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Original Article

Correlation between cerebral co-oximetry (rSO₂) and outcomes in traumatic brain injury cases: A prospective, observational study

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ABSTRACT

Background: Traumatic brain injury (TBI) is known to be an important reason for the increase in disabilities and deaths worldwide. Studies have demonstrated that brain tissue oxygen (PO₂) monitoring reduces mortality significantly but is a invasive method of monitoring. Therefore, there is a need to monitor cerebral ischemia in TBI by noninvasive methods. The study aims to correlate cerebral co-oximetry and possible outcomes in patients with TBI.

Methods: The study included 78 patients with TBI admitted in intensive care unit (ICU) with glasgow coma scale (GCS) of 8 or less than 8. Near-infrared spectroscopy monitor is applied to the patients immediately after admission to ICU; readings are noted every 4 hours up to first 48 hours, and outcomes studied as survival or neurological deficit are noted at 28 days.

Results: A total of 12 (15.4%) deaths were seen in this study. Survived patients were further divided into good recovery 33 (42.3%), moderate disability 21(26.9%), major disability 8 (10.3%), and persistent vegetative state 4 (5.1%). The rSO₂ values in surviving patients were ranging from mean of 60.74% (standard deviation [SD] 4.38) to a mean of 64.98% (SD 5.01), and the mean rSO₂ values in patients who died were ranging from a mean of 52.17% (SD 4.11) to a mean of 37.17% (SD 12.48). Lower rSO₂ values were correlating significantly with worse neurological outcome or death by using two independent sample t-test (p < 0.001).

Conclusion: Cerebral co-oximetry is a simple noninvasive method for predicting the outcomes in TBI and can be used to guide the management of these patients.

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Introduction

Traumatic brain injury (TBI) is known to be an important reason for increased disabilities and deaths and has been

designated as a “silent epidemic” of developed world.³ Pathophysiology of TBI starts with “primary injury” due to initial trauma and is followed by “secondary injury” which is caused by ongoing cerebral ischemia.^{1,2} Significant reduction in mortality can be achieved if cerebral ischemia is prevented

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after severe head injury.⁴ In case of TBI, treatment is directed toward maintaining cerebral perfusion pressure and prevention of cerebral ischemia which can be achieved by controlling raised intracranial pressure (ICP). Prognosis is poor in patients with TBI with raised ICP.^{5–8}

Studies have demonstrated that there is a marked improvement in outcomes in patients with TBI if brain tissue oxygen (PO₂) is monitored during treatment.^{2,9,10} Brain tissue PO₂ and ICP monitoring are invasive methods and are not routinely advised in many centers. Therefore, there is a need to monitor cerebral ischemia by non-invasive methods.

Brain tissue oxygenation needs to be maintained at all times and thus monitoring of the tissue oxygenation is vital.¹¹ However, it is difficult to monitor tissue oxygenation, and newer technologies focus on methods to do so.¹² Until recently, regional brain tissue oxygen measurement was practically not possible. Introduction of near-infrared spectroscopy (NIRS) has now made it easier to monitor because it is non-invasive.

Highlights of this study are the use of NIRS in cerebral rSO₂ monitoring. It is a non-invasive system capable of measuring the regional oxygenation and assessment of brain function through the intact skull.

In this study, we aim to correlate between regional saturation of oxygen in cerebral circulation (rSO₂) and outcomes in TBI cases after admission to intensive care unit (ICU). The main objective is to find out the relation between non-invasive measurement of cerebral rSO₂ and outcome in patients with severe head injury, which can be used as a guide for treatment.

Materials and methods

The study period was from December 2013 to July 2015, and it was conducted at a tertiary care hospital attached to medical college. Institutional ethical committee approval was obtained. Informed written consent was obtained from the relatives of the patients. This study is a prospective observational study which included 78 patients with severe head injury who were admitted in the intensive care unit (ICU) with a glasgow coma scale (GCS) of 8 or less than 8. The exclusion criteria were (a) patients with refractory hypotension at admission with a MAP of less than 55 mmHg despite administration of adequate fluid volume resuscitation and vasoactive drugs as indicated; (b) cardiac arrest survivors; and (c) head injury patients with major trauma to chest, abdomen, pelvis, and limbs.

Near-infrared spectroscopy (NIRS) monitor was applied to the patients immediately after admission to ICU, and readings were noted every 4 hours up to first 48 hours after admission. Data were recorded as per the case report format, which includes age, sex, comorbidities, GCS on arrival, and mean arterial pressure (MAP). The monitor used in this study was Nonin Equanox 7600 Regional Oximetry monitor (Fig. 1). Other clinical parameters such as SpO₂, electrocardiogram, heart rate, and non-invasive blood pressure were also recorded at the same time during NIRS monitoring.

