REVIEW ARTICLE

Specific intensive care management of patients with traumatic brain injury: Present and future

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ABSTRACT

Traumatic brain injury (TBI) is a major global problem and affects approximately 10 million peoples annually; therefore has a substantial impact on the health-care system throughout the world. In this article, we have summarized various aspects of specific intensive care management in patients with TBI including the emerging evidence mainly after the Brain Trauma Foundation (BTF) 2007 and also highlighted the scope of the future therapies. This review has involved the relevant clinical trials and reviews (from 1 January 2007 to 31 March 2013), which specifically discussed about the topic. Though, BTF guideline based management strategies could provide standardized protocols for the management of patients with TBI and have some promising effects on mortality and morbidity; there is still need of inclusion of many suggestions based on various published after 2007. The main focus of majority of these trials remained to prevent or to treat the secondary brain injury. The future therapy will be directed to treat injured neurons and may benefit the outcome. There is also urgent need to develop some good prognostic indicators as well.

Key words: *Clinical trials, head injury, intensive care management, traumatic brain injury*

INTRODUCTION

Traumatic brain injury (TBI) is a major global problem and affects approximately 10 million peoples annually; therefore has a substantial impact on the health-care system throughout the world.[1-3] This epidemic not only produces high mortality and morbidity, also significantly does affect the socio-economic lives of survivors and even, some may have long-term disabilities.[1-4]

The evidence-based guidelines for management of head injury patients provided by the Brain Trauma Foundation (BTF), has been modified and revised in 2007.[5] These guidelines could provide the standardized protocols for the management of patients with TBI. Thereafter, the results of various trials have been published and the major focus is mainly to minimize the secondary brain injury following the primary insults; however, results and conclusions of these trials are yet to be opted by standard guidelines.

In this article, we have summarized various aspects of specific intensive care management in patients with TBI including the emerging evidence mainly after the BTF 2007 and also highlighted the scope of the future therapies.

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MATERIALS AND METHODS

This is a narrative review based on PubMed search on the terms including "TBI," "head injury," "head trauma," "intensive care," "management." BTF guidelines were updated in 2007; however, they have included the evidences published until 2006.[5] 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 prehospital

management as well as general intensive care management in patients with TBI are also not included in this review.

Prehospital and general intensive care management

Secondary brain injuries have a substantial impact on the overall outcome in patients with TBI. These injuries appear minute to hours after the primary insults and therefore early recognization and prompt treatment can salvage most of the effects of secondary brain injuries or even may help to prevent them.

Thus, the actual management starts from the prehospital and also includes the management at the emergency department. The majority of initial management includes maintenance of an adequate airway, breathing and perfusion.[6] General intensive care of these patients further comprises of proper establishment of airway, ventilation, adequate sedation, avoidance of hypo/hyperglycemia, instituting normothermia, prevention of seizures, correction of anemia and coagulopathy, deep vein thrombosis prophylaxis, early nutritional therapies to avoid the hyper catabolic state, stress ulcer prophylaxis and maintenance of hygiene to minimize the infections.[5,7]

Specific management

Specific management of patients with TBI constitutes the application of specialized neuromonitoring as well as the maneuvers or therapies to optimize the cerebral hemodynamics and further prevent the effects of secondary brain insults.

Monitoring

Apart from the essential monitoring including pulse oximetry, electrocardiography, blood pressure measurement, end tidal carbon dioxide, core body temperature and input/output, some specific monitoring are being used in the management of patients with TBI.[5-7] These monitoring methods aim to give valuable information regarding intracranial pressure (ICP), brain oxygenation, cerebral perfusion pressure, cerebral blood flow (CBF) and electrical activity of the brain, which in turn guide the further treatment.

Intracranial pressure monitoring

Raised ICP (>20 mm Hg) is associated with high mortality.[5] The BTF clinical practice guidelines recommend that ICP monitoring should be performed in comatose patients with-

1. Glasgow Coma Scale (GCS) 3-8 with abnormal computed tomography (CT) scans
2. Normal CT scans with two or more of the following features at admission:
   - Age over 40,
   - Unilateral or bilateral motor posturing, or
   - A systolic blood pressure of less than 90 mm Hg.

Routine ICP monitoring is not indicated in patients with mild or moderate head injury. Although ICP monitoring is used frequently in cases with severe TBI; there have been evidences questioning this practice. A recent multicenter randomized controlled trial on 324 severe head injury patients compared a goal directed therapy (ICP < 20 mm Hg) using intraparenchymal ICP monitoring to a clinical examination and imaging based strategy and found no difference on the primary endpoint, which included survival time, impaired consciousness and functional status (at 3 months and 6 months) and neuropsychological status at 6 months. In this study, median length of intensive care units (ICU) stay as well as overall mortality was similar in both groups.[8] Though, this was a well-designed multicenter randomized clinical trial (RCT) and provided the class I evidence; the treatment distributions (more barbiturate therapy in pressure based regime vs. more hyperventilation and hypertonic saline in clinical examination based group) were not similar to both groups. Therefore, the final interpretation of this study is still debatable.

