

Intra Cranial Pressure (ICP) Monitoring in Traumatic Brain Injury; What is the Evidence?



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Abstract

Introduction: Although ICP (intracranial pressure) monitoring is widely advocated in managing TBI (traumatic brain injury) patients, successive guidelines for the management of severe TBI have documented the inadequate evidence of efficacy of ICP monitors.

Objective: We have conducted this review to evaluate and critically appraise the available literature addressing the role of ICP monitor in managing TBI, in order to aid managing such patients and highlighting areas where further research is required.

Methods: Ovid via Medline, PubMed, and Google scholar databases were searched for eligible studies, search results were then limited to studies in English language, Humans and studies published within the last 5 years. The included studies were critically appraised using the Critical Appraisal Skills Programme (CASP) tool, and each study has then been ranked using the Harbour and Miller hierarchy of ranking.

Results and conclusion: The appraised evidence ruled out any superiority in outcome with continuing managing ICP, however the value of knowing the precise ICP is not being challenged, yet this research works as a reminder for the principal of ICP monitoring to guide rather than dictate treatment of the cerebral physiology in severe TBI, the research also indicates that more research is needed to better understand the intracranial physiology in TBI patients.

Keywords: Traumatic brain injury; Intracranial pressure monitoring

Introduction

Traumatic Brain Injury (TBI) remains a leading cause of death and disability in young people [1]. In 2013-2014 there were approximately 445 head injury admissions per day to UK hospitals; that is approximately one admission every 3 minutes [2]. While in the United States, every 15 seconds someone suffers a TBI. Moreover TBI causes more deaths in young adults than all other diseases combined [3].

TBI is a heterogeneous condition in regards to aetiology, pathology, classification, severity and outcome. Therefore, TBI management rely heavily on close, careful, and frequent clinical assessment, patient's physiological data, laboratory results, and of course radiological investigations [4]. Raised intracranial pressure is potentially a life threatening condition, as this can result in compromising brain circulation and compression of the brainstem. Raised ICP is the commonest cause of death in patients with TBI, ICP monitoring is therefore, a reasonable

approach to detect progressive increase in ICP in these patients [5].

Although ICP monitoring is widely advocated in managing TBI patients, this recommendation is mainly based on physiological principles and the concept of preventing secondary brain injuries; due to hypoxia, swelling, etc., rather than concrete class I evidence [6]. Despite the lack of evidence, intracranial pressure (ICP) monitoring is widely adopted for managing severe traumatic brain injury, i.e. Glasgow Coma Scale (GCS) <8 (see below), and its use is suggested by numerous protocols [7,8]. Nevertheless successive guidelines for the management of severe traumatic brain injury have documented the inadequate evidence of benefits regarding usage of ICP monitors [9], therefore its use in guiding therapy has incomplete acceptance, even in high-income countries [10].

Severity of traumatic brain injury is classified by using Glasgow Coma Scale (GCS), as Mild: GCS 15-13. Moderate: GCS

12-9, and Severe: GCS 8 or less [8]. Appendix I contains a table for explaining the GCS. The Brain Trauma Foundation (BTF) recommends intracranial pressure (ICP) monitoring in managing severe TBI [7], while on the other hand, more recent guidelines in view of the results of the largest multicentre randomised clinical trial concluded that ICP guided management for TBI patients is not superior to care based on imaging and clinical examination alone [9]. Due to the existence of conflicting recommendations, the usage of ICP monitoring remains controversial, and a consensus is far from being reached.

This literature review will evaluate and critically appraise some of the available literature addressing the role of ICP

monitor in managing TBI, to aid managing such patients and highlighting areas where further research is required as the implementation of evidence based medicine provides high quality standard medical care at the lowest cost [11].

A critical analysis of the literature will be conducted using the Critical Appraisal Skills Programme CASP (2010) tool [12] and then each study will be ranked using the Harbour & Miller [13] hierarchy of ranking.

Search Strategy

Table 1 below summarises the search strategy used for the literature search.

Table 1: Search strategy.

