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Analgesia in undifferentiated abdominal pain: Is it safe?

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Background

Patients frequently present to emergency departments (EDs) with abdominal pain. The use of analgesia for this complaint has been debated for many years.[1–3] The fear of analgesics originated from the early edition of Cope's surgical text on the acute abdomen.[4] In the past decade there has been growing evidence demonstrating that opioid analgesia is safe and appropriate in ED patients with undifferentiated acute abdominal pain.[5–20] The literature has documented how pain is an inadequately treated symptom in the ED. This may be related, in part, to our current emergency medicine culture.[21–23] Specifically, with reference to abdominal pain, physicians appear reluctant, despite building evidence, to provide early, appropriate analgesia to their patients.[24–28]

Clinical question

When patients present to the ED with undifferentiated acute abdominal pain, can we safely treat their pain without increasing the risk of misdiagnosis?

Article chosen

Gallagher EJ, Esses D, Lee C, et al. Randomized clinical trial of morphine in acute abdominal pain. Ann Emerg Med 2006;48(2):150–60.[29]

Objective

To determine whether the administration of analgesia to patients with acute abdominal pain will reduce discomfort and improve clinically important diagnostic accuracy.

Population studied

Adults aged 21 years or older with atraumatic abdominal pain of less than 48 hours' duration judged by the emergency physician to require opioid analgesia. Those patients who had isolated flank pain, were pregnant, were allergic to the study medication (morphine), were self-medicated before arrival or enrollment, or had a systolic blood pressure of less than 100 mm Hg were excluded from the study.

Study design

Prospective, block-randomized, double-blind placebo-controlled trial.

Outcomes measured

The primary outcome of this study was the difference in clinically important diagnostic accuracy in the morphine-treated group compared with the placebo group. After review of the study data, 2 independent investigators defined this outcome as any diagnostic error between provisional and final diagnosis that could have been reasonably expected to have an adverse impact on the patient's health. This analysis resulted in 2 groups: one that included patients who were correctly diagnosed at the time of their initial evaluation and one in which a diagnostic error was determined upon the completion of full investigations. Where disagreement occurred (in 2 cases), patients were classified as "diagnostic errors."

Results

Of the 578 patients assessed for eligibility, 160 were randomly assigned to treatment with morphine (n = 80) or placebo (n = 80). A total of 153 patients were available for

analysis because one patient withdrew, one patient was lost to follow-up and data for 5 patients was incomplete.

There were no significant differences in baseline features although the distribution of final diagnoses were dissimilar between the 2 groups. Meaningful pain relief was achieved in the morphine group with a mean change in a 0 mm–100 mm visual analog pain scale of –33 mm (interquartile range [IQR] –8 to –73), while the mean change in the placebo group was –2 mm (IQR 1 to –16). The primary end point of diagnostic accuracy was not statistically different between the treatment (67 of 78 patients, 86%) or placebo (64 of 75 patients, 85%) groups. This difference was 1% (95% confidence interval [CI] –11% to 12%). The secondary outcome of the accuracy of the provisional disposition decision was also similar in the placebo (55%) and the morphine (58%) groups. There was one return visit that resulted in an admission and subsequent discharge with the same diagnosis of "nonspecific abdominal pain." Complications were similar in both groups.

Although the authors performed an efficacy analysis, a sensitivity analysis available in the online version of the article shows that an intention-to-treat analysis would not have altered their conclusions.[30]

Conclusions

The authors concluded that administration of morphine is safe and provides analgesia without impairing clinically important diagnostic accuracy.

Commentary

The treatment of patients with analgesia who suffer from undifferentiated abdominal pain is a safe practice that is supported by an existing body of research.

The authors acknowledge the limitations of their study in the online version of the article.[30] Their CI allows for as much as a 12% difference. The authors have taken great care to try to elucidate a clinically relevant outcome difference (i.e., a change in management that 2 independent reviewers believe could have reasonably impacted patient morbidity). Despite randomization, the 2 categories of nonspecific abdominal pain and biliary tract disease were unequally distributed by chance, a reflection of a relatively small sample size.

Gallagher and colleagues also cite threats to external validity,[30] including the collection of study participants by convenience sample and the lengthy study period. Providers were initially resistant to enrolling patients in the study because of the fear of providing analgesia to these patients, although this is unsupported by much of the published literature to date.[5–20] Assembly bias may have been generated by non-consecutive patient enrollment. Patients collected by convenience or because the physician suggested enrollment in a study may be a subset of the population unless all patients are contributed to the study. Spectrum bias may also be present here: patients in this study appear to have been those with maximal pain (99/100, 98/100). The authors also acknowledge that they enrolled a younger patient population (mean age 46 years) and that these patients received higher doses of analgesia than the geriatric population, affecting the generalizability of the study. A small, but not insignificant limitation of this study, may be that patients at low risk of misdiagnosis were preferentially recruited. We have no way to know the magnitude of this bias.