The role of non-invasive ICP monitoring methods including ocular ultrasound and transcranial Doppler (TCD) has also been investigated. In this regard, ocular ultrasound can be a potential bedside monitor, which rapidly assesses the raised ICP.[9] The optic nerve sheath diameter measurement was found to be well-correlated with the values of ICP and its value significantly increased to 7.0 ± 0.58 mm, when ICP rose in value to >20 mm Hg.[10] On the other hand, TCD also measures rise in ICP indirectly. Pulsatility index (difference between systolic and diastolic flow velocity, divided by the mean flow velocity), is found to be correlated with the increase in ICP.[11] It can signify either rise in the ICP or decrease in the cerebral perfusion pressure (CPP).[11] These non-invasive tools may be used when use of invasive monitoring cannot be used or rather contraindicated.[9-11] However, both tools need to be validated in randomized controlled trials before they can be recommended for routine use in patients with severe TBI.

Cerebral oxygenation monitor

The global oxygenation as well as the regional oxygen saturation measurement methods are being investigated and have gained popularity among many researches to guide different therapies in patients with TBI based on these parameters.[12-16] Jugular venous oxygen saturation measuring the global oxygen saturation and near infrared spectroscopy (NIRS) for measuring the regional oxygen saturation is the two monitors that are commonly used in patients with TBI.[12-16]

The ability to relate CBF and metabolism may be provided by the placement of a catheter in the jugular bulb.

Uncoupling of these two parameters can be determined by measuring cerebral venous oxygen saturation' which then permits the calculation of cerebral arterial-venous oxygen difference, which is a reflection of the relative adequacy of CBF to meet the metabolic needs of the brain. If the brain is hypoperfused, oxygen extraction will be increased and SjvO2 will be reduced.[12,13] On the other hand, if CBF is adequate for the brain's metabolic need, then SjvO2 will remain normal. This monitoring should be used in conjunction with moderate to severe hyperventilation therapy for patients with intracranial hypertension.

Brain tissue oxygen tension (PbtO2) is a measurement of focal cerebral oxygenation using an invasive probe (Licox) and is mainly used to monitor oxygenation of a critically perfused brain tissue. The normal PbtO2 ranges between 35 mm Hg and 50 mm Hg. A value of a PbtO2 < 15 mm Hg is considered a threshold for focal cerebral ischemia and treatment.[14,15] A systemic review of what type of studies highlighted that PbtO2 guided therapy coupled with ICP/CPP based therapy was associated with better patient's outcome and reduced mortality in comparison with ICP/CPP based therapy alone.[15] However, there is still need of a large randomized controlled trial to prove its effectiveness. NIRS offers non-invasive bedside measurement of direct regional cerebral arteriovenous (mixed) brain oxygenation. NIRS can also give the measurement of tissue perfusion.[16]

Microdialysis

Early predictors of ischemia are key factors for determining secondary brain injury and serve as a determinant of outcome. Microdialysis is one of the techniques that can be used to detect these markers of ischemia. Lactate-pyruvate ratio (L/P ratio) and glycerol concentrations were found to have a negative correlation with the patient's outcome.[17,18] Some investigators advocated that use of early microdialysis based therapies had a distinct advantage in better patient's outcome.

Electrophysiological monitoring

To know about the brain functions in patients with TBI, electroencephalogram (EEG) and evoked potential monitoring may be employed.[19,20] In one study, changes in somatosensory evoked potentials (SEP) have been shown to correlate with changes in ICP and can constitute a complementary tool to interpret ICP trends.[19] EEG-SEP monitoring reflects to remaining metabolic activity of brain parenchyma. However, EEG recordings usually get suppressed and difficult to interpret during deep sedation. Therefore, the role of electrocoricography in patients with TBI is not usually advocated; however, study showed that spreading depolarizations were associated with unfavorable outcome and opened the door for future therapeutic options based on these findings.[20]

ICP and CPP thresholds

Cerebral ischemia is the single most important secondary factor that influences the outcome after TBI; therefore maintenance of CPP has become a crucial factor for the management of patients with TBI. The controversies exist between the CPP based therapy and ICP based therapy.[21,22]

Concept of CPP target therapy was given by Rosner *et al*.[60] in 1996, who demonstrated an improvement in outcome when CPP was maintained above 70 mm Hg. However, in patients of severe TBI with the loss of vascular autoregulation, there occurs dissociation between CBF and metabolic requirements. In such circumstance, increasing CPP can lead to extravasation of fluid (cerebral edema), increased hydrostatic pressure across the cerebral capillary bed, which may culminate in vasogenic edema and intracranial hypertension. The trial based on low versus high CPP based treatment on 58 patients with moderate to severe TBI showed that in patients with more impaired cerebral autoregulation, CPP <50 mm Hg and CPP <60 mm Hg were associated with favorable outcome, whereas CPP >70 mm Hg and CPP >80 mm Hg were associated with unfavorable outcome.[21] There was no significant difference found in the outcome among those groups in which autoregulation was found to be intact.[21] Therefore, in cases of severe TBI and other patients with disrupted autoregulation, it is prudent to keep CPP at the lower level (below 70 mm Hg).

