Early Analgesia for Children With Acute Abdominal Pain

Robert Green, MD*; Blake Bulloch, MD‡; Amin Kabani, MD§; Betty Jean Hancock, MD‖; and Milton Tenenbein, MD§

ABSTRACT. *Objectives.* **The objectives of this study were to determine whether the administration of morphine to children with acute abdominal pain would impede the diagnosis of appendicitis and to determine the efficacy of morphine in relieving the pain.**

Methods. **This was a double-blind, randomized, placebo-controlled trial involving 5- to 16-year-old children who presented to the emergency department of a children's hospital with a chief complaint of acute abdominal pain that was thought by the pediatric emergency attending physician to require a surgical consultation. Subjects were randomized to receive intravenously administered morphine or normal saline solution. Clinical data and the emergency physician's confidence in his or her clinical diagnosis (0–100%) were recorded systematically with a standardized form. This was repeated 15 minutes after administration of the study medication. The surgeon assessed the child within 1 hour and completed a similar data collection sheet. Pain was assessed, with a color analog scale, before and after study medication administration. Each subject was monitored for 2 weeks after enrollment.**

Results. **One hundred eight children were enrolled; 52 received morphine and 56 received a placebo saline solution. There were no differences between groups in demographic variables or the degree of pain. There were no differences between groups in the diagnoses of appendicitis or perforated appendicitis or the number of children who were observed and then underwent laparotomy. The reduction in the mean pain score was significantly greater in the morphine group (2.2 vs 1.2 cm). The emergency physicians' and surgeons' confidence in their diagnoses was not affected by the administration of morphine.**

Conclusions. **Our data show that morphine effectively reduces the intensity of pain among children with acute abdominal pain and morphine does not seem to impede the diagnosis of appendicitis.** *Pediatrics* **2005;116: 978–983;** ***abdominal pain, analgesia, appendicitis, diagnosis, surgery.***

ABBREVIATIONS. CAS, color analog scale; ED, emergency department; CI, confidence interval; WBC, white blood cell.

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Pain is a common symptom among children presenting for care at emergency departments (EDs). Traditionally, the physician's focus has been on the diagnosis of the condition producing the pain, rather than on the relief of the pain. However, emergency physicians are now concerning themselves with the latter, and several authorities have produced position statements on the management of pain in EDs.[1–3]

Fifteen percent of school-aged children are brought to a physician because of abdominal pain, making this symptom a common presenting complaint in the pediatric ED.[4] The most common serious, pediatric, abdominal emergency is appendicitis.[5] As with adult patients, it has been thought that analgesic use among pediatric patients with surgical abdominal findings may impede the diagnosis. Theoretically, analgesia may mask pain and subsequently diminish the physical signs associated typically with a surgical condition. Current practice in pediatric emergency medicine and pediatric surgery dictates that children should not receive analgesics when presenting with acute abdominal pain.[6,7] This practice among children is a result of traditional teaching and only recently has been challenged in a manner similar to that for adults.[8]

There is a need to determine whether the practice of analgesic administration to pediatric patients with acute abdominal pain impedes the diagnosis of the condition causing the pain. The objectives of this study were to assess whether morphine would increase the rate of missed appendicitis, to determine its efficacy in treating acute pediatric abdominal pain, and to examine its effect on physician confidence in the diagnosis of the condition causing the pain.

METHODS

This study was conducted in the ED of a tertiary care, academic, pediatric ED with an annual census of 39 000. This facility is staffed by pediatric emergency medicine attending physicians. The study was a double-blind, randomized, placebo-controlled, clinical trial, with the primary outcome measure being the rate of missed appendicitis among children who received intravenous morphine treatment. The secondary outcomes were rates of perforated appendicitis, delays in diagnosis, pain relief, and confidence of pediatric emergency physicians and pediatric surgeons in the diagnoses. Ethics approval for this study was obtained from our university's institutional review board.

Male and female patients between the ages of 5 and 16 years (inclusive) who presented with nontraumatic abdominal pain of <48-hour duration were eligible for the study if, after assessment by the attending pediatric emergency physician, it was thought that a surgical consultation was warranted for a possible surgical condition. Exclusion criteria included allergy to opiates, previous

opiate use within the past 4 hours, hypotension, or the absence of a parent.

Children were enrolled 7 days per week between the hours of 8:00 AM and midnight. After midnight, often an attending surgeon was not available within the protocol time limits. The study center has 3 pediatric surgeons, but convenience sampling was used because 1 surgeon did not participate.

