Original Article

Intensive care management of head injury patients without routine intracranial pressure monitoring

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Background: Head injury contributes significantly to mortality and morbidity in India. Evaluation of the available trauma care facilities may help improve outcome. **Aim:** To evaluate the factors influencing the mortality of patients with head injury who had intensive care management and evolve strategies to improve outcome. **Setting and Design:** Retrospective study in a tertiary hospital where intracranial pressure monitoring (ICPM) is not routinely practiced. **Materials and Methods:** All patients with head injury managed in the intensive care unit in a two-year period were included. The factors evaluated were age, vital signs, Glasgow Coma scale score (GCS) at admission, pupillary light reflex (PR), oculocephalic reflex (OCR), hemodynamic stability, computerized tomography (CT) findings, diabetes mellitus, anemia, infections and abnormalities of serum sodium. **Results:** We analyzed 208 patients (202 without ICPM). In-hospital mortality was 64 (31%). Only 24 (11.5%) patients were admitted within one hour of injury, while one-third arrived after six hours. The clinical factors (at admission) that influenced mortality included age, GCS, PR, OCR and diastolic blood pressure (DBP). Effacement of the basal cisterns in the initial and repeat CT scans, hyperglycemia, hemodynamic instability and serum sodium imbalances were associated with higher mortality. The independent predictors of mortality by logistic regression were initial GCS, DBP, hemodynamic instability and effacement of cisterns on repeat CT. **Conclusions:** Mortality following head injury is high. Pre-hospital emergency medical services are disorganized. The key to reducing mortality within the limitations of our current trauma system is maintenance of DBP>70 mmHg and SBP >90 mmHg from the time of first contact.

Key words: Guidelines, intensive care, mortality, predictors, traumatic brain injury

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Societies with advanced emergency medical services (EMS) have reduced mortality in severe head injuries by "aggressive" pre-hospital and in-hospital management including intracranial pressure monitoring (ICPM).[1-5] However, India has limited resources in terms of infrastructure and manpower for managing such patients.[6,7] Other factors affecting outcome include age, Glasgow Coma scale score (GCS), pupillary reactivity (PR), early hypoxia and hypotension, brainstem reflexes and computed tomography scan (CT) findings.[8-19] Resource limitation in our trauma system restricts the routine use of aggressive pre- and in-hospital management strategies, like ICPM, for patients with head injury. We, therefore, attempted to evaluate the factors influencing mortality among patients with head injury managed in our intensive care unit (ICU) and evolve strategies to improve outcome in this resource-constrained environment.

Materials and Methods

This is a retrospective study of all patients admitted following head injury to the intensive care unit (ICU) of a neurosurgical center in India over a two-year period. All patients were evaluated and resuscitated. When indicated, they underwent appropriate surgical interventions before admission to the ICU. All patients were sedated and the majority of them were mechanically ventilated. Muscle relaxants and barbiturate coma were not used. The $PaCO_2$ was maintained at around 33-35 mmHg and PaO_2>100 mmHg. Intravenous mannitol (0.25 gm/kg/4-8 hourly) was used to reduce cerebral edema. Intracranial pressure monitoring was not used routinely. Normovolemia was ensured at all times. Hematological and biochemical parameters were monitored daily. Hyperglycemia was corrected to 180-200 mg/dl. The case records were reviewed by one person for the following information: initial post-resuscitation and subsequent ICU recordings of GCS,[20]

