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Study of Median Nerve Somatosensory Evoked Potentials in Severe Traumatic Brain Injury

[1]Swapna Patil and [2]Raji Thomas

[1]Department of PMR, Mahadevappa Rampure Medical College, Kalaburagi, India

[2]Department of PMR, Christian Medical College, Vellore, India

ABSTRACT

Patients with TBI can have a spectrum of physical disabilities with varying severity, depending on the structures or connections damaged and the severity. It is important to provide the clinical outcome after TBI. We are studying Median nerve Somatosensory Evoked Potentials in acute and subacute phases after TBI to predict clinical outcome in the recovery after TBI. To study Median nerve Somatosensory Evoked Potentials in patients with Traumatic Brain Injury within 1 month and at 3 months after the traumatic event. The study was conducted in the Department of Physical Medicine and Rehabilitation of Christian Medical College, Vellore. The study was approved by the Institutional Review Board of the Institution. Twenty one patients, 16 males (76.2%) and 5 females (23.8%) were included in the study. The mean age of the patients was 33.4 years (range: 9 years to 60 years). The mean duration of trauma was 19.33 days (range: 6-30 days, SD: 6.12). 10 patients had grade I, 8 patients had grade II and 3 patients had grade III initial Median SSEPs. 3 months after TBI, 11 patients had grade I, 6 patients had grade II and 4 patients had grade III Median SSEPs. Of the 8 patients with grade II initial SSEPs the second SSEP was grade I in two patients, grade III in one patient and grade II in 5 patients. Of the 3 patients with grade III initial SSEP, second SSEP was grade III in 2 patients whereas in 1 patient the SSEP improved to grade II. Median SSEPs improved in 27% and worsened in 11% patients. Median SSEPs with in one month of the traumatic brain injury co-relate significantly with short term outcomes (DRS, RLA, MBI, GOS and MMSE) 3 months after the injury($p<0.005$). Median SSEPs at 3 months also had statistically significant co-relation with outcomes (DRS, RLA, MBI-$p<0.005$).

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Key Words

Median nerve, somatosensory evoked potentials, severe traumatic brain injury

Corresponding Author

Swapna Patil,
Department of PMR, Mahadevappa Rampure Medical College, Kalaburagi, India
drswapnapatil@gmail.com

Author Designation

[1]Assistant Professor
[2]Professor

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INTRODUCTION

Traumatic Brain injury is one of the commonest causes of morbidity and mortality worldwide. Patients are left with varying degrees of physical, cognitive and behavioural sequelae. Outcomes after traumatic brain injury vary from vegetative state to mild/no disability[1]. A frequent question asked by the family members of a patient in vegetative state or minimally conscious state following traumatic brain injury is when the patient will recover to a state of consciousness. Prognostication is essential for counselling the family members about the possible outcomes and for planning rehabilitation measures. There are various methods of predicting prognosis in these patients[2].

The prognostic factors or models used for assessment have their own merits and demerits. Glasgow Coma Scale is commonly used as a predictor, however it can be affected by sedation, paralytic agents, or intoxication. Electrophysiological studies including Electroencephalography, Somatosensory Evoked Potentials, Brain stem Auditory Evoked Response and Event Related Potentials are useful for assessment of conscious level and for prognostication as they are not dependant on neurobehavioral responses and are not influenced by sedation or other medications used in treatment of Traumatic Brain injury. Hence this study was conducted to study Median nerve Somatosensory Evoked Potentials in patients with Traumatic Brain Injury within 1 month and at 3 months after the traumatic event.

MATERIALS AND METHODS

The study was conducted in the Department of Physical Medicine and Rehabilitation of Christian Medical College, Vellore. The study was approved by the Institutional Review Board of the Institution.

