BEST EVIDENCE TOPIC REPORTS

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

Edited by K Mackway-Jones

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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 Infirmary¹ or placed on the BestBETs website. Each BET has been constructed in the four stages that have been described elsewhere.² The BETs shown here together with those published previously and those currently under construction can be seen at <http://www.bestbets.org>.³ Four BETs are included in this issue of the journal.

- ▶ Terlipressin or somatostatin for the treatment of bleeding oesophageal varices
- ▶ Magnetic resonance imaging or bone scintigraphy in the diagnosis of plain x ray occult scaphoid fractures
- ▶ Diagnostic utility of arterial blood gases for investigation of pulmonary embolus
- ▶ Intranasal midazolam in patients with fits

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- 1 Carley SD, Mackway-Jones K, Jones A, *et al*. Moving towards evidence based emergency medicine: use of a structured critical appraisal journal club. *J Accid Emerg Med* 1998;15:220–2.
- 2 Mackway-Jones K, Carley SD, Morton RJ, *et al*. The best evidence topic report: a modified CAT for summarising the available evidence in emergency medicine. *J Accid Emerg Med* 1998;15:222–6.
- 3 Mackway-Jones K, Carley SD. [bestbets.org](http://www.bestbets.org): odds on favourite for evidence in emergency medicine reaches the worldwide web. *J Accid Emerg Med* 2000;17:235–6.

Terlipressin or somatostatin for the treatment of bleeding oesophageal varices

Report by Russel Boyd, *Consultant*
Checked by John Butler, *Consultant*

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Abstract

A short cut review was carried out to establish whether terlipressin or somatostatin is more effective at reducing acute bleeding in adults with known oesophageal varices. Altogether 170 papers were found using the reported search,

of which four 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

A 55 year old man presents to the Emergency Department with massive haematemesis. He has known oesophageal varices. He is tachycardic, peripherally shut down and continues to actively vomit fresh blood. You wonder if pharmacological treatment with terlipressin or somatostatin will be effective in reducing the bleeding.

Three part question

In [adults with known varices] is [terlipressin or somatostatin] more effective at [reducing acute bleeding]?

Search strategy

Medline OVID 1966–2005 February Week 1 and Embase OVID 1980–2004 Week 7: [(exp Gastrointestinal Hemorrhage/OR exp "Esophageal and Gastric Varices"/or oesophageal varices.mp.)] AND [(exp SOMATOSTATIN/AND terlipressin.mp. OR glypressin.mp. OR terlypressin.mp.)] LIMIT to humans and Eng Lang.

Search outcome

Altogether 170 papers were identified of which four were relevant to the clinical question. These four papers are shown in table 1.

Comment(s)

Four randomised controlled studies exist in this area. No significant difference in rates of cessation of bleeding were found between patients treated with either terlipressin or somatostatin.

▶ CLINICAL BOTTOM LINE

There appears to be no significant difference between terlipressin and somatostatin in their ability to control bleeding. The logistical advantage of four hourly bolus administration of terlipressin over the need for continuous infusions of somatostatin and the lower cost of terlipressin will be relevant when choosing between them.

Walker S, Kreichgauer HP, Bode JC. Terlipressin vs. somatostatin in bleeding esophageal varices: a controlled, double-blind study. *Hepatology* 1992;15:1023–30.

Pedretti G, Elia G, Calzetti C, *et al*. Octreotide versus terlipressin in acute variceal hemorrhage in liver cirrhosis. Emergency control and prevention of early rebleeding. *Clin Invest* 1994;72:653–9.

Fau F, Ruiz del Arbol L, Banares R, *et al*. Double-blind randomized controlled trial comparing terlipressin and somatostatin for acute variceal hemorrhage. *Gastroenterology* 1996;111:1291–9.

Walker S, Kreichgauer HP, Bode JC. Terlipressin (Glypressin) versus somatostatin in the treatment of bleeding esophageal varices—final report of a placebo-controlled, double-blind study. *Z Gastroenterol* 1996;34:692–8.

