In patients with head injuries who undergo rapid sequence intubation using succinylcholine, does pretreatment with a competitive neuromuscular blocking agent improve outcome? A literature review

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Abstract
A literature search was undertaken for evidence of the effect of succinylcholine (SCH) on the intracranial pressure (ICP) of patients with acute brain injury and whether pretreatment with a defasculating dose of competitive neuromuscular blocker is beneficial in this patient group. The authors could find no definitive evidence that SCH caused a rise in ICP in patients with brain injury. However, these studies were often weak and small. For those patients suffering acute traumatic brain injury the authors could find no studies that investigated the issue of pretreatment with defasculating doses of competitive neuromuscular blockers and their effect on ICP in patients given SCH. There is level 2 evidence that SCH caused an increase in ICP for patients undergoing neurosurgery for brain tumours with elective anaesthesia and that pretreatment with defasculating doses of neuromuscular blockers reduced such increases. It is unknown if this affects neurological outcome for this patient group.

Keywords: anaesthesia; neuromuscular blocking agent

Rapid sequence intubation (RSI) refers to the virtually simultaneous administration of a neuromuscular blocking agent and potent sedative agent to induce motor paralysis and unconsciousness to facilitate endotracheal intubation. This enables the securing of the airway, maintenance of oxygenation, and avoidance of hypercapnea and aspiration in the patient with head injury. Succinylcholine (SCH)/suxamethonium is the paralysing agent of choice for RSI because of its consistently rapid onset of action, ability to achieve excellent intubating conditions and a short duration of action.1 In controlled laboratory studies using healthy animals and an anaesthetic technique different from RSI, Lanier et al2 and Cotterill et al3 demonstrated that SCH administration was immediately followed by a rise in intracranial pressure (ICP) and that this rise could be blunted by the use of defasculating doses (10% of the normal paralysing dose) of competitive neuromuscular blockers.3 In patients with increased ICP secondary to brain tumours there is evidence that SCH causes further rises in ICP.4 5 This potentially detrimental effect can also be reduced by pretreatment with defasculating doses of competitive neuromuscular blockers in this patient group.6 Some have recommended that such pretreatment be extended to patients with head injuries7 and this advice is followed in the majority of emergency departments in the USA.8 Such a recommendation is also contained in the companion manual to the National Airway Management Course,9 an increasingly influential North American course that is now being taught in Europe. However, a recent survey of RSI practice in emergency rooms in England demonstrated the complete absence of such pretreatment.10 It is this disparity that prompted this review.

The review has two objectives. Firstly, to assess the human evidence that SCH causes an increase in ICP in patients with acute head injuries. Secondly, to assess the human evidence that pretreatment with a defasculating dose of a competitive neuromuscular blocking agent prevents a rise in ICP when SCH is administered to patients with acute head injuries.

Method
The relevant literature was identified by:
(1) Electronic searching of Medline (1966 onwards), EMBASE (1988 onwards) CINAHL and the Cochrane Library (2000 version 3). A combination of MeSH headings and text words were used (rapid sequence intubation or rapid sequence induction, suxamethonium or succinylcholine, neuromuscular block, vecuronium, pancuronium, rocuronium, and intracranial pressure) and the search was limited to human studies. For each database the same policy was adopted. The title and abstract were read by one of the authors and if thought relevant or possibly relevant the full paper was requested and appraised. This search was repeated independently by an experienced medical librarian and any additional abstracts were reviewed.

(2) The bibliographies of all appraised papers were searched and any relevant or possibly relevant papers reviewed.

The evidence that SCH causes a rise in ICP in patients with acute head injuries was evaluated to determine whether this is a clinically important phenomenon. For the purposes of this review acute was defined as <12 hours
from the time of injury. To evaluate the impact of pretreatment with a defasciculating dose of a competitive neuromuscular blocking agent on the effect of SCH on ICP, the three part question approach advocated by Sackett was used. This entails clearly specifying: (a) the patient or problem of interest; (b) the main intervention and comparison interventions; (c) the clinical outcome(s) of interest.

Thus our question is: In those patients who have suffered an acute traumatic brain injury (patient group) and who undergo rapid sequence intubation using SCH, does pretreatment with a defasciculating dose of a competitive neuromuscular blocker compared with no pretreatment (intervention and comparison) prevent or reduce rises in ICP (clinical outcome).

Each paper will be described in terms of levels of evidence for a treatment as follows: 1a Systematic review of randomised controlled trials. 1b Individual randomised controlled trial with narrow confidence intervals. 2a Systematic review of cohort studies. 2b Individual cohort study including low quality randomised controlled trial. 3a Systematic review of case-control studies. 3b Individual case-control study. 4 Case series and poor quality cohort and case-control studies. 5 Expert opinion with critical appraisal or based on physiology, bench research or first principles.

Results
The following papers investigated the issue of SCH and its effect on ICP.

(A) SCH does not change ICP, cerebral blood flow velocity or the electroencephalogram in patients with neurological injury.

Kovarik WD, et al (level of evidence 4)

This study included six patients with traumatic cerebral oedema who were intubated and ventilated in an ICU. They were investigated 1-5 days after injury. These patients were given SCH and this did not lead to rises in ICP. They did not have acute traumatic brain injury and this small study was not sufficiently powered to prove whether SCH by itself leads to a rise in ICP in patients with head injury.

