

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

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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

The pain of renal colic is due to obstruction of urinary flow by renal calculi, 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.¹ Both non-steroidal anti-inflammatory drugs (NSAIDs) and opioids provide pain relief in acute renal colic.²⁻³ Opioids have the advantages of cheapness, titratability, potency, and familiarity, but they do not act directly on the cause of pain and need to be given parenterally, which may limit their usefulness.⁴ NSAIDs act directly on prostaglandin release and have been shown to be effective, particularly when given intravenously.⁵ Compared with opioids, however, they are generally not titratable, have well recognised side effects, and may be less immediate and potent in their action.

Opioids and NSAIDs are currently recommended for acute renal colic, both alone and in combination.⁶⁻⁷ 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.⁸⁻⁹

We examined the relative benefits and disadvantages of NSAIDs and opioids. We also aimed to determine which of these drug types is most appropriate for managing pain in acute renal colic.

Methods

We obtained relevant trials from the Cochrane Renal Group's register; the Cochrane central register 2003; Medline and PreMedline; Embase; reference lists of nephrology textbooks, review articles and relevant trials; and the abstracts of conference proceedings. Trials were included for review if they were randomised controlled trials, compared any NSAID with any opioid given 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.

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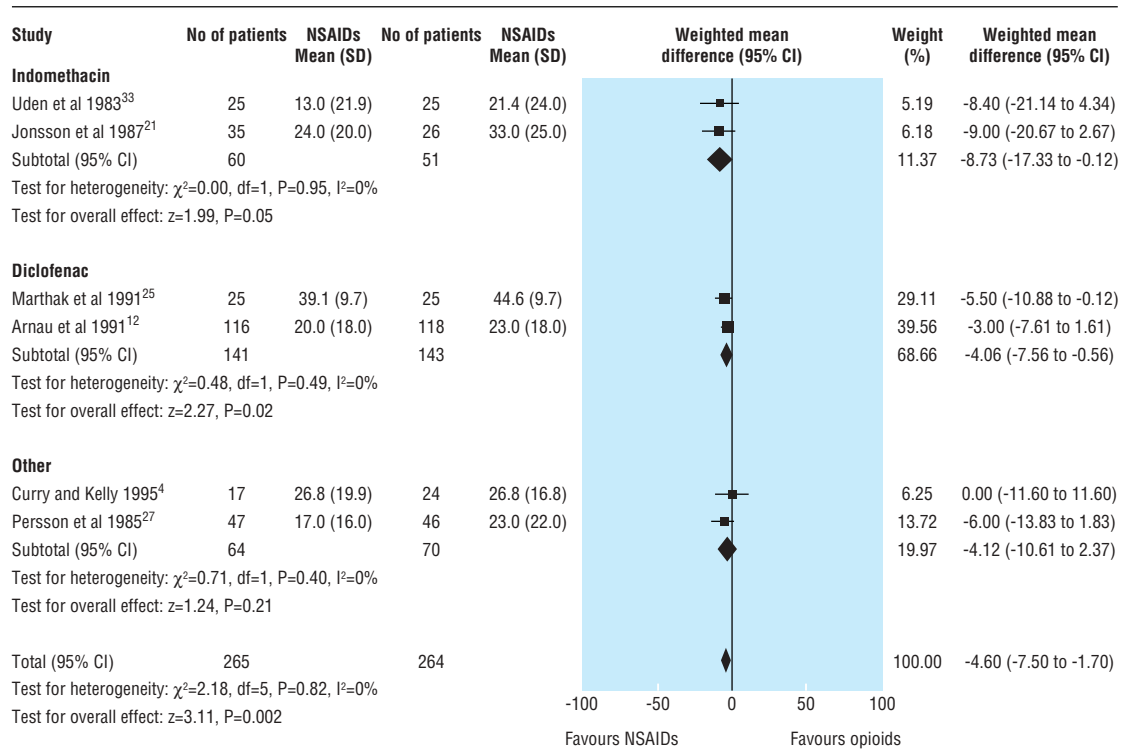


Fig 1 Patient rated scores on visual analogue scale for pain due to renal colic according to type of non-steroidal anti-inflammatory drug, excluding trials using ketorolac

Outcomes of interest were pain rated by patients on a validated pain scale, time to pain relief, need for rescue analgesia, rate of recurrence of pain, and number of patients with one or more adverse events. Major adverse events were defined as gastrointestinal bleeding, renal failure, hypotension, and respiratory depression.

Study quality was assessed independently by the two reviewers without blinding to authorship or journal, using the checklist developed for the Cochrane Renal Group (see bmj.com for criteria).¹⁰

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 also analysed the fixed effects model to ensure robustness. When continuous scales of measurement were used to assess the effects of treatment we used weighted mean differences.

Results

We identified 74 potentially relevant studies, of which 20 (1613 participants) were suitable for review (see bmj.com).^{2 8 9 11-27} Most studies included only those participants with renal calculi confirmed on subsequent testing using a variety of techniques. 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.^{16 26} Drugs were given by the parenteral route in all but three trials.^{12 14 25}

Many of the trials did not report variance data or outcomes in a form suitable for meta-analysis. Six studies had treatment arms in addition to NSAIDs and opioids^{9 11 14 17 19 22}; we analysed only data for the opioid

and NSAID groups for these trials. Two studies used a crossover design; we included only data from the precrossover phase of these trials.^{12 15}

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

No single study met all the quality criteria. Most studies did not meet quality criteria because of a lack of information rather than explicit reporting of methods that did not conform to the quality criteria.