These limitations ought to be taken in light of the accumulation of published evidence to date. Several weeks after this study was published, Ranji and colleagues published a meta-analysis and systematic review in the *JAMA Rational Clinical Examination Series*.[5] This metaanalysis seems to support Gallagher's conclusion.[29] Ranji and colleagues sought to answer several questions, 2 of which are important in this discussion:

1. "Does the administration of opiates alter the physical examination of patients with acute abdominal pain?" Although the studies did exhibit significant heterogeneity (I^2 = 62.1%, p = 0.003), the authors found that the administration of opiates did change the findings on physical examination of these patients (combined risk ratio 1.55, 95% CI 1.02–2.36).[5] The change in physical exam relates to the disease, not the patient, and is so termed a disease-oriented outcome.
2. "Does administration of opiates result in errors in clinical management of patients with acute abdominal pain?" This is the patient-oriented outcome of interest. A potential error in clinical management was defined as one resulting in possible delays in necessary surgery or the performance of potentially unnecessary surgery. The studies that reported this outcome showed no heterogeneity (I^2 = 0.0%, p = 0.67). There was no difference in the risk of incorrect management decisions (risk difference 0.1%, 95% CI –3.6% to 3.6%).[5]

The question of greatest importance is the patient-oriented one. We, therefore, used data from the studies selected by Ranji and collagues[5] and the results of Gallagher and colleagues' study[30] to determine whether the results would alter the metaanalysis in any meaningful way with respect to errors in clinical management. We used a random effects model to generate odds ratios with RevMan software (Review Manager, Version 4.2.8, Copenhagen:

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The Nordic Cochrane Centre, 2003). The results are shown in the forest plot in Figure 1 (the size of the data markers reflects the weight of the individual study). The studies exhibit no heterogeneity (I^2 = 0%, p = 0.72) and no differences in outcome (odds ratio 1.03, 95% CI 0.67–1.59).

These papers appear to provide support for the established emergency medicine practice of offering appropriate analgesia to patients with abdominal pain during their investigation phase. Beginning with the first edition of his text, *Early Diagnosis in the Acute Abdomen*, Cope[4] advised against the use of analgesia in patients until the surgeon had made his evaluation and decided whether or not surgery was needed. Such an attitude was in part justified by the variability in commercial morphine concentrations available at the time. This remained surgical dogma until the 1980s and 1990s, with few individuals retaining this view. In the 1990s emergency medicine literature and core curricula, providing analgesia to these patients was supported. In Rosen's 1998 fourth edition, the authors referenced the 2 prospective studies of ED analgesic use in these patients[6,7] and indicated that the evidence supported their safe use. In Rosen's fifth edition, published in 2002, the authors stated there was no evidence to support the withholding of analgesics in these patients.[31] In the most recent edition of Cope's *Acute Abdomen*, the authors recommend that analgesia not be withheld. "The realization, likely erroneous, that narcotics can obscure the clinical picture has given rise to the unfortunate dictum that these drugs should never be given until a diagnosis has been firmly established."[32]

There have been reported concerns about the ability of the patient who has received narcotic analgesia to provide informed consent. Published studies have refuted this argument.[33,34] Obtaining consent from a patient who has received narcotic analgesia should be individualized based on his or her capacity to understand and make rational decisions about his or her care. Lack of coercion is an additional requirement for informed consent. Coercion may be adjudged if patients are asked to give informed consent for surgery in the presence of untreated pain. Pain itself has also been recognized to cloud judgment and, therefore, some authors argue that analgesia enhances one's ability to provide informed consent.[1,35]

To date, there has not been a definitive, double-blind controlled trial of sufficient power to prove the safety of analgesia in ED patients with abdominal pain. The combined results of a series of small trials, however, suggest that before establishing a definitive diagnosis, analgesia is safe. The ethical implications of withholding analgesia from patients in pain prevent the need for further placebo-controlled studies of this population. Important, unanswered research questions still remain, for instance, what is the optimal and safe regimen for analgesia in this population? and what regimen do patients find most acceptable as part of their care in the emergency department?

Competing interests: None declared.