Keywords	The following key words were set to be recognised within article title, abstract, and/or keywords:
	Brain injury, Traumatic brain injury, Neurotrauma, Intracranial pressure (ICP).
Search Terms	Brain injury (OR) traumatic brain injury (OR) neurotrauma,
	Brain injury (OR) traumatic brain injury (OR) neurotrauma (AND) Intracranial pressure.
Limitations	The search was limited to the following:
	English Language.
	Humans.
	Between 2013 and current date.
Inclusion Criteria	The search included patients with traumatic brain injury; (eg. critically ill, multiple trauma, RTA victims, neurosurgical patients)
	The search also included systematic reviews, RCTs, cohort studies, and literature reviews.
Exclusion Criteria	The search excluded:
	Solely pregnant and post-partum patients.
	Neonates and paediatrics.
	Case reports.
	Descriptive reports.
Databases Used	Ovid SP (MedLine / Embase), PubMed, Google Scholar
Screening Evidencesd	Following the search, studies titles and abstracts were screened for relevance, inclusion and exclusion criteria, and non-qualifying articles were then excluded. Reference lists of included papers were reviewed with 'backward chaining' employed to gather pertinent papers for consideration.
Final Number	6 studies (1 RCT and 3 systematic reviews and 2 cohort studies) were identified, However limited by the nature of this short review; 3 studies will be critically appraised (1 RCT, and 2 systematic reviews).

Literature Review

This literature review includes detailed reviews of one Randomised controlled trial (RCT) and 2 systematic reviews performed in the last 5 years.

Randomised controlled trial

Chesnut et al. [9] conducted an RCT of intracranial-pressure monitoring in traumatic brain injury population, this was a multicentre trial conducted in 6 hospitals in South America (4 in Bolivia and 2 Ecuador). Participants were randomized to intracranial pressure monitoring (the pressure-monitoring group) or imaging and clinical examination (the imaging-clinical examination group) [9].

The primary objective of this trial, or what is often referred to as the (BEST: TRIP) trial (Benchmark Evidence from South American Trials: Treatment of Intracranial Pressure) was to assess whether the information derived from monitoring the intracranial pressure in patients with severe traumatic brain injury improves patient outcomes and medical practice or not. The randomization process was computer generated and the patients were stratified according to study site, severity of injury, and age. This is generally considered as a randomisation tool with low risk of bias ensuring even distribution of the baseline characteristics-potential confounding factors- between the two groups adding to the reliability and validity of the results [14].

The study was single blinded (only the outcome assessors were blinded from the group assignments) however both treating team and patients/families-when applicable-were aware of the group assignments. The limitation of the blinding process in this trial was perhaps understandably related to the nature of the intervention tested, as each group has a separate protocol for management, triggered by different clinical and monitoring data. Nonetheless the lack of blinding to the patients and the treating staff does raise the risks of performance bias.

In regards to the trial results, there was no significant difference in the primary outcome between the two groups. Six-month mortality was 39% in the pressure-monitoring group and 41% in the imaging-clinical examination group, accounting for a P value of 0.60. Although the number of days of brain-specific treatments-e.g. administration of hyperosmolar fluids and the use of hyperventilation-in the ICU was higher in the imaging-clinical examination group (mean of 4.8 days vs. 3.4 days respectively, $P=0.002$). The distribution of serious adverse events was similar in both groups.

Chesnut et al. [9] concluded that "For patients with severe traumatic brain injury, care focused on maintaining monitored intracranial pressure at 20mm Hg or less was not shown to be superior to care based on imaging and clinical examination" [9].

This study is ranked as 1+ in the Harbour & Miller [13] hierarchy of ranking for it being a well conducted RCT with a

low risk of bias.

Systematic reviews

Yuan et al. [15] conducted a systematic review and meta-analysis to assess the impact of intracranial pressure monitoring on mortality in patients with traumatic brain injury [15].

Advantages of the systematic reviews is that its quicker and cheaper method of collecting evidence in comparison to conducting new trials, it is also an objective and transparent approach for research synthesis, with low risk of bias if conducted appropriately. However this comes with the downside that its quality is dependent on the available trials and the reliability, validity and rigourousness of the included studies [16].

This review included a total of 14 studies, and has addressed a clearly focused question, whether ICP monitoring has any impact on mortality, intensive care unit (ICU) length of stay and/or hospital length of stay for patients with TBI [15].