Table 1

Author, date, and country	Patient group	Study type (level of evidence)	Outcomes	Key results	Study weaknesses
Walker S <i>et al</i> , 1992, Germany	50 episodes of endoscopically proven bleeding oesophageal varices in 33 patients	Double blinded randomised controlled trial	Cessation of active bleeding for 24 hours within 24 hours of randomisation	22/25 patients (80%) with terlipressin ceased bleeding whereas 19/25 (76%) of the somatostatin group ceased bleeding	Numbers too small to firmly exclude type 2 error No power study
Pedretti G <i>et al</i> , 1994, Italy	60 patients, previously diagnosed with hepatic cirrhosis, with current endoscopically proven variceal bleeds	Unblinded randomised controlled trial	Cessation of acute bleed and occurrence of rebleeding inside 24 hours	No statistical difference in cessation of bleeding; octreotide 76.6% (23/30) v terlipressin 53% (16/30)	Not blinded
Feu F <i>et al</i> , 1996, Spain	60 patients, previously diagnosed with hepatic cirrhosis, with current endoscopically proven variceal bleeds	Double blind randomised controlled trial	Cessation of bleeding for a 24 hour period inside 36 hours of randomisation	Cessation of bleeding in 64/80 patients (80%) treated with terlipressin and 68/81 patients (84%) treated with somatostatin. Statistical significance not reached	
Walker S <i>et al</i> , 1996, Germany	106 patient episodes of bleeding from endoscopically proven bleeding varices episodes in 72 patients	Double blind placebo controlled clinical trial	Cessation of bleeding for a 24 hour period within 24 hours of trial recruitment	91% (48/53) of terlipressin treated episodes and 81% (43/53) of the somatostatin treated episodes ceased bleeding. Statistical significance not reached	The inclusion of patients with multiple episodes who had variable numbers of sclerotherapy sessions may have introduced some bias

Magnetic resonance imaging or bone scintigraphy in the diagnosis of plain x ray occult scaphoid fractures

Report by Bernard Foex, *Consultant*, Peter Speake, *House Officer*

Checked by Rick Body, *Clinical Research Fellow*

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Abstract

A short cut review was carried out to establish whether magnetic resonance scanning or bone scintigraphy is better at identifying scaphoid fractures not apparent on plain x rays. Altogether 11 papers were found using the reported search, of which four 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 adult presents to the Emergency Department review clinic two weeks after falling onto his outstretched hand. A scaphoid fracture was suspected but no fracture was seen on plain scaphoid views. He continues to have scaphoid tenderness. You wonder whether a magnetic resonance scan would be better than a bone scan in confirming or excluding a scaphoid fracture.

Three part question

In an adult with a [clinically suspected scaphoid fracture] is [magnetic resonance imaging better than bone scintigraphy] at [reaching a diagnosis]?

Search strategy

Medline from 1966 until March Week 1 2005: ((fracture\$.af. OR fracture#.w..de. OR Hand-fracture#.de. OR hand-injury#.de.

OR fracture-nonunion#.de.) OR (scaphoid-fracture#.de.)) AND (Nuclear-Magnetic-Resonance-Imaging#.de. OR (magnet\$ ADJ reson\$ ADJ imag\$).mp. OR (magnet\$ ADJ reson\$ ADJ spect\$).mp. OR mri.af. OR nmr.af.) AND ((bone ADJ scan).mp. OR Bone-scintiscanning#.de. OR Medronate-Technetium-TC-99m#.de. OR Technetium-99m#.de. OR Whole-body-scintiscanning#.de. OR scintigraph\$.af.))

Search outcome

Altogether 23 papers were found. Only three addressed the question. One further paper was found by searching the references. These four papers are shown in table 2.

Comment(s)

Only 145 patients appear to have been entered into any sort of comparison between the two imaging modalities. Magnetic resonance imaging appears slightly superior in diagnosing occult scaphoid fractures. Magnetic resonance imaging also allows accurate diagnosis of clinically significant soft tissue injuries, which may otherwise be missed. It is also quicker to perform than a bone scan. However, some patients with claustrophobia will not tolerate it.

► CLINICAL BOTTOM LINE

Magnetic resonance imaging is the investigation of choice in the clinically suspected scaphoid fracture after negative initial and 10–14 day follow up x rays. A bone scan is a reasonable alternative in patients with claustrophobia.

Tiel-van Buul MM, Roolker W, Verbeeten BW, *et al*. Magnetic resonance imaging versus bone scintigraphy in suspected scaphoid fracture. *Eur J Nucl Med* 1996;23:971–5.

Thorpe AP, Murray AD, Smith FW, *et al*. Clinically suspected scaphoid fracture: a comparison of magnetic resonance imaging and bone scintigraphy. *Br J Radiol* 1996;69:109–13.

Fowler C, Sullivan B, Williams LA, *et al*. A comparison of bone scintigraphy and MRI in the early diagnosis of the occult scaphoid waist fracture. *Skeletal Radiol* 1998;27:683–7.

Kitsis C, Taylor M, Chandey J, *et al*. Imaging the problem scaphoid. *Injury* 1998;29:515–20.

