

BEST EVIDENCE TOPIC REPORTS

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

Edited by S D Carley

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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 practicing 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. Details on how to do a BET are available online at <http://www.bestbets.org/home/participation.html>

- ▶ Do non-steroidal anti-inflammatory drugs cause a delay in fracture healing?
- ▶ Rectal or intravenous non-steroidal anti-inflammatory drugs in acute renal colic
- ▶ Are antibiotics indicated following human bites?
- ▶ Nebulised furosemide in acute adult asthma

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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.

Do non-steroidal anti-inflammatory drugs cause a delay in fracture healing?

Report by Simon Clarke, *Consultant*
Checked by Fiona Lecky, *Consultant*
doi: 10.1136/emj.2005.028647

Abstract

A short cut review was carried out to establish whether there is any evidence that non-steroidal anti-inflammatory drugs (NSAIDs) might delay fracture healing. A total of 514 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. At present, although there are theoretical concerns about the adverse effects of NSAIDs on fracture healing, there is not enough clinical evidence to deny patients with simple fractures their analgesic benefits.

Clinical scenario

A 21 year old man attends the emergency department having sustained an undisplaced, closed fracture of his distal radius. You wonder whether giving the patient a course of NSAIDs will delay fracture healing.

Three part question

In [patients with simple fractures] do [NSAIDs compared with conventional analgesia] delay [fracture healing]?

Search strategy

Medline 1966–04/05 using the OVID interface. [(exp fractures OR fracture\$.mp OR fracture healing.mp) AND (exp anti-inflammatory agents, non-steroidal OR nsaid\$.mp OR anti-inflammatory\$.mp)] LIMIT to human. References of papers and suitable review articles were scrutinised for further possible articles.

Search outcome

A total of 514 papers were found of which three were relevant to the three part question. No further articles were discovered by the reference review.

Comment(s)

Inflammatory processes are integral to the early stages of fracture healing and there is theoretical concern that this may be inhibited by NSAIDs leading to delayed or even non-union. This worry seems to have been backed up by animal experimentation (primarily on rats); the two small randomised controlled trials did not give any clear evidence to suggest that this is translated into significant clinically adverse effects in humans. The case control study has raised a concern about the relation of NSAIDs to non-union that needs further evaluation. NSAIDs are effective analgesics for musculoskeletal trauma, so until more solid evidence becomes available, their use should not be discouraged.

▶ CLINICAL BOTTOM LINE

At present, although there are theoretical concerns about the adverse effects of NSAIDs on fracture healing, there is not enough clinical evidence to deny patients with simple fractures their analgesic benefits.

- Davis TRC, Ackroyd CE. Non-steroidal anti-inflammatory agents in the management of Colles' fractures. *Br J Clin Pract* 1988;42:184–9.
- Adolphson P, Abbassagan H, *et al*. No effects of piroxicam on osteopenia and recovery after Colles' fracture. *Arch Orthop Trauma Surg* 1993;112:127–30.
- Giannoudis PV, MacDonald DA, Matthews SJ, *et al*. Nonunion of the femoral diaphysis: the influence of reaming and non-steroidal anti-inflammatory drugs. *J Bone Joint Surg Br* 2000;82:655–8.

Table 1

Author, date, and country	Patient group	Study type	Outcomes	Key results	Study limitations
Davis, 1988, UK	100 patients >40 years with a 1st Colles' fracture given flurbiprofen 50/100 mg twice daily or placebo for 2/52	RCT	Functional recovery	Some early delay with active treatment (4-6/52) but no difference at 1 year	1. High dropout rate (24%) 2. Possibility of self-administered confounding treatments not accounted for
Adolphson, 1993, Sweden	42 post menopausal women with first Colles' fracture given piroxicam 20 mg once daily or placebo for 8/52	RCT	Radiological and functional recovery	No difference in recovery rate up to 12/52	1. Small study 2. Short follow up 3. Possibility of self-administered confounding treatments not accounted for 4. Randomisation process not specified and significant differences in demographics between groups
Giannoudis, 2000, UK	99 patients who had undergone intramedullary nailing of femoral shaft fractures over a 6 year period. 32 patients had suffered from a non-union while 67 had successful bone healing.	Case control study	The patients were telephoned with a questionnaire about a number of factors which included NSAID use. Their notes were scrutinised for the type of operative procedure and device used (which was the primary variable under investigation).	A significant difference was found in NSAID use between the non-union (62.5%) and successful healing (13.4%) groups ($p < 0.0001$). The non-union group tended to use NSAIDs for longer (21 v 1 week).	1. Authors attributed a causal relation to the association found between non-union and NSAID use. Prolonged NSAID use may have been result, rather than cause, of non-union 2. No data given as to the degree of matching of the control cases. 3. Not a typical ED patient population

Rectal or intravenous non-steroidal anti-inflammatory drugs in acute renal colic

Report by Caroline Lee, *Specialist Registrar*
Checked by Dhurga Gnanasegaram and Margaret Maloba, *Specialist Registrars*

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Abstract

A short cut review was carried out to establish whether rectal non-steroidal anti-inflammatory drugs (NSAIDs) are as effective as IV NSAIDs in the management of acute renal colic. Altogether 179 papers were found using the reported search, of which two 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. Rectal NSAIDs are an effective form of analgesia for patients with acute renal colic and have fewer side effects compared with intravenous NSAIDs.