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PR, oculocephalic reflex (OCR), focal neurological deficits, systolic blood pressure (SBP), mean arterial pressure (MAP) and diastolic blood pressure (DBP), serum electrolytes, hematology and bacteriological investigations. The CTs of the patients were reviewed for the predominant pathology, effacement of basal cisterns (ambient cistern obliterated bilaterally) and ventricles (lateral ventricles not visualized), presence of midline shift (based on position of septum pellucidum), subarachnoid hemorrhage and tissue tear hemorrhages. The CTs repeated during ICU admission were reviewed and categorized as "improved" (decreased cerebral edema, basal cisterns visualized, decreased midline shift) or "worsened" (increased cerebral edema, obliteration of the basal cisterns, increased midline shift, increased hematoma/ new hematoma and contusions). The patients who had "worsened" CT were grouped into those requiring surgical intervention for enlarging hematomas/contusions and those for whom surgery was not indicated. Definitions of terminology used: hyponatremia (serum sodium <135 mmol/L), hypernatremia (serum sodium >145 mmol/L), diabetes insipidus (DI, urine output >4 ml/kg/h for two consecutive hours or >3.5 liter/24 h with urine osmolality <300 mOsm/kg and serum sodium>145 mmol/L), hyperglycemia (blood glucose level [BGL] >110 mg/dL or 5.6 mmol/L), anemia (hemoglobin <10g/dL) and pneumonia (suspected upon the presence of new and/or progressive pulmonary infiltrates on chest radiograph in addition to two of the following criteria: fever > 38.3^0 C or hypothermia < 36^0 C, leukocytosis > 12 X 10^9 /L and purulent tracheobronchial secretions). Hemodynamic instability (HI) was categorized as absent (SBP>90 mmHg, with or without pressor drugs) and present (SBP<90 mmHg despite pressor drugs, excluding instability occurring prior to death). The data was analyzed to identify the factors responsible for the in-hospital mortality among these patients. All data are expressed as mean ± standard deviation (SD). Chi square test, Fisher exact test and Student's t test were used to determine the significance of the individual variables. Multivariate analysis by logistic regression was used to identify the independent predictors of mortality. SPSS 10 software was used for all statistical analysis.

Results

The records of 208 patients were analyzed. The majority of patients (180) were referrals from local hospitals, closer to the site of trauma, where initial resuscitation was performed. One hundred and ninety-nine patients (96%) arrived in our hospital without endotracheal intubation, despite 171 being referred from other hospitals and 124 having GCS <9. Data regarding initial arterial blood gas measurements were available for 139 patients and ten had PaO_2<60 mmHg. Prior to admission to the ICU, 56% of them underwent surgery. Sixty-four patients died (31%) and Table 1 shows that 22 died (34%) by the third day of injury.

The influence of various clinical factors on mortality is shown in Table 2. The clinical factors that had

Table 1: Days from admission to death

Day	Frequency	Cumulative percentage
1	5	7.8
2	10	23.4
3	7	34.4
4	5	42.2
5	10	57.8
6	3	62.5
7	6	71.9
8	3	76.6
9	1	78.1
10	3	82.8
11	2	85.9
12	1	87.5
13	1	89.1
15	2	92.2
16	2	95.3
18	1	96.9
21	1	98.4
25	1	100
Total	64	

Table 2: Influence of clinical variables on mortality

Clinical variables	Number N=208 (%)	Mortality N=64 (%)	*P* value
Age			
<15	33 (15.9)	7 (21.2)	
15-59	157 (75.4)	47 (29.9)	0.036
>59	18 (8.7)	10 (55.6)	
Gender			
Male	168 (80.8)	53 (31.5)	
Female	40 (19.2)	11 (27.5)	0.6
Time from injury to admission (hours)			
<1	24 (11.5)	8 (33.3)	
2-3	68 (32.7)	20 (29.4)	
4-6	47 (22.6)	14 (29.8)	0.9
7-12	36 (17.3)	12 (33.3)	
>12	33 (15.9)	10 (30.3)	
GCS at admission			
3-5	72 (34.6)	40 (55.6)	
6-8	103 (49.5)	21 (20.4)	<0.001
>8	33 (15.9)	3 (9.1)	
Pupil reactivity			
Equal and reacting	131 (63)	29 (22.1)	
Asymmetric and reacting	24 (11.5)	7 (29.2)	0.001
Non-reacting	50 (24)	27 (54)	
Couldn't test	3 (1.4)	1 (33.3)	
Oculocephalic reflex			
Normal	146 (70.2)	34 (23.3)	
Restricted	13 (6.3)	6 (46.2)	0.005
Absent	47 (22.6)	23 (48.9)	
Couldn't test	2 (1)	1 (50)	
Motor deficits			
Present	55 (26.4)	14 (25.5)	0.3
Absent	153 (73.6)	50 (32.7)	
*Systemic injury**			
Absent	188 (90.4)	58 (30.9)	
Chest injury	59 (2.4)	2 (40)	0.855
Lower limb fracture	6 (2.9)	1 (16.7)	
Upper limb fracture	9 (4.3)	3 (33.3)	