Table 2

Author, date, and country	Patient group	Study type (level of evidence)	Outcomes	Key results	Study weaknesses
Tiel-van Buul MM <i>et al</i> , 1996, the Netherlands	19 patients with clinically suspected scaphoid fracture and negative initial x rays	Diagnostic cohort	Scaphoid fracture	5 on MRI and BS	3 patients did not complete MR scan because of claustrophobia
			False positive False negative Agreement between methods	2 on BS 1 on MRI 11 of 16	
Thorpe AP <i>et al</i> , 1996, UK	61 patients (59 examinations) with signs of a scaphoid fracture but negative initial and 10 day follow up x rays	Diagnostic cohort	Scaphoid fractures	4 on BS and MRI	Only 52% attended follow up at 6 weeks for clinical evaluation and further x rays
			False positive Other significant injuries	3 BS and 1 MRI 3 on MRI only	
Fowler C <i>et al</i> , 1998, UK	45 patients with clinically suspected scaphoid fractures with negative initial and 7–10 day follow up x rays. Telephone follow-up at 12 months and then clinical evaluation and further x rays if indicated	Diagnostic cohort	Scaphoid fracture	6 on BS and MRI	2 patients did not complete MR scan because of claustrophobia. Only 8 patients followed up at 12 months (6 confirmed fractures and the 2 false positive on BS)
			False positive False negative Agreement between methods	2 BS 1 BS 40 of 43	
Kitsis C <i>et al</i> , 1998, UK	22 patients with suspected scaphoid fractures referred to a hand clinic after normal initial and 14 day follow up x rays. Follow up at 8 weeks for clinical evaluation and further x rays	Diagnostic cohort	Scaphoid fracture	3 in BS and MRI	Small study. 1 patient had BS and then missed MRI
			False positives Other significant injuries Agreement between methods	1 on BS 4 on MRI only 17 of 22	

BS, bone scintigraphy; MRI, magnetic resonance imaging.

Diagnostic utility of arterial blood gases for investigation of pulmonary embolus

Report by Margaret Maloba, *Specialist Registrar*
Checked by Kerstin Hogg, *Specialist Registrar*

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Abstract

A short cut review was carried out to establish the diagnostic utility of arterial blood gas analysis in patients with suspected pulmonary embolus. Altogether 459 papers were found using the reported search, of which six 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

A 28 year old woman presents to the Emergency Department with acute suspected pulmonary embolus (PE). You wonder whether normal arterial blood gases are sufficient to rule out PE.

Three part question

In [patients with clinical diagnosis of PE] do [arterial blood gases] aid in [making a definite diagnosis]?

Search strategy

Medline OVID1966–2005 Feb week 1 and Embase OVID 1980–2005 week 7: (exp pulmonary embolism/OR pulmonary embolus.mp.) AND (exp embolism/OR embol\$.mp. OR exp thromboembolism/OR thromboembol\$.mp.) AND (exp blood gas analysis/OR arterial blood gas\$.mp.)

Search outcome

Altogether 459 papers were found of which six directly addressed the question. These six papers are shown in table 3.

Comment(s)

Pulmonary angiography, the gold standard diagnostic tool in PE, has unacceptably high mortality and morbidity. At present, it cannot routinely be used in clinical practice. A reliable, cost effective, non-invasive test if identified would be of great use.

► CLINICAL BOTTOM LINE

Arterial blood gas analysis alone is of limited diagnostic utility in suspected PE.

Table 3

Author, date, and country	Patient group	Study type (level of evidence)	Outcomes	Key results	Study weaknesses
Cvitac O <i>et al</i> , 1989, USA	78 patients with angiographically proven PE and cardiopulmonary disease	Retrospective cohort	Sensitivity of hypoxaemia	76%	Excluded all patients with cardiopulmonary disease
Stein PD, 1995, USA	768 patients aged over 18 years with a clinical diagnosis of PE (part of the PIOPED study)	Prospective randomised controlled trial	NPV	Pco ₂ 65%	Recruitment bias—only those with written consent were recruited (approximately half of all suitable patients)
			Specificity	PO ₂ 68% Pco ₂ 50% PO ₂ 24% Pco ₂ 37%	
			PPV	PO ₂ 37% Pco ₂ 51%	
			Sensitivity	PO ₂ 81%	
Jeffrey S, 1997, USA	197 emergency department patients who underwent pulmonary angiography for presumed diagnosis of acute PE	Retrospective cohort	NPV	Pco ₂ >35 61%	Seriously ill patients possibly excluded because they were on oxygen
			Specificity	PO ₂ >80 66% Pco ₂ >35 51% PO ₂ >80 25%	Selection bias as only patients with angiography were recruited
Prediletto R <i>et al</i> , 1999, Italy	773 consecutive patients with suspected PE (part of the PISAPED study)	Prospective randomised controlled trial	PE present with normal PO ₂	14%	Not all patients had the gold standard (angiogram)
			PE present with normal Pco ₂	35%	
			PE absent with abnormal PO ₂ PE absent with abnormal Pco ₂	13% 55%	
Masotti L <i>et al</i> , 2000, Italy	118 patients aged over 65 years who had a VQ scan for suspected PE	Retrospective cohort	Blood gases in patients with and without PE	No significant differences	No gold standard. Minimal data and statistics given
Rodger MA <i>et al</i> , 2000, Canada	293 consecutive patients referred for imaging (VQ or pulmonary angiography)	Prospective cohort	Blood gases in patients with and without PE	No significant differences	Not all patients had the gold standard

NPV, negative predictive value; PE, pulmonary embolism; PPV, positive predictive value; VQ, ventilation-perfusion.

