ORIGINAL ARTICLE

General intensive care for patients with traumatic brain injury: An update

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ABSTRACT

Background: Traumatic brain injury (TBI) is a growing epidemic throughout the world and may present as major global burden in 2020. Some intensive care units throughout the world still have no access to specialized monitoring methods, equipments and other technologies related to intensive care management of these patients; therefore, this review is meant for providing generalized supportive measurement to this subgroup of patients so that evidence based management could minimize or prevent the secondary brain injury. **Methods:** Therefore, we have included the PubMed search for the relevant clinical trials and reviews (from 1 January 2007 to 31 March 2013), which specifically discussed about the topic. **Results:** General supportive measures are equally important to prevent and minimize the effects of secondary brain injury and therefore, have a substantial impact on the outcome in patients with TBI. The important considerations for general supportive intensive care unit care remain the prompt reorganization and treatment of hypoxemia, hypotension and hypercarbia. Evidences are found to be either against or weak regarding the use of routine hyperventilation therapy, tight control blood sugar regime, use of colloids and late as well as parenteral nutrition therapy in patients with severe TBI. **Conclusion:** There is also a need to develop some evidence based protocols for the health-care sectors, in which there is still lack of specific management related to monitoring methods, equipments and other technical resources. Optimization of physiological parameters, understanding of basic neurocritical care knowledge as well as incorporation of newer guidelines would certainly improve the outcome of the TBI patients.

Key words: *Evidence, secondary brain injury, supportive care, traumatic brain injury*

INTRODUCTION

Traumatic brain injury (TBI) is a growing epidemic throughout the world and may present as major global burden in 2020.[1-3] This burden has even found to be very high in some countries.[1,3] In addition, TBI not only increases the overall morbidity and mortality, but also, imposes substantial impact on quality-of-life.[4] Moreover, patients who survived from the primary insult, some may still have a long-term disability. In addition, the most of the victims are of younger age group. Timely and optimal management of the disease can significantly improve the outcome and decrease the mortality.[1-3,5]

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Some intensive care units throughout the world still have no access to specialized monitoring methods, equipments and other technologies related to intensive care management of these patients; therefore, this review is meant for providing generalized supportive measurement to this subgroup of patients so that evidence based management could minimize or prevent the secondary brain injury.[6,7] In this article, we have summarized various aspects of generalized intensive care management in patients with TBI.

METHODS

This is a narrative review based on PubMed search on the terms including "TBI," "head injury," "head trauma," "intensive care," "management." Brain Trauma Foundation guidelines were updated in 2007; however, they have included the evidences published till 2006.[8] Therefore, this review has involved the relevant clinical trials and reviews (from 1 January 2007 to 31 March 2013), which specifically discussed about the topic. The papers in any languages have been included. Pediatric and pregnant patients are not included in this review. The papers on pre-hospital as

well as specific neurosurgical management in patients with TBI are also not included in this review.

MANAGEMENT OF SEVERE HEAD INJURY

One of the most important considerations in severe head injury patients remain the early and prompt management of secondary brain injury, which is substantially salvageable and preventable; therefore, the management should also begin since out of the hospital period [Table 1]. This pre-hospital care should include emergent management of airway, breathing and circulation as well as timely shift patient in to advanced trauma center.[9]

Early evaluation of patient's neurological status should include Glasgow coma scale, pupil size and reaction and other signs of raised intracranial pressure or herniation such as deteriorating consciousness, appearance of new neurological deficits, seizures, shallow or irregular breathing with high blood pressure and reduced pulse rate.[10,11] In addition, severity and type of head injury should also be thoroughly evaluated as these sometimes associated with life-threatening injuries including major vessels rupture, visceral perforation and orthopedic trauma.[12]

Table 1: Classification of brain injury and factors affecting these in patients with TBI

