Towards evidence based emergency medicine: Best BETs from the Manchester Royal Infirmary

Edited by S D Carley

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
- Aspirin in the treatment of acute pulmonary embolism
- Bone Injection Gun placement of intraosseous needles
- Nebulised levalbuterol or albuterol for lowering serum potassium


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
Medline: 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


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**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>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 either outcome.</td>
</tr>
</tbody>
</table>

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http://www.bestbets.org/cgi-bin/bets.pl?record=00161

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**CLINICAL BOTTOM LINE**

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

**Comment(s)**

Poullis suggests in a letter that aspirin administration after diagnosis of PE in combination with heparin could have beneficial effects but needs further study. Although this question has been raised many times in our clinical practice there appears to be little discussion in the literature. One possibility may be, as some haematologists suggest, that aspirin is more likely to be useful when the final occluding event is a platelet clump. This is more common in the presence of arterial atheromatous plaques which rupture and attract platelets to the site. This occurs in coronary artery disease and in the carotid vessels where aspirin is advocated. In venous disease, where the vessel walls are relatively smooth and stasis is more important, clots are more likely to occur as a result of the activation of the clotting system. Another consideration is that patients with proved PE are generally anticoagulated initially with heparin, and then with warfarin. The additional benefit of aspirin is therefore likely to be small. Such a small benefit must be weighed against the additional bleeding complications from concomitant aspirin use.
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 into 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$ OR intraosseous. mp OR IO.mp] AND [BIG.mp OR auto-injector.mp OR auto$ 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.

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. This paper also used the screw tipped IO needle as the standard needle but in practice people may be more used to the standard straight needle. Waisman and Waisman suggest that they can be used successfully in practice. Olsen found 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.

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>Study weaknesses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calkins MD et al, 2000, USA</td>
<td>31 special operations corpsman 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>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Time to placement</td>
<td>BIG 70 s (SD 33), screw tip 88s (33) (not significant)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Rank of preference</td>
<td>BIG average rank 2.3, screw tip average rank 2.5 (not significant)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Time to placement</td>
<td>Success rate</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Complications</td>
<td>Time taken “1–2 minutes”</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>None in 24 hours or 4 months for respective groups</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>Study type</td>
<td>Using non-medical responders. By using cadavers there is no “clinical pressure” to achieve vascular access</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Observational study with no comparisons. 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 20/24 (83%) for BIG v 23/24 (96%) for the Jamshidi, p=0.3475</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Average time for placement</td>
<td>22.4 s for BIG v 42 s for Jamshidi</td>
</tr>
</tbody>
</table>

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 wide QRS and peaked T-waves. STAT electrolytes show a potassium level of 7.3. While starting calcium gluconate, glucose/insulin, nebulised albuterol and kayexalate you wonder if substitution of levalbuterol for albuterol would have the same lowering effect on serum potassium and have fewer side effects.

### Search strategy


### 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>
<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>Lipworth BJ, et al, 1997, UK</td>
<td>12 volunteers were randomised into 4 study groups: nebulised R-albuterol (200–3200 μg), S-albuterol (200–3200 μg), RS-albuterol (400–4400 μg) or placebo.</td>
<td>RCT crossover</td>
<td>FEV1, plasma potassium, plasma glucose, heart rate, G6PD, and urine plasma drug concentration at 1, 2, 4, 6, 8 hours after final dose</td>
<td>No significant differences were found in baseline plasma potassium values (no p values provided)</td>
<td>Small doses of study drugs used in healthy volunteers. Small sample size. Mean age (20±3) may not be representative of majority of population presenting with hyperkalaemia. Four consecutive small doses given at 30 minutes intervals may not be applicable to those patients presenting with pathological hyperkalaemia. Small sample size.</td>
</tr>
<tr>
<td>Gumbhir-Shah K, et al, 1999, USA</td>
<td>13 asthmatics subjects randomised to receive four cumulative doses of either nebulised 1.25 mg levalbuterol or 2.5 mg albuterol at 30 minutes intervals</td>
<td>RCT crossover</td>
<td>FEV1, plasma potassium, plasma glucose, heart rate, G6PD, 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>
<td>None severe. Included dizziness, tachycardia, nervousness (greater in R group), wheezing (greater in RS group). All events resolved spontaneously.</td>
</tr>
<tr>
<td>Lipdoll J, et al, 2001, Sweden</td>
<td>20 adult asthmatic patients were randomised into 4 study groups: nebulised R-albuterol (6.25–1600 μg), S-albuterol (6.25–1600 μg), RS-albuterol (12.5–5200 μg), or placebo.</td>
<td>RCT 4-way crossover</td>
<td>FEV1, heart rate, and plasma potassium levels before dosing, and change from baseline to 20 minutes after each dose</td>
<td>Differences/p values not documented Rapid increase in plasma potassium level (0.3-0.4 mmol/l) after placebo administration (no p value given)</td>
<td>Single K+ level was measured 30 minutes after study drug. Small sample size.</td>
</tr>
<tr>
<td>Pancu D, et al, 2003, USA</td>
<td>27 healthy adult volunteers; 6 nebulised normal saline, R-albuterol (10 mg), S-albuterol (6.1 mg) blinded, double blind, placebo controlled trial</td>
<td>Randomised, double blind, placebo controlled trials</td>
<td>Serum potassium values at baseline</td>
<td>No differences between any group: albuterol 3.9 (0.3) mmol/l, levalbuterol 4.1 (0.3) mmol/l, placebo 4.1 (0.3) mmol/l.</td>
<td>This study measured potassium changes in a small sample of healthy volunteers. The clinical significance of these small changes in potassium is uncertain and these changes may not be applicable to those patients presenting with pathological hyperkalaemia. Objective vital signs were only recorded in those patients reporting side effects.</td>
</tr>
</tbody>
</table>

- **SERUM POTASSIUM AT 30 MINUTES**: Albuterol reduced by 0.3 mmol/l, levalbuterol reduced by 0.3 mmol/l, placebo increased by 0.1 mmol/l; no significant difference between R and placebo (p<0.001). |

- **SERUM POTASSIUM AT 60 MINUTES**: Albuterol reduced by 0.3 mmol/l, levalbuterol reduced by 0.3 mmol/l, plasma showed no change. No significant difference between R and placebo. Both R and placebo better than placebo (p<0.001). |

- **SIDE EFFECTS**: Levalbuterol caused fewer reported side effects than albuterol. Levalbuterol v albuterol: total patient reporting symptoms, 22% v 78%; tremor, 22% v 78%; nervousness, 0% v 56%; palpitations, 0% v 56%; tachycardia, 0% v 44%; no p values provided.
Buccal midazolam as an alternative to rectal diazepam for prolonged seizures in childhood and adolescence
Richard Body and Mawra Ijaz

doi: 10.1136/emj.2005.024380

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