Key words: abdominal pain, analgesia, ethics

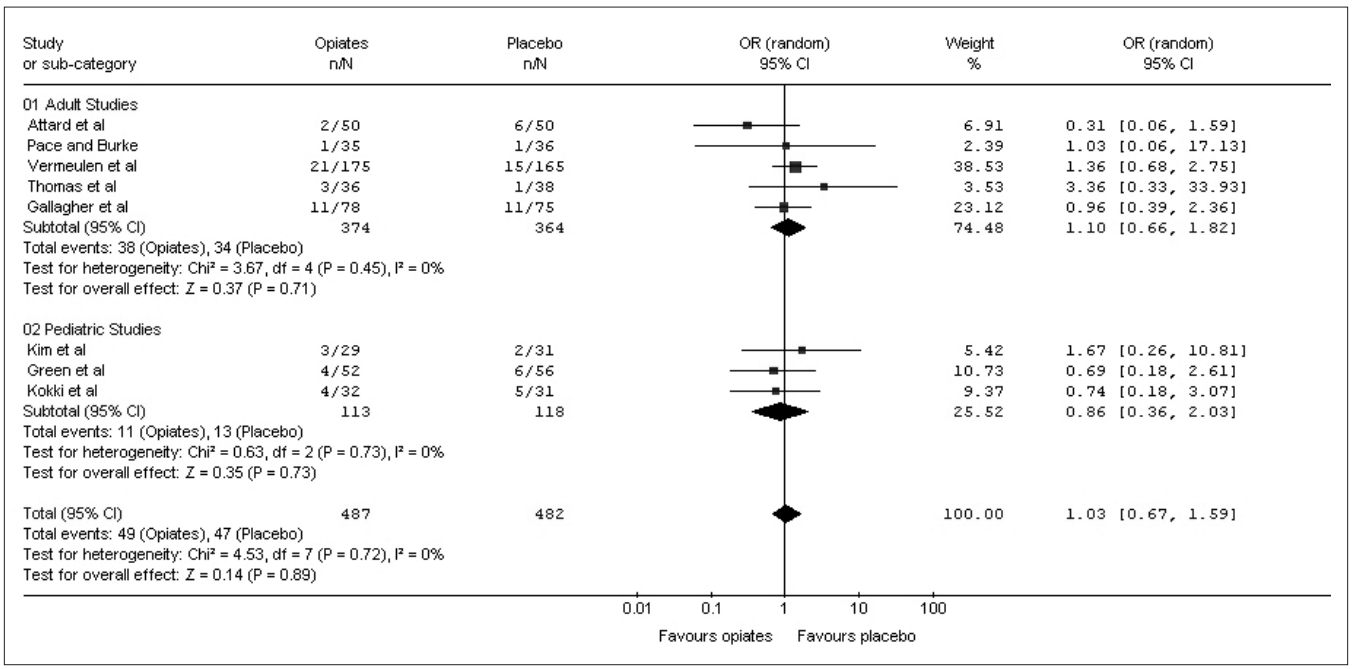

Fig. 1. Odds ratios (ORs) for incorrect management decisions with opiates. CI = confidence interval.