On the other hand, there is ICP based approach, which is known as Lund protocol, which aims to minimize the CPP target to a level (50 mm Hg) that avoids frank ischemia, but does not lead to further cerebral edema. Preservation of normal colloid pressure, reduction of blood pressure and reduction of cerebral blood volume are the three mechanisms, which decreases microvascular pressure, in turn, decreases edema formation. In RCT of 60 comatose patients with secondary brain ischemia following aneurysmal sub arachnoid hemorrhage and severe TBI, in comparison with CPP based therapy, modified (microdialysis based) ICP based Lund concept was found to be associated with a better outcome.[22] However, this approach has not been validated in large RCTs, not endorsed by the current clinical practice guideline by BTF.[5]

Ultimately, monitoring metabolic parameters in individual patients, such as brain tissue oxygen and L/P ratio as assayed by microdialysis, may allow further refinement of CPP targets on an individual basis.[22] Currently, the latest consensus is to use a CPP target of 50-70 mm Hg.[5] ICP and thus CPP can be controlled in a number of ways, including reduction in metabolic requirements using sedation, induced hyperventilation, hyperosmolar therapy, hypothermia and surgical adjuncts.

Despite all the above measures if ICP remains high then one should resort to below mentioned management strategies.

Induced hyperventilation

A reduction in PaCO2 causes cerebral vasoconstriction, thereby, reducing cerebral blood volume and consequently ICP.[23] When utilizing hyperventilation, a balance must be struck between the beneficial effect on ICP and the potential deleterious effect on CBF. Particularly in the first 24 h after TBI, CBF is reduced and aggressive hyperventilation can compound cerebral ischemia.[13,23] For this reason, hyperventilation should not be applied outside a dedicated neurointensive care setting when appropriate monitoring, such as jugular bulb oxygen saturation, can be employed.[5,13]

Hyperosmolar therapy

Hyperosmolar therapy is a key intervention for the management of cerebral edema and raised ICP after TBI.[24,25] It is indicated for acute increases in ICP as it has a rapid onset of action. Mannitol, an osmotic diuretic, is commonly employed for its immediate effect. It has plasma-expanding property and improves blood rheology due to reduction in hematocrit. Intravenous dose recommended is 0.25 g to 1 g/kg. Mannitol can be used on a repeated schedule. Monitoring of serum osmolality is useful so as to avoid systemic dehydration; serum osmolarity should not be allowed to increase to more than 320 mosmol/kg. Mannitol also establishes an osmotic gradient between plasma and brain cells reducing cerebral edema by drawing water across areas of intact blood–brain barrier into the vascular compartment. Major side-effects however, are electrolyte disturbances such as hyponatremia, hypokalemia and hypotension.[25] A systematic review from Cochrane data base including 4 RCTs showed that mannitol therapy for patients with raised ICP was found to be associated with some beneficial effect on mortality when compared with pentobarbital treatment; however may have a detrimental effect on mortality when compared to hypertonic saline.[26] In addition, ICP directed therapy possess a little benefit over therapy based on neurological signs as well as physiological parameters.[26]

On the other hand, hypertonic saline is being used as an alternative to mannitol.[25] It is available in a range of concentrations from 1.7% to 29.2% and numerous regimens have been described, making it difficult to draw conclusions about the optimal dose or concentration required to control ICP. Hypertonic saline produces a reduction in cerebral edema by moving water out of cells, reducing tissue pressure and cell size resulting in a decrease in ICP. Other advantages over mannitol include its effectiveness as a volume expander, without hyperkalemia and impaired renal function. Major side-effects are increasing sodium load and congestive heart failure.[27] Although equimolar infusion of 20% mannitol is as effective as 7.45% hypertonic saline (HSS) in decreasing ICP in patients with brain injury but in patients with severe TBI and elevated ICP refractory to previous mannitol treatment, 7.5% hypertonic saline administration showed a significant increase in brain oxygenation and improved cerebral and systemic hemodynamics.[24,28] Small trials have also investigated the effects of other hyperosmolar solutions including sodium bicarbonate and sodium lactate and these agents were found to have similar effects as mannitol or hypertonic saline.[29]

Existing literature do not support favoring boluses of hypertonic saline over mannitol in terms of ICP control in relation to the outcome and in fact questioned about the role of any osmotherapy in such cases.[25,30,31]