Three part question

In [patients with a clinical diagnosis of renal colic] is [PR NSAIDs better than IM NSAIDs] at [reducing pain (length and speed of analgesia)]?

Clinical scenario

A 21 year old male presents to the emergency department with sudden onset of left lumbar pain radiating to the groin. A clinical diagnosis of renal colic is made. You wonder whether rectal NSAIDs would be more effective than IV or IM NSAIDs?

Search strategy

Medline 1966–03/2005 using the OVID interface. [Exp Urinary Calculi OR exp Kidney Calculi OR renal colic.mp OR ureteric colic.mp OR renal calculi.mp OR kidney stone.mp] AND [exp Anti-Inflammatory Agents, Non Steroidal OR NSAID.mp] LIMIT to humans and English language. The Cochrane Library of systematic reviews Issue 1 2005: "renal colic OR NSAID".

Search outcome

A total of 179 papers were found of which two were relevant to the question. No additionally relevant citations were found in The Cochrane Library.

Table 2

Author, date, and country	Patient group	Study type (level of evidence)	Outcomes	Key results	Study weaknesses
Nelson CE <i>et al</i> , 1988, Sweden	84 patients from two emergency departments with a preliminary diagnosis of acute renal colic who later had diagnosis confirmed by IVU or urine sediment. Patients received one rectal and one IV injection Randomised to receive 100 mg indomethacin PR plus placebo IV injection (riboflavin coloured saline) in 37 patients OR placebo PR plus 50 mg indomethacin intravenously in 47 patients	Double blind RCT	Pain severity score (visual analogue scale 0-100) at 0, 10, 20, and 30 minutes after treatment Side effects Need for supplementary analgesia	Faster analgesic effect with IV v rectal at 10 minutes. Effective reduction in mean pain score for both groups (74, 39, 22, 14 for IV v 82, 41, 34, 22 for PR) Significantly more side effects in intravenous group (49%) v rectal group (17%) No significant difference in need for supplementary analgesia 21% IV v 34% PR Analgesia achieved faster in the intravenous group. Significant improvement in mean relative pain intensity in both groups More adverse reactions in intravenous group (44/80, 55%) v PR group (29/79, 37%) ($p = 0.03$) Need for supplementary analgesia in 27% of PR group v 9% of IV group ($p = 0.018$)	Excluded patients if could not retain rectal drug therefore did not analyse as intention to treat
Nissen I <i>et al</i> , 1990, Denmark	116 patients from 10 departments of surgery/urology with clinical symptoms of ureteric colic who were later proven to have a stone on IVU or on passage of stone. Randomised to receive 100 mg indomethacin PR or 50 mg indomethacin IV	Double blind RCT	Intensity of pain (visual analogue score 0-100) at 0, 10, 20, and 30 minutes after treatment Adverse events at time of treatment Need for supplementary analgesia	Analgesia achieved faster in the intravenous group. Significant improvement in mean relative pain intensity in both groups More adverse reactions in intravenous group (44/80, 55%) v PR group (29/79, 37%) ($p = 0.03$) Need for supplementary analgesia in 27% of PR group v 9% of IV group ($p = 0.018$)	Does not describe how study was randomised. Included 42 patients in analysis of adverse reactions who had no proven diagnosis

Table 3

Author, date, and country	Patient group	Study type (level of evidence)	Outcomes	Key results	Study weaknesses
Zubowicz VN and Gravier M, 1991, USA	48 patients with early (<24 hour) human bites to the hand	Prospective randomised controlled trial	Infection rate: placebo v oral cephalosporin v IV cephalosporin + penicillin G	Infection rate: 46.7% placebo v 0% oral/IV antibiotic (p<0.05)	Small study population within each group
Broder J <i>et al</i> , 2004, USA	127 patients with early (<24 hour) superficial human bites excluding to the hand, feet, or skin overlying joints	Prospective double blind placebo controlled trial	Infection rate: placebo v oral cephalosporin/penicillin	Infection rate: 1.6% placebo v 0% antibiotic (p>0.05)	Only investigated low risk bites

Comment(s)

There are many studies in the literature which compare intravenous with intramuscular NSAID use in acute renal colic. Unfortunately no studies were found comparing intramuscular NSAIDs with rectal NSAIDs, which are commonly used in our emergency departments. Rectal NSAIDs have advantages in busy departments by providing urgent analgesia when there are delays in staff available to cannulate the patient and the patient is vomiting.