Inclusion Criteria: twenty one patients with Traumatic brain injury (TBI) of less than one month duration seen in the Department of Physical Medicine and Rehabilitation of Christian Medical College, Vellore Duration of study was one and half year. Patients seen as outpatients in Brain Injury Clinic and those admitted for neurorehabilitation were included in the study after obtaining informed consent.

Exclusion Criteria:

- Patients with
- Neurological impairment before head trauma and peripheral neuropathy
- Focal lesions preventing the impulse from reaching the cortex
- Subdural or extradural collections which impede the recording of the cortical response were excluded from the study

MATERIALS AND METHODS

Neurological examination was done in all patients, which included Glasgow Coma scale, speech, cranial nerve, motor, sensory, cerebellar functions and gait assessment.

Outcomes Measures: Cognitive functions were assessed using:

- Mini-Mental Status Exam (MMSE)
- Rancho Los Amigos scale (RLA)

MMSE allows objective assessment of mental status. MMSE assess orientation to time and place, memory, attention, ability to name objects, follow verbal and written commands, write a sentence spontaneously and copy a complex figure. Scores range from 0-30. Rancho Los Amigos scale defines eight levels of cognitive functioning from “no response “to“ purposeful and appropriate.” It helps to identify the type of injury, severity, and cognitive functioning. Functional status and disability were assessed using:

- Modified Barthel Index (MBI)
- Disability Rating Scale (DRS)

Modified Barthel Index establishes the degree of independence of the patient during his routine activities. Scores range from 0 to 100[3]. Disability Rating Scale uses a continuous 30 point scale. It reflects change in arousal and awareness and in the cognitive functional and psychosocial areas. DRS scores have been correlated with 10 clinical levels of disability.

Glasgow Outcome Scale: (GOS) was used for overall assessment. GOS is one of the most widely used outcome scales. GOS is a five level classification scale. Glasgow Outcome Scale Extended (GOS-E) is a modification of the GOS. It has eight categories of outcomes, including dead, vegetative state, lower severe disability, upper severe disability, lower moderate disability, upper moderate disability, lower good recovery, and upper good recovery[4].

SSEP recording: Median nerve was stimulated using surface electrodes.

Stimulus Intensity and Rate: Monophasic square pulses of 0.2 milliseconds duration and 25 mA in intensity were given at 3Hz frequency.

Recording Parameters: Recording electrode impedances was kept below 5,000 ohms. Ground electrode was placed on the stimulated limb, proximal to the stimulation site. Recording amplifier filters were set at 30-3,000 Hz. Signal averaging with 500 stimulus trials was done.

Electrode Locations: SSEPs were recorded using standard EEG electrodes. Scalp electrode sites were determined using the international 10-20 system. Three channel recording was done for both Median. Electrode CP3 was placed midway between C3 and P3, and CP4 was midway between C4 and P4. CPi denotes ipsilateral and CPc contralateral CP3 or CP4, in relation to the limb being stimulated. CPz is placed midway between Cz and Pz. During median SSEP studies, electrodes were placed over Erbs point and cervical spine (C7) (E1 and E2 respectively).

Median SSEPs:

Stimulus Location: Median nerve is stimulated at the wrist with anode placed just proximal to the palmar crease and cathode between the tendons of Palmaris longus muscle, 3 cm proximal to the anode.

Montages/channels used for Median SSEPs:

- Channel 1: FPz-E1
- Channel 2: FPz-E2
- Channel 3: FPz-CP3 or CP4
- Channel 1 recorded the Erb's point potentials (EP). Channel 2 recorded the cervical potentials (N11 and N13). Channel 3 recorded subcortical far field potentials (N17) and near field cortical potentials (N22)

Recording of the waveforms: Evoked potential waveforms were named by the polarity of their peak (N or P to indicate negative or positive) and the time to maximal amplitude in milliseconds after stimulation. Wave forms were analysed for peak latencies and interpeak latencies. For median SSEPs, peak latencies of EP, N11, N13, N17 and N22 waveforms were measured. Interpeak latencies for EP to N13, N13 to N17 and EP to N17 were measured (Fig. 1 and 2). Patients were assessed clinically using the scales included in the study. SSEP studies were done first within one month of the event and then 3 months after the event. Outcome measures were obtained at 3 months as well.

