Clinical bottom line
While there is no direct evidence to answer the clinical question, the research available strongly suggests that it is reasonable to continue using standard wrist splints to immobilise patients with suspected scaphoid fractures.


Provenance and peer review Commissioned; internally peer reviewed.

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BET 3: IS KETAMINE A VIABLE INDUCTION AGENT FOR THE TRAUMA PATIENT WITH POTENTIAL BRAIN INJURY

Report by: Sian Hughes, CT3 (Emergency Medicine)

<table>
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<tr>
<th>Author, date and country</th>
<th>Patient group</th>
<th>Study type (level of evidence)</th>
<th>Outcomes</th>
<th>Key results</th>
<th>Study weaknesses</th>
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<tr>
<td>Filarovsky et al 2010, Canada</td>
<td>Narrative review article</td>
<td>Qualitative Literature review and expert opinion based on physiological data (level 5 evidence)</td>
<td>Opinion based conclusion</td>
<td>'ketamine appears to be the perfect agent for the induction of head injured patients for intubation.'</td>
<td>No attempt made at meta-analysis. Poor explanation of search strategy. Conclusions based on interpretation of individual case control/case studies</td>
</tr>
<tr>
<td>Sehdev et al 2008, Australia</td>
<td>Narrative review article</td>
<td>Qualitative Literature review and expert opinion based on physiological data (level 5 evidence)</td>
<td>Opinion based conclusion</td>
<td>'ketamine might be a suitable agent for induction of anaesthesia, particularly in those patients with potential cardiovascular instability.'</td>
<td>No attempt made at meta-analysis. Poor explanation of search strategy. Conclusions based on interpretation of individual articles</td>
</tr>
<tr>
<td>Grathwohl K et al, 2009, USA</td>
<td>Patients with traumatic brain injury undergoing operative neurosurgical intervention</td>
<td>Retrospective cohort with subgroup analysis of total intravenous anaesthesia (TIVA) patients and comparison of ketamine including regimens to non-ketamine including regimens. (Level of evidence 2b)</td>
<td>Good outcome (Glasgow Outcome Score 4--5), Mortality</td>
<td>79% patients in the ketamine group vs 72% patients in the non ketamine group (p=0.47), 8.5% in the ketamine group vs 2.2% in the non ketamine group (p=0.36)</td>
<td>Method of induction unregulated and unclear. Retrospective analysis renders the study open to multiple confounders. Ketamine used in tandem with other anaesthetic agents as part of TIVA. No raw ICP data provided</td>
</tr>
<tr>
<td>Goffit et al 1996, Israel</td>
<td>29 prehospital care patients with GCS&lt;8, following a single failed attempt at intubation using standard techniques. Head was the primary site of injury in 25 of these patients</td>
<td>Prospective cohort study (level of evidence 4)</td>
<td>Successful intubation following ketamine administration, Survival to hospital, Complications attributed to ketamine</td>
<td>19 patients (65.5%)</td>
<td>No comparator group. No standardised description of initial pharmacological/practical approach to intubation. No ICP data of any kind. No presentation of morbidity data. Large standardised ketamine dosage</td>
</tr>
<tr>
<td>Jabre et al 2009, France</td>
<td>104 trauma patients within 655 prospectively enrolled critically ill patients needing sedation for emergency intubation. No clarification of proportion with associated traumatic brain injury. Patients were randomly assigned to receive initial sedation for RSI with either 0.3 mg/kg Etomidate or 2 mg/kg Ketamine</td>
<td>Subgroup analysis within single blind prospective RCT (level of evidence 2b)</td>
<td>Maximum Sequential Organ Failure Assessment (SOFA) score during the first three days ICU admission, Mortality at 28 days</td>
<td>Mean SOFAmax for etomidate group 10.05(SD 3.5) vs 9.9(SD 2.8), Absolute difference 0.1 (95% CI 1.2 to 1.3), 26.3% (Etomidate group) vs 29.8% (Ketamine group), OR 0.8 (95% CI 0.4 to 2.0)</td>
<td>Approximately 30% initially recruited patients withdrawn following early critical care discharge, death or missing data. Underpowered for analysis of trauma patients and therefore at significant risk of type 2 error. Patients dying before arrival to hospital also excluded, a potential cohort of interest regarding the BET subject matter</td>
</tr>
</tbody>
</table>

ABSTRACT
A short cut review was carried out to establish whether ketamine is a viable induction agent in trauma patients with potential brain injuries. 276 papers were found using the reported searches, of which 5 presented the best evidence to answer the clinical question. The author, date and country of publication, patient group studied, study type, relevant outcomes, results and study weaknesses of these best papers are tabulated. It is concluded that there is no evidence to suggest harm with Ketamine use as induction agent for the patient with potential traumatic brain injury. The drug has major advantages in those patients with associated haemodynamic compromise and should potentially be regarded as the agent of choice.