► CLINICAL BOTTOM LINE

Rectal NSAIDs are an effective form of analgesia for patients with acute renal colic and have fewer side effects compared with intravenous NSAIDs.

Nelson CE, Nylander C, Olsson AM, *et al*. Rectal v. intravenous administration of indomethacin in the treatment of renal colic. *Acta Chir Scand* 1988;**154**:253–5.
Nissen I, Birke H, Olsen JB, *et al*. Treatment of ureteric colic. Intravenous versus rectal administration of indomethacin. *Br J Urol* 1990;**65**:576–9.

Are antibiotics indicated following human bites?

Report by **Dr Alma-Victoria Rittner and Dr Kevin Fitzpatrick, Senior House Officers**

Checked by **Dr Alasdair Corfield, Registrar**
doi: 10.1136/emj.2005.028662

Abstract

A short cut review was carried out to establish whether antibiotics are indicated for human bites. Eighty nine papers were found using the reported search, of which two 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. Prophylactic antibiotics should be given to all patients with human bites to the hands, feet, and skin overlying joints or cartilaginous structures, and to all patients with bites that penetrate deeper than the epidermal layer.

Three part question

In [healthy adults sustaining a human bite] do [prophylactic antibiotics] reduce [the incidence of infection]?

Clinical scenario

A healthy 25 year old man involved in an altercation with another man sustains a bite wound on the arm and presents to the Accident and Emergency Department. The wound is thoroughly cleaned and no signs of infection are present. You wonder whether prophylactic antibiotics are indicated to reduce the risk of wound infection in this patient.

Search strategy

Medline (1996–11/03) and Embase (1980–04/05). [human bites.mp OR exp Bites, Human/] and [penicillin.mp OR exp

Penicillins OR antibiotics.mp OR exp Anti-Bacterial Agents OR erythromycin.mp OR ERYTHROMYCIN OR augmentin. mp OR exp Amoxicillin-Potassium Clavulanate Combination OR cephalosporin.mp OR exp CEPHALOSPORINS/] and wound infection.mp OR exp Wound Infection OR exp Postoperative Complications OR exp Bacterial Infections OR exp Surgical Wound Infection/or infection rate.mp] LIMIT to human and English language. Cochrane Edition 1 2005: “human bites”.

Search outcome

Medline and Embase: the search produced 89 papers, two of which were relevant to the original question. Cochrane: 32 citations. One review on mammalian bites. No new relevant papers on human bites found.

Comment(s)

The first study showed a clear benefit of giving prophylactic antibiotics for human bites to the hand. The second study did not demonstrate any significant reduction of infection rate with antibiotics for low risk superficial human bites, which were defined as those bites that penetrated only the epidermis and did not involve the hands, feet, or skin overlying joints or cartilaginous structures. It may be that antibiotic treatment of the low risk bites described is unnecessary. Until further studies show no reduction in infection rates for human bites, antibiotics should be given to all patients except those presenting with superficial bites outwith the areas described above. No prospective randomised controlled trials have investigated which particular antibiotics should be prescribed, and therefore antibiotic choice should follow local guidelines until studies have shown a particular antibiotic to be the most effective.

► CLINICAL BOTTOM LINE

Prophylactic antibiotics should be given to all patients with human bites to the hands, feet, and skin overlying joints or cartilaginous structures, and to all patients with bites that penetrate deeper than the epidermal layer.

Zubowicz VN, Gravier M. Management of early human bites of the hand: a prospective randomized study. *Plast Reconstr Surg* 1991;**88**:111–14.
Broder J, Jerrard D, Olshaker J, *et al*. Low risk infection in selected human bites treated without antibiotics. *Am J Emerg Med* 2004;**22**:10–13.

Nebulised furosemide in acute adult asthma

Report by **Zui-Shen Yen, Emergency Physician**
Checked by **Shyr-Chyr Chen, Emergency Physician**
doi: 10.1136/emj.2005.028670

Abstract

A short cut review was carried out to establish whether the addition of nebulised furosemide to beta-agonist therapy improves outcomes in acute asthma. Altogether 87 papers

