



To Study the Effect of Vitamin C Supplementation on Brainstem Auditory Evoked Response in Diabetic Patients with Neuropathy

Authors

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Introduction

Neuropathy is the most common complication and greatest source of morbidity and mortality in diabetes patients. It is estimated that the prevalence of neuropathy in diabetes patients is approximately 25%.¹ In diabetic neuropathy patients other part of neurological system is also affected such as autonomous system, sensory and motor pathways. Auditory Brainstem Response (ABR) audiometry.

First described by Jewett and Williston in 1971. There are seven waves traditionally designated with roman numerals from I to VII. Wave I and II represent activity in cochlear nerve, wave III in cochlear nucleus, wave IV in superior olivary complex, wave V which is biggest and most consistent represent activity in nuclei of lateral lemniscus while wave VI and VII in the inferior colliculus.² Interpretation of the BAEPs usually involves measuring the absolute latency of the three most prominent vertex positive peaks I, III, and V, along with analysis of their relative inter-peak latencies (IPLs), which may provide some anatomical localisation of lesions. Conduction through the eighth nerve and the caudal brainstem is represented by the I to III IPL, while the III to V IPL probably represents transmission through the rostral brainstem and midbrain. Neuropathy is the most frequent late complication of DM. So far

most of the clinical and diagnostic studies on diabetic neuropathy have concerned only peripheral and autonomic nerve but recently with the refinement of evoked potential techniques detailed exploration of sensory pathway in central nervous system has been possible⁷. Brainstem auditory evoked potentials have obtained widespread clinical application in assessing neurologic and audiological problems. ABR audiometry is considered an effective screening tool in the evaluation of suspected retrocochlear pathology. In general, ABR exhibits a sensitivity of over 90% and a specificity of approximately 70-90%⁸ (Schmidt.et al., 2001).

Vitamin C also known as L-ascorbic acid, is a water-soluble vitamin that is naturally present in some foods, added to others, and available as a dietary supplement. Humans, unlike most animals, are unable to synthesize vitamin C endogenously, so it is an essential dietary component. Researcher have shown that vitamin C selectively restores the impaired endothelium-dependent vasodilation in the forearm resistance vessels of patients with insulin-dependent diabetes mellitus. These findings indicate that nitric oxide degradation by oxygen-derived free radicals contributes to abnormal vascular reactivity in humans with insulin-dependent diabetes mellitus.

Scientists have shown that vitamin C is especially significant to diabetic neuropathy because research shows that most diabetics have a lack of Vitamin C as a result of their illness rather than diet. Those suffering from diabetic neuropathy have an elevated level of vitamin C which the body has already used known as reduced Vitamin C. This implies that neuropathy places an extra strain on the body's Vitamin C stores. As a result, it is important for diabetics to get sufficient levels of this vitamin through supplementation or diet.

Aim

To study the effect of vitamin C supplementation on blood glucose and brainstem auditory evoked potential in diabetic patients with neuropathy.

Methodology

A case control study was carried out among diabetic patients visiting Neurology division of a tertiary care centre. Total of 120 cases of vitamin C deficient diabetic patients with poly neuropathy were examined and investigated out of which 60 patients were cases and other 60 patients were control. Group I(Control) comprised of 60 vitamin C deficient diabetic patients with poly neuropathy receiving OHA or Insulin. Group II (Case) comprised of 60 vitamin C deficient diabetic patients with poly neuropathy receiving Vitamin-C (1500mg/daily) orally along with OHA or Insulin. At the entry point of the study, the diabetic patients were given 1500mg of vitamin C daily for 6 months. Serum vitamin C concentration were estimated at 2, 4 and 6 months interval of time. Fasting blood glucose was done at first visit (at 0 weeks) and this was repeated subsequently at 2, 4 and 6 months respectively.

Brainstem Evoked Potential

ABR audiometry refers to an evoked potential generated by a brief click or tone pip transmitted from an acoustic transducer in the form of an insert earphone or headphone. The elicited waveform response is measured by surface electrodes typically placed at the vertex of the

scalp and ear lobes. The amplitude (microvoltage) of the signal is averaged and charted against the time (millisecond), much like an EEG. The waveform peaks are labelled I-VII. These waveforms normally occur within a 10-millisecond time period after a click stimulus presented at high intensities (70-90 dB normal hearing level [nHL])⁴

Recording one cm disc electrodes is filled with conducting jelly or paste are preferred. The electrode impedance should be kept below 5 k Ω s. The active(positive) electrode is typically placed on either the high forehead (Fz) or the vertex of the head (Cz) and the ground electrode on the low forehead, the reference(negative) electrode can be placed over the mastoid process behind the ear. Filter band pass 100-3000 Hz; Standard broadband click stimulation is used on the ear tested; Mono aural stimulation is used; The click intensity should be 60-70 dB above click perception threshold; The contra lateral ear receives masking noise of 30- to 40-dB lesser intensity; The first 10 ms are averaged, and 2-4000 responses may be averaged; At least 2 separate trials should be performed (Leslie et al., 2002).Mainly waves that appear at the human scalp in the first 10 msec after each stimulus (Picton et al.,1974). They are named according to their sequence in roman letters (from I to VII) (Chiappa et al., 1978)⁴⁸.

