

Papers

Systematic review of the relative efficacy of non-steroidal anti-inflammatory drugs and opioids in the treatment of acute renal colic

Anna Holdgate, Tamara Pollock

Abstract

Objective To examine the relative benefits and disadvantages of non-steroidal anti-inflammatory drugs (NSAIDs) and opioids for the management of acute renal colic.

Data sources Cochrane Renal Group's specialised register, Cochrane central register of controlled trials, Medline, Embase, and reference lists of retrieved articles.

Review methods Randomised controlled trials comparing any opioid with any NSAID in acute renal colic if they reported any of the following outcomes: patient rated pain, time to pain relief, need for rescue analgesia, rate of recurrence of pain, and adverse events.

Results 20 trials totalling 1613 participants were identified. Both NSAIDs and opioids led to clinically important reductions in patient reported pain scores. Pooled analysis of six trials showed a greater reduction in pain scores for patients treated with NSAIDs than with opioids. Patients treated with NSAIDs were significantly less likely to require rescue analgesia (relative risk 0.75, 95% confidence interval 0.61 to 0.93). Most trials showed a higher incidence of adverse events in patients treated with opioids. Compared with patients treated with opioids, those treated with NSAIDs had significantly less vomiting (0.35, 0.23 to 0.53). Pethidine was associated with a higher rate of vomiting.

Conclusions Patients receiving NSAIDs achieve greater reductions in pain scores and are less likely to require further analgesia in the short term than those receiving opioids. Opioids, particularly pethidine, are associated with a higher rate of vomiting.

Introduction

Renal colic, typically characterised by the sudden onset of severe pain radiating from the flank to the groin, is most commonly caused by the passage of calculi through the urinary tract. Renal colic has an annual incidence of around 16 per 10 000 people and a life time incidence of 2-5%.^{1 2}

The pain of renal colic is due to obstruction of urinary flow, with subsequent increasing wall tension in the urinary tract. Rising pressure in the renal pelvis stimulates the local synthesis and release of prostaglandins, and subsequent vasodilation induces a diuresis which further increases intrarenal pressure. Prostaglandins also act directly on the ureter to induce spasm of the smooth muscle.

As most renal calculi pass spontaneously, acute management should focus on rapid pain relief, confirmation of the diagnosis,

and recognition of complications requiring immediate intervention.³ Both non-steroidal anti-inflammatory drugs (NSAIDs) and opioids provide pain relief in acute renal colic.^{4 5} Opioids have the advantages of cheapness, titratability, potency, and familiarity, but there are concerns over dependency and drug seeking behaviour presenting as renal colic. Opioids do not act directly on the cause of pain and need to be given parenterally, which may limit their usefulness.⁶ NSAIDs act directly on prostaglandin release (the main cause of pain) and have been shown to be effective, particularly when given intravenously.⁷ Compared with opioids, however, they are generally not titratable, have well recognised side effects (including renal failure and gastrointestinal bleeding), and may be less immediate and potent in their action. A meta-analysis in 1994 suggested that NSAIDs were at least as effective as opioids in treating the pain of acute renal colic but this study did not specifically examine the difference in efficacy between NSAIDs and opioids.⁸

Opioids and NSAIDs are currently recommended for acute renal colic, both alone and in combination.^{9 10} The choice of agent is based on clinician's preference, personal experience, and institutional culture. Two studies examining the combined effect of opioids and NSAIDs have given conflicting results, and there is currently no evidence that NSAIDs reduce the amount of opioid required for control of pain.^{11 12}

We examined the relative benefits and disadvantages of NSAIDs and opioids, and aimed to determine which type of drug is most appropriate for the management of pain in acute renal colic.

Methods

We obtained relevant trials from the Cochrane Renal Group's specialised register of randomised controlled trials; the Cochrane central register of controlled trials 2003; Medline and PreMedline (1966 to 31 January 2003); Embase (1980 to 31 January 2003); reference lists of nephrology textbooks, review articles and relevant trials; and the abstracts of conference proceedings from nephrology meetings. Our search strategy was not limited by language, date, or publication status.¹³

Trials were included for review if they were randomised controlled trials, compared any NSAID with any opioid by any route, studied adults with a clinical diagnosis of acute renal colic, and had at least one of the predetermined outcomes of interest. We included combination therapies which contained an opioid or NSAID. NSAIDs included aspirin and cyclo-oxygenase-2 inhibitors but not paracetamol or dipyrrone. The efficacy of dipyrrone in renal colic has been reviewed previously.¹⁴

Outcomes of interest were patient rated pain on a validated pain scale, time to pain relief, need for rescue analgesia, rate of pain recurrence, and number of patients with one or more adverse events. Major adverse events were defined as gastrointestinal bleeding, renal failure, hypotension, and respiratory depression. Minor adverse events were defined as gastrointestinal disturbance without bleeding (vomiting, diarrhoea, pain), dizziness, and sleepiness.

Validity assessment and data abstraction

Study quality was assessed independently by the two reviewers without blinding to authorship or journal, using the checklist developed for the Cochrane Renal Group.¹⁵ Discrepancies were resolved by discussion. Criteria assessed were allocation concealment, intention to treat analysis, completeness to follow up, blinding of investigators, participants, and outcome assessors, and data analysis.

Identified titles and abstracts were screened independently by the two reviewers. Potentially relevant reviews were retained and the full text examined. Data extraction was carried out independently by the reviewers. When important data were not reported, we tried to contact the authors. Discrepancies between the reviewers were resolved by discussion.

Study characteristics and quantitative data synthesis

Whenever possible we classified the studies by age of participants, size and site of stones, and route and dose of drugs. Analysis was performed using meta-analytic software in Revman 4.1. The results for dichotomous outcomes (need for rescue analgesia, rate of pain recurrence, adverse event rate) are expressed as relative risks with 95% confidence intervals. We pooled data using the random effects model, but the fixed effects model was also analysed to ensure robustness. When continuous scales of measurement were used to assess the effects of treatment (patient rated pain scores, time to pain relief) we used weighted mean differences. Heterogeneity was analysed by a χ^2 test (one degree of freedom), and a P value of 0.05 or less was considered statistically significant.

