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What is new in neurocritical care: 2012

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The number of papers published in the field of neurocritical care is booming. A quick search in PubMed (filters "1/1/2012 to 31/12/2012" and "humans research") for the keyword "traumatic brain injury" (TBI) returns 1,869 references, "ischemic stroke" 2,058, "intracerebral hemorrhage" 1,072, and "subarachnoid hemorrhage" (SAH) 534. The aim of this short review was to underline some important issues, selected on the basis of personal judgement rather than on objective, formally established, criteria.

The epidemiology of TBI is changing, with more injuries in low- and medium-income countries, due to increasing car use, and a growing proportion of elderly patients in the western world [1, 2]. Despite a general trend toward better outcome in all age categories, older patients still have a higher mortality, while the proportion of patients with severe disability does not seem to increase [2]. The social cost of surviving TBI, including hospital costs, health resource utilization and home care, is difficult to quantify, but extremely important. Research on this issue performed in the USA [3] has indicated that outpatient care costs and nursing home stays are higher for older patients. Success in the acute phase, surviving the ICU, has to be weighed against long-term outcome.

Among the factors associated with long-term outcome after severe TBI, intracranial pressure (ICP) confirms its relevance. In 365 patients with TBI, average ICP in the first 48 h of monitoring was found to be a predictor of mortality and long-term neurobehaviour [4]. In that research, a composite score was used. Survival and functional outcome 6 months after trauma were worse in patients with higher ICP, with a threshold of 25 mmHg. Since ICP is known to affect outcome after severe TBI, raised ICP should be identified and treated. Updated guidelines for acute medical management of severe TBI in infants, children and adolescents have been issued recently [5]. In these guidelines specific indications for ICP monitoring are proposed, prudently rating the available evidence in support of ICP at the lowest level. However, studies addressing this issue are lacking.

Assessing the benefits of monitoring is a difficult task, because monitoring per se cannot improve outcome unless appropriate therapy is administered. In a recent study, the complex issue of the usefulness of ICP monitoring was approached in a more rigorous way, comparing treatments, rather than focusing on the presence/absence of ICP monitoring [6]. In six South American centres, 324 patients with severe TBI were randomized to receive one of two treatment schemes: management based on ICP monitoring versus a treatment algorithm based only on neurological responses and CT findings. The results did not demonstrate any significant advantage in those managed with ICP monitoring. This trial had an innovative design, clinically sound protocols and high-quality clinical data. However, it had limitations as well, and the final verdict on ICP is still awaited. The study was not powered to detect small improvements in the minority of patients who had raised ICP. Additionally, there is the issue of generalization, since the clinical scenario in the participating centres was peculiar: the prehospital system was still underdeveloped, mortality was high, and no rehabilitation was available after hospital discharge.

SAH remains a challenging and complex disease, with early threats, such as rebleeding and hydrocephalus, and late complications, such as vasospasm and ischaemia. Delayed ischaemia after SAH still affects one patient in four. A critical reduction in the diameter of vessels may lead to hypoperfusion and ischaemia, and has been interpreted in the past as the only cause of late ischaemia after SAH. Vasospasm, however, is not the only cause of delayed ischaemia, which may also depend on, for example, microthromboses and impaired

autoregulation [7]. Spreading depolarization, a wave of depolarization with alteration of the ionic gradients, depression of electrical activity and neuronal swelling, is receiving more attention, both as a consequence and as a potential trigger of further ischaemia [8].

Protection of the brain against further insults after SAH is extremely important. Magnesium, which inhibits excitatory glutamate release, and blocks the NMDA-glutamate receptors and voltage-dependent calcium channels, can be considered a neuroprotectant, and has been tested in several trials. The latest randomized trial of magnesium sulphate for SAH was recently published [9]. More than 1,200 patients with aneurysmal SAH were randomized in Europe and Chile to receive a fixed daily dose of 64 mmol magnesium sulphate or placebo for up to 20 days. Magnesium had no effect on outcome, unfortunately. A meta-analysis including this study and six previous randomized trials using magnesium for SAH has confirmed that intravenous magnesium does not affect outcome [9].

A lesson learned from TBI is that recovery after acute brain injury takes time, and that outcome at discharge from the ICU does not capture the patient's subsequent destiny. This has been investigated in patients with SAH [10] followed-up at 6 months. Interestingly, the majority of survivors, including those more severely affected, showed a trend of improvement over time.