(B) The effect of suxamethonium on ICP and cerebral perfusion pressure in patients with severe head injuries following blunt trauma.

Brown MM, et al (level of evidence 2)

Eleven intubated and ventilated patients with head injuries treated in an ICU were given SCH/normal saline in a double blind cross over trial. No significant increase in ICP was detected following SCH. These patients were studied within 48 hours of severe closed brain injury. Although not specified it is likely that most were studied >12 hours after injury. This paper suggests that in this patient group SCH does not cause an increase in ICP.

(C) Influence of SCH on lumbar cerebral spinal pressure in humans

Lam AM, et al (level of evidence 4)

Twenty four patients undergoing elective aneurysm clipping had their lumbar CSF pressure measured after induction of anaesthesia, administration of SCH and intubation. There was no significant change of ICP with the administration of SCH but it did increase with intubation. However, these patients did not have acute traumatic brain injury and had spinal CSF changes as the outcome.

(D) Control of cerebral perfusion pressure during induction of anaesthesia in high risk neurosurgical patients.

McLesky CH, et al (level of evidence 4)

Four patients undergoing elective neurosurgery for tumours did not demonstrate an increase in ICP with the administration of SCH but did with intubation. These patients did not have acute traumatic brain injury and this study was too small to provide any meaningful results.

(E) SCH-ICP effects in neurosurgical patients.

Marsh ML, et al (level of evidence 4)

Eight patients underwent elective surgery for brain tumours. Administration of SCH lead to a small but significant increase in ICP. The effect of intubation was not considered. These patients did not have acute traumatic brain injury and this study was too small to provide any meaningful results.

Only two papers investigated the effect of competitive neuromuscular blockade on the ICP changes related to SCH. Only one paper dealt with the use of defasciculating doses of a competitive neuromuscular blocking agent as a pretreatment. No paper contained all three ideal components of the question.

(1) Increases in ICP from SCH: prevention by prior non-depolarising block.

Minton MD, et al (level of evidence 4)

The patient group consisted of 19 patients undergoing elective neurosurgery for brain tumours. They were given thiopentone in two stages and intubated after the first administration of SCH. This caused a rise in ICP. The second administration of SCH was not accompanied by a rise in ICP in those patients who had undergone full neuromuscular block using vecuronium. This commonly quoted paper is a poor quality case-control study in which the patients served as their own controls. These patients did not have acute traumatic brain injury and did not undergo RSI. This paper suggests that SCH causes a rise in ICP in this patient group and that the rise could be ablated by full dose vecuronium (not the defasciculating dose).

(2) Defasculation with metocurine prevents SCH induced increases in ICP.

Stirt JA, et al (level of evidence 2)

Twelve patients undergoing elective neurosurgery for brain tumours having been pretreated with dexamethasone were randomly allocated pretreatment with metocurine (neuromuscular blocking agent)/normal saline, had anaesthesia induced and were then given succinylcholine but were not intubated. For those patients pretreated with metocurine, the ICP did not change significantly from the mean value observed before SCH, 14 mm Hg...
±2SE. For those given normal saline the ICP increased significantly from 11 mm Hg±2SE to 23 mm Hg±1SE. Although this study supports the concept of pretreatment, these patients did not have acute traumatic brain injury and did not undergo RSI.

Conclusions
No papers were identified with an ideal fit and level 1 evidence for our questions. The authors acknowledge that some potentially important papers may have been missed through the absence of hand searching of all possibly relevant journals but this was not likely and experts in this area were not able to identify any significant papers that were not evaluated. The authors could find no definitive evidence that SCH caused a rise in ICP in patients with brain injuries. However, these studies were often weak and small. For those patients suffering acute traumatic brain injury the authors could find no studies that investigated the issue of pretreatment with defasciculating doses of neuromuscular blocking agents and their effect on ICP in patients given SCH. There is level 2 evidence that SCH caused an increase in ICP for patients undergoing neurosurgery for brain tumours with elective anaesthesia and that pretreatment with defasciculating doses of neuromuscular blocking agents reduced such increases. It is unknown if this affects neurological outcome for this patient group.

It is concluded that there are no studies that satisfactorily answer our original questions. The question of the benefit of pretreatment with defasciculating doses of a competitive neuromuscular blocking agent is ideally suited to a prospective randomised controlled trial. The human literature suggests that patients with raised ICP secondary to SCH administration. Whether this effect is also seen in patients with head injury and whether mitigating this ICP rise would lead to an improved neurological outcome is not known. Until a properly conducted RCT is undertaken, emergency physicians will have to decide whether patients with raised ICP secondary to acute traumatic brain injury may similarly benefit from pretreatment with defasciculating doses of a competitive neuromuscular blocking agent.

Contributors
MC initiated the study, appraised the literature, wrote the paper and is the guarantor. SH undertook the literature search and appraised the literature. RW and MM discussed core ideas and contributed to the writing of the paper.

4 Lanier WL, Iaizzo PA, Milde JH. Cerebral function and muscle afferent activity following intravenous succinylcholine in dogs anesthetized with halothane: the effects of pretreatment with a defasciculating dose of pancuronium. Anesthesiology 1989;71:87-95.
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