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Motor nerve conduction, auditory evoked potential and visual evoked potentials in severely malnourished children vs healthy controls: An electrophysiological study

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Abstract: Severe acute malnutrition (SAM) is a significant public health problem in India and many developing countries. The prevalence of SAM remains at an alarming 7.7% according to the most recent NFHS-5 survey (2019-2021) covering 36 states and union territories (UTs). Malnutrition slows down the myelination process, thus preventing the increase in the caliber of myelinated nerve fibers. This study aimed to assess the effects of severe acute malnutrition on peripheral motor median and ulnar nerve conduction, auditory evoked potential, and visual evoked potential in children. The study group included 50 severely acute malnourished children of 6-59 months of age, recruited from SMTU, J.A. Group of the Hospital, G.R.M.C. Gwalior (M.P.), based on WHO classification for severe acute malnutrition. The control group consisted of 50 normally nourished healthy children of the same age group. Results showed a statistically significant decrease in motor nerve conduction velocity and delayed distal latencies in the median and ulnar motor nerves of both upper limbs in children with severe acute malnutrition. There were also significant differences in the mean latencies of the waves I to V and the mean interpeak latencies (IPLs) of the waves I-III and I-V on the right and left ears between the study and control groups. The study demonstrated significant alterations in mean latencies of wave p 100 in VEP. The present study shows a statistically significant alteration in electrophysiological parameters in children with severe acute malnutrition. This may be due to nutritional deficiency affecting the myelination of peripheral and central nerves, depending on the duration and severity of malnutrition.

Keywords: Severe acute malnutrition; Nerve conduction study; Mid upper arm circumference; Latencies; Auditory evoked potential; Visual evoked potential.

1. Introduction

Children are the world's most valuable resource and they are the foundation of the country. The development of the country can happen only if the children are healthy and fit. We are guilty of many errors and many faults, but our worst crime is abandoning the children, and neglecting the foundation of life. The World Health Organisation (WHO) defines 'severe acute malnutrition (SAM) as very low weight-for-height or a mid-upper arm circumference less than 115 mm, or by the presence of nutritional edema' [1]. Children suffering from SAM are nine times more likely to die in case of diseases due to their weakened immune systems [2,3]. The 2021 global hunger index ranked India 101 out of 135 countries with the serious issue of child wasting. At least one in five children under five years of age in India is wasted [4]. According to NFHS 5, the number of children under 5 years who are stunted (less height-for-age) in India has 35.5% and the number of underweight children (less weight-for-age) has 32.1% [5]. Malnutrition leads to permanent suboptimal physical and mental development resulting in mental retardation [6]. The behaviours and cognitive functions are impaired by malnutrition which is related to an altered emotional response to a stressful event [7].

CNS injuries caused by severe malnutrition can be shown clinically and electrophysiologically [8]. Malnutrition slows the process of myelination, thus preventing the increase in the calibre of myelinated nerve fibres [9]. Subclinical changes in CNS function may not be easily detected with the traditional method of medical assessment [10]. severely malnourished neonates and infants are most susceptible to the phase of exponential brain growth. So there is a need for early recognition and intervention to prevent permanent neurological sequelae. Few studies have individually found affected either nerve conduction study or auditory evoked potential or visual evoked potential in protein energy malnutrition patients. Early onset malnutrition cause more abnormalities in VEP and AEP. These could be due to a defect in myelination that ends in decreased synaptic efficiency in the auditory and visual systems. Malnutrition slows the process of myelination and prevents the increase in the diameter of nerve fibres [10].. Hence with the help of electro-physiologically, we can find the nervous system alteration in severely acutely malnourished children.

A nerve conduction study is a method to evaluate the status of peripheral nerves. Sachdev *et al*., & Kumar *et al.,* observed delayed motor nerve conduction velocities in children with protein energy malnutrition [11]. Brain stem auditory evoked potentials were recorded from ears and vertex in response to a brief auditory stimulus to assess the conduction in the auditory pathway up to the midbrain [12]. Visual evoked potentials are electrical differences recorded from the scalp in response to visual stimuli. The VEPS represent a mass response of cortical and sub-cortical areas. The VEPS consists of a series of waveforms of opposite polarity. The commonly used wavelengths are N-75, P-100 and N-145. The peak latency and peak-to-peak amplitudes of these waves were measured. The VEP can determine abnormalities such as latency prolongation, amplitude, combined latency and amplitude in P-100 wave in the optic pathway especially anterior to optic chiasma.