Type of traumatic brain injury	Management
Primary injury (direct mechanical impact)	Preventive management
Diffuse brain injury	
Brain concussion (loss of consciousness lasting <6 h)	
Diffuse axonal injury (loss of consciousness lasting >6 h)	
Focal brain injury	
Brain contusion (below or opposite the region of impact)	
Epidural hematoma (laceration of the middle meningeal artery)	
Subdural hematoma (tearing of the bridging veins)	
Intracerebral hematoma	
Secondary injury (minutes, hours, or days of the initial injury)	Target of TBI management
Aggravating factors	
Hypoxemia, hypercapnia	
Hypotension, low cardiac output	
Intracranial hypertension	
Biochemical and metabolic derangements	
Hyperthermia	
Seizures	
Hypo or hyperglycemia	

TBI: Traumatic brain injury

Monitoring

The two most important factors, which have a substantial impact on the outcome of patients with TBI remain hypoxemia and hypotension; therefore, warrant mandatory monitoring for these two variables, which include pulse oximetry and invasive blood pressure (IBP).[13,14] Here, it is also important to recognize the artifacts and failure of pulse oximetry to detect episodes of desaturation, especially in conditions with severe hypotension, cold extremities and movement of extremities; thereby mandates regular arterial blood gas (ABG) sampling. However, there is no consensus over frequency of sampling in TBI patients. The transducer of invasive blood pressure should be kept at the highest point or external meatus (circle of Willis) to reflect actual cerebral perfusion pressure (CPP). The monitoring of end tidal concentration of carbon dioxide (ETCO2) helps to know about the surrogate readings of PaCO2; however, baseline ABG should be carried out to know about the gradient.[15] Prolonged ventilation should be guided by PaCO2 values from ABG. Other essential monitoring should comprise of electrocardiography, core body temperature, intake/output and central venous pressure monitoring and serum electrolytes estimation. These monitoring provide useful information for optimal management in patients with TBI. Rarely, in certain conditions such as the presence of massive fluid or blood administration, patients with myocardial injury and pre-existing low ejection fraction, may require insertion of pulmonary artery catheter for monitoring of pulmonary capillary wedge pressure, cardiac output and stroke volume and guide the therapy according to mentioned parameters.[16]

An early non-contrast brain computed tomography (CT) scan is required to guide subsequent therapy including hematoma evacuation and/or decompressive craniectomy depending upon the signs of brain herniation (midline shift) and GCS of patient. The role of repeat CT scan is controversial; however, this should be used in patients with deteriorating consciousness, especially in younger age group and with severe head injury.[17,18] In fact, CT scan facility located in the trauma or emergency room has been found to reduce the time to acquire CT images and improves overall mortality.[19]

Positioning

There is no well-designed randomized controlled trial available to address this issue in patients with TBI; however general neuroanesthetic consideration for patient's positioning is applicable. Patients should be nursed in 15°-30° head up unless hemodynamically unstable or needing large doses of vasopressors, or prevented by unstable spinal or pelvic injuries. One must ensure that a cervical collar or head rotation does not cause venous obstruction. Head up position maximizes venous drainage

(preventing an increase in the venous cerebral blood volume) and minimizes ventilator associated pneumonia. Semi recumbent position (30° head up) also significantly reduces intracranial pressure (ICP) and improves CPP without any adverse effect on cerebral oxygenation.[20,21] A prospective observational study on the effect of different positions in cerebral and hemodynamic changes in 33 patients with TBI, subarachnoid hemorrhage, or craniotomy for tumor revealed that at 15-min postposition assessment mean change scores showed a downward trend for PbtO2 for all positions with statistically significant decreases observed for supine to head elevation of 30° and 45° and right and left lateral positioning with 30° head elevation; however, ICP decreased with supine to 45° and knee elevation, 30° and 45° head elevation and increased with right and left lateral 15° elevation.[22] Hemodynamic parameters were found to be similar in the various positions.

OXYGENATION AND VENTILATION

The major goal of mechanical ventilation is avoidance of hypoxemia and hypercarbia. In addition, ventilator strategies should comprise of low tidal volume (6-8 ml/kg ideal body weight) with application of 5-10 cm H_2O of positive end expiratory pressure (PEEP).[23,24] Plateau pressure should be kept below 30 cm H_2O. This low tidal volume strategy aims to reduce secondary, ventilator induced lung injury. In cases with acute lung injury/acute respiratory distress syndrome, application of moderate PEEP can be applied; however, increases in intrathoracic pressure can impair cerebral venous drainage and result in increases in ICP.[23,24] Therefore, particular attention needs to be paid when PEEP or intrathoracic pressures are increased, for the resultant effect on ICP.