Parameters measured are:

1. Absolute latency and amplitude,
2. Interpeak latencies(IPL),
3. Amplitude ratio of wave V/I or IV-V complex
4. Inter ear interpeak differences.

Normal value of different waves

For evaluating the level of improvements in the Brainstem Evoked Potential, the type II Diabetic patients with neuropathy were divided into two groups:

Group-I: Control group, were not given any vitamin C supplementation. patients were of

comparable ages were of normal weight for height, on usual diet. Renal and liver function test were normal.

Group-II: The study group, were given 1500 mg/day of vitamin C for 6 months.

BAEP always recorded with the same equipment using the stimulus either in the form of click or tone pip is transmitted to the ear via a transducer placed in the insert ear phone or head phone. Stimulation performed with a 25 x 18 cm screen with black and white checker-board pattern, each square with 1.1 cm sides. . The response evaluate by active electrodes placed on either the high forehead (Fz) or the vertex of the head (Cz) and the ground electrode on the low forehead, the reference(negative) electrode can be placed over the mastoid process behind the ear.

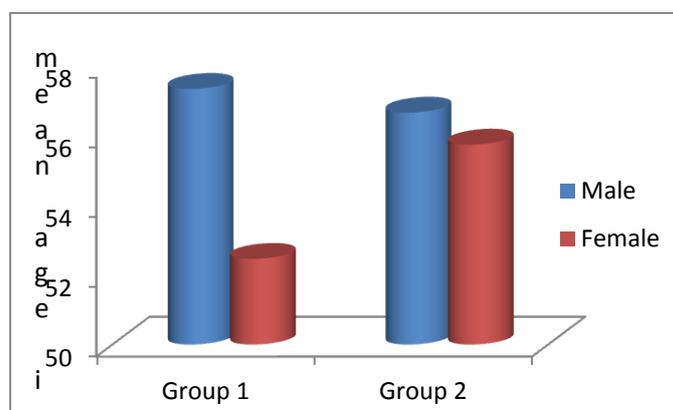
Statistical Analysis

Mean, Standard Deviation (S.D.) were calculated for each parameter. Data before and after administration of vitamin C were compared for

statistical analysis paired “t” test was performed and ‘p’ value were obtained for knowing the significance between different variables.

In Group I, 58.33% of patients belong to the 51-60 age group. 23.33% belongs to 41-50age group and 18.33% belongs to 61-70 age group of patients. No case was found in >70 age group. 9 males and 5 females were in the 41-50 age group. 29 males and 6 females were in 51-60 age group.10 males and 1 female was in 61-70 age group. Out of 60, 48 Males (80.00%) and 12 females (20%) were present in group I.

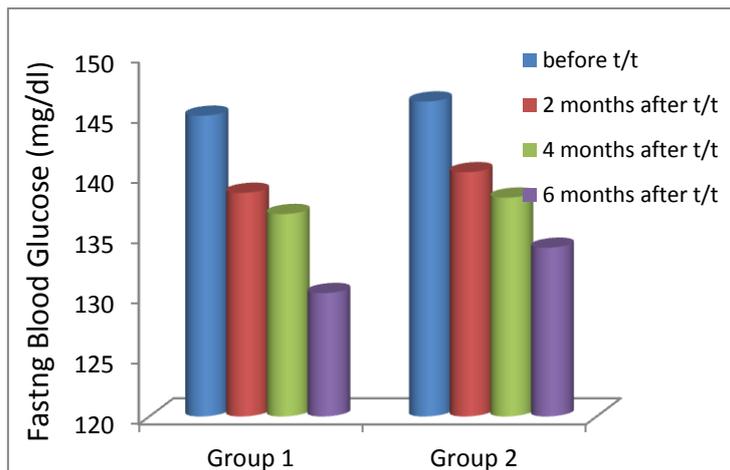
In Group II- 51.6% belongs to 51-60 age group. 31.6% belongs to 41-50 age and 16.6% belongs to 61-70 age group of Diabetic patients. No case was found in >70 age group. 15 males and 4 females were in 41-50 age group. 21 males and 10 females were in 51-60 age group. 9 males and 1 females were in 61-70 age group. Out of 60, 45 males (75%) and 15 females (25%) were present in group II.



