVEMP latency and amplitude measures significantly correlated with the caloric test in individuals with Meniere's disease. Similar findings were also reported by Chiarovano et al. (2011) who also concluded that the cVEMP responses are generated majorly in the saccular region while the oVEMP responses are from the utricular region.

Lack of correlation between the cVEMP and oVEMP measures has been attributed to the two different pathways involved in the generation of these potentials

(Huang, Wang & Young, 2012). The cVEMP test runs via the inferior vestibular nerve pathways, whereas the oVEMP runs via the superior vestibular nerve pathways (Huang et al., 2012). Also, since the amplitude of VEMP is dependent upon the muscle tension, no correlation between the cVEMP and oVEMP amplitude might be due to the fact that the muscle thickness for ocular muscle is lesser compared to the sternocleidomastoid muscles (Park et al., 2010). There might not be a significant correlation between the cVEMP and oVEMP but combining test of oVEMPs and cVEMPs may provide localization of pathology (Huang, Wang & Young, 2011).

Correlation between the Duration of Diabetes and Pure Tone Average with cVEMP and oVEMP Results

There was no correlation between the duration of diabetes with cVEMP or oVEMP results. Also, no significant correlation was obtained between puretone average and cVEMP and oVEMP results. Rajendran, Anandhalakshmi, Mythili and Rao (2011) reported that the duration of diabetes (above or below 10 years) has no effect in the incidence of hearing loss in the diabetic group. No correlation was reported between duration of diabetes and degree of hearing loss (Panchu, 2008) and duration of diabetes and abnormality of auditory brainstem responses (Zehra, Kaya, Gonen & Ilhan, 1999). Duration of diabetes might not be a significant factor in abnormality of the different tests rather the uncontrolled levels of the glucose might be a factor in damaging different structures (Panchu, 2008) such as the otolith organs as found in this study.

Most of the participants in the present study had minimal hearing loss (<30dBHL), a finding supported by many studies in literature. Several probable mechanisms of hearing loss in cases with diabetes have been proposed such as microangiopathy of the inner ear, neuropathy of the cochlear nerve, a combination of both, outer hair dysfunction and disruption of endolymphatic potential. The tissue effects of diabetes are thought to be related to the polyol pathway, where glucose is reduced to sorbitol. Sorbitol accumulation is implicated in neuropathy by causing a decrease in myoinositol content, abnormal phosphoinositide metabolism and decrease in Na+ K+ ATPase activity (Dennis et al., 2008). Since the auditory ABRs were normal in present study in all the participants of experimental group, it can be hypothesized that the lesion in individuals who participated for this study might be confined to the cochlear structures. Makishima and Tanaka (1971) have also reported a severe atrophy of the spiral ganglion in the basal and middle turns of the cochlea in diabetic patients with sensorineural hearing loss. Further no correlation between the puretone average and VEMP (cVEMP and oVEMP) results could be due to the fact that the structures involved in processing of the puretone signals and generation of VEMP (cVEMP and oVEMP) are different. It can be hypothesized that the level of glucose might have a differential effect on the two structures i.e it might affect the vestibular structures more than cochlear structures. However, there are no studies to support or refute this hypothesis.

Sign and Symptoms Exhibited by the Individuals with Diabetes and VEMP Results

On administering the Maryland dizziness questionnaire all the participants reported one or the other vestibular symptoms. Further, the client who exhibited these symptoms, most of them had abnormal/absent cVEMP and oVEMP. Based on the findings of this study (i.e absence of both the cVEMP and oVEMP in most of the subjects), it is expected that many more diabetic patients will have vestibular symptoms. Initially, when the general case history was taken, none of the participants reported vestibular symptoms. On intentional screening using the Maryland dizziness questionnaire vestibular symptoms were revealed indicating the importance of additional vestibular screening in the test battery for persons with diabetes mellitus. Most of the clients with vestibular symptoms had absent VEMP responses which indicated an otolith organ disorder (both utricle and saccule). The symptoms exhibited by the individuals with diabetes might be secondary to the damage of the otolith organs.

First, it is possible that this is not seen clinically because vertigo would probably be reported in the presence of functional asymmetry between the two inner ears. In diabetes mellitus and other metabolic diseases it is expected that there is a symmetrical impairment, which probably causes clinical symptoms only when the impairment severity increases. Second, some central compensation might be taking place in these individuals and hence they do not exhibit these symptoms clinically. Therefore, detail information about the vestibular symptoms should be collected from individuals with diabetes.

Conclusions

Diabetes can affect different vestibular structures. The site of lesion in individuals with diabetes can be confined to end organs rather than the neural system. The amplitude measures of cVEMP and oVEMP are more sensitive parameters than the latency measures. As the vestibular system is complex involving multiple structures, one must administer different tests to rule out pathology of each of these structures. Mostly the persons with diabetes remain asymptomatic probably because of bilateral distribution of the disorder or a probable central compensation, hence a detailed case history must be taken to rule out or detect any vestibular symptoms.

The study provides a thrust to long felt need for research in the field of vestibular assessment in individuals with diabetes. Present study opens a new research era in understanding the involvement of the sacculocollic and the utriculooccular pathway in individuals with diabetes. The vestibular evoked myogenic potentials may give an indication of the involvement of the different pathways of the vestibular system. Vestibular rehabilitation therapy (VRT) exercises are typically based on principles of vestibular adaptation of semicircular canal input. If otolith organ involvement is identified, then VRT exercises designed to stimulate otolithic adaptation may be more effective for managing a patient's symptoms.

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