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References

1. Graber MA, Ely JW, Clarke S, et al. Informed consent and general surgeons' attitudes toward the use of pain medication in the acute abdomen. Am J Emerg Med 1999;17:113-6.
2. Analgesia and the acute abdomen [Editorial]. BMJ 1979;2:1093.
3. Knopp RK, Dries D. Analgesia in acute abdominal pain: what's next? Ann Emerg Med 2006;48:161-3.
4. Cope Z, Silen W. The early diagnosis of the acute abdomen. New York (NY): Oxford University Press; 1921.
5. Ranji SR, Goldman LE, Simel DL, et al. Do opiates affect the clinical evaluation of patients with acute abdominal pain? JAMA 2006;296:1764-74.
6. Attard AR, Corlett MJ, Kidner NJ, et al. Safety of early pain relief for acute abdominal pain. BMJ 1992;305:554-6.
7. Pace S, Burke TF. Intravenous morphine for early pain relief in patients with acute abdominal pain. Acad Emerg Med 1996;3: 1086-92.
8. Vermeulen B, Morabia A, Unger PF, et al. Acute appendicitis: influence of early pain relief on the accuracy of clinical and US findings in the decision to operate–a randomized trial. Radiology 1999;210:639-43.
9. Thomas SH, Silen W, Cheema F, et al. Effects of morphine analgesia on diagnostic accuracy in emergency department patients with abdominal pain: a prospective, randomized trial. J Am Coll Surg 2003;196:18-31.
10. Kim MK, Strait RT, Sato TT, et al. A randomized clinical trial of analgesia in children with acute abdominal pain. Acad Emerg Med 2002;9:281-7.
11. Green R, Bulloch B, Kabani A, et al. Early analgesia for children with acute abdominal pain. Pediatrics 2005;116:978-83.
12. Kokki H, Lintula H, Vanamo K, et al. Oxycodone vs placebo in children with undifferentiated abdominal pain. Arch Pediatr Adolesc Med 2005;159:320-5.
13. Zoltie N, Cust MP. Analgesia in the acute abdomen. Ann R Coll Surg Engl 1986;68:209-10.
14. LoVecchio F, Oster N, Sturmann K, et al. The use of analgesics in patients with acute abdominal pain. J Emerg Med 1997;15:775-9.
15. Mahadevan M, Graff L. Prospective randomized study of analgesic use for ED patients with right lower quadrant abdominal pain. Am J Emerg Med 2000;18:753-6.
16. McHale PM, LoVecchio F. Narcotic analgesia in the acute abdomen—a review of prospective trials. Eur J Emerg Med 2001;8:131-6.
17. Brewster GS, Herbert ME, Hoffman JR. Medical myth: analgesia should not be given to patients with an acute abdomen because it obscures the diagnosis. West J Med 2000;172:209-10.
18. Thomas SH, Silen W. Effect on diagnostic efficiency of analgesia for undifferentiated abdominal pain. Br J Surg 2003;90:5-9.
19. Burke T, Mack S, Coward B, et al. The use of intravenous morphine for early pain relief in patients with acute abdominal pain [abstract]. Acad Emerg Med 1994;1:A51.
20. Quinn J. Debunking the myths of analgesia. CMAJ 1994; 151:914-5.
21. Rupp T, Delaney KA. Inadequate analgesia in emergency medicine. Ann Emerg Med 2004;43:494-503.
22. Todd KH. Emergency medicine and pain: a topography of influence. Ann Emerg Med 2004;43:504-6.
23. Miner J, Biros MH, Trainor A, et al. Patient and physician perceptions as risk factors for oligoanalgesia: a prospective observational study of the relief of pain in the emergency department. Acad Emerg Med 2006;13:140-6.
24. Shabbir J, Ridgway PF, Lynch K, et al. Administration of analgesia for acute abdominal pain sufferers in the accident and emergency setting. Eur J Emerg Med 2004;11:309-12.
25. Wolfe JM, Lein DY, Lenkoski K, et al. Analgesic administration to patients with an acute abdomen: a survey of emergency medicine physicians. Am J Emerg Med 2000;18-250-3.
26. Goldman RD, Crum D, Bromberg R, et al. Analgesia administration for acute abdominal pain in the pediatric emergency department. Pediatr Emerg Care 2006;22:18-21.
27. Green RS, Kabani A, Dostmohamed H, et al. Analgesic use in children with acute abdominal pain. Pediatr Emerg Care 2004;20:725-9.
28. Kim MK, Galustyan S, Sato TT, et al. Analgesia for children with acute abdominal pain: a survey of pediatric emergency physicians and pediatric surgeons. Pediatrics 2003;112:1122-6.
29. Gallagher EJ, Esses D, Lee C, et al. Randomized clinical trial of morphine in acute abdominal pain. Ann Emerg Med 2006;48:150-60.
30. Gallagher EJ, Esses D, Lee C, et al. Randomized clinical trial of morphine in acute abdominal pain. Ann Emerg Med. 2006; 48:160e1-160e4. Available: http://download.journals.elsevierhealth.com/pdfs/journals/01960644/PIIS0196064405019608.pdf (accessed 2006 Sept. 26).
31. Marx JA, Walls RM, Hockberger R, eds. Emergency Medicine: Concepts and Clinical Practice. 5th ed. St. Louis (MO): Mosby; 2002.
32. Silen W. Cope's Early Diagnosis of the Acute Abdomen. New York (NY): Oxford; 2000:5.
33. Vessey W, Siriwardena A. Informed consent in patients with acute abdominal pain. Br J Surg 1998;85:1278-80.
34. Kay R, Siriwardena AK. The process of informed consent for urgent abdominal surgery. J Med Ethics 2001;27:157-61.
35. Andress D, Pace S. Cognitive capacity after intravenous morphine administration. Ann Emerg Med 1992;21:1047.

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