We explored possible sources of heterogeneity (for example, participants, treatments, study quality). When sufficient randomised controlled trials were identified, we attempted to assess publication bias with a funnel plot.¹⁶

Results

Of 74 potentially relevant studies, we excluded 49 on review of the abstract (fig 1). Twenty five articles were retrieved for more detailed evaluation, of which five were excluded for failure to meet our inclusion criteria, leaving 20 trials for review.^{4 11 12 17-33}

Study characteristics

The 20 trials were conducted in nine countries, included 1613 participants, and were published between 1982 and 1999 (table 1). Most studies included only those participants with renal calculi confirmed on subsequent testing using a variety of techniques, specifically excluding patients without such a confirmation. Overall, the trials used five different NSAIDs and seven different opioids, although each trial used only one type of each drug. All but two trials used fixed doses of drugs, regardless of the patient's weight.^{22 32} Drugs were given by the parenteral route (intravenous or intramuscular) in all but three trials. In these three trials, NSAIDs were given orally or rectally and opioids were given parenterally.^{18 20 31}

Many of the included trials did not report variance data or outcomes in a form suitable for meta-analysis, and we were

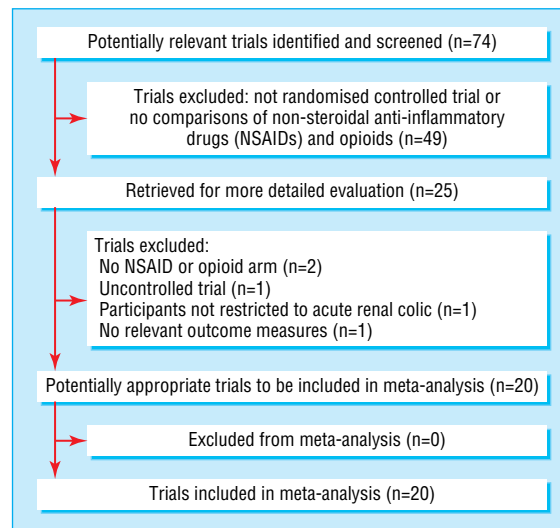


Fig 1 Flow of studies through trial

unable to gain any further information from the authors. Six studies had treatment arms in addition to NSAIDs and opioids^{12 17 20 23 25 28}; we analysed only data for the opioid and NSAID groups for these trials. Two studies used a crossover design, when the comparator drug was given if inadequate analgesia was achieved with the first drug. We included only data from the precrossover phase of these trials.^{18 21} One study included a third treatment arm with combined opioids and NSAIDs.¹¹ Data from this treatment arm were not included.

No trial reported time to pain relief, although several reported the proportion of patients with complete pain relief within a fixed time. We therefore used this proportion as an alternative outcome measure. No trials reported rates of pain recurrence or specifically reported serious adverse events such as renal dysfunction or gastrointestinal bleeding.

Overall, no single study met all the quality criteria (table 2). For most studies, quality criteria were not met owing to lack of information rather than explicit reporting of methods that did not conform to the quality criteria.

As the results from random and fixed effects models did not differ, we report only results from the random effects model.

Patient rated pain scores

Fifteen trials measured pain scores at enrolment and at a fixed time after the study drug had been given. In two trials this outcome was measured but not reported.^{19 20} Four trials reported data that were not suitable for pooled analysis.²⁹⁻³² All but one of these four trials showed a greater reduction in pain scores in the NSAID group than in the opioid group.³⁰ Nine trials reported pain on a 100 mm visual analogue scale; six recorded scores at 30 minutes,^{4 11 17 25 27 33} two at 20 minutes,^{21 22} and one at 60 minutes.²⁶ Seven of the nine trials favoured treatment with NSAIDs,^{11 17 21 25-27 33} one showed no difference,¹ and one showed lower pain scores in patients treated with opioids.²² Subgroup analysis by type of NSAID showed heterogeneity for studies using ketorolac but homogeneity among all other trials using any other type of NSAID. Combined analysis of the six trials not using ketorolac showed the visual analogue scale was on average 4.6 mm (95% confidence interval 1.7 mm to 7.5 mm) lower in patients receiving NSAIDs than in those receiving opioids (fig 2). Subgroup analysis by type and route of opioid did not explain heterogeneity. Addition of the three trials using ketorolac to the pooled analysis showed a similar effect. We could find no obvious biological or clinical explanation for this heterogeneity.

Table 1 Characteristics of included studies of efficacy of non-steroidal anti-inflammatory drugs compared with opioids for pain relief in acute renal colic