Corticosteroids

The role of steroids is at present inconclusive. In addition, the type of steroids and low dose versus high dose steroids are the issues, which need further considerations. The Corticosteroid Administration after Severe Head Injury trial showed increased mortality at 2 weeks (21.1% vs. 17.9%) as well as at 6 month (25.7% vs. 22.3%) when compared with placebo.[32,33] In this trial, 10,008 adults patients with head injury (GCS <14) within 8 h of injury were randomly allocated to either 48 h infusion of corticosteroids (methylprednisolone) or placebo. However, one RCTs on 150 patients with severe multiple trauma highlighted that low dose of steroids (hydrocortisone 200 mg/d for 5 days, followed by 100 mg on day 6 and 50 mg on day 7) may prevent hospital acquired pneumonia and found to decrease in the length of ICU stay.[34] The other results of other RCT on the role of low dose of steroids (hydrocortisone and fludrocortisones vs. double placebo) patients with TBI has yet to be published and may provide some important guidelines related to steroid use in this subgroup of patients.[35]

Temperature management

TBI initiates several metabolic processes that can exacerbate the injury.[36] Hyperthermia is one of the potential factors exaggerating the secondary injury. Hyperthermia may develop due to infections or some neurogenic mechanisms. Recent observational study of 7145 patients has shown that both degree and duration of early post head injury fever are strongly correlated with outcome.[37] It is prudent to keep the patients normothermic and antipyretics as well as surface cooling can be used to attain this.[36-38]

On the other hand, there is evidence that hypothermia may limit some of these deleterious metabolic responses

and improve the outcome.[39,40] However, the literature suggests that therapeutic hypothermia should be instituted as soon as practical (in the emergency room) and beneficial effect usually seen when it has been continued for at least 72 h.[40] In a RCT ($n = 82$), role of moderate hypothermia (32-33°C) in closed head injury (GCS 5-7) patients was found to hasten the neurologic recovery and improved the outcome.[41] A Cochrane review in 2009 analyzed 23 trials with a total of 1614 patients and found no evidence supporting the use of hypothermia during the treatment of TBI, but did find a statistically significant increased risk of pneumonia and other potentially harmful side-effects.[42] The important multicenter randomized controlled trial (The Eurotherm 3235 trial) on therapeutic hypothermia (32-35°C) in ICP reduction following TBI has recently been completed; however, its results is still awaiting and could be important to give better insight about this therapy.[43]

Barbiturate coma

Barbiturate coma is effective in reducing the ICP by suppressing cerebral metabolism, thus reducing cerebral metabolic demands and cerebral blood volume.[44] This therapy is associated with many complications including immunosuppression, infectious complications and hypotension. There is no clinical evidence of improved patient outcomes after barbiturate coma though an infusion of thiopentone to achieve EEG burst suppression is still commonly used when trying to control severe refractory intracranial hypertension.[44] Thiopentone was found to be better ICP reducing agent in comparison to pentobarbital; however, incidence of hypotensive episodes, outcome and mortality data were similar in both groups.[45] Recent Cochrane review (7 clinical trials, 341 patients) also showed no outcome benefit using the barbiturate therapy in patients with severe head injury; however, there was more frequent episodes of hypotension (1 in every four patients), which offset the improvement in ICP by decreasing the CPP.[44]

Surgical interventions

The surgical modalities, which are used for the treatment of refractory ICP, include lumbar drain, external ventricular drain and decompressive craniectomy. Though, lumbar drain had been shown to provide some beneficial effect in head injury patients having refractory ICP; it should be used with great caution due to potential risk of herniation.[46]

External ventricular drainage (EVD) involves placing a catheter into the ventricular system in to allow drainage of CSF. In conditions of reduced intracranial compliance, even drainage of a few milliliters of CSF can have a dramatic effect on ICP. The main advantage of this CSF drainage is that it can be inserted in intensive care without the need for transfer to an operating theater. The risks related to surgical placement are hematoma and infection. A retrospective review of 377 patients with head injury, found that in comparison to intraparenchymal ICP monitoring, use of EVDs in adult TBI patients was associated with prolonged ICP monitoring, ICU length of stay and more frequent device-related complications.[47] However, age of the patient, opening ICP and size of midline shift were found to be independent predictors for neurologic outcomes and mortality, when other variables were controlled.[47]

Decompressive Craniectomy (DECRA) is a surgical procedure in which a large area of the skull vault is removed and the dura opened to allow the brain to expand out of the confines of the rigid skull. It can be performed unilaterally during the evacuation of a specific space-occupying lesion or, in diffuse injury; a bifrontal craniectomy can be used to remove the most anterior part of the skull.[48] There is evidence to demonstrate that this procedure reduces ICP, but a beneficial effect on outcome is yet to be proven. A multicenter randomized controlled trial compared decompressive craniectomy (bifrontotemporoparietal) to standard care in 155 patients with refractory intracranial hypertension. This trial, DECRA trial (early DECRA in patients with severe TBI) showed that in spite of reduction in ICP and length of ICU stay, patients undergoing decompressive craniectomy (DC) were more likely to have unfavorable outcomes.[49] The possible explanation was accredited to neuronal stretch produced after the DC. However, overall mortality remained similar in both groups; therefore, change of practice based on this trial needs well-designed RCTs in the near future.