After emergency physician assessment, informed written consent was obtained from the parents and verbal assent was obtained from the children. For children who met the inclusion criteria, a premedication assessment form was completed by the emergency physician. Data collected on this form were clinical signs and symptoms, including the location of the pain, the presence or absence of abdominal tenderness, guarding, and psoas, obturator, and Rosving signs, and whether there was pain associated with jumping. The physician documented his or her diagnosis, with a degree of confidence ranging from 0% to 100%, on the form before the results of any laboratory testing or imaging studies were available.

A pain assessment was conducted with a validated color analog scale (CAS).[9] Children were asked to mark their current pain severity on the thermometer-shaped, standardized CAS anchored by the descriptors "no pain" and "worst pain." Children were asked to slide the marker to the point on the thermometer that best described the pain they were experiencing currently. The reverse side of this instrument has a numerical rating scale divided into unit marks separated by 0.25 cm, so that a number from 1 to 10 can be assigned to the individual assessments. A team of dedicated study nurses supervised compliance with the study protocol and administered all pain scales with a scripted dialogue.

Randomization was performed by the hospital pharmacy in a blinded manner, using a computer-generated, random-number list in blocks of 10. The pharmacy prepared identical syringes of morphine sulfate and normal saline solution as numbered prepacked syringes, to which all investigators and emergency staff members were blinded. Children were randomized to receive either 0.05 mg/kg morphine sulfate (maximum of 10 mg) or an equivalent volume of normal saline solution. Patients underwent continuous oxygen saturation monitoring, and vital signs were recorded by the study nurse every 10 minutes.

Fifteen minutes after administration of the study medication, the emergency physician reexamined the child and completed an identical assessment form, including an assessment of his or her confidence in the diagnosis. The study nurse repeated a pain scale assessment for the child at this time. All children were blinded to their initial CAS scores. If a child had ongoing pain, then the same dose of study medication was repeated at the emergency physician's discretion. The emergency physician reassessed the child within 15 minutes after the second dose. The emergency physician completed a second, identical, postmedication assessment form, and the study nurse repeated the pain scale assessment. Children who had ongoing pain after 2 doses of study medication (total dose of 0.1 mg/kg morphine sulfate) did not receive additional medication until assessment by the pediatric surgeon.

Surgical assessment had to be performed within 1 hour after the initial study medication infusion. Attending pediatric surgical staff members or a senior surgical resident (postgraduate year 4 or higher) completed a surgical assessment form and arranged disposition. The surgical assessment form evaluated abdominal tenderness, guarding, the presence of positive or negative psoas, obturator, and Rosving signs, and whether there was pain with jumping. The surgeon was then asked to make a diagnosis and to indicate his or her confidence in the diagnosis, from 0% to 100%. Additional analgesia and other medications were administered at the surgeon's discretion.

Children were monitored if they were admitted to the hospital. All children who were discharged from the hospital received follow-up telephone calls from the study nurse within 2 weeks, to ensure that no surgical condition had been missed. Operating room and pathology reports were reviewed for final diagnoses for all children who underwent laparotomy.

Mean pain scores were analyzed with repeated-measures analysis of variance. The χ^2 test or Fisher's exact test (when appropriate) was used for comparisons of proportions, and the t test was used for comparisons of means. All statistical analyses were performed with SAS software, version 8.2 (SAS Institute, Cary, NC).

RESULTS

During the 25-month study period from February 1, 2000, to March 30, 2002, 162 patients were eligible for our study. Of these, 54 were not enrolled because they met exclusion criteria ($n = 17$), refused ($n = 16$), or were missed ($n = 21$). A total of 108 children completed the study (Fig 1).

Fifty-two patients were randomized to receive morphine, whereas 56 received normal saline solution. The groups were similar with respect to mean initial pain scores, physical findings, and time from study drug administration to surgical assessment (Table 1).

The outcomes for the 108 children are shown in Table 2. Appendicitis was missed for only 1 child, and this patient was in the normal saline solution group. There was no difference between groups in the diagnosis of appendicitis ($P = .25$) or perforated appendicitis ($P = .51$) or in the number of children who were observed and then underwent laparotomy ($P = .77$). Overall, there were 31 patients in the morphine group and 26 in the placebo group who