Due to demyelination delay in the conduction produced by focal demyelination in visual pathways can be detected by VEPS. Today the availability of more sensitive and non-invasive methods like the Nerve conduction study, Brain stem auditory and visual evoked potential to evaluate subtle alteration in CNS function allows us to better correlate SAM with possible early brain alteration.

2. Aims and objective

To Compare Motor Nerve Conduction, Auditory Evoked Potential and Visual Evoked Potential in Severely Acute Malnourished Children and Normal Nourished Children, age group of 6 months to 59 months".

3. Material and methods

This study was conducted in the Post Graduate Laboratory, Department of Physiology, Gajra Raja Medical College Gwalior, Madhya Pradesh. The case-control study was conducted from March 2021 to November 2021. The children were recruited from the severe malnutrition treatment unit (SMTU), at Kamla Raja Hospital, Gwalior. The study group consisted of 50 SAM children, who had severe malnutrition according to IAP and WHO classification. The control group consisted of 50 children with normal height for their age.

Ethical committee approval was obtained from the institution before commencing the study.

The study's aim and nature were explained to the Parents/guardians. Informed written consent was obtained from the Parent/Guardian of the child before the test. A detailed clinical, anthropometry, and neurological examination were done. Nerve conduction Brainstem auditory and visual evoked potential were measured using a four-channel RMS EMG-EP MARK II machine.

Nerve Conduction Study - A computerized 4-channel RMS EMG-EP machine was used in the study. The filter was set at 2HZ and 5KHZ for motor studies. The sweep speed was set at 5ms/division for MNCS. Once centimetre disc recording electrode will use for motor study. The supramaximal stimulus was delivered in order to get an adequate response.

4. Auditory evoked potential

AEPs response w recorded using a surface electrode applied to the ipsilateral earlobe and vertex. The vertex electrode is best placed in the midline anterior to anterior fontanelle and the earlobe electrode may be placed over the mastoid, as the earlobe is very small. The ground electrode was placed in the mid-forehead. It comprises 5 or more waves in the 10 milliseconds of stimulus. Waves- I, II, III, IV and V were considered for our study. We recorded latencies (I, II, III, IV and V) and interpeak latencies (I-III, III-V, I-V). This is usually set about 65 decimals above the hear-in threshold which was delivered by the headphones and the opposite ear masked by white noise AEP is of very low voltage, around 2000 thousand responses were recorded so that AEP can be extracted by averaging from the background noise.

5. Visual evoked potential

Flash VEPs were recorded with a stimulus with a rate of 0.5HZ and 1000ms sweep time. In children above 1 year, we give stimulation at a rate of 1.9HZ and sweep time 500ms and bend pass 1 to 100 HZ. In recording the VEP the active electrode was positioned 1 inch above the inion (oz.), referencing to the centre of the forehead with a ground electrode on the vertex of the head (CZ), in each recording the 100 sweeps averaged. We recorded p-100 latency, amplitude and duration in VEP bilaterally.

6. Inclusion criteria

Severely malnourished children in the age group of 6 - 59 months based on anthropometric measurements like weight for age and height for age according to WHO criteria

7. Exclusion criteria

Genetic, metabolic, and endocrine causes for short stature, eye and ear pathology were excluded from the study. Statical analysis was done by using SPSS version 20. The result was analyzed using an unpaired student "t" test. Values were expressed as mean with standard deviation. The control group was compared with severely malnourished children. P-value < 0.05 was considered statistically significant

8. Procedure

The aim and procedure of the test were explained to the subject and Parents/guardians. A complete examination of the external ears was done. To achieve complete relaxation hypnotic chloral hydrate 50 mg /kg was used in children above 18 months. The subject was asked to avoid applying hair oil after the last head bath. Skin preparation was done by gently abrading and degreasing before applying electrodes. Electrodes were placed according to the 10- 20 international system of EEG electrode placement.

9. Results

We included 20 (40.0%) females and 30 (60.0%) males as a case in our study, with the same distribution in control. (Table 1) showed the anthropometrical values of SAM were significantly different from the control. Tables 2 and 3 depict that Mean distal latency and velocities of the median and ulnar nerve were significantly reduced in children with severe acute malnutrition($p < 0.01$). There was no significant change in the amplitudes of both group.

The mean and the standard deviations of absolute peak latency and interpeak latency in milliseconds of AEPs in the study and control groups are shown in (Table 4). A significant prolongation of absolute peak latencies in I, II, and IV, and I, III, and IV were seen in the Left and Right ears respectively. There were significant differences in the mean of interpeak latencies (IPLs) of the waves I-III and I-V on the right ear between the study and control groups ($P < 0.05$). There was no statistically significant difference in IPLs of the left ear.