Study	Country	Group (No of participants; No of men), interventions	Outcomes	Notes
al-Sahlawi and Tawfik 1996 ¹²	Kuwait	Group 1 (50; 34), indomethacin 100 mg intravenously; group 2 (50; 37), pethidine 100 mg, lysine-acetyl salicylate 1.8 g intravenously	Complete relief at 30 minutes, rescue analgesia, adverse events	Group 3 excluded from analysis because of drug type (acetyl salicylate)
Arnau et al 1991 ¹⁷	Spain	Group 1 (116; 63), diclofenac 75 mg intramuscularly; group 2 (118; 61), pethidine 100 mg intramuscularly	Pain score*, rescue analgesia, adverse events	Two groups (n=217) not included because of drug type (dipyrone)
Cordell et al 1994 ¹⁸	United States	Group 1 (31; 18), indomethacin 100 mg rectally; group 2 (20; 18), morphine 5-10 mg intravenously	Adverse events	Crossover trial, post crossover data not included
Cordell et al 1996 ¹¹	United States	Group 1 (35; 28), meperidine 50 mg intravenously; group 2 (36; 30), ketorolac 60 mg intravenously	Pain score*, rescue analgesia, adverse events	Group 3 (n=35) receiving combined non-steroidal anti-inflammatory drug and opioid not included
Curry and Kelly 1995 ⁴	New Zealand	Group 1 (17), tenoxiam 40 mg intravenously; group 2 (24), pethidine 75 mg intravenously. Overall, 75% men	Pain score*, rescue analgesia, adverse events	
Hetherington and Philip 1986 ¹⁹	United Kingdom	Group 1 (28), pethidine 100 mg intramuscularly; group 2 (30), diclofenac 75 mg intramuscularly. Overall, 48 men	Rescue analgesia, adverse events	
Indudhara et al 1990 ²⁰	India	Group 1 (33), diclofenac 150 mg orally; group 2 (31), pethidine 50 mg intramuscularly. Overall, 73% men	Pain relief measured but not defined, adverse events	Group 3 (n=30) not included because of drug type ("baralgin")
Jonsson et al 1987 ²¹	Sweden	Group 1 (26; 24), oxyconchloride 5 mg and papaverine 50 mg intravenously; group 2 (35; 30), indomethacin 50 mg intravenously	Pain score*, adverse events	Crossover trial, data from postcrossover period not included
Larkin et al 1999 ²²	United States	Group 1 (33; 26), ketorolac 60 mg intramuscularly; group 2 (37; 27), meperidine 100-150 mg intramuscularly	Pain score*, rescue analgesia, adverse events	
Lehtonen et al 1983 ²³	Finland	Group 1 (93; 69), indomethacin 50 mg intravenously; group 2 (31; 26), pethidine 50 mg intravenously	Complete relief at 30 minutes, rescue analgesia, adverse events	Group 3 not included because of drug type (dipyrone)
Lundstam et al 1982 ²⁴	Sweden	Group 1 (34; 25), diclofenac 50 mg intramuscularly; group 2 (32; 25), "spasmofen" (combination of multiple narcotics) 1 ml intramuscularly	Adverse events	Pain relief measured but not well defined and therefore not analysed
Marthak et al 1991 ²⁵	India	Group 1 (25; 17), diclofenac 75 mg intramuscularly; group 2 (25; 20), pethidine 75 mg intramuscularly	Pain score*, complete relief at 30 minutes, adverse events	Second study comparing diclofenac with dipyrone not included
Oosterlinck et al 1990 ²⁶	United Kingdom and Belgium	Group 1 (45; 32), ketorolac 10 mg intramuscularly; group 2 (37; 29), ketorolac 90 mg intramuscularly; group 3 (39; 29), pethidine 100 mg intramuscularly	Pain score*, complete relief at 60 minutes, adverse events	Patients from group 1 not included in visual analogue scale analysis owing to inability to combine data
Persson et al 1985, ²⁷	Sweden	Group 1 (48; 35), indoprofen 400 mg intravenously; group 2 (46; 35), oxicone 10 mg and papaverine 20 mg intramuscularly	Pain score*, complete relief at 30 minutes, adverse events	
Quilez et al 1984 ²⁸	Spain	Group 1 (24; 14), diclofenac 75 mg intramuscularly; group 2 (14; 8), pentazocine 30 mg intramuscularly	Complete relief at 30 minutes, adverse events	Group 3 (n=23) not included because of drug type (hyoscine)
Sandhu et al 1994 ²⁹	United Kingdom	Group 1 (76; 59), ketorolac 30 mg intramuscularly; group 2 (78; 58), pethidine 100 mg intramuscularly	Adverse events	Data for pain scores and rescue analgesia not used in analysis due to format of information
Sommer et al 1989 ³⁰	Denmark	Group 1 (27; 17), "ketogan" 3 ml intramuscularly; group 2 (29; 22), diclofenac 75 mg intramuscularly	Complete relief at 30 minutes, adverse events	Pain scores measured but not reported
Thompson et al 1989 ³¹	United Kingdom	Group 1 (29), pethidine 100 mg "injection"; group 2 (29), diclofenac 100 mg rectally†	Complete relief at 30 minutes, rescue analgesia, adverse events	Change in pain score but not absolute scores reported
Nicolas Torralba et al 1999 ³²	Spain	Group 1 (24), ketorolac 30 mg intramuscularly; group 2 (24), tramadol 1 mg/kg subcutaneously†	Rescue analgesia, adverse events	Pain scores but no variance given
Uden et al 1983 ³³	Sweden	Group 1 (25; 20), indomethacin 50 mg intravenously; group 2 (25; 22), hydromorphone chloride atropine 2 mg subcutaneously	Pain score*, complete relief at 30 minutes, rescue analgesia, adverse events	

*Measured by visual analogue scale.

†Number of men not reported.

Table 2 Assessment of quality criteria for trial of efficacy of non-steroidal anti-inflammatory drugs and opioids for pain relief in acute renal colic