Hypocapnia can cause cerebral vasoconstriction and may exaggerate the cerebral ischemia.[25] Therefore, it should be used only for emergent management of life-threatening intracranial hypertension when other therapies are refractory or would not be possible to use at that time. Moreover, when it is used, PaCO2 should be normalized as soon as possible. On the other hand, permissive hypercapnia should be avoided because of its cerebral vasodilatory effect that can cause substantial rise in ICP.

Prolonged ventilation is often required in severe head injury patients. There is a considerable debate about the optimal timing for tracheostomy in critically ill-patients. However, it has been shown that an early tracheostomy in trauma patients in general is associated with shorter duration of mechanical ventilation and intensive care unit (ICU) length of stay without an adverse effect on ICU or hospital mortality. Early tracheostomy is advocated in patients with persistently low GCS (< 5), chest infections, conditions requiring frequent endotracheal suctioning or signs of very slow recovery.[26,27]

Hemodynamic support

Systemic hypotension in conjunction with TBI increases the risk of mortality and worse functional outcomes long-term outcomes as assessed using the Glasgow Outcomes Scale.[10] Hypotension increases the chance for secondary brain injury because of hypoperfusion and impaired oxygen delivery to the injured brain according to Brain Trauma Foundation (BTF) guidelines, systemic hypotension is defined as systolic BP of less than 90 mmHg; however, some studies advocated that patients with isolated moderate to severe TBI should be considered hypotensive for systolic blood pressure <110 mmHg.[8,10,28,29] Occasionally, patients with TBI may be severely hypertensive, which can result in cardiac dysfunction. Patients may exhibit evidence of myocardial ischemia. For the treatment of hypertension an infusion of a short acting beta blocker, like esmolol, is very useful. These agents do not cause cerebral vasodilatation, when compared with nitrates and calcium channel blockers and therefore do not increase cerebral blood volume and ICP.[30]

Isotonic fluids are the first line of choice for pre-hospital fluid resuscitation and there is evidence that this is equally effective when compare to hypertonic — dextran solution.[31] Hypertonic solutions have potential to support CPP and reduce ICP; however, clinical trials of early administration to these patients have also failed to show any benefit. Colloids, especially albumin has been shown to be associated with higher mortality in severe TBI patients; therefore, cannot be recommended at present.[32,33]

SEDATION/ANALGESIA/SUCTIONING

Adequate analgesia and sedation minimize pain, anxiety and agitation, reduce the cerebral metabolic rate of oxygen (CMRO2) consumption and facilitate mechanical ventilation.[34,35] This is achieved with sedative drugs and opioids. A short acting benzodiazepine like midazolam is commonly used, which is very effective both as a sedative and as an anticonvulsant. Prolonged use of midazolam can result in significant accumulation. Propofol may have benefits over midazolam because of its superior metabolic suppressive effects and favorable shorter half-life. However, it is not recommended in hypothermic patients as it has a tendency to accumulate and precipitate hyperlipidemia. Propofol infusion syndrome (metabolic acidosis, cardiac dysfunction and rhabdomyolysis) is also a known complication when used as prolonged infusion in ICU.[36] This has been most commonly reported with infusion rates greater than 5 mg/kg/h or when infusions

have been used for more than 48 h. Studies on propofol versus midazolam and ketamine versus sufentanil, found no difference between agents in relation to cerebral hemodynamics. In addition, a systematic review on randomized control trials concluded that there was no advantage in using one agent over another.[35] There was no difference in the overall outcome, intracranial pressure or CPP in patients with severe TBI.[35] Barbiturates are used less commonly for sedation because of the high-risk of cardiovascular depression and increased risk of infection. However, they still have a role when other methods of controlling ICP have failed.[37] The role of the highly specific alpha-2 agonist Dexmedetomidine has also been investigated for ICU sedation in patients with TBI. The sedation profile of this drug was found to be similar to propofol.[38] The advantage of this drug is that it results in less or no respiratory depression; however, the major concerns remain the hemodynamic instability (bradycardia, hypotension) associated with it. This drug is also a useful adjunct for awake intubation. This drug can be used for the agitated patients (alcoholics, substance abuse) who require reliable, serial neurological testing to monitor the course of their TBI without producing respiratory depression and obviate the need for further intubation.[39]