*Patients with abdominal injury are not admitted in our ICU a significant influence on mortality by univariate analysis are age, GCS at admission, PR, OCR and DBP at admission. The mean SBP and mean MAP in the survivors (117±14 mmHg and 88±12 mmHg respectively) were not significantly different from that in those who died (115±20 mmHg and 85±16 mmHg respectively) ($P = 0.4$). However, the DBP in the survivors was higher (74 ±13 mmHg) than in those who died (70±16 mmHg) ($P = 0.03$). Only one patient had a SBP <90 mmHg and two patients had MAP <60 mmHg, whereas 37 (18%) had DBP <70 mmHg.

The CTs of 200 patients were available for review. The CT findings and the corresponding mortality are shown in Table 3 ($P = 0.022$). Among patients with extradural hematoma (EDH), 13 had GCS 3-5 and 12 had non-reacting pupils. Only one patient (GCS=8, pupils equal and reacting) of the seven patients with EDH admitted within 3h of injury died, whereas nine (GCS 3-5=7, GCS 7=2, non-reacting pupils in seven) of 22 admitted after three hours died.

Midline shift of more than 3 mm was found in 156 patients and 34% of them died compared to 23% in those with lesser shift. ($P = 0.156$). Effacement of the cisterns was seen in 151 patients and their mortality rate was 38% as against 13% in those with visible cisterns ($P = 0.001$). One hundred and sixty-four of 200 patients underwent repeat CT scans while in the ICU. Most of the scans were done between 12 and 48h of admission to the ICU. The repeat CT scan findings are shown in Table 4 ($P = 0.001$). Twenty-seven of 46 patients (58.7%) with effacement of basal cisterns in the repeat CT scan died compared to 23 of 118 patients (19.5%) with visible cisterns ($P < 0.001$).

The influence of various ICU factors on mortality is shown in Table 5. Mechanical ventilation (MV) was required in 184 patients. The mean duration of ventilation was 6.4 ± 5.2 days in those who died and 6.3 ± 5.7 days in the survivors ($P = 0.889$). Pneumonia was present in 83 (40%) patients and increased with the number of days spent in the ICU (Pearson correlation coefficient 0.697, $P = 0.001$). Only six patients underwent ICPM and hence this didn't influence mortality.

A mathematical prediction model was evolved based on logistic regression of all the parameters that had a significant influence on the outcome on univariate analysis. Initial GCS at admission, DBP at admission, presence or absence of hemodynamic instability during ICU stay and status of cisterns on repeat CT was found to influence the outcome significantly [Table 6]. Probability of Survival (P) = $1 / (1 + e^{-z})$, where z = [(0.08 x DBP) + (0.19 x IGCS) - (3.4 x HI) - (1.2 x CRC) − 3.7].

Table 3: CT scan findings and mortality

CT Scan findings	Mortality (%)	Total
Normal CT	0	2
Diffuse edema	1 (5.6)	18
Contusion	4 (13.8)	29
Extradural hematoma	10 (34.5)	29
Acute subdural hematoma	13 (44.8)	29
Depressed fracture	1 (20)	5
Multiple hematomas / contusions	34 (39.1)	87
Traumatic Subarachnoid hemorrhage alone	0	1
Total	63 (31.5)	200

Table 4: Repeat CT scan findings and mortality

Repeat CT scan findings	Mortality (%)	Total
Improved	9 (12)	75
Worsened -non-operable lesion	25 (51)	49
Worsened -required surgery	16 (40)	40
Total	50	164