Future therapies

Homeostatic cellular processes governing calcium influx, mitochondrial function, membrane stability, redox balance, blood flow and cytoskeleton structure often become dysfunctional after TBI. Most of the therapies are being developed toward the minimization of secondary brain injuries and includes hyperbaric oxygen therapy (HBOT), neuroprotective agents and gene/stem cell therapy.[50-56]

In HBOT, 100% oxygen at environmental pressures greater than 1 atmosphere absolute is administered for respiration in an airtight vessel. Therefore, there is a substantial increase in partial pressure of oxygen to the tissues that can help to improve the oxygen delivery to the injured brain tissue and also reduces brain edema. This therapy has shown some promising results to decrease the overall mortality in patients with severe TBI; however, there were no substantial improvement found related to neurological outcome of these patients.[50] In addition, the potential side-effects of oxygen toxicity are also concern. Thus, large well-defined controlled trials are needed to prove its effectiveness in patients with TBI.

TBI generates many pro-inflammatory mediators and leads to secondary brain injury. The main goal of developing future neuroprotective treatments for TBI is to minimize the detrimental and neurotoxic effects of these inflammatory mediators and help in the regeneration and repair after injury.[51-54] Many agents such as selfotel, pegorgotein (PEG-SOD), magnesium, deltibant and dexanabinol, statins were investigated; however found to be ineffective in clinical trials. The beneficial role of other agents such as progesterone, thyrotropin-releasing hormone and cyclosporine has yet to be tested in large trials. The other potential area of the target is apoptotic pathways. Many agents are being investigated to block the intermediate pathways related to apoptosis. However, the apoptotic changes are also essential for normal functioning of cells; therefore, blocking the pathways by these agents would lead to possible potential complications.[51-54]

Genes that are implicated in TBI outcome include APOE, MAO-A, BDNF, NOS3, IL-6, NEFH, SLC6A4, COMT, PPP3CC and KIBRA genes. These genes are linked with modulations of various mechanisms including CBF, autoregulation and cerebral edema.[54] Further researches are warranted to implicate these genetic studies and identify new genes, which could affect the outcome.

The stem cell transplant is another area of potential interest, which could affect the future therapy in patients with TBI. These therapies are usually focused to repair the various types of injured neural tissues. However, this is still in infancy phase and needs future research to establish its effectiveness.[55,56]

Prognosis

Prognostic indicators are usually the reflection of effectiveness of management strategies. Canadian multicenter retrospective study recently highlighted the prognosis of patients with severe TBI.[57] In the study of 720 patients, the overall hospital mortality was 31.7% and ranged from 10.8% to 44.2% across centers. Most deaths (70.2%) were associated with withdrawal of life-sustaining therapy, ranging from 45.0% to 86.8% across centers and mainly occurred within 3 days of care.[57] In the recent study, the same group of investigators has further shown that there exist a significant variation in the perceptions of neurologic prognosis and in clinical decision making on the level of care was found among intensivists, neurosurgeons and neurologists. Therefore, there exist wide variations of treatment protocols as well as prognostic methods among different centers and warrant future trials to formulate better prognostic criteria as well as standardized protocols.[58] Further to this, the effects of genetic and biological variables on prognosis/outcome needs to be re-integrated for the development of better resuscitative and rehabilitative management protocols.[59]

DISCUSSION

Several trials have been conducted and published after the BTF guidelines-2007. The trial on specialized neuromonitoring such as ICP monitoring does not support the routine use of it and indeed found to have a similar outcome results when compared the conventional methods for neurological assessment including clinical as well as imaging.[8] The role of other forms of non-invasive monitoring methods including ocular ultrasound and TCD has yet to be proven in well-designed RCTs; however these can be of value to give prompt diagnosis of raised ICP and may be utilized for the cases in which invasive monitoring cannot be used.[9-11] The other neuromonitoring methods pertaining to brain oxygenation, metabolism and electrophysiological activities have been investigated in small trials; therefore warrant future RCTs.[12-20] There is some evidence for using the jugular venous oxygen saturation monitoring in cases of raised ICP, which may require moderate to severe hyperventilation.

