Expert Opinion

Conventional treatments for severe head injury: are they effective, ineffective, or even harmful?

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SINCE the middle of the 1990s, most neurotrauma centres have followed the guidelines or recommendations put forward by the US Traumatic Coma databank (1), the European brain trauma consortium (2) or some local protocols such as the Addenbrooke algorithm (3), for the treatment of severe brain trauma. Even though these guidelines differ in details, they include essentially the same therapeutic components, such as osmotherapy, barbiturate therapy, preservation of cerebral perfusion pressure (CPP) with vasopressors and moderate hyperventilation. To date, there have been no randomised studies proving the effectiveness of any of the guidelines available today or their various components regarding outcome following a severe head injury; no specific therapy or guideline has been shown to be more effective than another and no single therapy has been identified to allow improvement in outcome. We lack scientific support for the use of osmotherapy (4, 5), high-dose barbiturate therapy (6), active cooling (7), vasopressors, or continuous CSF drainage. We also lack scientifically based guiding of the optimal CPP, degree of sedation, type of nutrition and how to handle fluid therapy and blood volume. Except for the studies showing that marked hyperventilation should be avoided (8), we also lack scientific guiding on how to handle ventilatory resuscitation, such as PEEP and inhalation regime. We lack studies defining the optimal haemoglobin concentration in head-injured patients, but a restrictive blood transfusion policy is often recommended, and low haemoglobin levels have reached a high degree of acceptance. No clinical neuroprotective drug trial has so far shown any beneficial effect on outcome after severe head injury (9).

Even though there are signs of immediate beneficial effects of some therapies, the long-term effects are not predictable. Osmotherapy may be beneficial in the short run by reducing intracranial pressure (ICP), but this does not necessarily mean an improved outcome, as more long-term adverse effects in terms of renal insufficiency, electrolyte disturbances, and rebound ICP-increasing effects may worsen outcome (4). Similarly, the short-term ICP-reducing effect of barbiturate therapy may turn into adverse effects when barbiturates are given for many days or in high concentrations due to negative pulmonary effects with secrete stagnation, electrolyte disturbances, and cardio-inhibitory effects (10). Acceptance of low haemoglobin concentrations may be justified by avoiding negative transfusion effects and the possibly beneficial effects of a subnormal viscosity, but low haemoglobin concentration may also mean a suboptimal oxygen-delivery capacity, and difficulties in maintaining normovolaemia and normal blood pressure (11, 12). Vasoconstrictor therapy (e.g. noradrenalin, phenylephrin) increases blood pressure and may reduce ICP in the short run due to a cerebral vasoconstrictor effect. Vasoconstrictor therapy may increase the overall cerebral blood flow, but can compromise the circulation in and around the most injured areas of the brain, despite an increase in arterial pressure. Further, vasoconstrictor therapy may increase brain oedema in the long run due to increased transcapillary filtration through an opened blood–brain barrier when the arterial pressure is increased (11). Also, the initial beneficial cerebral blood flow effects by inotropic drugs may turn into adverse effects by increased transcapillary

filtration and aggravation of brain oedema as a consequence of precapillary vasodilation in combination with raised arterial pressure. Vasoconstrictor therapy is also associated with ARDS (13), and may induce intestinal ischaemia and renal insufficiency. CSF drainage to reduce ICP is sometimes used in patients with ventricular drainage and may initially be beneficial due to its ICP-reducing effect, but with continuous drainage there is a risk of ventricular collapse. Intermittent sedation with frequent wake-up tests gives some information on the status of the patient, but may cause a stress-induced increase in ICP and increased catecholamine concentrations with compromised cerebral circulation around contusions (11).

Thus, in spite of the good intentions when formulating protocols and guidelines, when all aspects of the current treatment are considered, it is far from granted that it will be beneficial for the final outcome, and some of the components are also potentially harmful for outcome.

Two recently published outcome studies have raised doubts about the effectiveness of the conventional treatments of severe head injury. A comprehensive analysis of trauma patients in England and Wales from 1989 to 2003 by Patel et al. (14) showed that no improvement was observed for head-injured patients between 1995 and 2003. Lack of improved outcome after head injury during the same period was also shown in a British study by Hyam et al. (15). These results are interesting and worrying in view of the fact that the quality of both general intensive care and pre-hospital care has improved over the same period, resulting in a better outcome for trauma patients without severe head injury (14). Thus, it seems that the more protocol-driven guidelines introduced in the middle of the 1990s have not improved outcome. The following questions must be raised. Is the conventional treatment ineffective or are these patients so ill that outcome cannot be improved further, irrespective of therapy?

The lack of scientific support for the use of the most common therapeutic components and, considering the discouraging results from the outcome studies mentioned above (14, 15), require careful considerations and an open mind regarding alternative approaches of severe head injury. New therapeutic components to be evaluated in clinical studies, for example, may be the use of low-dose steroid therapy to compensate for post-traumatic adrenal insufficiency in analogy to what has been recommended for sepsis (16), and reducing

contusion bleedings by early strengthening of coagulation (17). There are demands for further studies on decompressive craniotomy (18) as well as on the use of hypertonic saline (19) as to whether these measures are of value not only by their initial ICP-reducing effects, but also by improving outcome. The Lund concept is a comprehensive alternative therapy of severe head injury, mainly based on physiological principles for brain volume and cerebral perfusion regulation, which, in essential aspects, differs from the more traditional guidelines (11). The Lund therapy has never been tested in a randomised study, but its main principles have been confirmed experimentally (11), and outcomes from series reported so far with the Lund therapy are very promising (20–23). The CPP levels in an update of the US guidelines have emerged towards those accepted in the Lund therapy after analysis of randomised studies.

In order to further improve and develop care of these patients, it is important to increase the understanding of the complex mechanisms behind brain oedema development and cerebral perfusion (oxygenation) of traumatic brain injury. The different physiological haemodynamic and other disturbances and their impact on the injured brain still remain a challenge in further research. The motives of performing solid scientific studies comparing conventional and alternative treatment approaches of traumatic brain injuries have been strengthened.

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