Study	Allocation concealment	Intention to treat analysis	Completeness of follow up	Investigators blinded	Participants blinded	Outcome assessors blinded
al-Sahlawi and Tawfik 1996 ¹²	Insufficient information	Insufficient information	Insufficient information	Insufficient information	Insufficient information	Yes
Arnau et al 1991 ¹⁷	Insufficient information	Insufficient information	Insufficient information	Insufficient information	Insufficient information	Yes
Cordell et al 1994 ¹⁸	Adequate	Only patients with diagnosis confirmed on subsequent investigations included in analysis	Insufficient information	Yes	Yes	Yes
Cordell et al 1996 ¹¹	Adequate	Yes; all patients with clinical diagnosis	Insufficient information	Yes	Yes	Yes
Curry and Kelly 1995 ⁴	Adequate	Only patients with diagnosis confirmed on subsequent investigations included in analysis	Reported	Yes	Yes	Yes
Hetherington and Philip 1986 ¹⁹	Insufficient information	Only patients with diagnosis confirmed on subsequent investigations included in analysis	Insufficient information	Insufficient information	Yes	Yes
Indudhara et al 1990 ²⁰	Insufficient information	Insufficient information	Insufficient information	Insufficient information	NO	Insufficient information
Jonsson et al 1987 ²¹	Adequate	Only patients with diagnosis confirmed on subsequent investigations included in analysis	Insufficient information	Yes	Yes	Yes
Larkin et al 1999 ²²	Adequate	Only patients with diagnosis confirmed on subsequent investigations included in analysis	Reported	Yes	Yes	Yes
Lehtonen et al 1983 ²³	Insufficient information	Insufficient information	Insufficient information	Insufficient information	Insufficient information	Yes
Lundstam et al 1982 ²⁴	Insufficient information	Only patients with diagnosis confirmed on subsequent investigations included in analysis	Insufficient information	Insufficient information	Insufficient information	Insufficient information
Marthak et al 1991 ²⁵	Insufficient information	Insufficient information	Insufficient information	Insufficient information	Insufficient information	Insufficient information
Oosterlinck et al 1990 ²⁶	Insufficient information	Only patients with diagnosis confirmed on subsequent investigations included in analysis	Reported	Insufficient information	Insufficient information	Yes
Persson et al 1985 ²⁶	Insufficient information	Yes; all patients with clinical diagnosis	Insufficient information	Insufficient information	Insufficient information	Insufficient information
Quilez et al 1984 ²⁸	Insufficient information	Insufficient information	Insufficient information	Insufficient information	Insufficient information	Insufficient information
Sandhu et al 1994 ²⁹	Insufficient information	Yes; all patients with clinical diagnosis	Insufficient information	Insufficient information	Yes	Insufficient information
Sommer et al 1989 ³⁰	Insufficient information	Only patients with diagnosis confirmed on subsequent investigations included in analysis	Reported	Insufficient information	Yes	Insufficient information
Thompson et al 1989 ³¹	Insufficient information	Only patients with diagnosis confirmed on subsequent investigations included in analysis	Insufficient information	Insufficient information	No	Insufficient information
Nicolas Torralba et al 1999 ³²	Insufficient information	Insufficient information	Insufficient information	Insufficient information	Insufficient information	Insufficient information
Uden et al 1983 ³³	Insufficient information	Insufficient information	Insufficient information	Insufficient information	No	Yes

Of the 13 trials with reported results, 10 found lower pain scores in patients treated with NSAIDs, two showed no difference, and only one found lower pain scores in patients treated with opioids.

Failure to achieve complete pain relief

Nine trials (647 participants) reported the proportion of patients who failed to achieve complete pain relief at 30 or 60 minutes after receiving the study drug.^{12 23 25-31 33} No study found a significant difference in the proportion of patients with complete pain relief, and there was no significant heterogeneity between studies. Combined analysis of these studies showed a trend towards a higher rate of complete pain relief in patients treated with NSAIDs, but this finding was not significant (relative risk

0.87, 0.74 to 1.03; fig 3). Subgroup analysis by NSAID or opioid type did not show significant benefit for any one drug.

Need for rescue analgesia

Ten trials (854 participants) reported the need for rescue analgesia within four hours of giving the study drug.^{4 11 12 17 19 22 23 31-33} The decision to use rescue analgesia was generally determined by clinician's preference in all trials, and the decision to give further analgesia had no objective criteria in eight of the studies. In four trials, pethidine was given if further analgesia was needed 30 minutes after the study drug had been given.^{4 11 12 17} In the remaining trials the drug used for rescue analgesia was either not specified, was a second dose of the study drug, or was the alternate study drug. The pooled analysis showed no statistical

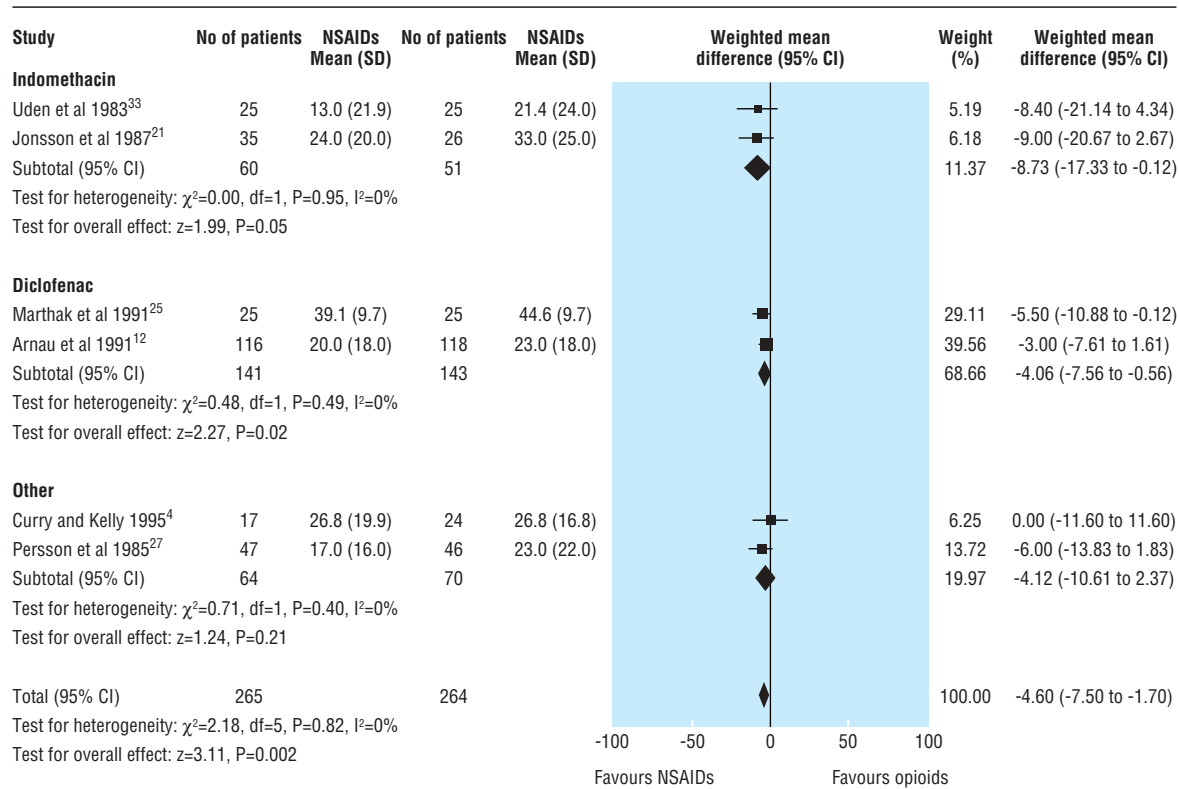


Fig 2 Patient rated scores on visual analogue scale for pain due to renal colic according to type of non-steroidal anti-inflammatory drug, excluding trials using ketorolac

heterogeneity, and patients receiving NSAIDs were significantly less likely to require rescue analgesia than those receiving narcotics (0.75, 0.61 to 0.93; fig 4). Subgroup analysis of only those trials with blinding of investigators and participants continued to show in favour of NSAIDs. All but one of the pooled trials used pethidine as the opiate (dose range 50-150 mg).³³ Based on this analysis, approximately 16 patients would require treatment with a NSAID rather than with an opioid for one additional patient to avoid the need for rescue analgesia.