Near-infrared spectroscopy (NIRS) monitor probes were attached over forehead bilaterally. Monitoring was

Fig. 1 – Near-infrared spectroscopy monitor used in the study.

continuously performed for 48 hours, and data were recorded every 4 hours. Cerebral oximetry (rSO₂) values less than 50 for more than a minute is defined as low cerebral oxygen saturation, values between 50 and 60 are taken as borderline low rSO₂, and values more than 60 are taken as normal rSO₂.

Statistical analysis

Data analysis was performed using SPSS software (Statistical package for Social Sciences), version 21.0. Qualitative data were expressed as frequency and percentage (%). Quantitative data variables were expressed as descriptive statistics [mean, standard deviation (SD) and so forth]. Data were analyzed as mean $\pm$ SD separately for patients survived and died with time on X axis and rSO₂ on Y axis. Also, rSO₂ values at 4-hour interval up to 48 hours were recorded, and the outcomes were noted at 28 days. Comparison among patients who died and survived was performed using Kolmogorov–Smirnov test and Mann–Whitney U test.

Results

A total of 78 patients with severe head injury were studied. Data collected were demographic data, initial GCS, MAP on admission, rSO₂ values at 4-hour interval, and outcomes at 28 days. Age group included in the study was between 16 and 75 years. The patient characteristics are given in Table 1.

The mortality rate found in this study was 15.4%. The survived patients (84.6%) were further divided into four groups according to neurological recovery: good recovery (42.3%), moderate disability (26.9%), major disability (10.3%), and persistent vegetative state (5.1%) as per the Glasgow Outcome Scale (Table 2 and Fig. 2).

Patients who survived had a mean rSO₂ values higher than those who died (Table 3 and Fig. 3). The rSO₂ values in surviving patients that ranged from a mean of 60.74% (SD 4.38) to a mean of 64.98% (SD 5.01) were observed during the first 48 hours of admission to ICU. The mean rSO₂ values in patients who died ranged from a mean of 37.17% (SD 12.48) to a mean of 52.17% (SD 4.11). In this study, we found that mean rSO₂ values were significantly lower in patients who died, and

Table 1 – Patient characteristics.

	Number of patients	Percentage (%)
Gender		
Male	65	83
Female	13	16.7
Age group		
≤ 30	3	3.8
31–40	11	14.1
41–50	18	23.1
51–60	14	17.9
61–70	20	25.6
>70	12	15.4
Comorbidity		
Present	18	23.1
Absent	60	76.9
Comorbidities		
Anemia	1	1.3
Diabetes mellitus	5	6.4
Hypertension	8	10.3
DVT	2	2.6
RHD	2	2.6
Seizure	1	1.3

DVT, deep vein thrombosis; RHD, rheumatic heart disease.

the results showed a statistically significant difference between the mean rSO₂ values with respect to outcomes ($p < 0.001$). Data were analyzed by calculating area under the curve and average of rSO₂ values of patients who died and survived. Also, distribution of rSO₂ between the survived and died patients suggests that higher baseline rSO₂ has better probability of survival (Fig. 4).

The outcomes are further studied after dividing the patients into groups with values less than or equal to 50, between 51 and 60, and more than 60 (Table 4). It was observed that patients with persistently low values of rSO₂ (less than 50) were significantly correlated with poor outcomes.

Table 2 – Outcome.

Outcome	Number of patients	Percentage (%)
Survive	66	84.6
Death	12	15.4
Total	78	100.0

Fig. 2 – Bar diagram showing various outcomes in this study.

Discussion

The international traumatic data bank has defined severe head injury as a GCS of 8 or less at 6 hours after injury after neurosurgical resuscitation or deterioration to GCS of 8 or less within 48 hours of injury and lasting for at least 6 hours.¹³ Management involves ICU admission and can be either conservative or surgical and is decided by the extent of injury and computed tomography (CT) findings. There is a possibility of sudden deterioration in the condition of these patients due to secondary ischemia. ICP and brain tissue oxygenation measurement is advisable in all patients of TBI, but it is invasive, and therefore, we need to switch to an effective non-invasive method to do so.

