Best evidence topic reports (BETs) summarise the evidence pertaining to particular clinical questions. They are not systematic reviews, but rather contain the best (highest level) evidence that can be practically obtained by busy practising clinicians. The search strategies used to find the best evidence are reported in detail in order to allow clinicians to update searches whenever necessary. Each BET is based on a clinical scenario and ends with a clinical bottom line which indicates, in the light of the evidence found, what the reporting clinician would do if faced with the same scenario again. The BETs published below were first reported at the Critical Appraisal Journal Club at the Manchester Royal Infirmary or placed on the BestBETs website. Each BET has been constructed in the four stages that have been described elsewhere. The BETs shown here together with those published previously and those currently under construction can be seen at http://www.bestbets.org. Four BETs are included in this issue of the journal.

### Buccal midazolam as an alternative to rectal diazepam for prolonged seizures in childhood and adolescence

**Report by Richard Body, Senior House Officer**  
**Checked by Mawra Ijaz, Staff Grade**

**doi**: 10.1136/emj.2005.024380

**Abstract**

A short cut review was carried out to establish whether buccal midazolam is better than rectal diazepam for treating prolonged seizures in childhood and adolescence. Eight papers were found using the reported search, of which two 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. A clinical bottom line is stated.

**Clinical scenario**

An 11 year old girl, known to be epileptic, is brought to the Emergency Department with a prolonged seizure. You have no intravenous access at this point. A colleague recently mentioned that buccal midazolam is an available alternative to rectal diazepam. You are aware that this would be easier and more socially acceptable in the situation, but wonder if it would be as efficacious.

**Three part question**

In [children with prolonged seizures] does [buccal midazolam or rectal diazepam] lead to [quicker resolution of seizures]?

**Search strategy**


**Search outcome**

Eight papers were identified, two of which were relevant to the three part question (table 1). Cochrane: Nine hits, none of which was relevant.

**Comment(s)**

Buccal midazolam is gaining in popularity as a treatment for prolonged seizures in children. It overcomes many of the disadvantages associated with rectal diazepam, including difficulty of administration in wheelchair users and in tonic seizures, potentially unpredictable absorption with constipation and bowel movements and social unacceptability, particularly in older children. Nasal midazolam has also been used, although the greater surface area of the buccal mucosa could potentially confer advantages with regard to absorption.

One small trial suggests that buccal midazolam is at least as effective as rectal diazepam and one suboptimally designed telephone survey suggested a degree of parental satisfaction with the drug. However, the patient group in the randomised controlled trial is very different from that presenting to emergency departments. There remains a paucity of evidence regarding this topic.

**Clinical bottom line**

Buccal midazolam may be equal or superior to rectal diazepam for treatment of prolonged seizures in children but more evidence is needed for emergency patients.

Aspirin in the treatment of acute pulmonary embolism

Report by Caroline Lee, Senior Clinical Fellow
Checked by Craig Ferguson, Clinical Research Fellow

doi: 10.1136/emj.2005.024398

Abstract
A short cut review was carried out to establish whether aspirin is a useful adjunct in the treatment of acute pulmonary embolism. No papers were found using the reported search to answer the clinical question. A clinical bottom line is stated.

Clinical scenario
A 50 year old woman presents to the emergency department with shortness of breath and pleuritic chest pain, following a flight from Australia. Examination is unremarkable except for tachypnoea and mild hypoxia. Chest x ray is also normal, so you aim to treat for suspected pulmonary embolus (PE). You know that aspirin is used in the treatment of other acute thromboembolic conditions such as stroke or myocardial infarction, and in the prophylaxis of deep vein thrombosis/PE. You wonder if aspirin would also be beneficial in the treatment of acute PE?

Three part question
In [a patient with suspected acute pulmonary embolus] is [aspirin] effective in [reducing morbidity and mortality]?