Adverse events

The definition of adverse effects varied between trials, and many trials included any complaint recorded on general questioning after the study drug had been given. No trial specifically defined or reported serious adverse events such as gastrointestinal

bleeding or renal impairment. Most trials had a short period of follow up (maximum 24 hours).²⁹ All studies included reporting of adverse events, and all but four trials^{11 17 28 31} reported the total number of patients mentioning any adverse event, rather than total number of adverse events. Most of these 16 trials showed a higher incidence of adverse events in patients who were treated with opioids, but there was significant heterogeneity between studies. Subgroup analysis by type of opioid, route of opioid administration, and type of NSAID did not explain this heterogeneity. This heterogeneity may be explained by the ad hoc nature of reporting adverse events in most trials.

Vomiting was reported as a specific adverse event in 10 trials (826 participants), with no evidence of heterogeneity. The pooled analysis showed significantly less vomiting in patients

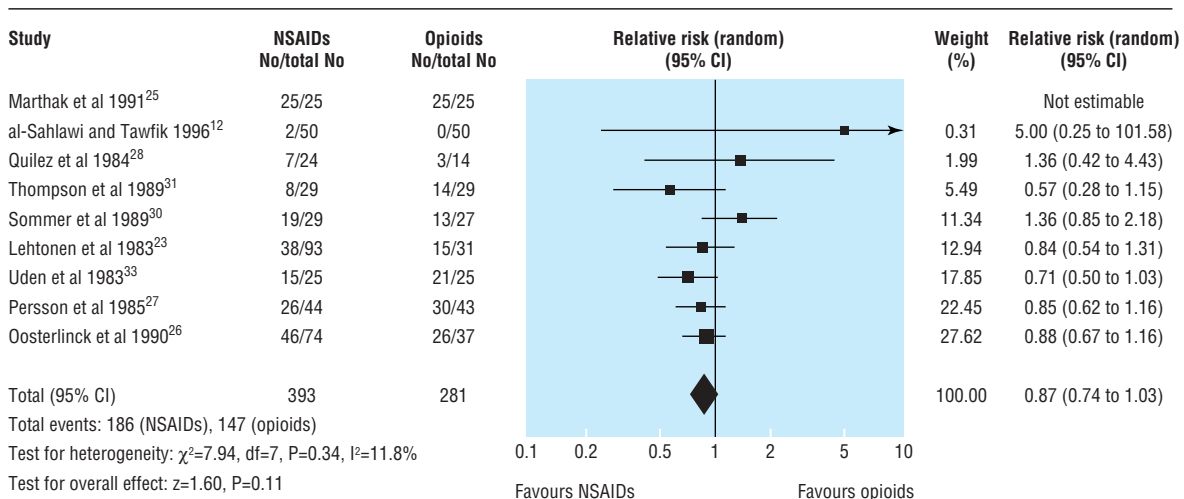


Fig 3 Number of patients failing to achieve complete pain relief from renal colic after receiving anti-inflammatory drugs (NSAIDs) or opioids

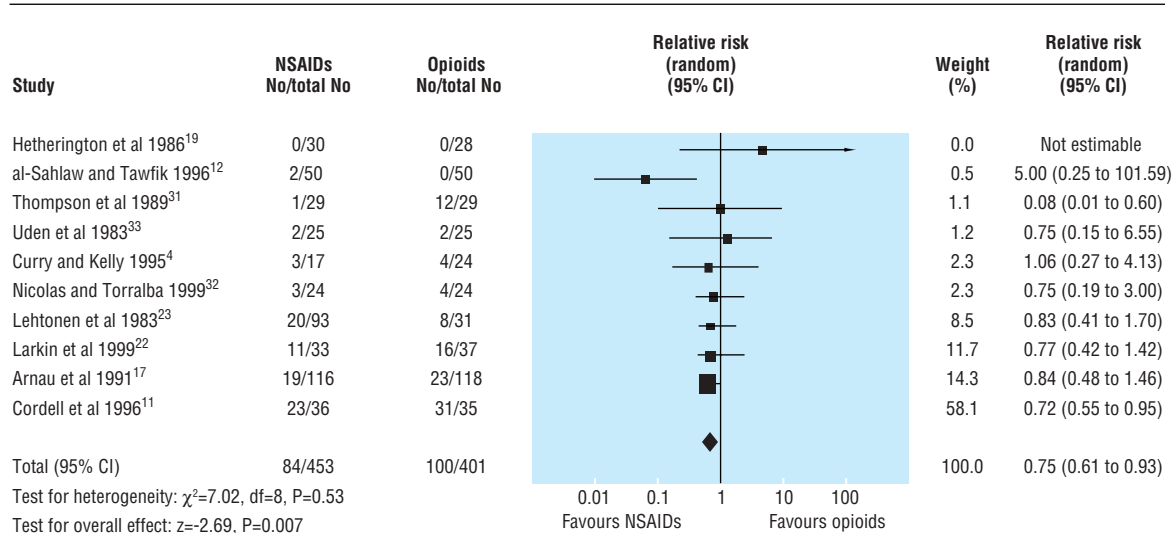


Fig 4 Number of patients requiring rescue analgesia after treatment with non-steroidal anti-inflammatory drugs (NSAIDs) or opioids for acute renal colic

treated with NSAIDs than in those treated with opioids (0.35, 0.23 to 0.53; fig 5); overall rate 5.8% in patients treated with NSAIDs and 19.5% in patients receiving opioids. Thus for every seven patients treated with NSAIDs rather than with opioids, one less patient will experience vomiting. Subgroup analysis by type of narcotic showed that the risk of vomiting was particularly dominant in patients receiving pethidine (0.30, 0.18 to 0.49). Adverse event rates did not vary according to dosage of opioid.