Statistical Methods: Descriptive statistics, including mean, standard deviation and range were done for continuous data. Univariate analysis of the data for SSEP and outcome scales was done for correlation using chi square test. $p>0.05$ was considered as significant.

RESULTS

Twenty one patients, 16 males (76.2%) and 5 females (23.8%) were included in the study. The mean age of the patients was 33.4 years (range: 9 years to 60 years). The mean duration of trauma was 19.33 days (range: 6-30 days, SD: 6.12). At initial assessment of GCS score, as many of the patients were on tracheostomy, only motor and visual components were analysed and the verbal component being non-numerical (Vt). The mean of combined visual and motor components of GCS at entry into the study was 7.90 (range: 6 to 9, SD: 0.77). There were 12 patients with GCS 8, 4 patients each with GCS 7 and GCS 9 and one patient with GCS 6.

The mean RLA score at initial assessment was 3.1 (SD: 0.63), with range of 2-4. The DRS score at initial assessment was 21.76 (SD: 1.95), with range of 16 to 24. MMSE and MBI could not be assessed at initial assessment due to low level of sensorium. On categorising the patients further, according to DRS, of the total 21 patients, 14 patients were in vegetative state and 7 were in severe disability state. According to RLA grading, 16 patients were in stage 3 or less that is, either generalised or localised response to external stimuli. The remaining 5 patients were in RLA stage 4 that is confused agitated state (Table 1).

Somatosensory Evoked Potentials: Median SSEP studies was done initially and after 3 months.

According to grading of SSEPs, 10 patients had grade I, 8 patients had grade 2 and 3 patients had grade 3 initial Median SSEPs. (Table 2) 3 months after TBI, 11 patients had grade I, 6 patients had grade II and 4 patients had grade III Median SSEPs.

Changes in SSEPs Over Time:

Median SSEPs: Of the 10 patients with grade 1 SSEPs, 3 months later, nine patients continued to have grade 1 SSEP, whereas SSEP of 1 patient worsened to grade 3 (However the patient who worsened from grade 1 to grade 3, clinically improved from RLA stage 3-7 and DRS from 22-15) (Table 3).

Of the 8 patients with grade 2 initial SSEPs the second SSEP was grade I in two patients, grade 3 in one patient and grade 2 in 5 patients. Of the 3 patients with grade III initial SSEP, second SSEP was grade III in 2 patients whereas in 1 patient the SSEP improved to grade 2 (Table 4). Median SSEPs of grade 1 and 2, two patients worsened to lower grades (11%).

Clinical Outcome Scales Assessed 3 Months After Injury: Three months after the event, assessments were repeated using the clinical outcome scales. The mean MMSE was 18.81 (SD: 9.73), range being 0-30. The mean RLA score was 7.05 (SD: 1.66), with the range of 3-8. The mean MBI score was 72.1 (SD: 33.96), with a range of 0 to 100. The mean DRS score was 5.57 (SD: 7.33), with a range of 0-23 (Table 5 and 6).

Comparison of Grades of SSEPs and Clinical Outcomes: The initial Median SSEPs was co-related with outcomes at 3 months.