Analgesia is provided with regular doses of acetaminophen and infusion or boluses of opioids, such as morphine, fentanyl or remifentanil. All these have minimal effects on cerebral hemodynamics in adequately resuscitated patients.[40] Neuromuscular blocking drugs are used to minimize coughing and straining, which may increase ICP and is provided with boluses or infusion of non-depolarizing muscle relaxants Atracurium and rocuronium are preferred. There should always be monitoring of the degree of muscle paralysis with a twitch monitor.[41] Prolonged use of neuromuscular blocking agents is associated with an increased incidence of critical illness myopathy.

During suctioning of endotracheal tube, precipitation of cough may dramatically raise the ICP; therefore, mandates to use of boluses of shorter acting agents propofol/opioids/lidocaine before suctioning. The general recommendations of suctioning in ICU patients should also be applicable to patients with TBI and include preoxygenation before and after suctioning, keeping suction pressure minimal, shorter suctioning duration (<15 s), avoidance of carina stimulation and suctioning only when absolute necessary.[42]

Sodium and water balance

In the TBI patient with raised ICP, sudden changes in serum sodium concentration and osmolarity must be avoided since these factors impact on the nature and degree of cerebral edema.[43] The maintenance fluid of choice is normal saline with supplemental potassium. TBI patients are susceptible to disorders of sodium and water balance. Causes include central diabetes insipidus (CDI), cerebral salt wasting (CSW) syndrome and syndrome of inappropriate anti-diuretic hormone (SIADH) secretion.[44] The former condition (CDI) manifests as hypernatremia while later two (CSW, SIADH) present as hyponatremia.[44] The sodium level should be kept between 140 mmol/ml and 150 mmol/ml. Hypotonic fluids can result in swelling of cerebral cells and increases in ICP.[38]

Nutritional support

Early nutritional support is recommended, aiming to meet full nutritional requirements once hemodynamic stability is achieved. Furthermore, early aggressive nutritional support enhances immunologic function by increasing CD4 cells, CD4-CD8 ratios and T-lymphocyte responsiveness. Early enteral nutrition (EN) has also found to be associated with better hormonal profile; therefore, may be related to a better outcome.[45] The route of administration may differ according to the overall clinical condition of patient, but there is no difference in the outcome after severe TBI between enteral or parenteral nutrition.[46] It has been recommended that 140% of resting metabolic expenditure in non-paralyzed patients and 100% in paralyzed patients should be replaced. At least 15% of calories should be protein.[8] Study on patients with moderate TBI showed nitrogen balance was similar with both types of therapy. Parenteral nutrition leads to greater hyperglycemia and there was no difference between the routes in regards to early inflammatory response and clinical outcome.[46] In other multicenter cohort study, EN (145 patients) within 48 h post-injury compared to non EN (152 patients) was found to be associated with better survival, GCS recovery and outcome among TBI patients, particularly in those with a GCS score of 6-8.[47] In this study, the hazard ratio for non EN patients was found to be 14.63.[47] In another prospective randomized controlled study (104 patients) on comparison between two enteral sites (transpyloric versus gastric feeding) revealed that transpyloric route had reduced the incidence of overall and late pneumonia and improved nutritional efficacy in severe TBI patients.[48]

Glycemic control

The stress response in trauma patients, including those with severe TBI, generates a hyper catabolic state leading to rapid muscle protein breakdown and hyperglycemia. In patients with TBI, hyperglycemia was associated with higher ICP, a longer stay in hospital, worse neurological outcome and reduced survival.[49] There is substantial evidence highlighting the adverse effects of hyperglycemia in critically ill-patients. On the other hand, tight glycemic control regime was found to be associated with more episodes of hypoglycemia and less favorable outcome. In a study, of 88 patients with TBI, intensive insulin therapy