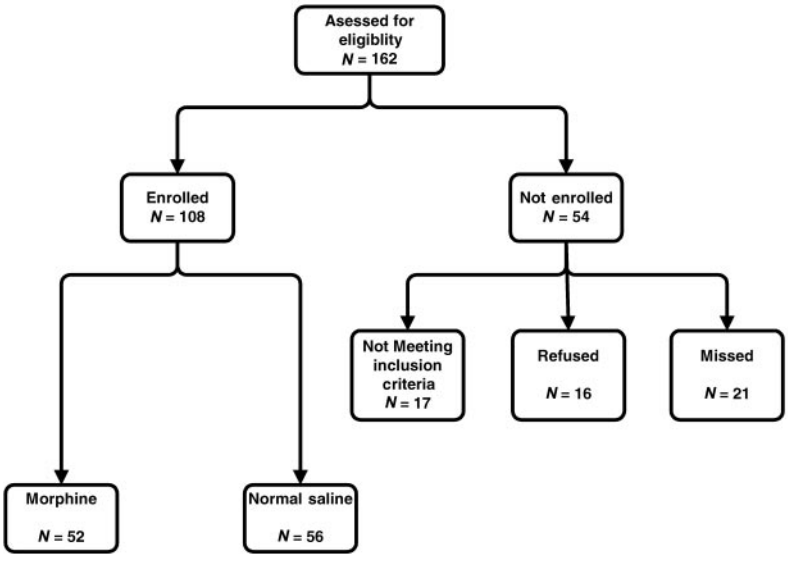

Fig 1. Study flowchart.

TABLE 1. Initial Assessment Before Study Drug Administration

	Morphine	Placebo	*P* Value
Mean initial pain score (95% CI)	6.65 (6.27–7.03)	6.66 (6.29–7.02)	.98
Right lower quadrant tenderness, %	100	100	1.00
Positive Rosving sign, %	49.0	55.4	.51
Positive psoas sign, %	69.2	67.9	.88
Positive obturator sign, %	49.1	51.8	.77
Involuntary guarding, %	55.8	50.0	.55
Voluntary guarding, %	65.4	69.6	.64
Time from study drug to surgical assessment, min	38.5 (33.4–43.6)	44.4 (38.1–50.8)	.15

TABLE 2. Outcomes

	No. of Patients	
	Morphine (*N* = 52)	Normal Saline Solution (*N* = 56)
Laparotomy immediately after ED assessment	25	24
Appendicitis (perforated)	24 (12)	22 (11)
Normal appendix	1	2
Admitted for observation after ED assessment	19	22
Laparotomy	7	6
Appendicitis (perforated)	7 (3)	4 (1)
Normal appendix	0	2
No laparotomy	12	16
Urinary tract infection	0	1
Ovarian cyst	0	1
Self-resolving pain	12	14
Discharged home after ED assessment	8	10
Self-resolving pain	5	9
Subsequent laparotomy for appendicitis	1 (4 mo later)	1 (5 d later)
Pneumonia	1	0
Urinary tract infection	1	0

had final diagnoses of appendicitis. Perforated appendicitis occurred for 27 patients, with no difference between groups ($P = .51$). Laparotomies were performed for 4 patients with normal appendices in the placebo group and 1 in the morphine group. The incidences of other diagnoses and self-resolving abdominal pain were not different between the groups ($P = .70$).

Of the 41 children admitted for observation, 13 underwent a laparotomy subsequently, ie, 7 in the morphine group and 6 in the placebo group. All 7 children in the morphine group had appendicitis (3 perforated), as did 4 in the placebo group (1 perforated). There was no difference in the proportions of patients admitted for observation and subsequently found to have appendicitis (7 of 19 patients in the morphine group and 4 of 22 patients in the placebo group; $P = .29$).

Both groups experienced reductions in recorded CAS scores, as assessed by self-report. The mean pain scores and 95% confidence intervals (CIs) before and after morphine or placebo administration are shown in Table 3. Figure 2 shows that the reduction in the mean pain score was 2.2 cm in the morphine group, compared with 1.2 cm in the placebo group ($P = .015$).

TABLE 3. Pain Scores

	Pain Scores (95% CI)	
	Before Administration	After Administration
Morphine	6.65 (6.27–7.03)	4.50 (4.11–4.88)
Normal saline solution	6.66 (6.29–7.02)	5.55 (5.17–5.93)

The emergency physicians thought that the pain had diminished for 46 (88.5%) children who received morphine, compared with 33 (63.5%) children in the placebo group ($P = .0005$). No emergency physician thought that the pain grew worse in either group, but physicians thought that the pain was unchanged for 6 (11.5%) children in the morphine group and 23 (44.2%) children in the placebo group ($P = .0002$).