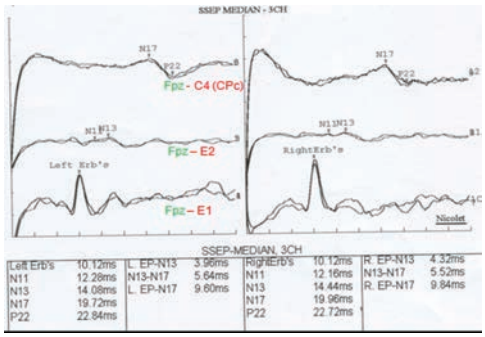

Fig. 1: Median SSEP recording

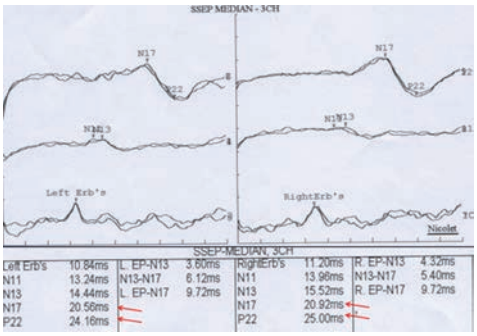

Fig. 2: Median SSEPs recording showing bilaterally prolonged latencies

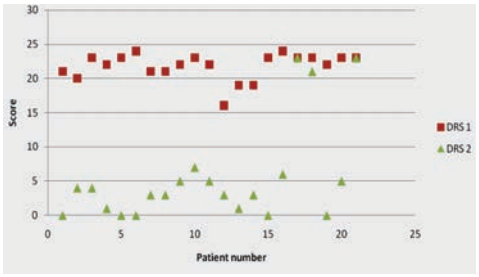

Fig. 3: DRS scores at initial assessment and at 3 months for each patient

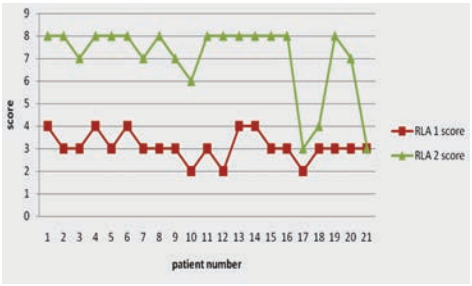

Fig. 4: RLA scores at initial assessment and at 3 months for each patient

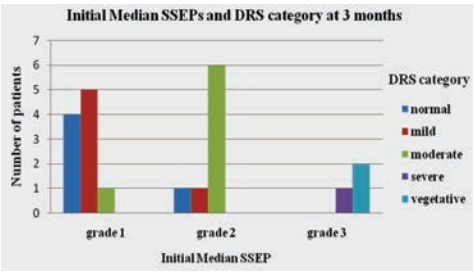

Fig. 5: Initial Median SSEP grades and DRS category at 3 months

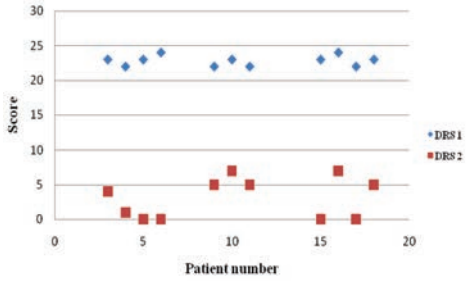

Fig. 6: Comparison of improvement in DRS scores at initial assessment and after 3 months for patients in grade 1 and 2 initial median SSEPs for patients who were in vegetative state

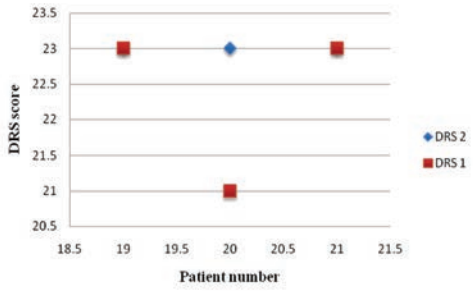

Fig. 7: Comparison of improvement in DRS scores at initial assessment and after 3 months for patients in grade 3 initial median SSEPs for patients who were in vegetative state

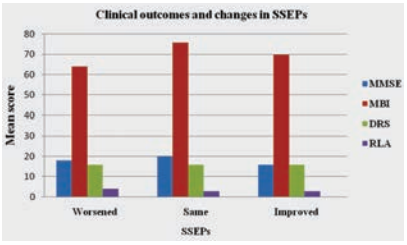

Fig. 8: Differences in clinical outcomes in patients with improvement, worsening or no change of SSEP grades

