CLINICAL TRIALS REPORT

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Does Intracranial Pressure Monitoring Improve Outcome After Severe Traumatic Brain Injury?

Cremer OL, van Dijk GW, van Wensen E, et al.: **Effect of intracranial pressure monitoring and targeted intensive care on functional outcome after severe head injury.** *Crit Care Med* 2005, **33:**2207–2213.

Rating: •Of importance.

Introduction: Severe traumatic brain injury (TBI) is responsible for at least 52,000 deaths per year in the United States alone, and up to 90,000 additional persons suffer permanent neurologic impairment. Disability after TBI results in considerable loss of both productive years and income potential, with an estimated cost to society of about $40 billion dollars annually [1].

The outlook for victims of trauma has improved, however. Mortality after severe TBI has declined from over 40% in the 1970s to less than 20% over the past decade [1,2]. Development of treatment protocols and enhancement of resuscitation techniques at the prehospital and hospital levels, coupled with advances in critical care, understanding of TBI physiopathology, and more aggressive therapies, are primarily responsible for this improvement. Interestingly, these improvements in outcome have occurred without the benefit of many positive randomized controlled trials. Recently, results from prospective, randomized controlled trials of TBI-directed therapies such as hypothermia [3] and corticosteroids [4] have been inconclusive or disappointing.

There is conflicting evidence with regard to many standard therapeutic interventions for the TBI patient, with most current treatment guidelines based on nonrandomized clinical trials, pathophysiologic hypotheses, and expert opinion [5]. The current widely accepted rationale for intracranial and cerebral perfusion pressure (ICP/CPP)-guided therapy after TBI originates from similar sources, as well as from observational studies associating elevated ICP [6] and hypotension [7] with poor outcome. Pathologic studies indicate that secondary injury after TBI is often ischemic in nature, making hemodynamic augmentation to maintain an adequate CPP a reasonable therapeutic intervention to improve outcome after TBI [2,8,9].

Although ICP monitoring is here to stay, it is used inconsistently, being considered a standard of care at some centers and used rarely, if ever, at others. Thus, this large observational cohort study is of importance because it addresses an important clinical question with the best level of evidence that is currently available.

Aims: To evaluate the impact on outcome of ICP/CPP-guided therapy versus conventional medical management in patients with severe TBI.

Methods: This study was a prospective assessment of outcomes from a retrospectively treated cohort of 333 patients with severe TBI (Glasgow Coma Scale < 8) who survived beyond 24 hours and who were transported to two different Dutch Level I Trauma Centers over a period of 5 years. Interventions were center dependent. In Center A (n = 122), management was driven by clinical and CT findings, no patient had ICP monitoring, and mean arterial pressure (MAP) was maintained at greater than 90 mm Hg. In Center B (n = 211), management was driven by an ICP/CPP resuscitation protocol, 67% of patients had ICP monitors, and 48% had jugular venous oxygen saturation monitors. The goals for ICP and CPP were less than 20 mm Hg and greater than 70 mm Hg, respectively.

Results: The main results of this study were that 1) mortality and functional outcome (Glasgow Outcome Scale) at 12 months were comparable between two groups, 2) mechanical ventilation and length of stay in the intensive care unit were significantly prolonged in patients at Trauma Center B (ICP/CPP-guided therapy), and 3) sedatives, vasopressors, mannitol, and barbiturates were used more frequently in Center B.

Discussion: The authors concluded that the ICP/CPP-guided treatment increases the intensity of medical therapy, potentially adding costs to health care and without significant improvement in outcomes or reduction in mortality.

Editor's comments

This study is important because it addresses a question that will probably never be answered by a randomized controlled trial: does ICP monitoring improve outcome after severe TBI? This study represents a significant effort to answer this question, and deserves close attention and scrutiny.

Cremer et al. compared two different treatment strategies for TBI in two separate hospitals. The results contradict the experience of previous studies in which protocolized ICP/CPP-driven management was associated with improved outcomes [2,8,9]. Although these studies used historical control groups, Cremer et al. used a nonrandomized concurrent control group and the evaluation of outcomes was done in a prospective fashion. Nevertheless, the results of this study should be interpreted with caution.

First, there is the obvious problem that this study was not a prospective, randomized controlled trial. This means that it is impossible to be sure that the comparison evaluates the two medical management strategies independently, without contamination from confounding variables such as referral bias, practice variations regarding end-of-life care, intensity of rehabilitation care, and a host of other variables.

Second, although demographic variables and severity of brain injury were well balanced between the two groups, a significantly higher proportion of patients in Center B (ICP/CPP management) were victims of high-energy trauma (motor vehicle accident [35% vs 26%; $P = 0.002$]), had hypotension on admission (12% vs 5%; $P = 0.04$), and were anemic (10% vs 5%; $P = 0.08$). There may have been important imbalances between the two groups.

Third, a total of 122 patients treated at Center A without an ICP probe were compared with 211 patients in Center B, of whom only 142 (67%) received the ICP probe. Even so, all patients in this group were included in the statistical analysis in an intention-to-treat basis. Among center B patients, the two thirds who received ICP monitoring were younger, had worse Glasgow Coma Scale motor scores, a higher frequency of respiratory failure, more often had diffuse injury on CT (rather than mass lesions), and underwent fewer emergent neurosurgical evacuations. Thus it appears that patients allocated to the ICP probe at Center B were clinically worse, and that the decision to allocate these patients to an ICP probe may have been biased. When the authors analyzed only patients with ICP probes (on-treatment analysis) by adjusting for age, best motor score greater than 4, presence of two nonreactive pupils, CT scan category, injury cause, and surgical evacuation, the results were similar. However, it remains unclear if statistical adjustment alone could fully compensate for the significant baseline differences between the center A "standard management" patients and the highly selected and very sick center B ICP-monitored patients.

The results of this study parallel the results of similar observational nonrandomized studies of pulmonary artery catheter (PAC) use in critically ill patients. In a recent meta-analysis of 5051 patients, Shah et al. [10] concluded that PAC use neither increased overall mortality or days in hospital nor conferred any benefit. We believe that these results may be related to the lack of an effective treatment strategy that is linked to the results of PAC data at the bedside. When the use of PAC as a monitoring device was to a clear predefined therapeutic intervention, improvement in some measures of outcome can be detected. In a recent report from the National Heart, Lung, and Blood Institute Acute Respiratory Distress Syndrome (ARDS) Clinical Trials Network, the use of PAC-guided conservative strategy of fluid management was not associated with important changes in mortality, but had a significant impact on improvement of lung function and shortened duration of mechanical ventilation and intensive care days without increasing nonpulmonary organ failure [11].

In summary, the provocative study by Cremer et al. does not prove that ICP/CPP monitoring is of little value. It only allows us to conclude that limiting the use of ICP probes for ICP/CPP-guided therapy may reduce hospital resource utilization, such as ventilator days [5]. We support the author's call for better prospective trials designed to test effective therapies guided by available neuromonitoring techniques that may potentially limit secondary brain damage after severe TBI.

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