Physician confidence in diagnoses was not altered for children who received morphine. Emergency physicians recorded no change in their confidence in diagnoses after patients received either morphine or placebo. The emergency physician confidence in diagnoses was 68.9% in the morphine group before study medication administration, compared with 65.5% in the placebo group. After morphine administration, physician confidence increased to 69.5% (effect size: 1.2%; 95% CI: −2.9% to 5.3%), compared with 70.9% in the placebo group (effect size: 5.3%; 95% CI: 2.7–7.9%). Similarly, there was no demonstrable effect of morphine on the surgeons' confidence in diagnoses. The surgeons were 73.8% confident of their diagnoses for the morphine group, compared with 73.6% for the placebo group (effect size: 0.01%; 95% CI: −0.39–0.40%).

Two children in our study were discharged from the hospital after receiving the study medication and subsequently returned with acute appendicitis. One child was in the morphine group and returned 4 months later with a perforated appendix. This child

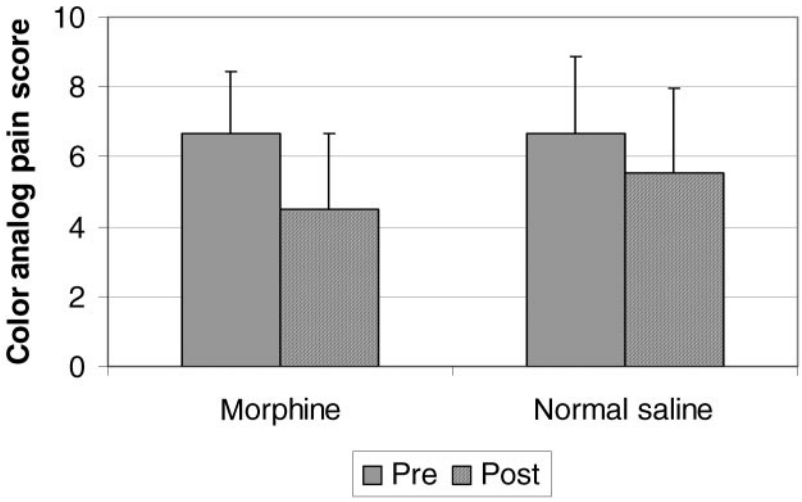

Fig 2. Mean (and SD) pain scores before (Pre) and after (Post) administration of morphine or normal saline solution for 108 children with acute abdominal pain (morphine versus normal saline solution: $P = .15$).

was asymptomatic in the interval between study enrollment and return to the hospital, making it unlikely that morphine had any effect in delaying the diagnosis. The other child was in the placebo group and returned 5 days later with acute appendicitis.

All children were monitored specifically for apnea, hypoxemia, hypotension, or changes in the level of consciousness. These adverse events were not observed in either group.

Four of the 13 children who underwent a laparotomy after being admitted to the hospital for observation were found to have a perforated appendix and intraabdominal infection. Their operations were performed 20 to 48 hours after presentation to the ED. Their case histories are as follows.

Patient 1 (randomized to the morphine group) was 12 years of age when she visited the ED because of abdominal pain that had begun 4 days previously, in the periumbilical region. During the previous 3 days, her pain had been in the suprapubic region and she had been vomiting. Diarrhea began 1 day before presentation, and the patient had dysuria. She had experienced a normal menstrual period 2 weeks previously. She walked with a hunched-over gait, and her vital signs were as follows: heart rate: 96 beats per minute; respiratory rate: 28 breaths per minute; temperature: 38.0°C; blood pressure: 122/76 mm Hg. There were decreased bowel sounds, with suprapubic tenderness. The patient had a positive psoas sign and rebound tenderness. Admission to the surgical inpatient unit was arranged. The following investigation results were obtained: white blood cell (WBC) count: 17 800 cells per mm^3 (14 600 neutrophils per mm^3); urinalysis: normal findings. A sonogram of the patient's abdomen found no abnormality; the report stated, "The appendix is well visualized and appears normal pre and post compression. A normal appearing appendix." The patient experienced pain requiring 3 doses of morphine through the night. In the morning, the surgeon noted tenderness and rebound tenderness in both lower quadrants but greater on the left side. Laparotomy was performed 20 hours after presentation to the ED. Free pus was found in the peritoneal cavity. The perforated appendix was found in the high pelvic region on the sacral promontory, with the sigmoid colon wrapped around the left side of it. Infected exudate was found on the sigmoid mesentery. The patient fared well after her operation and was discharged from the hospital 5 days later.