Table 5: Other factors influencing mortality

Factors influencing mortality	Mortality (%)	Total	*P* value
Mechanical ventilation			
Yes	63 (34)	184	0.029
No	1 (4)	24	
Hemodynamic instability			
Absent without pressor drugs	14 (11)	126	
Absent with pressor drugs	15 (35)	43	0.001
Present despite pressor drugs	35 (90)	39	
Hypo/hypernatremia			
Present	32 (40)	80	0.023
Absent	32 (25)	128	
Diabetes insipidus			
Present	19 (68)	28	0.001
Absent	45 (25)	180	
Hyperglycemia			
Present	14 (47)	30	0.041
Absent	50 (28)	178	
Anemia			
Present	32 (37)	87	0.111
Absent	32 (26)	121	
Pneumonia			0.003
Present	16 (19)	83	
Absent	48 (38)	125	
Urinary tract infection			
Present	4 (19)	21	0.220
Absent	60 (32)	187	
Septicemia			
Present	4 (67)	6	0.074
Absent	60 (30)	202	
Central nervous system infection			
Present	4 (67)	6	0.074
Absent	60 (30)	202	

Discussion

This study evaluates the factors influencing outcome in patients with head injury managed in an ICU in India, without routine ICP monitoring. The independent predictors of in-hospital mortality are initial GCS, DBP at admission, presence or absence of hemodynamic instability during ICU stay and the status of CRC.

Most cities in India have a poorly networked trauma system. The EMS personnel are largely untrained and ambulances poorly equipped. Consequently, onlookers often transport patients with brain injury to the nearest clinic, which is usually unable to provide appropriate

Table 6: Significant variables in the logistic regression equation

	B	S.E.	Wald	df	*P* value	Odds ratio	95% confidence interval for odds ratio	
							Lower	Upper
Hemodynamic instability (Present=1, absent=2)	-3.433	0.762	20.279	1	0.000	0.032	0.007	0.144
Cisterns on repeat CT (CRC) (Effaced=1, visible=2)	-1.214	0.532	5.207	1	0.022	0.297	0.105	0.843
Diastolic BP at admission	0.077	0.028	7.871	1	0.005	1.081	1.024	1.141
Initial GCS at admission (IGCS)	0.190	0.095	3.958	1	0.047	1.209	1.003	1.458
Constant	-3.714	2.060	3.252	1	0.071	0.024		

treatment. This picture is reflected in the care received by our patients prior to admission to our hospital. Most patients had an unprotected airway despite being referred from other hospitals. Surprisingly, though about one-third of the patients were admitted after six hours of injury, time from injury to admission did not influence outcome. This is counter-intuitive and in fact, one study which evaluated two trauma systems with vastly different EMS capabilities found that an inadequate EMS results in fewer patients arriving at the hospital within one hour of injury and leads to increased mortality following head injury.[5] However, the concept of the "golden hour" has never been proved with respect to brain injury patients and may well be an "urban legend".[21,22] Life-threatening, but potentially treatable injuries are up to six times more likely to lead to death in a country with no organized trauma system than in one with an organized, resourced trauma system.[23] The high mortality in our patients with EDH is probably a reflection of a disorganized EMS as suggested by Bricolo *et al*.[24]

Early hypotension is an important predictor of outcome and can be reduced by an efficient EMS.[6,10,14] Unlike previous reports, we found that initial DBP rather than SBP predicted mortality.[25] The prognostic value of DBP was probably unveiled because only one patient had SBP<90 mmHg. While the maintenance of SBP >90 mmHg in most patients shows our EMS in good light, maintaining DBP above a certain threshold is probably equally important because two-thirds of the cardiac cycle and resultant cerebral perfusion, is spent in diastole. The presence of hemodynamic instability (SBP<90 mmHg) during ICU stay is also an independent predictor of mortality. We should therefore attempt to maintain both DBP> 70 mmHg and SBP >90 mmHg during transport and the in-hospital management of patients with head injury.