CLINICAL SCENARIO
A 26-year-old male is brought to the Emergency Department after being struck by a car. His Glasgow coma scale on arrival is 8/15 with obvious evidence of head injury and thoracoabdominal trauma. He has a profusely bleeding scalp wound and is tachycardic. You decide to undertake a rapid sequence intubation (RSI) and begin drawing up ketamine as an induction agent. Your colleagues raise a collective eyebrow and ask you to defend your choice of agent. You offer cardiovascular stability and familiarity as two main indications. They remain concerned about the risk of raising intracranial pressure (ICP) and insist that Ketamine is contraindicated in head injured patients. They are unable to cite any evidence to support this view. You wonder whether they are right.

THREE-PART QUESTION
In (adults with head injury necessitating emergency intubation) does (the use of ketamine as an induction agent, compared to any other standard agent) lead to (increased morbidity/mortality)?

SEARCH STRATEGY
Medline and Embase using the OVID interface Medline (1948 to week 4 September 2011): ((ketamine.mp) or (exp ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketamine)) or (ketame
keta-mine/) AND ((exp intubation, intra-tracheal/) or (rapid sequence induction. mp) or exp (anesthesia, general/) or (rapid sequence intubation.mp)) AND ((intra-cranial pressure.mp) or (exp intracranial pressure/) or ICP.mp) AND ((head injury. mp) or (exp cranioencephal trauma/) or (head injury5.mp)) EMBASE (1990 to week 4 September 2011): (((exp ketamine/)) AND (((exp intracranial hypertension/) OR (exp head injury/)) AND (exp anesthesia, induction) OR (exp endotracheal intubation/))). Both search strategies were limited to English language, humans and adults. The Cochrane database of systematic reviews was also searched for any articles including the term ketamine.

SEARCH OUTCOME
Two hundred and seventy-six articles were identified. Of these, 18 were deemed directly relevant and assessed by abstract. Following further review, 5 papers were retained for critical appraisal. Of these articles, two narrative literature reviews and a predefined subgroup analysis within a prospective single blind randomised controlled trial (RCT) formed the highest level of evidence. All five articles are reviewed below:

COMMENT
The only controlled trial comparing ketamine as an induction agent to any other pharmacotherapy for RSI in patients with traumatic brain injury (TBI) is the paper by Jabre et al. Although predefined, the subgroup analysis of trauma patients within the overall cohort is underpowered and the authors are non specific about the prevalence of traumatic brain injury within this group. Thus the highest level of evidence to answer the predefined question is 2b only. Initial concerns with ketamine use in head injured patients originate from small case control studies in the early 1970’s. Ketamine administration for diagnostic pneumoventriculography in spontaneously breathing patients and procedural sedation in those with abnormal CSF flow dynamics has previously demonstrated a potentially detrimental rise in ICP. (Gibbs 1972, Evans et al 1971, Gardner et al 1971, Shapiro et al 1972 and List et al 1972). This rise was most pronounced in those with abnormal cerebrospinal fluid (CSF) pathways, with a consequent drop in cerebral perfusion pressure (CPP). However, the healthy patients involved in these studies actually demonstrated a rise in mean arterial pressure (MAP) and a concomitant increase in cerebral blood flow with intravenous ketamine usage, at doses compatible with induction. Calculations of CPP from this published data are suggestive that ketamine actually improves cerebral perfusion. Thus, in the absence of obstructed CSF flow pathways, this data goes some way to support the use of ketamine in head injured patients rather than refute it. Ketamine has been increasingly utilised in the prehospital environment in recent years, (Sibley et al 2011) based on maintenance of airway reflexes, predictability and cardiovascular stability. Indeed, hypotension unarguably increases mortality and worsens secondary brain injury: ketamine has the potential to limit hypotensive sequelae in those necessitating emergency intubation. Prehospital practice has now encouraged adoption in secondary care, with increasing use of ketamine based agents for sedation in the emergency department. (Senser S et al 2011). Critical care physicians have also warned to its use in limiting physiological disturbance during temporarily distressing procedures such as endotracheal suction and for prolonged sedation, even in known TBI, (Bar-Joseph et al 2009 and Sibley et al 2011). In these patients, often with ICP monitors, a further evidence base is emerging to refute the previously proposed physiological disadvantages of the drug.

LEVEL OF EVIDENCE
Level 2—Studies considered were neither 1 or 3.

Clinical bottom line
There is no evidence to suggest harm with Ketamine use as induction agent for the patient with potential traumatic brain injury. The drug has major advantages in those patients with associated haemodynamic compromise and should potentially be regarded as the agent of choice.

BET 4: IS INTRanasAL FENTANYL BETTER THAN PARENTERAL MORPHINE FOR MANAGING ACUTE SEVERE PAIN IN CHILDREN?

Report by: Sandeep Rahul Kusre, Senior House officer
Search checked by: Jonathan Costello, Consultant
Institution: Royal Free Hospital, Pond Street, London, UK

ABSTRACT
A short cut review was carried out to establish whether intranasal fentanyl is better than parenteral morphine for managing acute severe pain in children. 51 papers were found using the reported searches, of which 4 presented the best evidence to answer the clinical question. The author, date and country of publication, patient group studied, study type, relevant outcomes, results and study weaknesses of these best papers are tabulated. It is concluded that intranasal fentanyl is an effective and safe alternative to IV or IM morphine.
BET 3: Is ketamine a viable induction agent for the trauma patient with potential brain injury

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