Patient rated pain scores and failure to achieve complete pain relief

Fifteen trials measured pain scores at enrolment and at a fixed time after the study drug had been given. Four trials reported data that were not suitable for pooled analysis.²³⁻²⁶ All but one of these four trials showed a greater reduction in pain scores in the NSAID group than in the opioid group.²⁴ Nine trials reported pain on a 100 mm visual analogue scale; seven of these trials favoured treatment with NSAIDs, one showed no difference, and one showed lower pain scores in patients treated with opioids. 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 1). Of the 13 trials with reported results, 10 found lower pain scores in patients treated with

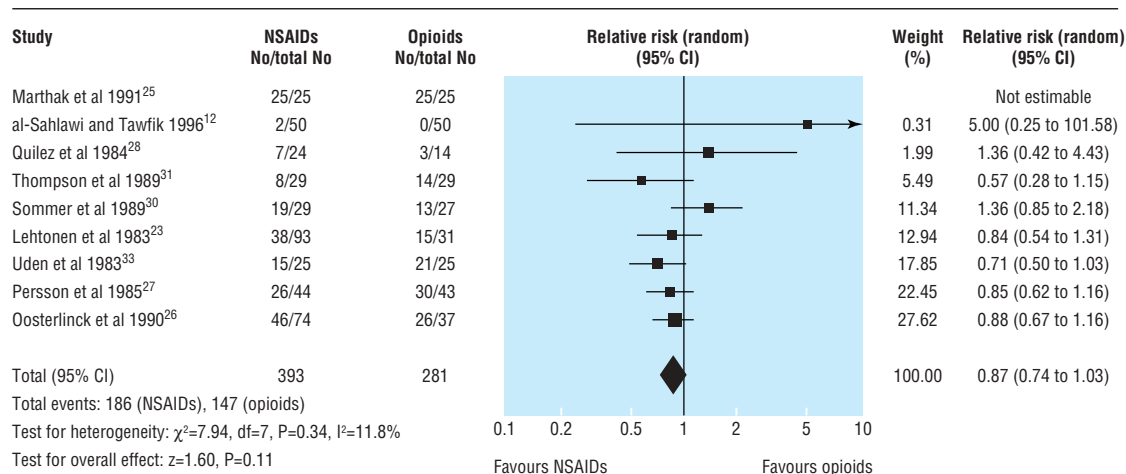


Fig 2 Number of patients failing to achieve complete pain relief from renal colic after receiving anti-inflammatory drugs (NSAIDs) or opioids

NSAIDs, two showed no difference, and only one found lower pain scores in patients treated with opioids.

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.^{9 17 19–25 27} No study found a significant difference in the proportion of patients with complete pain relief. Combined analysis of these studies showed a trend towards a higher rate of complete pain relief in patients treated with NSAIDs (fig 2).

Need for rescue analgesia

Ten trials (854 participants) reported the need for rescue analgesia within four hours of giving the study drug.^{2 8 9 11 13 16 17 25–27} In four trials, pethidine was given if further analgesia was needed 30 minutes after the study drug had been given.^{2 8 9 11} In the remaining trials the drug used for rescue analgesia was not specified, was a second dose of the study drug, or was the alternate study drug. Patients receiving NSAIDs were significantly less likely to require rescue analgesia than those receiving narcotics (relative risk 0.75, 0.61 to 0.93). All but one of the pooled trials used pethidine as the opiate.²⁷ On the basis of 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

No trial specifically defined or reported serious adverse events. Most trials had a short period of follow up (maximum 24 hours).²³ All but four trials reported the total number of patients mentioning any adverse event, rather than total number of adverse events.^{8 11 22 25} Most of these 16 trials showed a higher incidence of adverse events in patients treated with opioids, but there was significant heterogeneity between studies.

Vomiting was reported as a specific adverse event in 10 trials (826 participants). The pooled analysis showed significantly less vomiting in patients treated with NSAIDs than in those treated with opioids (0.35, 0.23 to 0.53). 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).

Discussion

Our systematic review shows that non-steroidal anti-inflammatory drugs (NSAIDs) have slightly better efficacy than opioids for relieving the pain of acute renal colic with significantly fewer adverse events. Results favoured NSAIDs for the three outcomes of pain scores at a specified time after the study drug had been given, for the proportion of patients who achieved complete pain relief within a fixed time, and for the need for rescue analgesia, although this finding was significant for only two of these 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. In the subgroup of patients receiving NSAIDs other than ketorolac, there was a statistically significant reduction in pain scores of 4.6 mm, but this difference is unlikely to be clinically important.^{28 29}

NSAIDs and opioids did not differ significantly in the proportion of patients who achieved complete pain relief in the short term. 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.

Adverse events were generally higher 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

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

showed a clear association with opioids, particularly pethidine.

Several studies have shown that NSAIDs and opioids provide at least equivalent levels of post-operative analgesia, with higher rates of nausea, vomiting, and dizziness in patients treated with opioids.³⁰⁻³⁴ Our findings that NSAIDs provided slightly better analgesia with fewer side effects than opioids are in keeping with these studies.

Limitations and conclusion

The applicability of our findings may be limited because most of the studies reviewed included only 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. In general, analysis of means rather than medians is unlikely to introduce bias unless the distribution of scores is severely skewed.³⁵

All the included trials used fixed doses of opioids. The standard practice in most emergency departments is to titrate opioids to effect, and this limits the applicability of our findings to everyday practice.⁵

Opioids, particularly pethidine, are associated with a higher rate of vomiting than NSAIDs. We therefore recommend an NSAID rather than an opioid for treating patients with acute renal colic. If opioids are to be used either because of contraindications to NSAIDs or ease of titratability, pethidine should be avoided.

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