Table 1: Initial and 3 month median and tibial SSEPs

Median SSEPs	Initial	3 months
Absent on both sides	3 (14.3%)	4(19%)
Absent on one side and normal on other side	2 (9.5%)	1 (4.8)
Absent one side and prolonged on other side	2 (9.5%)	-
Prolonged on one side and normal on other side	1 (4.8%)	2(9.5%)
Prolonged on both sides	3 (14.3%)	3 (14.3%)
Normal	10 (47.6%)	11 (52.4%)

Table 2: Number of patients in each grade of SSEPs

	No. of patients	
Median SSEPs	Initial	At 3 months
Normal (grade 1)	10	11
Impaired (grade 2)	8	6
Absent (grade 3)	3	4

Table 4: Changes in Median SSEPs over time

	Second Median SSEP-No of patients			
First Median SSEP-No of patients	Grade I	Grade II	Grade III	Total
Grade I	9	0	1	10
Grade II	2	5	1	8
Grade III	0	1	2	3
Total	11	6	4	21

Table 6: Clinical outcome scales 3 months after injury

Parameter	Mean (SD)	Range
Mini Mental Status examination score	18. 81 (9.73)	0-30
Rancho Los Amigos score	7.05 (1.66)	3-8
Modified Barthel Index score	72.1 (33.96)	0-100
Disability Rating Score	5.57 (7.33)	0-23

Table 7: Grades of initial Median SSEPs and clinical outcomes

	RLA (1)	DRS (1)	MMSE (2)	RLA (2)	MBI (2)	DRS (2)
Grade I	3.30	21.10	24.20	7.80	91.80	1.80
Grade II	3.00	22.12	19.12	7.50	74.50	4.00
Grade III	2.67	23.00	-	3.33	-	22.33
Kruskal wallis test	2.73	3.67	9.78	10.23	9.96	10.85
Sig	.25	.16	.008	.006	.007	.004

Table 8: Grades of second Median SSEPs and clinical outcomes

	RLA (1)	DRS (1)	MMSE (2)	RLA (2)	MBI(2)	DRS (2)
Grade I	3.36	21.09	23.82	7.91	92.18	1.82
Grade II	2.83	22.83	14.83	6.50	58.50	7.33
Grade III	2.75	22.00	11.00	5.50	37.25	13.25
Kruskal wallis test	4.51	3.21	3.12	6.27	5.35	9.024
Sig	.104	.201	.077	.012	.021	.011

Table 9: SSEPs grades and clinical outcome based on GOS at 3 months

	Glasgow outcome scale			
	Favourable	Unfavourable	Pearson chi square value (sig)	Likelihood ratio (sig)
First Median SSEPs				
Grade I	9	1	15.16 (0.001)	13.94 (0.011)
Grade II	8	0		
Grade III	0	3		
Second Median SSEPs				
Grade I	9	2	3.21 (0.20)	2.79 (0.24)
Grade II	5	1		
Grade III	2	2		
Grade II	5	1		
Grade III	7	4		

Table 10: RLA difference and initial median SSEP grades

Initial Median SSEPs/mean RLA scores	RLA (2)	RLA (1)	Difference	Wilconxon signed ranks test value (significance)
Grade I	7.67	2.83	4.83	-2.23(0.026)
Grade II	7.43	2.86	4.57	-2.42 (0.015)
Grade III	3.33	2.67	0.67	-1.41 (0.15)

Initial Median SSEPs and Clinical Outcomes: Patients with initial Median SSEPs in all the 3 grades were all initially either in vegetative state or severely disabled state according to DRS and they were having generalised/localised responses or were in confused agitated state according to RLA grading. SSEP grades did not co-relate with initial RLA/DRS scores. However a significant co-relation was seen with outcomes at 3 months. Patients with grade 1 and 2 Median SSEPs at initial assessment, improved over time as indicated by the improvement in the RLA, MBI and DRS scores at 3 months, whereas patients with grade III SSEPs initially did not improve to the same extent. This was statistically significant for changes in MMSE (p-0.008), RLA (p-0.006), MBI (p-0.007) and DRS scores (p-0.004) (Table 7).