Other subgroup analysis and publication bias

Data were insufficient for subgroup analysis by participants' age and sex, size and site of stone, or drug dose for all outcomes. As all opioids and all but three NSAIDs were given parenterally it was not possible to analyse the effect of different routes of administration other than intravenous and intramuscular. Insufficient trials were available to perform funnel plot analysis.

Discussion

Our systematic review shows that non-steroidal anti-inflammatory drugs (NSAIDs) have better efficacy than opioids for relieving the pain of acute renal colic. Results favoured NSAIDs for the three outcomes of pain scores at a specified time

after the study drug had been given, proportion of patients who achieved complete pain relief within a fixed time, and the need for rescue analgesia, although the differences reached significance for only two of the three outcomes.

Both opioids and NSAIDs showed a clinically important analgesic effect in patients with acute renal colic, with a noticeable reduction in pain scores over time. Significant heterogeneity between studies did not allow pooled analysis of pain scores for all studies, but qualitatively most studies showed lower pain scores for patients receiving NSAIDs rather than opioids, although the differences were small. In the subgroup of patients receiving NSAIDs other than ketorolac, there was a statistically significant reduction in pain scores of 4.6 mm. This difference is unlikely to be clinically important, however, as previous studies have shown the minimum clinically important difference in visual analogue scales to be around 9-13 mm.^{34 35}

No significant difference was found between NSAIDs and opioids in the proportion of patients who achieved complete pain relief in the short term. Our findings are consistent with the review by Labrecque et al, which also found a non-significant increase in the proportion of patients achieving complete pain relief when treated with NSAIDs rather than with other analge-

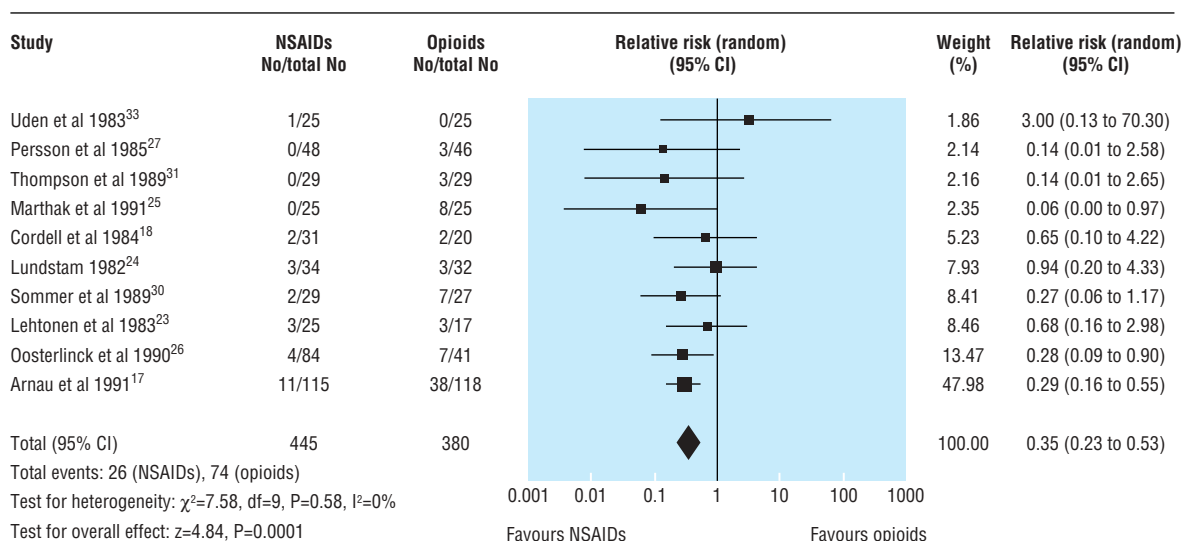


Fig 5 Incidence of vomiting as adverse event in patients receiving non-steroidal anti-inflammatory drugs (NSAIDs) or opioids for acute renal colic

sics.⁸ In our review the results varied widely between studies, with some showing almost all patients and others showing less than half of the patients achieving complete pain relief. This may reflect the wide range of agents, doses, and routes of administration for the study drugs.

Although both NSAIDs and opioids led to clinically important analgesia, a greater number of patients who received opioids required rescue analgesia within an hour of receiving the study drug. As nine of 10 trials pooled for this analysis used pethidine, this finding may not be generalisable to all opioids. The lack of clear objective guidelines for giving a rescue drug may also limit interpretation of this finding.

Adverse events were generally more common in patients receiving opioids than NSAIDs, but the ad hoc nature of reporting these events makes interpretation of this finding difficult. The specific adverse event of vomiting showed a clear association with opioids, particularly pethidine. Although no studies reported serious adverse events, the short follow up period and failure to specifically record renal dysfunction and gastrointestinal bleeding necessitates cautious interpretation of these results.

The comparative efficacy NSAIDs and opioids has been examined in several clinical settings. Several studies have shown that NSAIDs and opioids provide at least equivalent levels of postoperative analgesia, with higher rates of nausea, vomiting, and dizziness in patients treated with opioids.^{36–40} Similar results have been found in patients with acute biliary colic and isolated limb injuries and after lithotripsy.^{41–44} Our findings that NSAIDs provided slightly better analgesia with fewer side effects than opioids are in keeping with these studies, although the finding of improved analgesia in patients with renal colic may relate to the local synthesis and release of prostaglandins specific to this condition.

Limitations

We aimed to assess the effect of treatment in patients with a clinical diagnosis of renal colic because in practice most patients will be treated initially on the basis of a presumptive diagnosis. The applicability of our findings may be limited because most of the studies reviewed only included patients who had renal calculi confirmed on subsequent testing.