Search strategy

Table 1

<table>
<thead>
<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>
</tr>
</thead>
<tbody>
<tr>
<td>Scott RC et al, 1999, UK</td>
<td>79 seizure episodes in 24 young people aged 5–22 years with severe epilepsy living at a residential centre</td>
<td>PRCT</td>
<td>Termination of seizure within 10 minutes of drug administration</td>
<td>Response to midazolam in 30 (75%) of 40 episodes; response to rectal diazepam in 23 (59%) of 39 episodes (p=0.016)</td>
<td>Small sample size (no power calculation)</td>
</tr>
<tr>
<td></td>
<td>Randomised to receive either 2 ml (10 mg) buccal midazolam or 10 mg rectal diazepam upon having a seizure lasting longer than three minutes</td>
<td>Mean time to termination of seizure</td>
<td>Six minutes for midazolam and eight minutes for diazepam (p=0.01)</td>
<td>Nearly half the seizure episodes occurred in the same two patients</td>
<td></td>
</tr>
<tr>
<td>Wilson MT et al, 2004, UK</td>
<td>53 young people aged 3–21 years identified from hospital prescriptions for nasal/buccal midazolam over a 16 month period</td>
<td>Telephone survey</td>
<td>Parental preference</td>
<td>24 of 40 families had used both rectal diazepam and buccal/nasal midazolam: 20/24 (83%) preferred midazolam</td>
<td>Aims of the study were to evaluate effectiveness and convenience of nasal/buccal midazolam in terminating prolonged seizures in the community. The study was not appropriately designed to investigate other outcomes. Patient group selected having already had midazolam prescribed. This may be because they had already stated a preference for midazolam, introducing selection bias. Further, not all prescriptions may have been identified. No sample size calculation and no statistical analysis Not all results were reported (for example parents were asked to grade ease of use from 1 to 5, no results were given)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Termination of seizures</td>
<td>33/40 who used midazolam (83%)</td>
<td></td>
</tr>
</tbody>
</table>

Wilson MT, MacLeod T, O'Regan ME. Nasal/buccal midazolam use in the community. Arch Dis Child 2004;89:50–51.
http://www.bestbets.org/cgi-bin/bets.pl?record=00161

CLINICAL BOTTOM LINE
There is no published evidence to support the use of aspirin in the treatment of acute pulmonary embolism.

Bone Injection Gun placement of intraosseous needles

Report by Andrew Curran, Specialist Registrar
Emergency Medicine
Checked by Ayan Sen, Clinical Fellow
doi: 10.1136/emj.2005.024406

Abstract
A short cut review was carried out to establish whether the Bone Injection Gun is better than a standard intraosseous (IO) needle at obtaining IO access. A total of 129 papers were found using the reported search, of which three represent 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. A clinical bottom line is stated.

Clinical scenario
A 23 year old shocked patient is brought to the Emergency Department resuscitation room. The trauma team are trying to gain vascular access. After five minutes of being unable to gain intravenous access you remember a recent training session on a Bone Injection Gun (BIG) and you wonder if this would be better to use than the standard IO needles that you have previously used?

Three part question
In [patients requiring IO access] is [the Bone Injection Gun better than standard IO needles] at [safely and rapidly acquiring IO access]?

Search strategy
Medline 1966-01/05 using the OVID interface. [exp Infusions, Intraosseous OR intraosseous infusion$.mp OR intraosseous.mp OR IO.mp] AND [BIG.mp OR auto-injector.mp OR auto$.mp OR bone injection gun.mp] LIMIT to English

Search outcome
Altogether 129 papers were found, of which three were relevant to the three part question.

Table 2

<table>
<thead>
<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>
</tr>
</thead>
<tbody>
<tr>
<td>Calkins MD et al, 2000, USA</td>
<td>31 special devices carpal testing 4 IO devices on cadavers; BIG, screw tip IO needles (2 other devices not relevant to the three part question so results not given)</td>
<td>Randomised experimental trial</td>
<td>Success rate</td>
<td>BIG 94%, screw tip 97% (not significant)</td>
<td>Using non-medical responders. By using cadavers there is no “clinical pressure” to achieve vascular access</td>
</tr>
<tr>
<td>Waisman M and Waisman D, 1997, USA</td>
<td>19 patients for resuscitation in whom IV access could not be achieved within 10 minutes and 31 adults with fractures receiving regional anaesthesia</td>
<td>Prospective case series</td>
<td>Time to placement</td>
<td>BIG 70 s (SD 33), screw tip 88s (33) (not significant)</td>
<td>Animal study. Anaesthetised subjects. Small numbers. Lack of follow up in resuscitation group</td>
</tr>
<tr>
<td>Olsen D, 2002, USA</td>
<td>Adult dogs randomised to either IO gun or a Jamshidi IO needle, 24 dogs in each group</td>
<td>PRCT (animal)</td>
<td>Successful placement</td>
<td>BIG 23/24 (96%) for BIG v 23/24 Jamshidi, p = 0.3475</td>
<td>Animal study. Anaesthetised subjects. Direct relevance to humans questionable. Single operator did all procedures. They explain increased failure rate for BIG to be due to poor landmark identification rather than device failure</td>
</tr>
</tbody>
</table>

Comment(s)
There are no published studies looking at the use of the BIG in live adults or children. Though this would be ideal it is unlikely to be achievable as IO placement is a rare event and there would be ethical and consent issues. We must therefore extrapolate data from other models. The paper by Calkins et al shows that the technique itself is easy to learn by non-medical trained responders, this may have implications for its use in prehospital care. The BIG has a higher failure rate in anaesthetised dogs but explained this was due to poor landmark identification rather than device failure. The differences in time to placement are unlikely to be clinically significant. From a clinical perspective there appears to be little to choose between them and issues such as cost and training may influence local decisions.