Table 4

Author, date, and country	Patient group	Study type (level of evidence)	Outcomes	Key results	Study weaknesses
Nannini LJ <i>et al</i> 1992 Canada	20 patients with acute asthma randomised to inhaled salbutamol/furosemide (age 31 (SD 11)) or inhaled salbutamol/normal saline (age 41 (SD 12))	PRCT	PEFR (percentage increase)	Salbutamol/furosemide 83 (SD 61) % v salbutamol/normal saline 35 (SD 24) % at 30 minutes, $p < 0.05$	Small sample Unclear randomisation and blinding procedure Unknown exclusion and inclusion criteria Poor comparability of baseline data between two groups Small sample
Karpel JP <i>et al</i> , 1994, USA	24 patients (age 18–45) with acute asthma randomised to nebulised furosemide or nebulised metaproterenol or nebulised metaproterenol/furosemide	PRCT	FEV1	No statistical difference between the metaproterenol group and the metaproterenol/furosemide group	Small sample Unclear randomisation and blinding procedure Post hoc analysis of patients with short duration of exacerbations
Pendino JC <i>et al</i> , 1998, Canada	42 patients (age 18–45) with acute asthma randomised to nebulised salbutamol/furosemide or salbutamol/normal saline	PRCT	PEFR (percentage increase) in all patients PEFR (percentage increase) in patients with short duration of exacerbations (<8 hours)	No significant difference in PEFR between both groups at 15 minutes and 30 minutes. Salbutamol/furosemide 82 (SD 48) % and 113 (SD 49) % v salbutamol/normal saline 35 (SD 40) % and 61 (SD 35) %, at 15 minutes ($p = 0.03$) and 30 minutes ($p = 0.014$) respectively	Small sample Unclear randomisation and blinding procedure Post hoc analysis of patients with short duration of exacerbations

were found using the reported search, of which two presented the best evidence to answer the clinical question. A further relevant paper was found on scanning the references of these papers. The author, date and country of origin, patient group studied, study type, relevant outcome, results, and study weaknesses of the best papers are tabulated. There is currently insufficient evidence to support the routine addition of nebulised furosemide to standard beta agonist therapy in acute asthma in adults

Three part question

In [an adult with asthma] is [nebulised beta agonist with nebulised furosemide better than nebulised beta agonist alone] at [improving airflow and reducing morbidity]?

Clinical scenario

A known asthmatic adult patient is brought into the emergency department with signs consistent with acute asthma. Little improvement is noted with nebulised beta agonist therapy. You wonder if adjunctive nebulised furosemide would provide any benefit.

Search strategy

Medline 1966–12/04 and Embase: Drugs & Pharmacology 1980–01/03 using the OVID interface, The Cochrane Library, Issue 2, 2005. Medline: [(exp furosemide OR furosemide\$.mp OR lasix\$.mp) AND (nebuli\$.mp OR vapor\$.mp OR inhal\$.mp OR aerosoli\$.mp) AND (exp asthma OR exp asthma, exercise-induced OR asthma\$.mp OR exp bronchial spasm OR bronchial spasm\$.mp OR bronchospasm\$.mp)] LIMIT to human AND English language. Embase: [(exp furosemide OR furosemide\$.mp OR lasix\$.mp) AND (nebuli\$.mp OR vapor\$.mp OR inhal\$.mp OR aerosoli\$.mp) AND (exp asthma OR exp exercised induced asthma OR exp allergic asthma OR exp occupational asthma OR exp

bronchospasm OR bronchial spasm\$.mp OR bronchospasm\$.mp)] LIMIT to human AND English language. Cochrane Library: “furosemide”.

Search outcome

Altogether 87 papers from Medline and 156 from Embase were found of which two were considered to be original research of high quality (randomised controlled trials) and relevant to the topic of interest. A further reference was found after scanning of paper references. These three papers are summarised in table 1. Thirty four papers were found in the Cochrane Library, none of which were relevant to the three part question.

Comment(s)

A number of mechanisms have been postulated to explain the bronchodilating effect of nebulised furosemide, including: (1) induction of relaxant prostaglandins; (2) blockade of mediator production from inflammatory cells; (3) regulation of ion exchange in the airway epithelium. Of the few randomised controlled studies that relate to the efficacy of nebulised furosemide in the treatment of acute adult asthma, samples remain small and conflicting results persist. More large scale studies are needed to determine whether nebulised furosemide has any therapeutic benefit in acute adult asthma.

► CLINICAL BOTTOM LINE

There is currently insufficient evidence to support the routine addition of nebulised furosemide to standard beta agonist therapy in acute asthma in adults.

Nannini LJ, Pendino JC, Molfino NA, *et al*. Inhaled furosemide and salbutamol in acute asthma. *Am Rev Respir Dis* 1992;**145**:A422.

Karpel JP, Dworkin F, Hager D, *et al*. Inhaled furosemide is not effective in acute asthma. *Chest* 1994;**106**:1396–400.

Pendino JC, Nannini LJ, Chapman KR, *et al*. Effect of inhaled furosemide in acute asthma. *J Asthma* 1998;**35**:89–93.