Pain scores were reported in all studies as means with variance, although it is well recognised that data from visual analogue scales are often skewed and therefore may be more accurately analysed as medians. We were unable to access individual patient data to assess whether comparison of medians rather than means may have altered our findings. In general, however, analysis of means rather than medians is unlikely to introduce bias unless the distribution of scores is severely skewed.⁴⁵

All the included trials used fixed doses of opioids, rather than titration of opioids to an appropriate level of pain relief. The standard practice in most emergency departments is to titrate opioids to effect rather than to give single large boluses, and this limits the applicability of our findings to everyday practice.⁹ The wide variety of drug types and doses used in the studies make it difficult to identify appropriate dosing regimens for clinical practice.

Conclusion

Single bolus doses of NSAIDs and opioids provide pain relief for patients with acute renal colic. Patients receiving NSAIDs, however, achieve greater reduction in pain scores and are less likely to require further analgesia in the short term. Opioids, particularly pethidine, are associated with a higher rate of vomiting than NSAIDs. We therefore recommend a NSAID rather than an opioid. If opioids are to be used either because of contraindications

What is already known on this topic

Both non-steroidal anti-inflammatory drugs (NSAIDs) and opioids provide analgesia in acute renal colic

NSAIDs have well recognised side effects

What this study adds

NSAIDs achieve slightly greater reductions in pain scores than opioids in patients with renal colic

Patients with renal colic are less likely to need rescue analgesia if treated with NSAIDs

Opioids, particularly pethidine, are associated with a higher rate of vomiting and other adverse effects

to NSAIDs or ease of titratability, we recommend that pethidine be avoided.

This review was conducted with substantial support and advice from the Cochrane Renal Group, Sydney, Australia.

Contributors: AH and TP were involved in all stages of study design, data collection, data analysis, and manuscript preparation. AH will act as guarantor for the paper.

Competing interests: None declared.

Ethical approval: Not required.

- 1 Stewart C. Nephrolithiasis. *Emerg Med Clin North Am* 1988;6:617-30.
- 2 Drach GW. Urinary lithiasis: etiology, diagnosis, and medical management. In: Walsh PC, Refik AB, Stamey TA, Vaughan ED, eds. *Campbell's urology*. 6th ed. Philadelphia, WB Saunders, 1992:2085-156.
- 3 Holdgate A, Hardcastle J. Renal colic: a diagnostic and therapeutic review. *Emerg Med* 1999;11:9-16.
- 4 Curry C, Kelly AM. Intravenous tenoxicam for the treatment of renal colic. *NZ Med J* 1995;108:229-30.
- 5 Smailly AJ. Analgesia in renal colic. *Ann Emerg Med* 1997;29:296.
- 6 Reich JD, Hanno PM. Factitious renal colic. *Urology* 1997;50:858-62.
- 7 Tramer MR, Williams JE, Carroll D, Wiffen PG, Moore RA, McQuay HJ. Comparing analgesic efficacy of non-steroidal anti-inflammatory drugs given by different routes in acute and chronic pain: a qualitative systematic review. *Acta Anaesthesiol Scand* 1998;42:71-9.
- 8 Labrecque M, Dostaler L-P, Rouselle R, Nguyen T, Poirier S. Efficacy of non-steroidal anti-inflammatory drugs in the treatment of acute renal colic. *Arch Intern Med* 1994;154:1381-7.
- 9 Nicholson F. Renal colic. In: Cameron P, Jelinek G, Kelly AM, Murray L, Heyworth L, eds. *Textbook of adult emergency medicine*. Edinburgh: Churchill Livingstone, 2000:372-4.
- 10 Moll J, Peacock WF. Urologic stone disease. In: Tintinalli JE, Kelen GD, Stapczynski JS, eds. *Emergency medicine: a comprehensive study guide*. 5th ed. New York: McGraw-Hill, 1999:640-5.
- 11 Cordell WH, Wright SW, Wolfson AB, Timerding BL, Maneatis TJ, Lewis RH, et al. Comparison of intravenous ketorolac, meperidine, and both (balanced analgesia) for renal colic. *Ann Emerg Med* 1996;28:151-8.
- 12 al-Sahlawi KS, Tawfik OM. Comparative study of the efficacy of lysine acetylsalicylate, indomethacin and pethidine in acute renal colic. *Eur J Emerg Med* 1996;3:183-6.
- 13 Holdgate A, Pollock T. Nonsteroidal anti-inflammatory drugs versus opioids for acute renal colic. *Cochrane Database Syst Rev* 2004;(1):CD004137.
- 14 Edwards JE, Meseguer F, Faura C, Moore RA, McQuay HJ. Single dose dipyron for acute renal colic. *Cochrane Database Syst Rev* 2003;(4):CD003867.
- 15 Willis NS, Mitchell R, Craig JC. Renal Group. In: *Cochrane library*, Issue 4. Chichester: Wiley, 2003.
- 16 Egger M, Davey-Smith G, Schneider M, Minder C. Bias in meta-analysis detected by a simple graphical test. *BMJ* 1997;315:629-34.
- 17 Arnau JM, Cami J, Garcia-Alonso F, Laporte JR, Palop R. Comparative study of the efficacy of dipyron, diclofenac sodium and pethidine in acute renal colic. *Eur J Clin Pharmacol* 1991;40:543-6.
- 18 Cordell WH, Larson TA, Lingeman JE, Nelson DR, Woods JR, Burns LB, et al. Indomethacin suppositories versus intravenously titrated morphine for the treatment of ureteral colic. *Ann Emerg Med* 1994;23:262-9.
- 19 Hetherington JW, Philip NH. Diclofenac sodium versus pethidine in acute renal colic. *BMJ* 1986;292:237-8.
- 20 Indudhara R, Vaidyanathan S, Sankaranarayanan A. Oral diclofenac sodium in the treatment of acute renal colic. A prospective randomized study. *Clin Trials J* 1990;27:295-300.
- 21 Jonsson PE, Olsson AM, Petersson BA, Johansson K. Intravenous indomethacin and oxycodone-papaverine in the treatment of acute renal colic. A double-blind study. *BJU Int* 1987;59:396-400.
- 22 Larkin GL, Peacock WF, Pearl SM, Blair GA, D'Amico F. Efficacy of ketorolac tromethamine versus meperidine in the ED treatment of acute renal colic. *Am J Emerg Med* 1999;17:6-10.