On top of database searches, the authors did conduct personal contact with experts and authors for clarification on study details and/or missing data, contributing for a rigorous review. Nevertheless the authors neither declared nor published a protocol for their systematic review. In contrast to the recommended and increasingly adopted guidelines for systematic reviews, to ensure the quality of evidence provided, and decrease the chances for selection and performance bias [17].

In this review, most statistical analyses were performed using the review manager software [15]. The statistical level of significance this was set to be 5%, and the results of all 14 studies including 24,792 patients were analysed. The review results suggested that there is no evidence that ICP monitoring decreased the risk of death (pooled OR 0.93 [95% CI 0.77-1.11], $p=0.40$). However, 7 of the included studies -all published after 2012-revealed that ICP monitoring was significantly associated with a decrease in mortality than no ICP monitoring (pooled OR 0.56 [95% CI 0.41-0.78], $p=0.0006$). ICU length of stay were significantly longer for the group subjected to ICP monitoring (mean difference [MD] 0.29 [95% CI 0.21-0.37]; $p<0.00001$).

This systematic review was graded as 2++, for being a high quality systematic review of mainly cohort studies as well as a single RCT with a very low risk of confounding or bias.

Mendelson et al. [18] conducted a systematic review to examine the relationship between intracranial pressure monitors (ICP) monitors and mortality in traumatic brain injury (TBI) [18]. The review addressed a clear question, the population under study was the patients with TBI, intervention was ICP monitor devices, and the outcome was any effect on mortality. The search included two databases only: MEDLINE (1966-October 2011) and EMBASE (1977-October 2011) and has included 6 retrospective observational studies as no RCT

were conducted then on the topic. Moreover there was no risk of bias assessment conducted for the involved data; this is usually done in systematic reviews to assess the quality of evidence, which is an important process to ensure the included papers are rigorous, valid, and minimally biased [17].

In regards to base line characteristics all six studies had at least one clinical variable that differed significantly between the group of patients that received ICP monitoring and the controls. Patients in whom an ICP monitor was inserted were younger, had higher injury severity scores, more hypotension, and lower GCS [18]. One also notices the significant heterogeneity between the included studies, as well as within each study; this precluded performing a pooled analysis—a method frequently used in epidemiology when individual studies are either too small or too heterogeneous to allow any definite conclusion [19].

The results suggested few points; firstly there were frank differences both within and between studies in terms of which patients were chosen for ICP monitoring, the definition of severe TBI, the type of ICP monitor used. Secondly patients with ICP monitors had different clinical characteristics and received more ICP targeted therapy in the ICU.

Lastly, four studies found no significant relationship between ICP monitoring and survival, while the other two studies demonstrated conflicting results. For example: one study showed an overall harm to ICP monitor insertion on univariate analysis ($p < 0.032$), however, after controlling for injury severity and mechanism, ICP monitoring was associated with improved survival ($p < 0.015$) [20].

Discussion

Until the current time, the use for ICP monitors in guiding the management of traumatic brain injury is debatable. While successive guidelines for management of traumatic brain injury recommend the use of ICP, it is still a level II recommendation from the Brain Trauma Foundation (BTF) in patients with severe TBI (Glasgow Coma Scale (GCS) ≤ 8) [21]. Nonetheless, despite these recommendations, the use of ICP exhibits a significant variation across different hospitals and countries. This is related to the conflicting or absent clinical evidence as to the benefit of ICP monitoring [18].

Consecutive guidelines, however; documented the inadequate evidence in this topic, and have been calling for randomised controlled trials, while addressing the ethical dilemma for not providing the best available management (ICP monitoring) for the control group. This ethical issue was solved after Chestnut et al. [9] identified a group of intensivists in South America who routinely managed TBI without ICP monitors, with the same efficacy and comparable patients' outcome, hence the BEST TRIP trial [9].