(Table 5) depicted the mean value of the latencies of N75 were almost the same in SAM and normally nourished children, the mean value of P100 was found statistically significant with a p-value<0.05, and N145 is not observed as statistically significant.

Table 1. Distribution of participants according to Age & Gender

Age Group (In years)	Severely acute malnourished (SAM) (N=50)		Normal (N=50) N (%)		(χ^2p-value)
	Male (30) n (%)	Female (20) n (%)	Male (32) n (%)	Female (18) n (%)	
<1.5	7 (14.0)	5 (10.0)	7 (14.0)	4(8.0)	0.53 (df=9) (0.99) Not Significant
1.5-3	10 (20.0)	6(12.0)	11 (22.0)	6(12.0)	
3-4	7 (14.0)	5(10.0)	9 (18.0)	5(10.0)	
>4	6 (12.0)	4(8.0)	5 (10.0)	3(6.0)	
Mean Age (SD)	2.73±1.30		2.83±1.23		

Table 2. Comparison of Median motor nerve conduction parameters in case and control

Median motor nerve conduction parameters		Severe acute malnourished Mean ± SD	Normal Mean ± SD	t (p) value
Latency(msec)	L	3.27±1.7	2.19±0.7	4.26 (0.01*)
	R	2.66±0.9	1.85±0.6	5.50 (0.01*)
Amplitude(mv)	L	3.68±2.1	4.34±2.0	-1.60 (0.122)
	R	3.91±2.3	4.60±1.9	-1.61 (0.11)
Velocity(m/s)	L	34.31±12.3	47.70±18.3	-4.29 (0.01*)
	R	34.39±16.7	42.10±14.6	-2.46 (0.01*)

* Significant Statistically (L=Left, R-Right, msec=Mili second, mv-Mili Volt, m/s = Meter per second)

Table 3. Comparison of Ulnar motor nerve parameters in case and control

Ulnar motor nerve conduction parameters		Severe acute malnourished Mean ± SD	Normal nourished Mean ± SD	t (p) value
Latency (msec)	L	2.52±0.3	2.29±0.4	2.90 (0.005*)
	R	2.42±0.3	2.18±0.4	3.223 (0.002*)
Amplitude (mv)	L	3.51±0.9	4.14±1.1	-3.047 (0.003*)
	R	3.45±1.2	3.95±1.1	-2.196 (0.030*)
Velocity (m/s)	L	35.96±5.8	39.96±3.2	-4.281 (0.01*)
	R	39.49±8.5	44.54±5.9	-3.433 (0.001*)

* Significant Statistically

Table 4. Comparison of auditory evoked potentials and mean latencies in malnourished case and control

Auditory Evoked Potential (AEP) in msec	Site of Ear	Severely acute malnourished (Case-SAM) Mean ± SD	Normal (Control) Mean ± SD	t test value (p)
Wave I	L	1.68±0.35	1.52±0.39	2.1 (0.036*)
	R	1.79±0.22	1.582±0.401	3.2 (0.002*)
Wave II	L	2.78±0.47	2.56±0.42	2.40 (0.018*)
	R	2.74±0.42	2.70±0.20	0.54 (0.58)
Wave III	L	3.47±0.54	3.44±0.42	0.27 (0.79)
	R	3.84±0.52	3.59±0.22	3.10 (0.003*)
Wave IV	L	4.97±0.59	4.73±0.62	1.98 (0.05*)
	R	5.03±0.64	4.79±0.34	2.28 (.0.02*)
Wave V	L	5.71±0.54	5.59±0.52	1.18 (0.24)
	R	5.73±0.54	5.72±0.32	0.15 (0.88)
IPL I-III	L	1.79±0.70	1.93±0.45	-1.069 (0.29)
	R	1.99±0.57	1.77±0.43	2.13 (0.03*)
IPL III-V	L	2.24±0.76	2.14±0.64	0.72 (0.47)
	R	2.16±0.73	2.156±0.51	0.04 (0.96)
IPL I-V	L	4.04±0.57	4.07±0.55	-0.28 (0.78)

Table 5. Comparison of Visual Evoked Potentials in Case and Control

Visual Evoked Potential (VEP)	Site of eye	SAM Mean ± SD	Normal nourished Mean ± SD	t test value (p)
N 75	L	69.879±9.208	69.054±4.543	0.569(0.571)
	R	66.458±4.509	65.827±8.023	0.485(0.629)
P 100	L	103.71±4.902	100.848±8.509	2.063(0.042)
	R	103.014±3.991	99.483±7.366	2.980(0.004)
N 145	L	145.449±9.604	140.843±9.3977	2.424(0.017)
	R	143.533±12.005	140.330±11.712	1.381(0.170)
Amplitude	L	5.023±2.017	5.007±1.290	0.047(0.963)
	R	5.273±3.020	4.802±1.525	0.985(0.327)

10. Discussion

Maturation of the peripheral nervous system in the form of myelination begins during the fourth month of fetal life and it is complete at around 5 years of age [13].