- 23 Lehtonen T, Kellokumpu I, Permi J, Sarsila O. Intravenous indomethacin in the treatment of ureteric colic. A clinical multicentre study with pethidine and metamizol as the control preparations. *Ann Clin Res* 1983;15:197-9.
- 24 Lundstam SOA, Leissner K-H, Wahlander LA, Kral JG. Prostaglandin-synthetase inhibition with diclofenac sodium in treatment of renal colic: comparison with use of a narcotic analgesic. *Lancet* 1982;i:1096-7.
- 25 Marthak KV, Gokarn AM, Rao AV, Sane SP, Mahanata RK, Sheth RD, et al. A multi-centre comparative study of diclofenac sodium and a dipyrrone/spasmolytic combination, and a single-centre comparative study of diclofenac sodium and pethidine in renal colic patients in India. *Curr Med Res Opin* 1991;12:366-73.
- 26 Oosterlinck W, Philip NH, Charig C, Gillies G, Hetherington JW, Lloyd J. A double-blind single dose comparison of intramuscular ketorolac tromethamine and pethidine in the treatment of renal colic. *J Clin Pharm* 1990;30:336-41.
- 27 Persson NH, Bergqvist D, Melander A, Zederfelt B. Comparison of a narcotic (oxicone) and a non-narcotic anti-inflammatory analgesic (indoprofen) in the treatment of renal colic. *Acta Chir Scand* 1985;151:105-8.
- 28 Quilez C, Perez-Mateo M, Hernandez P, Rubio I. Usefulness of a non-steroid anti-inflammatory, sodium diclofenac, in the treatment of renal colic. Comparative study with a spasmolytic and an opiate analgesic. *Med Clin (Barc)* 1984;82:754-5. [In Spanish.]
- 29 Sandhu DP, Lacovou JW, Fletcher MS, Kaisary AV, Philip NH, Arkell DG. A comparison of intramuscular ketorolac and pethidine in the alleviation of renal colic. *BJU Int* 1994;74:690-3.
- 30 Sommer P, Kromann-Andersen B, Lendorf A, Lyngdorf P, Moller P. Analgesic effect and tolerance of Voltaren and Ketogan in acute renal or ureteric colic. *BJU Int* 1989;63:4-6.
- 31 Thompson JF, Pike JM, Chumas PD, Rundle JS. Rectal diclofenac compared with pethidine injection in acute renal colic. *BMJ* 1989;299:1140-1.
- 32 Nicolas Torralba JA, Rigabert Montiel M, Banon Perez V, Valdelvira Nadal P, Perez Albacete M. Ketorolaco intramuscular frente a Tramadol subcutaneo en el tratamiento inicial de urgencia del colico renal. *Arch Esp Urol* 1999;52:435-7.
- 33 Uden P, Rentzhog L, Berger T. A comparative study of the analgesic effects of indomethacin and hydromorphone-chloride-atropine in acute, ureteral-stone pain. *Acta Chir Scand* 1983;149:497-9.
- 34 Todd KH, Funk KG, Funk JP. Clinical significance of reported changes in pain severity. *Ann Emerg Med* 1996;27:485-9.
- 35 Gallagher EJ, Liebman M, Bijur PE. Prospective validation of clinically important changes in pain severity measured on a visual analog scale. *Ann Emerg Med* 2001;38:633-8.
- 36 Smith LA, Carroll D, Edwards JE, Moore RA, McQuay HJ. Single-dose ketorolac and pethidine in acute postoperative pain: systematic review with meta-analysis. *Br J Anaesth* 2000;84:48-58.
- 37 McEvoy A, Livingstone JI, Cahill CJ. Comparison of diclofenac sodium and morphine sulphate for postoperative analgesia after day case inguinal hernia surgery. *Ann R Coll Surg Engl* 1996;78:363-6.
- 38 Zackova M, Taddei S, Calo P, Bellochchio A, Zanella M. Ketorolac vs tramadol in the treatment of postoperative pain during maxillofacial surgery. *Minerva Anesthesiol* 2001;67:641-6.
- 39 DeAndrade JR, Maslanka M, Reines HD, Howe, D, Rasmussen GL, Cardea J, et al. Ketorolac versus meperidine for pain relief after orthopaedic surgery. *Clin Orthop* 1996;1:302-12.
- 40 Shende D, Das K. Comparative effects of intravenous ketorolac and pethidine on peri-operative analgesia and postoperative nausea and vomiting (PONV) for paediatric strabismus surgery. *Acta Anaesthesiol Scand* 1999;43:265-9.
- 41 Dula DJ, Anderson R, Wood GC. A prospective study comparing i.m. ketorolac with i.m. meperidine in the treatment of acute biliary colic. *J Emerg Med* 2001;20:121-4.
- 42 Henderson SO, Swadron S, Newton E. Comparison of intravenous ketorolac and meperidine in the treatment of biliary colic. *J Emerg Med* 2002;23:237-41.
- 43 Rainer TH, Jacobs P, Ng YC, Cheung NK, Tam M, Lam PK, et al. Cost effectiveness analysis of intravenous ketorolac and morphine for treating pain after limb injury: double blind randomised controlled trial. *BMJ* 2000;321:1247-51.
- 44 Chia YY, Liu K. Prospective randomized trial of intravenous tenoxicam versus fentanyl and tramadol for analgesia in outpatient extracorporeal lithotripsy. *Acta Anaesthesiol Sin* 1998;36:17-22.
- 45 Streiner DL, Norman GR. *Health measurement scales—a practical guide to their development and use*, 2nd ed. Oxford: Oxford University Press, 1995.

(Accepted 1 April 2004)

doi 10.1136/bmj.38119.581991.55

Department of Emergency Medicine, St George Hospital, Gray St, Kogarah, NSW 2217, Australia

Anna Holdgate *deputy director*

Tamara Pollock *registrar*

Correspondence to: A Holdgate holdgatean@sesahs.nsw.gov.au