Median SSEPs at 3 Months After TBI and Clinical Outcomes: Similarly, patients with grade 1 and 2 Median SSEPs at 3 months had better RLA, MBI and DRS scores than those patients who had grade 3 SSEPs at 3 months and this was statistically significant for RLA (p-0.012),MBI (p-0.021) and DRS(p-0.011) (Table 8).

SSEPs and GOS: Three months after the event, based on the Glasgow outcome scale (GOS), 10 patients (47.6%) had good recovery, 7 (33.4%) had moderate recovery, one patient had severe disability (4.8%) and 3 (14.3%) were in vegetative state. Using GOS patients were categorised into favourable and unfavourable outcome groups. Favourable outcome includes the categories of moderate disability and good recovery. Unfavourable outcome includes the categories of death, vegetative state and severe disability.

17 out of 18 patients with grade 1 and 2 initial Median SSEPs had favourable outcome on GOS whereas as all the 3 patients with grade 3 initial Median SSEPs had unfavourable outcome and this difference in outcome was statistically significant (p-0.001). There was no co-relation between Median SSEPs 3 months after the TBI and the outcome based on GOS (Table 9).

Analysis of subgroup of patients in vegetative state (based on DRS): There were 14 patients in vegetative state at initial assessment based on DRS scores. Among these patients, Initial Median SSEPs were grade I in 5, grade 2 in 6 and grade 3 in 3 patients. Of the 3 patients with initial grade 3 Median SSEP, 2 patients continued to be in vegetative state while the third patient was left with severe disability. Patients who had initial Median SSEPs of grade 1 or 2, emerged into higher grades on DRS, 4 patients became normal and 7 had mild to moderate disability (Table 10).

Further the difference in the mean DRS scores in this group at the two different time intervals was 19.82 for patients with initial Median SSEPs of grade 1 and 2 and 0.67 for patients with initial Median SSEPs of grade 3. This was statistically significant (p-0.003) for patients with either grade 1 or grade 2 initial Median SSEPs (Fig. 1-5).

Analysis of Subgroup of Patients with Low RLA Scores (i.e. 3 or Less): There were 16 patients with initial RLA score 3 or less i.e, those with localised or generalised response to stimulus. Among these patients, of the 13 with Grade 1 or 2 SSEPs, 10 improved to normal (RLA score 8) functioning and 3 improved to a state of automatic appropriate response (RLA score 7). Of the 3 patients with grade 3 initial SSEPs, 2 remained in the same stage (RLA 3 or less) and one improved to confused agitated state (RLA score 4).

Further the difference in the RLA scores in this group at the two different time intervals was 4.83 for patients with initial Median SSEPs of grade 1, 4.57 for patients with initial Median SSEPs of grade 2 and 0.67 for patients with initial Median SSEPs of grade 3. The improvement was statistically significant for grade 1 and 2 initial Median SSEP ($p<0.05$) (Fig. 6 and 8).

SSEPs Changes Over Time and Co-Relation with Outcomes: There was no significant correlation between the changes in Median SSEPs after 3 months with the clinical improvement. In median SSEP, 16 patients continued to have the same grade of SSEP, 3 patients improved to better grade and 2 patients worsened in terms of SSEP grade. There was no statistically significant difference in change in outcome between these 3 categories of patients.