In this study, cerebral co-oximetry of patients was performed using NIRS monitor, which is a portable and easy-to-use device with disposable bifrontal electrodes. Data recorded were real time, continuous, and it does not involve any invasive procedure. It uses four wavelengths of light to measure both oxygenated and deoxygenated hemoglobin, adjusting for potential confounding effects of light scattering and other extraneous chromophores (light-absorbing substances) in the tissue bed. A proprietary algorithm combines the information from all wavelengths and light paths in fractions of a second and converts it to a percent-oxygenated hemoglobin value for the targeted deep tissue. The measurement is completely independent of the pulsatile flow. Nonin EQUANOX NIRS monitor used in this study updates measurements every 1.4 s. This rapid update speed is important for noting desaturation events quickly.

Ferrari et al.¹⁴ pioneered and studied NIRS extensively. In 1993, the first commercial device was marketed in the USA after the Food and Drug Administration approval. Since then, several studies on correlation of NIRS with CT and magnetic resonance imaging findings in patients with intracranial hemorrhage preoperatively have shown good sensitivity of NIRS.^{16–18} One of the highlights of the monitor is its portability which enables it to be used while transport of a patient with TBI.¹⁵

In our study, continuous real-time cerebral co-oximetry was performed for first 48 hours in ICU. The rSO₂ values noted were correlated with various outcomes at 28 days. It was found that lower rSO₂ values were correlating significantly with worse neurological outcomes, and patients with higher values had better outcomes. The mortality in our study is 15.4%, and most of these patients had rSO₂ values less than 50 during the study period. Also, in patients with rSO₂ values below 50, the probability of death or persistent vegetative state is high. Hence, we can say that lower rSO₂ values suggestive of regional cerebral ischemia area are a marker of poor neurological outcomes. Monitoring rSO₂ with NIRS can prove to be useful in taking important decisions regarding treatment of patients with TBI.

There are various factors determining outcomes in severe TBI, and prevention of secondary brain injury remains an important goal out of which maintaining blood pressure and tissue oxygenation is of prime importance.^{19–23} The commonly used predictors of outcome both individually or in combination include age, GCS score, pupillary reactivity, early

Table 3 – Comparison of the outcomes of patients who died (0) with that of patients who survived (1).

Outcome	AUC		Average	
	0	1	0	1
Mean	2232.17	3038.79	47.39	63.27
Median	2232.00	3082.00	46.42	63.96
SD	232.85	205.52	3.20	4.23
Min	1698	2388	42.23	49.92
Max	2598	3436	53.92	71.23
Range	900	1048	11.69	21.31
IQR	260	241	4.52	4.87
Tests of normality				
Outcome	Kolmogorov–Smirnov test			
		Statistic	df	Sig.
0	AUC	.179	12	.200
	Avg	.202	12	.188
1	AUC	.142	66	.002
	Avg	.157	66	.000
Mann–Whitney U test				
Variable	Outcome	Mean rank	Asymp. Sig. (two tailed)	
AUC	0	6.92	0	
	1	45.42		
Avg	0	6.92	0	
	1	45.42		
Outcome	rSO2	Mean–SD	Mean	Mean + SD
0	0	46.61511	52.08	57.552
0	4	48.05829	52.17	56.275
0	8	46.52785	50.58	54.639
0	12	47.37758	49.92	52.456
0	16	45.30958	50.00	54.690
0	20	42.9894	48.83	54.677
0	24	39.90327	47.00	54.097
0	28	39.95759	46.42	52.876
0	32	39.04649	46.17	53.287
0	36	38.87053	44.75	50.629
0	40	26.96898	40.33	53.698
0	44	26.08519	38.83	51.581
0	48	24.68517	37.17	49.648
1	0	56.36658	60.74	65.118
1	4	57.07957	61.26	65.436
1	8	57.27349	61.85	66.423
1	12	57.73873	62.44	67.140
1	16	57.90961	62.88	67.848
1	20	57.02583	62.89	68.762
1	24	56.73949	63.20	69.654
1	28	57.72727	63.77	69.818
1	32	58.85948	64.08	69.292
1	36	59.61079	64.71	69.813
1	40	60.21747	64.97	69.722
1	44	59.81251	64.79	69.763
1	48	59.97872	64.98	69.991

AUC, area under the curve; IQR, interquartile range; SD, standard deviation.

hypoxia and hypotension, brain stem reflexes, and CT findings.²⁴ In our study, we found that lower rSO2 values were associated with unfavorable outcomes. Also, previous studies have found that there was increase in unfavorable outcomes with increasing age despite having less severe TBI.^{25–28} In our study, 41% patients were aged more than 60 years.