Overall, the BEST TRIP trial is a well conducted RCT, addressing a genuine clinical debate, with it being prospective, and having a comprehensive nature of outcomes, addressing

mortality, morbidity and quality of life after discharge, adds to its strengths [9]. Nevertheless was it really testing the ICP as an intervention? The trial divided the study population into two groups (ICP group, and clinical assessment & imaging group) each has a separate management protocol. Hence one can argue it is in fact trial for the management protocol of TBI rather than the use of ICP, based on the fact that ICP monitor was not the sole difference between the control and intervention groups. However if we have to accept that by inserting an ICP monitor clinicians are obliged to manage raised ICP as required and have to tailor the management plan accordingly, this “two treatment protocols” trial could be the maximum possible, limited by the ethical and clinical obligations to patients.

Secondly the external validity of this trial is questionable, and the results are far from generalizable, as finding similar groups of intensivists who are competent and comfortable in managing TBI without ICP monitors is difficult these days, especially in the developed world where the equipment and facilities are readily available. Furthermore there are differences in pre-hospital care, in-hospital management, and post discharge rehabilitation services for TBI patients across different countries, and these differences may affect outcomes as well.

Moreover the trial did not comment on the number nor the cost of CT scans performed for the control group, this could be outweighing the costs for the ICP monitors, and adding to the risk of radiations to patients. Lastly the ICP cut off pressure for treatment in this trial was set at 20mm Hg, in contrast to previous studies where ICP of >25 was found to increase the mortality rate [5]. This could be criticised as different units use different cut off pressure points, hence the need for appreciating the need for diverting the attention from the absolute number to the underlying pathophysiology of TBI and the patient's overall condition.

With regards to the meta-analysis conducted by Yuan et al. [15], the study examined the association between ICP monitoring and outcome in patients with TBI. Fourteen studies compared mortality in TBI in an ICP monitoring group and a “no-ICP monitoring” group and reported no evidence that ICP monitoring decreased the odds of death. Interestingly subgroup analysis revealed that ICP monitoring was significantly associated with a decrease in mortality compared to the “no-ICP monitoring” in studies published after 2012; is there any clinical significance for that regardless of statistical significance? This remains a theory requiring further testing. Despite the above the isolated benefit of ICP monitoring in severe TBI is still not clear.

The main weaknesses of this review were the scarcity of the included studies together with the significant heterogeneity of the study sample and the outcome of interest despite applying the appropriate statistical analysis tools. This could be related to the fact that different management protocols are adopted for raised ICP. Therefore further effort should focus on standardizing ICP monitoring and on identifying clinical subgroups of TBI patients who may benefit from ICP monitoring.

While Mendelson AA et al. [18] review to examine the relationship between intracranial pressure monitors (ICP) monitors and mortality in traumatic brain injury (TBI) included six observational studies with 11,371 patients; four studies found no significant relationship between ICP monitoring and survival, while the other two studies demonstrated conflicting result.

ICP monitoring may still influence outcomes independently and hence deserves more attention. However, being a monitoring device, a distinction must be made between the information obtained from the ICP monitor and the interventions initiated based on this information. The overall accuracy of the ICP monitors was investigated by Zacchetti et al (2015), and was confirmed that the pressure readings are highly accurate and average error between ICP measures is clinically negligible (Figure 1 & 2).

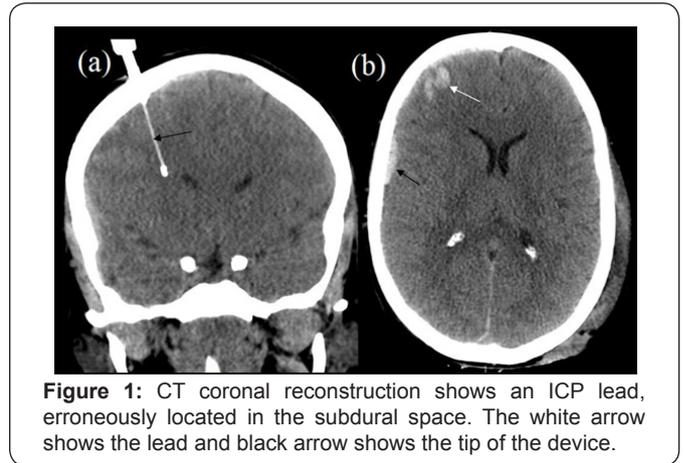


Figure 1: CT coronal reconstruction shows an ICP lead, erroneously located in the subdural space. The white arrow shows the lead and black arrow shows the tip of the device.