	GROUP I (n=60)				GROUP II (n=60)			
	Before treatment	After Treatment			Before treatment	After Treatment		
		2months	4 months	6months		2months	4 months	6months
Mean	0.60	0.62	0.63	0.62	0.63	0.68	0.72	0.86
S.D	+/- 0.051	+/-0.042	+/-0.060	+/- 0.046	+/-0.055	+/-0.047	+/-0.058	+/-0.060
S.E.M	0.010	0.014	0.008	0.013	0.009	0.012	0.01	0.009
% Change Over Baseline	3%				33%			
p Value	>0.05 (I.S)				<0.01 (H.S.)			

S. Vitamin C (mg/dl) Before and After Treatment.

Fasting Blood Glucose before and after treatment:



Latency (ms) of Waves In B.A.E.P of Left Ear before and after Treatment

Wave	Value in (ms) in Study Group (60)				Value in (ms) in Controls group (60)			
	Before treatment	After treatment			Before treatment	After treatment		
		2 months	4 months	6 months		At 1st visit	2 months	4 months
I	1.94±0.10	1.80±0.09	1.70±0.08	1.60±0.12	1.84±0.14	1.88±0.16	1.84±0.17	1.88±0.16
III	4.48±0.20	4.10±0.22	3.90±0.22	3.76±0.16	4.47±0.18	4.42±0.20	4.50±0.16	4.38±1.8
V	6.60±0.25	6.24±0.20	5.82±0.32	5.70±0.30	6.49±0.31	6.50±0.28	6.52±0.29	6.6±0.28
I-III IPL	2.53±0.30	2.34±0.18	2.20±0.24	2.11±0.21	2.56±0.32	2.56±0.29	2.54±0.32	2.61±0.28
III-V IPL	2.36±0.25	2.21±0.34	2.16±0.28	2.10±0.24	2.51±0.25	2.44±0.31	2.46±0.26	2.50±0.29
I-V IPL	4.61±0.30	4.40±0.24	4.23±0.26	4.10±0.24	4.40±0.21	4.53±0.24	4.59±0.25	4.50±0.22

Discussion

Total 120 cases of diabetic neuropathy patients were subdivided into two groups, of 60 patients in each group. Group-I Control group were not given any Vitamin C supplementation. Group-II consists of study population who were given 1500 mg/day vitamin C for 6 months.

Patients were distributed according to different age starting from > 40 years and according to sex. In group I maximum number of patients (n=35) were in 50-60 age years and in group II maximum number of patients (n=31) were in age group 50-60 years. In both group maximum number of patients were in 50-60 years age group.

In group I there were 48 male patients and 12 female patients (M:F ratio 4.0:1) and in group II there were 45 males and 15 females (M:F ratio 3.0:1). In both group males are affected more than females. Similar findings were observed by R Pradeepa & et.al. (2008).

Average age of males was 57.34 + 0.531 years and of females was 52.46+0.561 years in group I. In group II Average age of males was 56.66+0.624 years and of females was 55.74 + 1.587 years.

Mean duration of diabetes in group I was 20.83 ± 0.76 as compared to 22.83±0.83 in group II. Maximum no. of patients in both groups were having duration of diabetes between 11 to 15 years.

In our study, in group I family history of diabetes was present in 62% of cases and in group II family history was present in 54% of cases. Vishwanathan M (1994) found prevalence (62%) of diabetes in families of diabetic patients in Indian population.

Total 120 cases of diabetic neuropathy patients were subdivided into two groups.

Group-I: were not given any vitamin C supplementation.

Group-II: the study population were given 1500 mg of vitamin C per day for 6 months.

Serum vitamin C, Fasting Blood Glucose was measured before and after treatment at 2, 4 and 6 months. Latency of Brainstem Evoked Potential was investigated at above schedule.

The results of the present study are summarized below:

In Group I – 58.33% of patients belong to the 51-60 age group. 23.33% belongs to 41-50 age group and 18.33% belongs to 61-70 age group of patients. No case was found in >70 age group. 9 males and 5 females were in the 41-50 age group. 29 males and 6 females were in 51-60 age group. 10 males and 1 female was in 61-70 age group. Out of 60, 48 Males (80 %) and 12 females (20 %) were present in group I.

In Group II- 51.60 % belongs to 51-60 age group. 31.6% belongs to 41-50 age and 16.6% belongs to 61-70 age group of Diabetic patients. No case was found in >70 age group. 15 males and 4 females were in 41-50 age group. 21 males and 10 females were in 51-60 age group. 9 males and 1 females were in 61-70 age group. Out of 60, 45 males (75%) and 15 females (15%) were present in group II.