Cvitac O. Improved use of arterial blood gas analysis in suspected pulmonary embolism. *Chest* 1989;**95**:48–51.

Stein PD, Goldhaber SZ, Henry JW. Arterial blood gas analysis in the assessment of suspected acute pulmonary embolism. *Chest* 1996;**109**:78–81.

Jones JS. Use of the alveolar-arterial oxygen gradient in the assessment of acute pulmonary embolism. *Am J Emerg Med* 1998;**16**:333–7.

Prediletto R, Miniati M, Tonelli L, et al. Diagnostic value of gas exchange tests in patients with clinical suspicion of pulmonary embolism. *Crit Care* 1999;**3**:111–16.

Masotti L, Ceccarelli E, Cappelli R, et al. Arterial blood gas analysis and alveolar-arterial oxygen gradient in diagnosis and prognosis of elderly patients with suspected pulmonary embolism. *J Gerontol A Biol Sci Med Sci* 2000;**55A**:M761–M764.

Rodger MA, Carrier M, Jones GN, et al. Diagnostic value of arterial blood gas measurement in suspected pulmonary embolism. *Am J Resp Crit Care Med* 2000;**162**:2105–8.

Intranasal midazolam in patients with fits

Report by **Martin Smith, Consultant**
Checked by **Simon Carley, Consultant**

doi: 10.1136/emj.2005.025726

Abstract

A short cut review was carried out to establish whether intranasal midazolam was effective for stopping fits. Altogether 36 papers were found using the reported search, of which four 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

A 14 year old boy with known epilepsy attends the Emergency Department having had a fit at school. His teacher is with him. She tells you that he was fitting for approximately 20 minutes. She also tells you that they have rectal diazepam at school but the staff were reluctant to administer it. You check the patient and find him to be postictal but otherwise well. You wonder if midazolam, which can be administered intranasally, would successfully terminate epileptic fits.

Three part question

In [a fitting patient with no intravenous access] can [intranasal midazolam] stop [the fit]?

Search strategy

Medline OVID 1966 to 2005 Feb week 2 and Embase OVID 1980–2004 Week 7: [exp epilepsy/OR epilepsy.mp OR exp seizures/OR seizure\$.mp OR convulsion\$.mp. OR fit\$.mp.] AND [exp midazolam/OR midazolam.mp. OR exp

Table 4

Author, date, and country	Patient group	Study type (level of evidence)	Outcomes	Key results	Study weaknesses
O'Regan ME <i>et al</i> , 1996, UK	19 epileptic children in the neurophysiology laboratory given intranasal midazolam	Experimental	Electroencephalographic (EEG) evidence or clinical cessation of fits	15/19 patients showed either EEG changes or clinical improvement	Population different from that seen as an emergency No control of other medications Small numbers
Kendall JL <i>et al</i> , 1997, USA	2 patients in the Emergency Department	Case report	Clinical evidence of cessation of fits	Both patients stopped fitting	
Scheepers M <i>et al</i> , 1998, UK	2 patients in the Emergency Department	Case report	Clinical evidence of cessation of fits	Both patients stopped fitting	
Mahmoudian T and Zadeh MM, 2004, Iran	70 children aged 2 months to 15 years Intravenous diazepam v intranasal	Clinical trial	Time to seizure control	2.94 min v 3.58 min	No randomisation

benzodiazepines/OR benzodiazepines.mp.] AND [exp administration intranasal/OR nasal\$.mp. OR nose.mp.]

Search outcome

Altogether 36 papers were identified. On reading the abstracts four papers were found to be of interest to the question. These four papers are shown in table 4.

Comment(s)

The standard of evidence is poor. Properly conducted trials comparing the efficacy of intranasal midazolam are needed.

► CLINICAL BOTTOM LINE

Intranasal midazolam appears to be effective at controlling seizures.

O'Regan ME, Brown JK, Clarke M. Nasal rather than rectal benzodiazepines in the management of acute childhood seizures? *Dev Med Child Neurol* 1996;**38**:1037–45.

Kendall JL, Reynolds M, Goldberg R. Intranasal midazolam in patients with status epilepticus. *Ann Emerg Med* 1997;**29**:415–17.

Scheepers M, Scheepers B, Clough P. Midazolam via the intranasal route: an effective rescue medication for severe epilepsy in adults with learning disability. *Seizure* 1998;**7**:509–12.

Mahmoudian T, Zadeh MM. Comparison of intranasal midazolam with intravenous diazepam for treating acute seizures in children. *Epilepsy Behav* 2004;**5**:253–5.