Patient 2 (randomized to the normal saline solution group) was 11 years of age when he visited the ED because of generalized abdominal pain that had been present for the past 15 hours. This had been preceded by a 7-day history of flu-like symptoms (sore throat, malaise, and fever). Amoxicillin treatment had been started 1 day before presentation. The patient had a poor appetite and no vomiting or diarrhea. His vital signs were as follows: heart rate: 112 beats per minute; respiratory rate: 20 breaths per minute; temperature: 37.3°C; blood pressure: 122/77 mm Hg. The patient had generalized tenderness over his abdomen, slightly increased in the right lower quadrant, and no rebound tenderness. Admission to the surgical inpatient unit was arranged. The following investigation results were obtained: WBC count: 12 900 cells per mm^3 (11 400 neutrophils per mm^3); urinalysis: normal findings. The findings of an abdominal radiograph were consistent with gastroenteritis. During the first 24 hours in the hospital, the patient experienced 6 episodes of diarrhea, with no vomiting, and his pain diminished. During his second night in the hospital, his temperature increased to 39.5°C and the patient was found to have marked tenderness in the right lower quadrant. Laparotomy was performed 48 hours after presentation to the ED. A periappendiceal abscess was found in the middle lower abdomen, extending toward the right. The patient fared well after surgery and was discharged from the hospital 6 days later.

Patient 3 (randomized to the morphine group) was 10 years of age when he visited the ED because of 3 days of lower abdominal pain in both quadrants. There had been no nausea, vomiting, diarrhea, dysuria, or anorexia. The patient's vital signs were as follows: heart rate: 84 beats per minute; respiratory rate: 24 breaths per minute; temperature: 36.7°C; blood pressure: 116/67 mm Hg. The patient had

normal bowel sounds and left lower quadrant tenderness, with rebound tenderness. Admission to the surgical inpatient unit was arranged. The following investigation results were obtained: WBC count: 11 500 cells per mm^3 (9500 neutrophils per mm^3); urinalysis: normal findings. The results of an abdominal radiograph were normal. The patient's abdominal pain persisted during the first 24 hours in the hospital. The patient was allowed fluids and had no emesis. At 13 hours, he was found to have mild left lower quadrant tenderness, with no guarding or rebound tenderness. His temperature increased to 39.1°C on the evening of his first hospital day, 24 hours after admission. However, his abdominal findings were unchanged. The patient slept well through the night and was afebrile in the morning. He had some abdominal tenderness. The results of an abdominal sonogram were normal. Later that day, however, the patient experienced marked right lower quadrant pain and tenderness. Laparotomy was performed 43 hours after presentation to the ED. A small amount of pus was encountered after entry into the peritoneal cavity. The cecum had turned up on itself in a cranial manner, with the appendix being adherent behind the ileum toward the middle of the abdomen, in a wall of omentum. Free pockets of pus were found. The patient fared well after surgery and was discharged from the hospital 6 days later.

Patient 4 (randomized to the morphine group) was 5.5 years of age when she visited the ED because of abdominal pain that had begun 1 day previously. The pain was generalized and progressive in severity. The patient had vomited once and passed 1 normal stool. She had a 2-day history of sore throat, cough, and rhinorrhea. Fever began 8 hours before arrival. The patient preferred to lie still, and her vital signs were as follows: heart rate: 199 beats per minute; respiratory rate: 20 breaths per minute; temperature: 38.3°C; blood pressure: 119/74 mm Hg. The patient had normal bowel sounds, with tenderness in both lower quadrants and a distended bladder. After voiding, she seemed more comfortable and her abdomen seemed softer. Admission to the surgical inpatient unit was arranged. The following investigation results were obtained: WBC count: 8500 cells per mm^3 (6800 neutrophils per mm^3); urinalysis: 2 to 6 pus cells per high-power field. No imaging studies were performed. The patient was allowed clear fluids, and there was no emesis. In the morning, the patient's temperature was 38.1°C and her condition was judged to be improved. The patient seemed to be more comfortable, and her pain seemed diminished. Her abdomen was soft, and she had periumbilical and right lower quadrant abdominal pain. The notation in the record at that time stated, "I do not think this is appendicitis." Several hours later, the patient's abdomen was distended and she had decreased bowel sounds and increased tenderness. Laparotomy was performed 23 hours after presentation to the ED. The appendix was found behind the bladder. There was purulent exudate confined to the periumbilical region. The patient fared well after surgery and was discharged from the hospital 3 days later.