(IIT) (maintenance of blood glucose between 80 mg/dL and 110 mg/dL with continuous insulin infusion), did not improve the neurological outcome; however, it did increase the episodes of hypoglycemia.[50] Another randomized controlled trial (RCT) (targeting blood glucose of 80-120 mg/dL) has also concluded the similar findings; however, the IIT was associated with shorter ICU stays and infection rates.[51] In meta-analysis of 9 RCTs out of 1260 studies, IIT has also shown no benefit on mortality nor on long term outcome; however, it does decrease infection rates.[52] In addition, one RCT study on tight glycemic control (80-110 mg/dL) in 13 patients with severe TBI showed that there could be an abrupt increase in cerebral metabolic crisis (critical reductions in glucose and elevations of lactate/pyruvate ratio) measured by microdialysis and therefore mild hyperglycemia (120-150 mg/dL) may be important to provide continuous glucose supply to the brain in this critical period.[53]

Peptic ulcer prophylaxis

Severe TBI is a well-recognized risk factor for stress ulcers (Cushing's ulcers) and also found to be associated with increased plasma cortisol level in this subgroup of patients.[54] Even though, the level of evidence supporting the use of antacids in this selected high-risk group of patients is insufficient, necessitating regular prescription of peptic ulcer prophylaxis, it is not yet clear, which is the ideal agent, dose or route of administration. H2 blockers like ranitidine or proton-pump inhibitors (omeprazole, pantoprazole, esomeprazole) should be routinely used as stress ulcer prophylaxis.[55]

Anemia, hemostasis and deep venous thrombosis (DVT) prophylaxis

Anemia following severe TBI may be detrimental and sometimes requires blood transfusion. Transfusion of packed RBCs has been shown to improve cerebral oxygenation (Pbto2) without significant effect on cerebral metabolism.[56] Strikingly, brain tissue oxygenation was not associated with baseline hemoglobin concentration or low Pbto2.[57] Erythropoietin (EPO) stimulates the production of red blood cells and can protect the injured neurons at the time of hypoxia produced after TBI.[58] Therefore, it can help to prevent and modulate secondary brain injury. Use of EPO was found to be associated with improve in neurological outcome. In RCT of 54 patients with diffuse axonal injury, EPO (2000 U) showed better neurological recovery at 2 weeks.[59] Similarly, in the study of 566 patients with severe TBI, use of EPO was associated with significant lower mortality (9.3% vs. 25.3%) and there was no statistically significant difference in the incidence of morbidities including DVT and pulmonary embolism.[60] Bleeding is also a major issue in patients with TBI, especially associated with other injuries, in this regard, tranexamic acid (TXA) has been shown to reduce blood loss in surgical patients and the risk of death in patients with traumatic bleeding.[61] The role of TXA in patients with TBI associated hemorrhage is at present inconclusive; however, recent clinical randomization of an antifibrinolytic in significant hemorrhage showed some promising results in these cases.[62]

The incidence of DVT is related to the type and severity of injuries. It is reported to be 3-30% depend upon the severity of head injury, associated other injuries and prophylaxis used.[63-66] There are different methods of preventing venous thrombosis, including thromboembolic deterrent stockings, sequential compression devices, low-dose unfractionated heparin (UH), low-molecular weight heparin (LMWH) or a combination of these. Although LMWH seems better than UH in preventing DVT, the incidence of adverse events is low with either option. The use of chemical thromboprophylaxis should be used after proper review of serial CT scans and consultation with neurosurgeons. Most of the studies on this topic are retrospective in nature; thus, warrants a well-defined RCT in near future to address this issue.[63-66]

Hygiene

As for all intensive care patients, chest physiotherapy, frequent turning, eye care and full hygiene care must be provided. Laxatives are prescribed to ensure regular bowel opening to reduce the risk of intra-abdominal hypertension and its systemic repercussions. Frequent dressing of catheters and catheter sites minimizes the risk of infection. Oral hygiene should also be given utmost importance as poor oral hygiene has shown to favor bacterial colonization and the evolution of nosocomial infections. Oral decontamination with chlorhexidine has been shown to decrease oropharyngeal colonization in surgical intensive care; therefore, can decrease the incidence of nosocomial infections, length of ICU stay and mortality.[67]

