

Analgesia in Patients With Acute Abdominal Pain: To Withhold or Not to Withhold?

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SYSTEMATIC REVIEW SOURCE

This is a systematic review abstract, a regular feature of the *Annals'* Evidence-Based Emergency Medicine (EBEM) series. Each features an abstract of a systematic review from the Cochrane Database of Systematic Reviews and a commentary by an emergency physician knowledgeable in the subject area. The source for this systematic review abstract is Manterola C, Astudillo P, Losada H, et al. Analgesia in patients with acute abdominal pain (Cochrane Review). In: *Cochrane Database Syst Rev*. 2007;(3):CD005660. The *Annals'* EBEM editors assisted in the preparation of the abstract of this Cochrane systematic review, as well as the Evidence-Based Medicine Teaching Points.

OBJECTIVE

The objectives of this review were primarily to examine whether the literature supports the appropriate use of opioid analgesia in the treatment of patients with acute abdominal pain and secondarily to assess changes in patient comfort while patients await definitive diagnosis and final treatment decisions.

DATA SOURCES

The authors searched the Cochrane Central Register of Controlled Trials (CENTRAL, Issue 4, 2006), MEDLINE (1966 to 2006), and EMBASE (1980 to 2006). The searches were not limited by language or publication status.

STUDY SELECTION

Randomized controlled trials were examined that compared any opioid analgesia to no analgesia administered before any intervention, regardless of outcomes. The studies included adult patients (16 years and older) with acute abdominal pain, without any sex restrictions.

The primary outcome measure was the accuracy of management decisions. The secondary outcome measures included change in intensity of pain by visual analogue scale,

change in the patient's comfort level, rate of treatment error, and time taken for the diagnosis to be made.

DATA EXTRACTION AND ANALYSIS

Two reviewers independently selected trials from electronic search results, using a priori inclusion criteria applied to the titles and abstracts of the citations and full-text versions of any potentially relevant studies. Two reviewers extracted information based on trial design, participants, randomization, and exclusions after randomization procedures.

The reviewers were blinded to the authors' identity. Data were pooled with a random-effects model (RevMan Analysis; version 1.0.5), and heterogeneity was tested using a χ^2 test. Quantitative analyses were based on intention-to-treat results; however, in the case of significant clinical heterogeneity, no pooling was completed. Data were reported as either relative risks (RR) or weighted mean differences, as appropriate, with their respective 95% confidence intervals (CIs). The authors performed a sensitivity analysis based on the quality assessment.

MAIN RESULTS

Six studies involving 669 patients (363 opioid and 336 placebo patients) were selected for this systematic review. All 6 trials analyzed the use of opioids (morphine, tramadol, or papaveretum) compared with a placebo (normal saline solution) administered in an equivalent volume and similar manner to all study subjects. Before randomization, the opioid and placebo groups had similar pain intensities (weighted mean difference visual analogue scale = 0.13; 95% CI -0.15 to 0.42). Not surprisingly, patients after receiving analgesics were more comfortable (RR = 0.05; 95% CI 0.01 to 0.19) compared with those receiving placebo and had reduced pain (weighted mean difference visual analogue scale = -1.94; 95% CI -2.92 to -0.95).

The Table contains a summary of outcomes from each trial, reported as RR with their respective 95% CIs. Only the study by LoVecchio et al¹ found any significant change in the physical examination results between the opioid and control groups. An altered physical examination result in the opioid-treated patients

Table. Comparison of major outcomes between reviewed trials of pain control in patients with abdominal pain.

Study	(n) Intervention (Dose)	(n) Control	Changes in Physical Examination Result	Errors in Decisionmaking	Incorrect Diagnosis	Morbidity	Accurate Management Decisions
LoVecchi et al	(32) Morphine (5-10 mg)	(16) Normal saline solution	8.00 (1.16-55.07)	Not estimable	1.50 (0.17-13.30)		Not estimable
Pace et al	(35) Morphine (10 mg)	(36) Normal saline solution	0.34 (0.01-8.14)		0.51 (0.24-1.12)	5.14 (0.26-3.37)	
Thomas et al	(38) Morphine (15 mg)	(36) Normal saline solution	1.02 (0.56-1.87)		1.11 (0.59-2.06)		
Mahadeva et al	(33) Tramadol (1 mg/kg)	(33) Normal saline solution	1.27 (0.68-2.38)				
Attard et al	(50) Papaveratum (20 mg)	(50) Normal saline solution		0.33 (0.07-1.57)	0.22 (0.05-0.98)	Not estimable	0.33 (0.07-1.57)
Vermeulen et al	(175) Morphine (10 mg)	(165) Normal saline solution		1.19 (0.63-2.27)	1.19 (0.63-2.27)	Not estimable	1.19 (0.63-2.27)

All data are RRs with 95% CIs.

did not persist (RR=1.32; 95% CI 0.67 to 2.59) when the other 3 studies were meta-analyzed together with the trial by LoVecchi et al. None of trials found a significant risk in the opioid compared with control groups for any of the outcomes summarized in the Table. Meta-analysis of each outcome across the studies failed to find any increased risk in the opioid versus control group for errors in decisionmaking (RR=0.77; 95% CI 0.23 to 2.54), incorrect diagnoses (RR=0.81; 95% CI 0.48 to 1.37), morbidity (RR=5.14; 95% CI 0.26 to 103.37), or accurate management decisions (RR=0.77; 95% CI 0.23 to 2.54). Finally, opioid anesthesia did not significantly (weighted mean difference=-1.00; 95% CI -1.52 to -0.48) increase the time taken to discharge the abdominal pain patients from the hospital.