The present study also demonstrates the importance of commonly used predictors of outcome including age, GCS score, pupillary reactivity, brainstem reflexes and CT findings.[8-15,17-19] These variables, however, cannot be modified by our management.

Abnormalities of serum sodium may be markers of injury severity and are usually considered to be due to hypothalamic/pituitary damage but can also be caused by excessive mannitol administration.[10] The incidence of sodium abnormality in this study is similar to that in centers using ICPM[26,27] and hence, it is unlikely that our use of mannitol without ICPM was responsible. SIADH is not discussed because it was not evaluated systematically. A tighter control of sodium balance seems appropriate but is unlikely to make a significant difference in mortality.

Rovlias and Kostou reported that among patients with severe head injury, a blood glucose level (BGL) greater than 200 mg/dl was associated with worse outcome.[28] Parsons *et al*. have demonstrated, using magnetic resonance spectroscopy in patients with acute stroke, that hyperglycemia causes increased brain lactate and this in turn causes at-risk hypoperfused tissue to progress to infarction.[29] Blood glucose level maintained between 80 and 110 mg/dl reduced mortality in surgical ICU patients compared to when BGL was maintained between 180 and 200 mg/dl.[30] This improvement in outcome was related to achieving normoglycemia rather than the dose of insulin administered.[31] Blood glucose level >110 mg/dl is associated with higher mortality in this study, however, revision of our target for glycemic control to 80-110 mg/dl may not reduce mortality since it is not an independent predictor of outcome.

The incidence of pneumonia is similar to that reported by Ewig *et al*.[32] Antibiotic prophylaxis beyond 24h can increase late-onset pneumonia due to Gram-negative enteric bacilli and Pseudomonas.[32] Prophylactic antibiotics on the first day of ventilation has however been shown to decrease the incidence of ventilator-associated pneumonia and reduce duration of ICU stay.[33] Our findings suggest a need to a change our practice of continuing with prophylactic antibiotics beyond 24h.

Our present in-hospital mortality is high. Secondary complications, rather than the primary injury, were probably responsible for the mortality because two-thirds of the deaths occurred after the third day. Reported mortality rates range from 3-29% at best.[2,3,5,34,35] However, there are reports of higher mortality from systems which are better equipped than ours-38% by Shreiber *et al*. and 20% at 48h increasing to 47% at six months by Boto *et al*.[36,37] These outcomes, however, may not be comparable because of differences in the patient population. Recently, another center in India reported that mortality following severe head injury was 46%

and poor EMS was one of the factors held responsible.[38] The CRASH trial which included a heterogeneous group of patients reported a two-week mortality of 34.8% for patients with severe head injury who did not receive corticosteroids.[39] Is the higher mortality in our study related to the fact that ICPM was not routinely practiced? Unfortunately, this question cannot be answered with the available data. Some studies which have compared outcomes between centers where ICPM is routine with those where it is rarely or never practiced have found that the former have significantly better outcomes,[1,40] whereas Cremer *et al.* found no significant difference in mortality (33% versus 34% respectively).[41] Three surveys in different countries (USA, Canada and the UK) have found use of ICPM in 50-75% centers but only about 20% of neurosurgeons feel with a high level of confidence that this actually improves outcome.[1,42,43] The material requirements for ICPM can be quite low in India but the manpower required to monitor and manage a patient on ICPM often proves to be serious deterrent, as in our ICU.[44]

The two key limitations of this study are firstly, the retrospective nature of the analysis and secondly, the use of in-hospital mortality as an end-point for evaluation of outcome because the actual mortality at follow-up is likely to be higher.

Conclusions

Mortality following head injury is high in a resource-constrained environment. Pre-hospital emergency medical services are disorganized. Initial GCS at admission, DBP at admission, presence or absence of hemodynamic instability during ICU stay and status of cisterns on repeat CT can influence the outcome significantly. Despite the limitations of our trauma care system, mortality among our patients with head injury can be reduced if every caregiver, from the site of injury to the ICU, maintains hemodynamic stability (DBP>70 mmHg and SBP>90 mmHg) at all times.

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