The CPP based regime seems more plausible in comparison to ICP based therapy and optimum CPP could not be determined; however, higher CPP (>70 mm Hg) has no distinct advantage and may even associated with complications.[21,22] Lower limit of CPP would depend upon various factors including intact autoregulation, associated with other hemorrhagic injuries and needs to be defined. The role of hyperventilation is limited and should be avoided in first 24 h.[23] The medical management of raised ICP remains osmotherapy; however no distinct advantage of one agent (mannitol) was seen over other (hypertonic saline).[24-31] Even, the role of osmotherapy in patients with TBI is also questioned.[29-31] The corticosteroids have been associated with increases mortality and poor outcome.[34,35] Similarly, the role of barbiturate coma is inconclusive and showed higher risks of complication; therefore cannot be recommended.[44,45] In addition, therapeutic hypothermia has shown some promising role in very few trials; however majority of literature do not support it.[39-43] Hyperthermia should be promptly treated.[36-38] Normothermia is advocated in many trials. The surgical therapies to reduce ICP including lumbar drain, EVD and decompressive craniectomy are also found to be ineffective to produce a favorable outcome and needs further large RCTs.[46-49]

CONCLUSION

Though BTF guideline based management strategies could provide standardized protocols for the management of patients with TBI and have some promising effects on

mortality and morbidity; there is still need of inclusion of many suggestions based on various published after 2007. The main focus of majority of these trials remained to prevent or treat secondary brain injury. The future therapy will be directed to treat injured neurons and may benefit the outcome. There is also urgent need to develop some good prognostic indicators as well.

