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Editorial

Decompressive craniectomy in traumatic brain injury – time for randomised trials?

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Research into the intensive care aspects of traumatic brain injury is currently directed at both pathophysiological mechanisms and treatment options. In terms of pathophysiology, progress has been achieved in the understanding of the mechanisms involved including brain swelling, raised intracranial pressure and derangements in cerebral blood flow and metabolism. In terms of novel treatment modalities, however, despite considerable effort, the magic bullet of neuroprotection remains elusive. Clinical trials of drugs and other specific treatment modalities have so far failed to provide class I evidence (standards) of benefit [8, 10, 12]. Improvements in the management of this heterogeneous group of patients have been seen in other areas including prevention (road and other safety legislation), pre-hospital care (medical treatment at the scene), immediate hospital care (trauma teams and centres) and acute hospital care (specialised neuro-intensive care units with protocol-driven therapy). There remains, however, significant morbidity and mortality, with trauma being the commonest cause of death under the age of 40 years, and head injury still contributing to the majority of these deaths [3].

Why have we failed to demonstrate efficacy in the clinical trials of potential neuroprotective drugs? There are several reasons [8, 10, 12] but perhaps the most fundamental is that these agents tend to target specific metabolic pathways e.g. the glutamate receptor and whilst effective at blocking one or even several of these mechanisms, there are many other ongoing processes that contribute to further cerebral injury. More global therapeutic measures are currently applied including barbiturates and hypothermia. Whilst both these modalities are thought to be effective in the management of selected patients, they are associated with side effects, notably cardiovascular and respiratory complications, and critical evaluation in terms of a Cochrane analysis for barbiturates [13] and a recent large randomised trial for hypothermia [4] have not proved positive. The approach of raising blood pressure using inotropes to improve the cerebral perfusion pressure to above 70 mm Hg has also been associated with significant cardiovascular complications [14].

Is there another approach? If brain swelling, increase in intra-cranial pressure, reduction in cerebral blood flow and energy failure plays a major role in the pathogenesis of head injury, interception of this cycle will theoretically improve outcome. Indeed, both hypothermia and barbiturates act, amongst other mechanisms, by reducing energy demand. One of the simplest ways in which this cycle can be broken, however, is by a surgical option – craniectomy i.e. opening of the skull to convert the tight closed box surrounding the brain into an open box. This concept is similar to the decompression of other body compartments subjected to high pressure, for example, fasciotomy for compartment syndrome. Decompression of the brain has been in existence for hundreds of years, initially in terms of trephination by the Ancient Greeks and more recently by Kocher approximately one hundred years ago. Kocher stated that ''if brain pressure

exists without CSF pressure then pressure must be relieved by opening the skull''. While decompressive craniectomy has been practised for many years it is only relatively recently that it is being performed in the context of modern and highly supportive neuro-intensive care. The ability to perform this operation in the context of sophisticated pre and post-operative intensive care, in terms of ventilatory support, cardiovascular support and general and specific monitoring (particularly ICP monitoring) is one of the prime reasons for its current renaissance. The operation is currently being performed in several neurosurgical centres world-wide, with different approaches in terms of the timing of the surgery, the type of the surgery and context of the surgery in terms of its place in protocol-driven management [7]. Applying decompressive craniectomy after other treatment options (ventilation, paralysis, nursing head up, mannitol, inotropes, moderate hyperventilation, hypothermia and barbiturates) have failed to control ICP is one approach but raises many issues concerning the role of the procedure i.e. if and when to operate.

What are the potential advantages and disadvantages of decompressive craniectomy for the management of raised ICP following traumatic brain injury? Whilst the theory that opening the tight skull will reduce ICP, improve blood flow, improve energy status and reduce swelling is attractive, this concept has yet to be proved in terms improving clinical outcome. There is, however, evidence that the operation does favourably influence intra-cranial pressure as a surrogate endpoint [7, 16]. Furthermore, decompressive craniectomy does have potential advantages over other neuro-protective therapies. It has a global action not restricted to one metabolic pathway and it is unlikely to suffer from the same systemic side effects (respiratory and cardiovascular) as other medical options notably barbiturates and hypothermia. It does, however, involve a major operative procedure with the risk of haemorrhage, injury to the cerebral cortex and injury to the venous sinuses. In fact, despite several series of the operation reported in the literature, the complication rate of the operation is unclear. Whether decompressive craniectomy increases the incidence of hydrocephalus also remains to be seen. A consideration of the pathophysiological concepts that underpin the Lund protocol for head injury management [6] would suggest that decompressive craniectomy might predispose to further oedema formation. There is also the question of later skull reconstruction which itself is associated with morbidity, predominantly infection. Finally, one of the major concerns is that decompressive craniectomy may save life at the expense of increasing the number of patients in vegetative state and severe disability. Fortunately, recent outcome studies of protocols including decompressive craniectomy, have not supported this concept [11].

Should decompressive craniectomy be the subject of a randomised clinical trial? Evidence based treatment for the management of patients with head injury is sparse. The Brain Trauma Foundation Guidelines for the management of patients with severe head injury cite only three categories of Class I evidence on the role of hyperventilation, anticonvulsants and steroids [2]. Despite this published Class I evidence there is a further on-going trial looking at the potential benefit of steroids [9]. The recently published Brain Trauma Foundation Guidelines on the management of patients with mass lesions were unable to cite any examples of Class I evidence [1]. There is therefore a continuing need for good quality prospective studies in this field. There are strong arguments for decompressive craniectomy to be evaluated as a prospective randomised study. Following traumatic brain injury, raised intra-cranial pressure refractory to standard treatment measures (sedation, ventricular CSF drainage, mild hyperventilation, mannitol) is a common problem [15]. The current evidence predominantly small series (class II and III evidence) from individual centres have demonstrated a wide range of outcomes, with no clear consensus regarding the indications for the operation. The concern that outcome will be shifted from death to vegetative shift and severe disability can only be addressed by large outcome studies.

If studies can demonstrate a reduction in the rate of severe disability and persistent vegetative state with progression to good recovery, there will be profound social and economic advantages. The main arguments against such studies is that several potential recruiting centres already utilise decompressive craniectomy and may therefore find it difficult to randomise patients with implications for complicated data analysis in terms of crossover. Overall, however, the fact that there are several series in the literature which are supportive of decompressive craniectomy, with evidence that the operation does reduce ICP and that ICP is related to outcome [5] strongly supports proceeding with randomised studies.

Three large multi-centre randomised studies of decompressive craniectomy have been proposed – an Australasian, an American and a European Study. While all three studies have the same overall objective –

addressing the role of decompressive craniectomy in traumatic brain injury they have several differences notably in terms of power and thresholds. The fact that these studies address slightly different parameters may be useful in extrapolating decompressive craniectomy into a wider clinical arena. There is also considerable on-going debate in terms of the nuances of the type of decompression (unilateral versus bilateral, anterior and posterior limits of the flap, the creation of vascular tunnels to reduce venous congestion).

In conclusion, the concept of performing decompressive craniectomy for raised and refractory ICP in patients with traumatic brain injury in the context of modern neuro-intensive care is attractive. It provides a global approach in terms of neuro-protection with the potential for avoiding the side effects of hypothermia and barbiturates. There are several series from individual centres demonstrating good results in terms of ICP control and outcome with strong arguments for proceeding with large multi-centre studies. Whether decompressive craniectomy represents progress along the path towards the holy grail of a gold standard of neuro-protection remains to be seen.

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