Others

The other factors, which could potential to cause secondary brain injury, are seizures, hyperthermia as well as hypothermia. Seizures precipitate tremendous increase in CMRO2, ICP and may potential to incite secondary brain injuries. Therefore, prevention and optimal management of seizures is necessary to improve the overall outcome. However, guidelines suggest only anti-seizure medications for the high-risk patients, which include GCS score <10, cortical contusion, depressed skull fracture, subdural hematoma, epidural hematoma, intracerebral hematoma, penetrating TBI and occurrence of seizures within 24 h of injury.[8]

Hyperthermia has also been associated with the increase in CMRO2, ICP and poor neurological outcome; therefore should aggressively treat.[68,69] Current evidence favors normothermia; the trials on therapeutic hypothermia did

not show any beneficial effects on neurological outcome or survival.[70] In addition, hypothermia was found to be associated with cerebrovascular adverse events on rewarming and possibly with pneumonia in adult patients.[70]

DISCUSSION

General supportive measures are equally important to prevent and minimize the effects of secondary brain injury and therefore, have a substantial impact on outcome in patients with TBI. The important considerations for general supportive ICU care remain the prompt recognitionand treatment of hypoxemia, hypotension and hypercarbia [Table 2]. Evidence based guidelines have found to decrease in morbidity and mortality in patients with TBI.

Table 2: Components of general intensive care for head injury patients

Components	Focus
Positioning	To reduce venous congestion
	To reduce ICP, optimizes CPP
Ventilation	To optimize cerebral oxygenation
	To achieve normocarbia (therapeutic transient hyperventilation)
	Minimization of peak and plateau pressure rise
Sedation/analgesia	Prevention of cough/gag to minimize the risk of increase in ICP
	Reduce pain, anxiety and minimize cerebral oxygen consumption
	Synchronize mechanical ventilation
Electrolytes	Na^+ balance to minimize cerebral edema formation
	Early recognition of CSW, DI, or SIADH
Nutrition	Assist in early recovery, to maintain nitrogen balance
	Normalization of gut functions
	Reduce the incidence of infections
Glycemic control	Maintenance of adequate glucose to brain
	Prevention of hyper catabolic state
Seizure control	Prevention of excessive rise in $CMRO_2$
	Prevention of rise in ICP
	Prevention of secondary injury
Ulcer prophylaxis	Prevention and treatment of crushing's ulcer
	Prevention of steroid induced gastric morbidities
Anemia, hemostasis and DVT prophylaxis	Maintenance of adequate cerebral and other tissue oxygenation
	Maintenance of adequate hemostasis
	Prevention of DVT and PE
Hygiene	Prevention of infection
Hypothermia/ hyperthermia	Maintenance of normothermia
	Avoidance of shivering

ICP: Intracranial pressure; CPP: Cerebral perfusion pressure; CSW: Cerebral salt wasting; DI: Diabetes insipidus; SIADH: Syndrome of inappropriate anti-diuretic hormone; DVT: Deep venous thrombosis; PE: Pulmonary embolism; $CMRO_2$: Cerebral metabolic rate of oxygen

Most of the evidences are found against the use of routine hyperventilation therapy, tight control blood sugar regime, use of colloids and late nutritional therapy as well as parenteral nutrition therapy in patients with severe TBI.

Some of the major areas, which still require well-designed RCTs include the effect of patient positioning on cerebral hemodynamic, redefining the outcome based blood pressure targets (90 mm systolic versus higher), ventilation strategies (pressure controlled vs. volume controlled), sedation protocols and acid prophylaxis. The other areas which also need further attentions include target hemoglobin for blood transfusion in TBI patients, role of EPO, hemostatic agent and role of pharmacological DVT prophylaxis.

CONCLUSION

Several trials, after the BTF-2007, have yet to be adopted by standard guidelines and would certainly impart better outcome in this subgroup of patients. There is also a need to develop some evidence based protocols for the health-care sectors, in which there is still lack of specific management related to monitoring methods, equipments and other technical resources. Optimization of physiological parameters, understanding of basic neurocritical care knowledge as well as incorporation of newer guidelines would certainly have a substantial impact on the outcome of the TBI patients.

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