In Total- out of 120 diabetic patients 93 were males (77.5%), 27 were females (22.5%)

- In Both Group Patients were distributed according to different age starting from > 40 years and according to sex. In both group maximum number of patients were in 50-60 years age group.
- Average age of males was 57.34 ± 0.531 years and of females was $52.46 \pm .561$ years in group I. In group II Average age of males was 56.66 ± 0.624 years and of females was 55.74 ± 1.587 years. In group I Average age of total male and female were 55.23 ± 0.457 years and in group II were 56.10 ± 0.576 years.
- Mean duration of diabetes in group I was 20.83 ± 0.76 years as compared to 22.83 ± 0.83 years in group II.

In Group I; Mean Baseline value for S. vitamin C (mg/dl) is 0.60 ± 0.051 and after treatment values at 2 months is 0.63 ± 0.060 , 4 months 0.63 ± 0.060 , at 6 months 0.62 ± 0.046 respectively. In this group we observed that difference in S. vitamin C (mg/dl) values before and after 6 months of vitamin C (mg/dl) supplementation was significant (P value >0.05).

In Group II; Mean Baseline value for S. vitamin C (mg/dl) is 0.63 ± 0.055 and after treatment values at 2 months is 0.68 ± 0.047 , 4 months 0.72 ± 0.058 , at 6 months 0.86 ± 0.060 respectively. In this group there was highly significant (P value <0.01) difference in S. vitamin C (mg/dl) between before and after 6 months of treatment.

In present study values for Mean fasting blood glucose level in group I before treatment (i.e. first visit) was 144.96 ± 0.95 mg/dl as compared to 130.24 ± 0.79 mg/dl values of after treatment. This difference was considered Significant between before and after treatment values for fasting blood glucose levels ($p < 0.01$)

In group II values for mean fasting blood glucose level before treatment (i.e., first visit) was 146.14 ± 1.17 mg/dl as compared to 134.00 ± 0.93 mg/dl values of fasting blood glucose after 6 months treatment. This Difference was also considered Significant.

In present study mean value for latency of left ear In group I before treatment (i.e. first visit) Mean value for latency of left ear was wave I: 1.84 ± 0.16 , wave III: 4.47 ± 0.18 , wave V: 6.49 ± 0.31 , wave I-III IPL: 2.56 ± 0.32 , wave III-V IPL: 2.51 ± 0.25 , wave I-V IPL: 4.40 ± 0.21 compared to wave I: 1.88 ± 0.16 , wave III: 4.38 ± 1.8 , wave V: 6.6 ± 0.28 , wave I-III IPL: 2.61 ± 0.28 , wave III-V IPL: 2.5 ± 0.29 , wave I-V IPL: 4.58 ± 0.22 respectively after treatment (i.e after 6 months). This difference was Statistically Insignificant ($p > 0.05$).

In group II before treatment was wave I: 1.94 ± 0.10 , wave III: 4.48 ± 0.20 , wave V: 6.60 ± 0.25 , wave I-III IPL: 2.53 ± 0.30 , wave III-V IPL: 2.36 ± 0.25 , wave I-V IPL: 4.61 ± 0.30 , compared to wave I: 1.60 ± 0.12 , wave

III:3.76±0.16, wave V:5.70±0.30, wave I-III IPL:2.11±0.21, wave III-V IPL: 2.10±0.24, wave I-V IPL:4.10±0.24 respectively after 6 months of treatment. This Difference was considered significant (p<0.01).

In present study mean value for right ear:

In Group I before treatment (i.e. first visit) Mean value for amplitude of right ear was wave I:1.80±0.13 wave III:4.36±0.18 wave V:6.5±0.3 wave I-III IPL:2.5±0.31 wave III-V IPL:2.5±0.29 wave I-V IPL:4.6±0.22 compared to wave I:1.84±0.16 wave III : 4.26±1.7 wave V:6.61±0.29 wave I-III IPL: 2.63±0.29 wave III-V IPL:2.50±0.30 wave I-V IPL: 4.58±0.22 respectively after 6 months of treatment. This difference was Statistically Insignificant (p>0.05).

In Group II before treatment was wave I:1.78±0.13, wave III:4.40±0.22, wave V:6.5±0.33, wave I-III IPL:2.5±0.3, wave III-V IPL:2.38±0.28, wave I-V IPL:4.4±0.38 compared to wave I: 1.61±0.05, wave III:3.75±0.20, wave V: 5.78±0.34, wave I-III IPL:2.1±0.27, wave III-V IPL:2.34±0.22, wave I-V IPL:4.2±0.25 respectively after 6 months of treatment. This Difference was considered significant (p<0.05).

Conclusion

In **Group I** without vitamin C supplementation results of fasting blood glucose level were significant. In **Group II** Effect of vitamin C supplementation on fasting blood glucose were significant. Results for improvement in latency of BAER of both ears were significant in group 2. Results were insignificant in group 1. Vitamin C supplementation helps to improve latency in patients of diabetic neuropathy.

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