Rescuing brain tissue after ischaemic stroke is a matter of time, and for this reason stroke care requires organization to bring the right candidates to the appropriate hospital, with the shortest "door to needle" time. Intravenous thrombolysis improves survival and independence when performed up to 4.5 h after stroke. This interval may perhaps be extended to 6 h according to the findings of a large (>3,000 patients) multicentre trial [11]. Interestingly, patients older than 80 years, often excluded from previous studies, constituted more than 50 % of those randomized, and benefits were also documented in this subgroup.

Older and sicker patients with TBI or ischaemic stroke have to be treated. New mechanisms should be explored to better understand and treat ischaemia after SAH. Old certainties, such as ICP monitoring, have to be rediscussed. Long-term outcome, well beyond ICU discharge, needs to be considered. Neurocritical care has to adapt to a changing world.

References

1. Rosenfeld JV, Maas AI, Bragge P, Morganti-Kossmann MC, Manley GT, Gruen RL (2012) Early management of severe traumatic brain injury. Lancet 380:1088–1098
2. Stocchetti N, Paternò R, Citerio G, Beretta L, Colombo A (2012) Traumatic brain injury in an aging population. J Neurotrauma 29:1119–1125
3. Thompson HJ, Weir S, Rivara FP, Wang J, Sullivan SD, Salkever D, Mackenzie EJ (2012) Utilization and costs of health care after geriatric traumatic brain injury. J Neurotrauma 29:1864–1871
4. Badri S, Chen J, Barber J, Temkin NR, Dikmen SS, Chesnut RM, Deem S, Yanez ND, Treggiari MM (2012) Mortality and long-term functional outcome associated with intracranial pressure after traumatic brain injury. Intensive Care Med 38:1800–1809
5. Kochanek PM, Carney N, Adelson PD, Ashwal S, Bell MJ, Bratton S, Carson S, Chesnut RM, Ghajar J, Goldstein B, Grant GA, Kissoon N, Peterson K, Selden NR, Tasker RC, Tong KA, Vavilala MS, Wainwright MS, Warden CR (2012) Guidelines for the acute medical management of severe traumatic brain injury in infants, children, and adolescents–second edition – chapter 3. Indications for intracranial pressure monitoring. Pediatr Crit Care Med 13(Suppl 1):11–17
6. Chesnut RM, Temkin N, Carney N, Dikmen S, Rondina C, Videtta W, Petroni G, Lujan S, Pridgeon J, Barber J, Machamer J, Chaddock K, Celix JM, Cherner M, Hendrix T (2012) A trial of intracranial-pressure monitoring in traumatic brain injury. N Engl J Med 367:2471–2481
7. Dhar R, Scalfani MT, Blackburn S, Zazulia AR, Videen T, Diringer M (2012) Relationship between angiographic vasospasm and regional hypoperfusion in aneurysmal subarachnoid hemorrhage. Stroke 43:1788–1794
8. Woitzik J, Dreier JP, Hecht N, Fiss I, Sandow N, Major S, Winkler M, Dahlem YA, Manville J, Diepers M, Muench E, Kasuya H, Schmiedek P, Vajkoczy P (2012) Delayed cerebral ischemia and spreading depolarization in absence of angiographic vasospasm after subarachnoid hemorrhage. J Cereb Blood Flow Metab 32:203–212
9. Dorhout Mees SM, Algra A, Vandertop WP, van Kooten F, Kuijsten HA, Boiten J, van Oostenbrugge RJ, Salman RA, Lavados PM, Rinkel GJ, van den Bergh WM (2012) Magnesium for aneurysmal subarachnoid haemorrhage (MASH-2): a randomised placebo-controlled trial. Lancet 380:44–49
10. Navi BB, Kamel H, Claude Hemphill J 3rd, Smith WS (2012) Trajectory of functional recovery after hospital discharge for subarachnoid hemorrhage. Neurocrit Care 17:343–347
11. The IST-3 collaborative group, Sandercock P, Wardlaw JM, Lindley RI, Dennis M, Cohen G, Murray G, Innes K, Venables G, Czlonkowska A, Kobayashi A, Ricci S, Murray V, Berge E, Slot KB, Hankey GJ, Correia M, Peeters A, Matz K, Lyrer P, Gubitz G, Phillips SJ, Arauz A (2012) The benefits and harms of intravenous thrombolysis with recombinant tissue plasminogen activator within 6 h of acute ischaemic stroke (the third international stroke trial [IST-3]): a randomised controlled trial. Lancet 379:2352–2363