DISCUSSIONS

In our patients, SSEPs abnormalities evolved after traumatic brain injury during the study period. Three out of 11 patients with grade 2 or 3 initial Median SSEPs, improved to better grades after 3 months whereas 2 out of 18 patients with initial grade 1 or 2 Median SSEPs worsened to lower grades after 3 months. There was no significant co-relation between the changes in the SSEP grades and the clinical outcome, as only the initial SSEPs had strong co-relation with the clinical findings at 3 months after TBI. This is similar to the findings in two other studies by Claassen and Hansen and Mazzini *et al*.[5] where the SSEPs evolved over the study period and these changes were heterogeneous and did not have strong co-relation with the final outcomes assessed[6].

The initial Median SSEP grades co-related with the clinical outcomes assessed at 3 months after the TBI. Patients with grade 1 and 2 SSEPs had good outcome with improvement in the MMSE, RLA, MBI and DRS scores which were significant ($p<0.005$). The initial median SSEP grades also co-related with GOS at 3 months, with patients with grade I and II SSEPs, having favourable outcome ($p<0.004$). The Median SSEPs done 3 months after the TBI also co-related with clinical outcomes assessed at 3 months but only for RLA and MBI. Initial Tibial SSEPs co-related with MMSE and 3 month Tibial SSEPs co-related with MBI. Eleven patients in Vegetative state (based on DRS scores) with initial Median SSEPs of grade 1 and 2, improved to higher levels of consciousness, while 3 patients in vegetative state with grade III SSEPs remained in the vegetative state or with severe disability. There was also significant difference in the DRS score at initial assessment and at 3 months after the TBI in the group with initial median SSEP of either grade 1 or 2 (p-0.03). At initial assessment, of the 16 patients with

generalized or localized response on RLA grading, only those with initial Median SSEPs of grade 1 and 2 improved to higher levels at 3 months, whereas those with SSEPs of grade III remained at the same level. The difference in the outcomes according to RLA score of patients with initial Median SSEP grades of I and II was significant ($p<0.05$).

Thus initial SSEPs reliably predicted the short term outcome at 3 months. Patients with normal or abnormal SSEPs abnormalities had good short term outcome, while those with bilateral absent SSEPs had poor outcome. This is similar to the other studies where SSEPs were noted to have good co-relation with clinical outcome after TBI[7-9]. This result is clinically very significant in that early SSEPs can help to predict if the patient will emerge out of vegetative state. This predictive value of SSEPs in prognostication after TBI can be useful in the setting where results from other modalities could be affected by patient or environmental factors.

In our study, Median SSEPs co-related with clinical outcomes. This was in contrast to a similar study by Mazzini *et al*.[6] where lower limbs SSEPs were better than upper limbs SSEPs for predicting outcome. Initial Median SSEPs done within one month after the TBI had better correlation with short term (at 3 months) outcome measures than the SSEPs done at 3 months after the TBI, especially the Median SSEPs. In the study by Houlden *et al*.[8] SSEP grades on days 1, 3, and 7 co-related significantly with Glasgow Outcome Scale and Barthel scores and of them, day 3 SSEP corelated better than others. Other studies also have noted that early SSEPs are better predictors of outcome after TBI than SSEPs studies done later.

CONCLUSION

Median SSEPs improved in 27% and worsened in 11% patients. Median SSEPs with in one month of the traumatic brain injury co-relate significantly with short term outcomes (DRS, RLA, MBI, GOS and MMSE) 3 months after the injury($p<0.005$). Median SSEPs at 3 months also had statistically significant co-relation with outcomes (DRS, RLA, MBI-$p<0.005$). In patients with vegetative state at initial assessment, normal or impaired SSEPs predicted good outcome or emergence to higher levels of consciousness at 3 months, Changes in SSEPs over time do not co-relate with the change in outcomes. In addition to clinical examination and neuroimaging, SSEPs can be useful for prognostication after TBI. This is especially true in the acute phase when clinical examination which depends on neurobehavioral responses can be confounded due to sedative medications, metabolic abnormalities or other physical disabilities.

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