Review of literature on predictors of final outcomes after TBI suggests that initial GCS is an important factor.^{29–36} In contrast to this, some studies³⁷ reviewed early prediction of

outcomes of patients with TBI and found that initial GCS after admission in ICU and eventual outcomes had insignificant correlation. Furthermore, GCS 6 hours after presentation showed significant correlation with outcomes. Also, some patients with lower scores had good neurologic recovery indicating contribution of other factors involved. Therefore, accurate prediction of outcomes immediately after TBI is difficult suggesting that these patients should be treated aggressively regardless of initial neurologic status.

Fig. 3 – Comparison of the outcomes of patients who died (0) with that of patients who survived (1).

Fig. 4 – Box-and-whisker plot showing distribution of rSO2 between survived and died shows that higher baseline rSO2 has better probability of survival.

In our study, it was found that the rSO2 values were reduced within first 4 hours of presentation and hence, it can be said that rSO2 values can prove to be the first indicator of worse neurological outcomes. NIRS monitoring in severe head injury patients can provide first sign of cerebral hypoxia and can prove to be vital in the management of these patients.

Also, few studies^{38,39} had stated that NIRS does not reflect significant changes in cerebral oxygenation, but the sample size in these studies was less, and the comparison was done with jugular venous oxygen saturation. In contrast to our study, which had a good sample size, NIRS showed significant changes in cerebral oxygenation which correlated with other clinical parameters.

Limitations

Despite the good predictability of NIRS for outcomes, there are few limitations in this study. A number of factors such as age, multiple injuries, hypotension, pupillary reflexes, hypoxia, and extent of injury affect the outcomes as mentioned in various studies. But many of these factors are also indirectly affecting the cerebral oxygenation and hence NIRS values. Also, there are factors such as frontal edema, injuries, or postoperative dressing over forehead, which makes the

Table 4 – rSO₂ values are divided as low (≤ 50), borderline (51–60), and normal (> 60) and were noted at 4-hour interval and studied in terms of various outcomes of this study at 28 days.

rSO ₂		Outcome					Total number of patients
		Good recovery	Moderate disability	Major disability	Persistent vegetative state	Death	
At baseline	≤ 50	0	0	0	0	3	3
	51–60	12	8	8	3	9	40
	> 60	21	13	0	1	0	35
4th hour	≤ 50	0	0	0	1	3	4
	51–60	6	7	8	3	9	33
	> 60	27	14	0	0	0	41
8th hour	≤ 50	0	0	1	0	5	6
	51–60	4	6	7	4	7	28
	> 60	29	15	0	0	0	44
12th hour	≤ 50	0	0	0	1	8	9
	51–60	4	9	7	3	4	27
	> 60	29	12	1	0	0	42
16th hour	≤ 50	0	0	1	1	8	10
	51–60	1	11	4	3	4	23
	> 60	32	10	3	0	0	45
20th hour	≤ 50	0	0	1	1	7	9
	51–60	1	9	6	3	5	24
	> 60	32	12	1	0	0	45
24th hour	≤ 50	0	1	1	2	9	13
	51–60	1	7	5	2	2	17
	> 60	32	13	2	0	1	48
28th hour	≤ 50	0	0	2	2	10	14
	51–60	0	8	2	1	2	13
	> 60	33	13	4	1	0	51
32nd hour	≤ 50	0	0	1	2	9	12
	51–60	0	6	4	2	3	15
	> 60	33	15	3	0	0	51
36th hour	≤ 50	0	0	1	0	10	11
	51–60	0	3	1	4	2	10
	> 60	33	18	6	0	0	57
40th hour	≤ 50	0	0	0	0	10	10
	51–60	1	5	5	4	1	16
	> 60	32	16	3	0	0	51
44th hour	≤ 50	0	0	0	0	11	11
	51–60	1	1	4	4	0	10
	> 60	32	20	4	0	0	56
48th hour	≤ 50	0	0	0	0	11	11
	51–60	0	1	6	4	0	11
	> 60	33	20	2	0	0	55

placement of NIRS probes difficult and hence can give abnormal values.

Near-infrared spectroscopy (NIRS) monitoring is relatively expensive and has single-use patient sensors. Further studies are recommended for other clinical applications after a thorough cost–benefit analysis.

Conclusion

Cerebral co-oximetry is an important tool for monitoring patients with TBI. It is helpful in detecting regional ischemia early and also predicting the outcomes of severe head injury cases, which can be beneficial in taking important decisions in management of these patients. Therefore, NIRS monitor can be recommended as a useful monitor to be kept in ICU as a part of the armamentarium of the treating physician along with other monitors.

Conflicts of interest

All authors have none to declare.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at <https://doi.org/10.1016/j.mjafi.2018.08.007>.

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