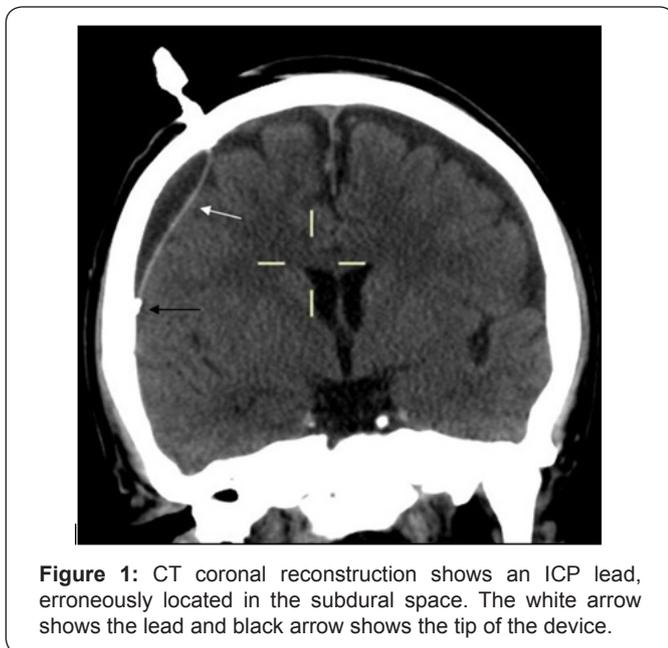


Figure 1: CT coronal reconstruction shows an ICP lead, erroneously located in the subdural space. The white arrow shows the lead and black arrow shows the tip of the device.

Conclusion

Significant part of managing TBI patients is to prevent, identify, and manage secondary brain injury. This is centred on ICP monitoring, which is generally a safe method and does provide accurate data for guiding the management. However ICP monitoring is not without risks, such as infection, malplacement, haemorrhage, or malfunction, and as with any monitoring in the ICU, the goal is to both obtain accurate data and initiate interventions that positively affect outcomes.

Although previous evidence ruled out any superiority in outcome with continuously monitoring intracranial pressure, however the value of knowing the precise intracranial pressure is not being challenged, yet what could be gathered from this research is to re-evaluate the principal of manipulating monitored intracranial pressure as part of targeted treatment of severe traumatic brain injury, and target the cerebral physiology instead. In other words the dissenting publications should not lead to questions of ICP monitor use in total, but rather indicate that more research is needed to understand the intracranial physiology in TBI patients better, to use ICP monitoring in a more targeted and effective fashion.

Appendix I (Table 2)

Table 2: Glasgow Coma Scale [8].

Aspect	1	2	3	4	5	6
Best eye response	No eye opening	Opens eyes in response to painful stimuli	Opens eyes in response to voice	Opens eyes spontaneously	N/A	N/A
Best verbal response	No verbal response	Incomprehensible sounds	Utters inappropriate words	Confused, disoriented	Oriente, converses normally	N/A
Best motor response	No motor response	Extension to painful stimuli (decerebrate response)	Abnormal flexion to painful stimuli (decorticate response)	Flexion / Withdrawal to painful stimuli	Localizes painful stimuli	Obeys commands

Appendix II

Harbour and Miller [13] hierarchy of evidence [14]:

1++ High quality meta analyses, systematic reviews of RCTs or RCTs with a very low risk of bias.

1+ Well conducted meta analyses, systematic reviews of RCTs, or RCTs with a low risk of bias.

1- Meta analyses, systematic reviews of RCTs, or RCTs with a high risk of bias

2++ High quality systematic reviews of case-control or cohort studies. High quality case-control or cohort studies with a very low risk of confounding, bias, or chance and a high probability that the relationship is casual.

2+ Well conducted case-control or cohort studies with a low risk of confounding, bias or chance and a moderate probability that the relationship is casual.

2- Case-control or cohort studies with a high risk of confounding, bias, chance and a significant risk that the relationship is not casual.

3. Non-analytic studies, e.g. case reports, case series.

4. Expert opinion.

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