REFERENCES

1. Corrigan JD, Selassie AW, Orman JA. The epidemiology of traumatic brain injury. J Head Trauma Rehabil 2010;25:72-80.
2. Hyder AA, Wunderlich CA, Puvanachandra P, Gururaj G, Kobusingye OC. The impact of traumatic brain injuries: A global perspective. NeuroRehabilitation 2007;22:341-53.
3. Gean AD, Fischbein NJ. Head trauma. Neuroimaging Clin N Am 2010;20:527-56.
4. Feigin VL, Theadom A, Barker-Collo S, Starkey NJ, McPherson K, Kahan M, *et al*. Incidence of traumatic brain injury in New Zealand: A population-based study. Lancet Neurol 2013;12:53-64.
5. Bullock MR, Povlishock JT. Brain Trauma Foundation, American Association of Neurological Surgeons, Congress of Neurological Surgeons, AANS/CNS Joint Section on Neurotrauma and Critical Care. Guidelines for the Management of Severe Traumatic Brain Injury. 3rd ed. J Neurotrauma 2007;24 Suppl 1:S1-106.
6. Badjatia N, Carney N, Crocco TJ, Fallat ME, Hennes HM, Jagoda AS, *et al*. Guidelines for prehospital management of traumatic brain injury 2nd edition. Prehosp Emerg Care 2008;12 Suppl 1:S1-52.
7. Mateen FJ. Neurocritical care in developing countries. Neurocrit Care 2011;15:593-8.
8. Chesnut RM, Temkin N, Carney N, Dikmen S, Rondina C, Videtta W, *et al*. A trial of intracranial-pressure monitoring in traumatic brain injury. N Engl J Med 2012;367:2471-81.
9. Cammarata G, Ristagno G, Cammarata A, Mannanici G, Denaro C, Gullo A. Ocular ultrasound to detect intracranial hypertension in trauma patients. J Trauma 2011;71:779-81.
10. Soldatos T, Karakitsos D, Chatzimichail K, Papathanasiou M, Gouliamos A, Karabinis A. Optic nerve sonography in the diagnostic evaluation of adult brain injury. Crit Care 2008;12:R67.
11. Gura M, Elmaci I, Sari R, Coskun N. Correlation of pulsatility index with intracranial pressure in traumatic brain injury. Turk Neurosurg 2011;21:210-5.
12. Zabolotskikh IB, Mindiiarov Alu, Babakov AS, Konareva TI. Intracranial pressure and jugular venous oxygenation influence on outcome in patients with severe traumatic brain injury. Anesteziol Reanimatol 2011;4:50-5.
13. Bhatia A, Gupta AK. Neuromonitoring in the intensive care unit. II. Cerebral oxygenation monitoring and microdialysis. Intensive Care Med 2007;33:1322-8.
14. Rosenthal G, Hemphill JC 3rd, Sorani M, Martin C, Morabito D, Obrist WD, *et al*. Brain tissue oxygen tension is more indicative of oxygen diffusion than oxygen delivery and metabolism in patients with traumatic brain injury. Crit Care Med 2008;36:1917-24.
15. Nangunoori R, Maloney-Wilensky E, Stiefel M, Park S, Andrew Kofke W, Levine JM, *et al*. Brain tissue oxygen-based therapy and outcome after severe traumatic brain injury: A systematic literature review. Neurocrit Care 2012;17:131-8.
16. Calderon-Arnulphi M, Alaraj A, Slavin KV. Near infrared technology in neuroscience: Past, present and future. Neurol Res 2009;31:605-14.
17. Omerhodzić I, Dizdarević K, Rotim K, Hajdarpasić E, Niksić M, Bejtić-Custović E, *et al*. Cerebral microdialysis: Perioperative monitoring and treatment of severe neurosurgical patient. Acta Clin Croat 2011;50:13-20.
18. Karathanou A, Paterakis K, Pakopoulou M, Tasiou A, Hadjigeorgiou G, Chovas A, *et al*. Biochemical markers analyzed using microdialysis and traumatic brain injury outcomes. J Neurosurg Sci 2011;55:173-7.
19. Amantini A, Fossi S, Grippo A, Innocenti P, Amadori A, Bucciardini L, *et al*. Continuous EEG-SEP monitoring in severe brain injury. Neurophysiol Clin 2009;39:85-93.
20. Hartings JA, Bullock MR, Okonkwo DO, Murray LS, Murray GD, Fabricius M, *et al*. Spreading depolarisations and outcome after traumatic brain injury: A prospective observational study. Lancet Neurol 2011;10:1058-64.
21. Johnson U, Nilsson P, Ronne-Engström E, Howells T, Enblad P. Favorable outcome in traumatic brain injury patients with impaired cerebral pressure autoregulation when treated at low cerebral perfusion pressure levels. Neurosurgery 2011;68:714-21.
22. Dizdarevic K, Hamdan A, Omerhodzic I, Kominlija-Smajic E. Modified Lund concept versus cerebral perfusion pressure-targeted therapy: A randomised controlled study in patients with secondary brain ischaemia. Clin Neurol Neurosurg 2012;114:142-8.
23. Curley G, Kavanagh BP, Laffey JG. Hypocapnia and the injured brain: More harm than benefit. Crit Care Med 2010;38:1348-59.
24. Francony G, Fauvage B, Falcon D, Canet C, Dilou H, Lavagne P, *et al*. Equimolar doses of mannitol and hypertonic saline in the treatment of increased intracranial pressure. Crit Care Med 2008;36:795-800.
25. Ropper AH. Hyperosmolar therapy for raised intracranial pressure. N Engl J Med 2012;367:746-52.
26. Wakai A, Roberts I, Schierhout G. Mannitol for acute traumatic brain injury. Cochrane Database Syst Rev 2007;1:CD001049.
27. Fink ME. Osmotherapy for intracranial hypertension: Mannitol versus hypertonic saline. Continuum (Minneap Minn) 2012;18:640-54.
28. Oddo M, Levine JM, Frangos S, Carrera E, Maloney-Wilensky E, Pascual JL, *et al*. Effect of mannitol and hypertonic saline on cerebral oxygenation in patients with severe traumatic brain injury and refractory intracranial hypertension. J Neurol Neurosurg Psychiatry 2009;80:916-20.
29. Ichai C, Armando G, Orban JC, Berthier F, Rami L, Samat-Long C, *et al*. Sodium lactate versus mannitol in the treatment of intracranial hypertensive episodes in severe traumatic brain-injured patients. Intensive Care Med 2009;35:471-9.
30. Bulger EM, Hoyt DB. Hypertonic resuscitation after severe injury: Is it of benefit? Adv Surg 2012;46:73-85.
31. Grände PO, Romner B. Osmotherapy in brain edema: A questionable therapy. J Neurosurg Anesthesiol 2012;24:407-12.
32. Roberts I, Yates D, Sandercock P, Farrell B, Wasserberg J, Lomas G, *et al*. Effect of intravenous corticosteroids on death within 14 days in 10008 adults with clinically significant head injury (MRC CRASH trial): Randomised placebo-controlled trial. Lancet 2004;364:1321-8.
33. Edwards P, Arango M, Balica L, Cottingham R, El-Sayed H, Farrell B, *et al*. Final results of MRC CRASH, a randomised placebo-controlled trial of intravenous corticosteroid in adults with head injury-outcomes at 6 months. Lancet 2005;365:1957-9.
34. Roquilly A, Mahe PJ, Seguin P, Guitton C, Floch H, Tellier AC, *et al*. Hydrocortisone therapy for patients with multiple trauma: The randomized controlled HYPOLYTE study. JAMA 2011;305:1201-9.
35. Asehnoune K, Roquilly A, Sebille V, Corti-TC trial group. Corticotherapy for traumatic brain-injured patients — The Corti-TC trial: Study protocol for a randomized controlled trial. Trials 2011;12:228.
36. Childs C. Human brain temperature: Regulation, measurement and relationship with cerebral trauma: Part 1. Br J Neurosurg 2008;22:486-96.