These 4 children demonstrate the well-known heterogeneity of the presentation and clinical course of appendicitis and the challenge of making this diagnosis for some children. Common to all 4 of these children was the fact that their inflamed appendix was not in the right lower quadrant, which is the likely explanation for their atypical presentations and clinical courses. Their clinical courses demonstrate that the delays in diagnosis and the development of perforation were not consequences of analgesic administration.

DISCUSSION

Pain is one of the most common presenting symptoms in primary care practice. Some estimate that 5% of patients seek medical attention for a variety of painful conditions.[10] These patients expect pain relief. However, the practice of analgesic use in the ED is a relatively recent topic in the literature. Wilson and Pendleton[11] retrospectively reviewed 198 charts of patients with "painful medical and surgical conditions," such as chest pain, abdominal pain, and renal colic, and found that 56% of these patients received no analgesia. Although 44% did receive some analgesia, 69% of them waited >1 hour. The authors concluded that "oligoanalgesia" is prevalent in the ED setting. Other studies have also demonstrated inadequate analgesia use in the ED.[12,13]

This has also been studied among children. Friedland et al[14] retrospectively reviewed the charts of pediatric patients who presented to the ED with 3 painful conditions. They found that children with sickle cell crisis received analgesia 100% of the time but those with long-bone fractures and burns received analgesia in only 31% and 26% of cases, respectively. The authors concluded that there was suboptimal use of analgesia for children.

The realization that frequently physicians do not provide their patients with optimal analgesia has led to widespread concern, with many organizations publishing policies that integrate the need for pain management with an ethical obligation.[1–3,14,15] Abdominal pain is often a diagnostic challenge. Surgical practice has dictated that no analgesic should be given to these patients, for fear of obscuring the diagnosis. An editorial in the *British Medical Journal* addressed this issue in 1979,[16] but studies were conducted only more recently. Zoltie and Cust[17] were the first to address this issue and others followed,[18–20] by comparing opiate use with placebo use among adults with acute abdominal pain. All found analgesic use to be safe and effective in reducing pain without increasing morbidity.[17–20] These studies changed practice in adult emergency medicine and adult general surgery. It is now the accepted standard of care to provide pain relief to adults with acute abdominal pain, before definitive diagnosis and before surgical assessment.

Typically, children with acute abdominal pain requiring surgical referral are not provided with analgesia. This stems from a combination of traditional surgical teaching, limited confidence in the assessment of pediatric acute abdominal conditions by referring physicians, and healthy skepticism in the

extrapolation of adult data to the pediatric population.[21] Unfortunately, despite the frequency of abdominal pain as a presenting complaint in the pediatric ED, only 1 previous study addressed this issue. Kim et al[8] randomized 60 children to received morphine or placebo and found a significant reduction in pain scores between the study groups, with no change in the number of areas of abdominal tenderness or decrease in the diagnostic accuracy between the study groups. In their study, however, surgeons evaluated children both before and after study medication administration; in our study, the surgeons performed their evaluation after the intervention.

One of our primary outcome variables was whether morphine administration would result in an increase in missed appendicitis cases. This condition was missed for only 1 child, who was treated with placebo. The number of patients with a normal appendix who underwent an appendectomy can also indicate diagnostic accuracy; there were 5 such patients, 4 of whom were treated with placebo.

Another of our primary outcome variables was whether morphine decreased acute abdominal pain among children. Our data demonstrated a significant decrease in abdominal pain, as measured with a CAS. A statistically significantly greater decrease in mean pain scores was found for the group that received morphine, compared with the placebo group. Statistical significance does not necessarily indicate clinical significance. Previous studies demonstrated that reductions in mean pain scores, with the CAS, must be at least 2 cm to be clinically significant.[9] Children in our placebo group had a reduction of 1.2 cm and, although it was statistically significant, this was likely not clinically significant. The reduction of 2.2 cm in the morphine group was both statistically and clinically significant.

Studies among adults with acute abdominal pain concluded that analgesic use may increase diagnostic accuracy.[19] In our study, there was no difference between groups in diagnostic accuracy or confidence in diagnoses by emergency physicians or surgeons.

The sample size is a limitation of this study. A post hoc sample size calculation determined that this study had a power of 0.16 to detect a difference in missing the diagnosis of appendicitis. From this, it was calculated that >1000 children per group would need to be enrolled in a randomized, controlled trial to attain a power of 0.80.

Our data showed that morphine effectively reduced the intensity of pain among children with acute abdominal pain, and it seems that morphine does not mask the physical signs of acute appendicitis. A multicenter trial to study this issue in more depth may be warranted.

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