CONCLUSION

According to the evidence available, the authors conclude that the use of opioid analgesics in acute abdominal pain significantly improves patient comfort without compromising treatment decisions. Further randomized controlled trials are necessary to establish the most effective pain-relieving protocols in abdominal pain patients.

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COMMENTARY: CLINICAL IMPLICATION

Abdominal pain is the most common complaint for patients presenting to emergency departments (EDs) in the United States.² The patient with abdominal pain requires a diagnostic evaluation, including medical history, physical examination, and laboratory tests. If an abdomen condition needing surgery is

suspected, the patient will require evaluation by the appropriate surgical team. Traditional surgical practice has been to withhold analgesics from these patients before physical examination or diagnostic confirmation to prevent “masking” of signs and symptoms, which may lead to missed or delayed diagnoses. Historically, surgical textbooks, including the influential *Cope's Early Diagnosis of the Acute Abdomen*, have perpetuated this practice myth without any supporting evidence,³ which has led to the common practice in many EDs in which physicians routinely wait to administer analgesics to patients with acute abdominal pain until they have been examined by a surgeon.⁴

The studies reviewed in this Cochrane review challenge the longstanding practice of withholding analgesia in patients with acute abdominal pain. Experimental evidence suggests that, when compared with placebo, analgesia administration to patients with acute abdominal pain does not significantly increase the risk of diagnostic error or incorrect management decisions.^{1,5-9} In addition, these studies demonstrate that providing this analgesia results in significant improvements in patient comfort.^{1,5} Finally, the use of analgesics in acute abdominal pain does not appear to delay the diagnosis or lead to increased morbidity.

Despite these promising results, there are some areas of concern. First, these results were based on a small number of trials and a small total sample size, especially given the prevalence of the phenomenon being studied. Second, although there exist sufficient data to indicate that administering analgesia may be more beneficial than withholding it in patients with acute abdominal pain, insufficient data exist to conclude that diagnostic delays and errors are equivalent with the 2 approaches. Another recent meta-analysis examining the role of analgesia in evaluating patients with acute abdominal pain found that opioids might change the physical examination result but have a negligible impact on incorrect management decisions.¹⁰ Third, there is a need for further randomized controlled clinical trials to establish the most effective analgesic

regimen in patients with acute abdominal pain. Finally, future randomized controlled clinical trials will also need to include elderly patients because physical examinations in this patient group may produce more subtle examination findings.

The increased availability of imaging studies has made repeated physical examinations less important for making the final diagnosis of acute abdomen. The reported accuracy of ultrasonography in diagnosing appendicitis, the most common abdominal surgical emergency, varies between 75% and 90% in sensitivity and between 95% and 100% in specificity.¹¹ Studies evaluating the efficacy of high-resolution computed tomography show sensitivities of 90% to 100% and specificities of 83% to 97% for the diagnosis of acute appendicitis.¹² Further studies should evaluate how opioid administration may affect the request for and interpretation of imaging studies.

TAKE-HOME MESSAGE

Despite the traditional practice of withholding analgesia from patients with acute abdominal pain until a definitive diagnosis has been established, this review reveals that administering opioid analgesia to patients with abdominal pain improves patient comfort and does not increase diagnostic error. Further randomized clinical trials are needed to fully elucidate the role of opioid analgesia in the diagnosis and management of acute abdominal pain. Until further evidence is generated, emergency physicians should treat their patients humanely and administer opioid analgesia to patients with acute abdominal pain.

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EBEM TEACHING POINT

Blinding of the reviewers: Traditional narrative reviews of the medical literature are often written by experts in their fields who subjectively choose which articles are included and depend on their own experience to critically review the validity of each reference. The methods used in nonsystematic reviews result in a potentially biased answer to the clinical question. In an effort to achieve the best evidence synthesis of the medical literature, systematic reviews and meta-analysis have been developed. These secondary analyses of the medical literature are designed to reduce bias as much as possible. For example, high-quality systematic reviews use exhaustive search strategies to reduce the chance of publication bias and detailed efforts to avoid selection bias. Finally, objectively structured methodologies for determining study quality, qualitative or quantitative synthesis, and results reporting are components of high-quality systematic reviews. Even with these safeguards in place, the potential for

bias exists whenever humans are involved in the judgment process.

Blinding and independence of the reviewers are commonly used strategies of attempting to further reduce bias. Reviewer blinding of study identification can take the form of simply masking the authors' names, as was done in the present abstracted Cochrane review. More expansive reviewer blinding schemes have been developed that involve differential photocopying of each section of the article. For example, an individual reviewer will have access to the methods section but be blinded to the authors, results, and conclusions of each article. This reviewing scheme can be time consuming, especially when multiple reviewers are responsible for judging the quality and tabulating the results of a large number of primary sources. Concerns about the time and complexity required for reviewer blinding have led some to question the value of masking in secondary analyses.¹³⁻¹⁵

Studies of reviewer blinding in meta-analyses have reported mixed results. All these studies compared quality scoring of the same meta-analysis between blinded and nonblinded reviewers. Berlin¹³ found no effect of reviewer blinding. Yet Moher et al¹⁴ found a statistically higher quality score in blinded compared with nonblinded meta-analyses, whereas Jadad et al¹⁵ observed that blinding resulting in lower-quality scores than open assessments. Clearly, no consensus exists for the value of reviewer blinding in secondary analyses. Perhaps a meta-analysis of these studies of reviewer blinding is justified; of course the question would still remain whether this analysis should be masked.

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CORRECTION

In the October 2008 issue, in the letter to the editor by Luten and Broselow (“Standardization of Production Concentration in Emergency Dosing: A Response to Fineberg and Arendts,” pages 477-478), the authors’ disclosures were not included. Drs. Luten and Broselow have been involved both academically and commercially with the Broselow Tape™ and other color-coded medical products. We regret this error.