CLINICAL BOTTOM LINE
The Bone Injection Gun appears to be equivalent in terms of success and possibly (but not clinically significantly) faster to use than standard IO needles at achieving IO access.

Nebulised levalbuterol or albuterol for lowering serum potassium

Report by Herald Ostovar, Senior EM Resident
Checked by Dr Jeffrey Jones, Research Director of the Emergency Medicine Residency Program and Dr Michael Brown, Director of the Emergency Medicine Residency Program
doi: 10.1136/emj.2005.024414

Abstract
A short cut review was carried out to establish whether nebulised levalbuterol is better than or equivalent to albuterol
for lowering serum potassium. Seven papers were found using the reported search, of which three 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. A clinical bottom line is stated.

Three part question
In [patients with hyperkalaemia] is [levalbuterol better than albuterol] at reducing [serum potassium]?

Clinical scenario
A 67 year old man presents to the emergency department with chest pain and syncope. The electrocardiogram shows a diagnosis of hyperkalaemia. The author, date and country of publication, patient group studied, study type, relevant outcomes, results and study weaknesses of these best papers are tabulated. A clinical bottom line is stated.

Three part question
In [patients with hyperkalaemia] is [levalbuterol better than albuterol] at reducing [serum potassium]?

Clinical scenario
A 67 year old man presents to the emergency department with chest pain and syncope. The electrocardiogram shows a diagnosis of hyperkalaemia.

Search strategy
Medline 1966–October 2004 using the OVID interface. [levalbuterol.mp OR exp Albuterol (or albuterol or salbutamol).mp OR exp bronchodilator agents/OR exp adrenergic beta-agonists/OR beta-agonists.mp] AND [exp stereoisomerism/OR enantiomers.mp OR racemic.mp] AND [hyperkalemia.mp. or exp hyperkalaemia/OR hyperkalaemia. mp OR exp potassium] LIMIT TO human AND English language

Search outcome
Seven papers were found of which three were irrelevant to the study question. The remaining four papers are shown in table 3.

Comment
Equipotent nebulised levalbuterol appears to be as effective as albuterol in lowering serum potassium in healthy and asthmatic adults. Studies comparing these two medications in hyperkalaemic patients with comorbidities and on various medications would be helpful in establishing their comparative efficacy in treating common presenters to the emergency department.

Clinical bottom line
Nebulised levalbuterol appears to be as effective as albuterol in lowering serum potassium in adults.

Table 3

<table>
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<tr>
<th>Author, date and country</th>
<th>Patient group</th>
<th>Study type (level of evidence)</th>
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<tr>
<td>Lipworth BJ, UK, 1997</td>
<td>12 volunteers were randomised into 4 study groups</td>
<td>RCT crossover</td>
<td>Pharmacodynamics at extrapolmonary</td>
<td>No significant differences were found in baseline plasma potassium values (no p values provided)</td>
<td>Small doses of study drug used in healthy volunteers Small sample size Mean age (20-34) may not be representative of majority of population presenting with hyperkalaemia Four consecutive small doses given at 30 minute intervals may not be applicable to those patients presenting with pathological hyperkalaemia Small sample size</td>
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<td>Gumbhir-Shah K, USA, 1999</td>
<td>13 asthmatic subjects randomised to receive four cumulative doses of either nebulised 1.25 mg levalbuterol or 2.5 mg albuterol at 30 minute intervals</td>
<td>POR crossover</td>
<td>(2 receptors (Bronchus, Plasma potassium, heart rate) measured at 0-100 minutes at 20 minute intervals)</td>
<td>No significant differences between R and RS albuterol in reduction of plasma potassium levels (AUC p=0.17)</td>
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<td>Lofwall J, et al, 2001, Sweden</td>
<td>20 adult asthmatic patients were randomised into 4 study groups, nebulised R albuterol (0.25-1600 µg), 5 albuterol (0.25-1600 µg), 85 albuterol (12.5-5000 µg) or placebo</td>
<td>RCT crossover</td>
<td>FEV1, Plasma potassium, Plasma glucose, heart rate, QTc interval, and urine plasma drug concentration at 1, 2, 4, 6, 8 hours after final dose</td>
<td>No significant differences between R and RS albuterol in reduction of plasma potassium levels (AUC p=0.17)</td>
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<td>Pancu D, et al, 2003, USA,</td>
<td>27 healthy adult volunteers, 9 nebulised normal saline, 9 albuterol (10 mg), 9 levalbuterol (2.5 mg)</td>
<td>Randomised, double blind, placebo controlled trial</td>
<td>Serum potassium values at baseline</td>
<td>No differences between any group: albuterol 3.9 (0.3) mEq/l, levalbuterol 4.1 (0.3) mEq/l, placebo 4.1 (0.3) mEq/l</td>
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