37. Li J, Jiang JY. Chinese Head Trauma Data Bank: Effect of hyperthermia on the outcome of acute head trauma patients. J Neurotrauma 2012;29:96-100.
38. Badjatia N. Hyperthermia and fever control in brain injury. Crit Care Med 2009;37:S250-7.
39. Urbano LA, Oddo M. Therapeutic hypothermia for traumatic brain injury. Curr Neurol Neurosci Rep 2012;12:580-91.
40. Fox JL, Vu EN, Doyle-Waters M, Brubacher JR, Abu-Laban R, Hu Z. Prophylactic hypothermia for traumatic brain injury: A quantitative systematic review. CJEM 2010;12:355-64.
41. Marion DW, Penrod LE, Kelsey SF, Obrist WD, Kochanek PM, Palmer AM, *et al*. Treatment of traumatic brain injury with moderate hypothermia. N Engl J Med 1997;336:540-6.
42. Sydenham E, Roberts I, Alderson P. Hypothermia for traumatic head injury. Cochrane Database Syst Rev 2009;2:CD001048.
43. Andrews PJ, Sinclair HL, Battison CG, Polderman KH, Citerio G, Mascia L, *et al*. European society of intensive care medicine study of therapeutic hypothermia (32-35°C) for intracranial pressure reduction after traumatic brain injury (the Eurotherm3235Trial). Trials 2011;12:8.
44. Roberts I, Sydenham E. Barbiturates for acute traumatic brain injury. Cochrane Database Syst Rev 2012;12:CD000033.
45. Pérez-Bárcena J, Llompart-Pou JA, Homar J, Abadal JM, Raurich JM, Frontera G, *et al*. Pentobarbital versus thiopental in the treatment of refractory intracranial hypertension in patients with traumatic brain injury: A randomized controlled trial. Crit Care 2008;12:R112.
46. Tuettenberg J, Czabanka M, Horn P, Woitzik J, Barth M, Thomé C, *et al*. Clinical evaluation of the safety and efficacy of lumbar cerebrospinal fluid drainage for the treatment of refractory increased intracranial pressure. J Neurosurg 2009;110:1200-8.
47. Kasotakis G, Michailidou M, Bramos A, Chang Y, Velmahos G, Alam H, *et al*. Intraparenchymal vs extracranial ventricular drain intracranial pressure monitors in traumatic brain injury: Less is more? J Am Coll Surg 2012;214:950-7.
48. Tagliaferri F, Zani G, Iaccarino C, Ferro S, Ridolfi L, Basaglia N, *et al*. Decompressive craniectomies, facts and fiction: A retrospective analysis of 526 cases. Acta Neurochir (Wien) 2012;154:919-26.
49. Cooper DJ, Rosenfeld JV, Murray L, Arabi YM, Davies AR, D'Urso P, *et al*. Decompressive craniectomy in diffuse traumatic brain injury. N Engl J Med 2011;364:1493-502.
50. Bennett MH, Trytko B, Jonker B. Hyperbaric oxygen therapy for the adjunctive treatment of traumatic brain injury. Cochrane Database Syst Rev 2012;12:CD004609.
51. Darkazalli A, Levenson CW. Tracking stem cell migration and survival in brain injury: Current approaches and future prospects. Histol Histopathol 2012;27:1255-61.
52. Kumar A, Loane DJ. Neuroinflammation after traumatic brain injury: Opportunities for therapeutic intervention. Brain Behav Immun 2012;26:1191-201.
53. McConeghy KW, Hatton J, Hughes L, Cook AM. A review of neuroprotection pharmacology and therapies in patients with acute traumatic brain injury. CNS Drugs 2012;26:613-36.
54. Loane DJ, Faden AI. Neuroprotection for traumatic brain injury: Translational challenges and emerging therapeutic strategies. Trends Pharmacol Sci 2010;31:596-604.
55. Ugoya SO, Tu J. Bench to bedside of neural stem cell in traumatic brain injury. Stem Cells Int 2012;2012:141624.
56. Dardiotis E, Grigoriadis S, Hadjigeorgiou GM. Genetic factors influencing outcome from neurotrauma. Curr Opin Psychiatry 2012;25:231-8.
57. Turgeon AF, Lauzier F, Simard JF, Scales DC, Burns KE, Moore L, *et al*. Mortality associated with withdrawal of life-sustaining therapy for patients with severe traumatic brain injury: A Canadian multicentre cohort study. CMAJ 2011;183:1581-8.
58. Turgeon AF, Lauzier F, Burns KE, Meade MO, Scales DC, Zarychanski R, *et al*. Determination of neurologic prognosis and clinical decision making in adult patients with severe traumatic brain injury: A survey of Canadian intensivists, neurosurgeons, and neurologists. Crit Care Med 2013;41:1086-93.
59. Stevens RD, Sutter R. Prognosis in severe brain injury. Crit Care Med 2013;41:1104-23.
60. Rosner MJ, Rosner SD, Johnson AH. Cerebral perfusion pressure: management protocol and clinical results. J Neurosurg. 1995;83:949-62.

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