This study has shown significant alteration in the electrophysiological parameters in the Nerve conduction study, Brainstem Auditory Evoked Potential, and Visual evoked potential in children with severe acute malnutrition. Motor nerve conduction velocities were significantly reduced in children with SAM. There was a statistically significant difference in distal latencies and velocities of the median and ulnar motor nerve between SAM patients and controls. The amplitude of these nerves were higher in control in comparison to SAM but could not establish the significance statistically.

Ghosh S *et al.*, [14] They reported a significant reduction in motor nerve conduction velocity in children with severe PEM and ongoing long-term malnutrition. Osuntokun BO [15] reported that motor nerve conduction velocity decreased to the greatest extent in the more severe cases of PEM. Similarly, Sachdeva, Taori, and Pereira [16] reported delayed nerve conduction velocities in 12 kwashiorkor children between the ages of one to four years.

In the present study, AEP Recordings of absolute peak latencies of waves I, II, III, and IV, V and Interpeak latency of I - III, III - V in SAM were significantly prolonged but could not establish statistically significant results in both ears when compared to the normal nourished group. Vandana and Tandon OP [17] measured auditory evoked potential responses in 20 chronic malnourished children of 3 - 6 years of age and found that there is significant prolongation in peak latencies of waves I, II, III, IV. Interpeak latencies of I - III and III - V were also prolonged as malnutrition affects the peripheral developmental process of auditory pathways in the brainstem. Odabas *et al.*, [18] found an increase in the absolute latencies of wave I-V and interpeak latency I-V and III-V indicating the involvement of peripheral as well as central pathways in malnourished children Miller, (2013) assessed visual evoked potentials (VEP) and detected PEM-related morphological brain changes via MRI. The mean value of the latencies of N75 were almost the same in SAM and normally nourished children, the mean value of P100 was found statistically significant with a p-value<0.05, and N145 is not observed as statistically significant. This present study's finding is the opposite of Durmaz *et al.*, (1999), who found no difference between malnourished infants and controls concerning a component of comparable latency to P2. P2 is the most consistent component of the fVEP, particularly in young infants, and by 100 days of age, its latency is similar to that of the P2 of adults (Benavente *et al.*, 2005).

Aspects of brain development, such as dendrite arborization and synaptogenesis other than myelination, can explain the prolongation of latencies in BAEP rather than fVEP, as in our present study. Very rare or no data is available about VEP in malnourished children. The fVEP latencies of wave IV (N2) were not significantly different between the two groups, although they showed the tendency of prolongation in all patients, which was more pronounced in the SAM group. As a result, we can conclude that severe malnutrition with low protein levels causes prolonged BAEP and partially prolonged VEP. Further studies must be carried out to show the reversibility of this detected deterioration and also to confirm clinical improvement according to the treatment regimens. This may help predict the prognosis of such patients with PEM.

11. Conclusion

In the present study, NCS, and AEP appeared more sensitive and early indicators of these changes than VEP. The findings suggest that electrophysiological abnormalities depend on the duration and severity of malnutrition. So these electrophysiological tests can be used to detect malnutrition at its early stage. Nutritional deficiency during the development of the brain has a long-lasting effect on learning abilities, and psychomotor development, But whether it is reversible or irreversible after nutritional rehabilitation needs to be evaluated.

With the help of advanced electrophysiological methods, the need for screening, early diagnosis, health education, and initiating nutritional support at the appropriate time will help the children to improve their academic performance and to become successful achievers in the future. It is concluded that further studies are needed to substantiate these changes, especially in a large number of patients with various duration of malnutrition. These changes in our group of subjects support our hypothesis and need further confirmation in patients with a longer duration of disease.

12. The limitations of the current literature

The relatively small number of participants and lack of follow-up to severe acute malnourished subjects after discharge. Larger multi-centre studies and longer follow up are necessary to seek deeper into the detailed impact of malnutrition along with its connecting neuronal pathways with the exploration of other possible involved mediators. The weight-for-age diagnostic criteria used to determine the severity of malnutrition might not accurately reflect the severity of malnourishment. We did not know the presence or extent of all comorbid conditions or the effect of medications or environmental influences. We were also limited in our ability to fully explore the role of systemic infections.

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