

## Opioid administration for acute abdominal pain in the pediatric emergency department

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### ABSTRACT

*The use of opioid analgesia for acute abdominal pain of unclear etiology has traditionally been thought to mask symptoms, alter physical exam findings, delay diagnosis, and increase morbidity and mortality. However, studies in children and adults have demonstrated that administering intravenous opioids to patients with acute abdominal pain induces analgesia but does not delay diagnosis or adversely affect diagnostic accuracy. This review discusses the effects of opioid administration on pain relief and diagnostic accuracy in children with moderate to severe acute abdominal pain who have been evaluated in the emergency department. We hold that current evidence supports the administration of opioids to children with acute abdominal pain, and future trials will help determine safe and effective timing and dosing related to opioid administration.*

*Key words: opioids, children, abdominal pain, emergency department*

### INTRODUCTION

Acute appendicitis is the most common serious pediatric abdominal emergency<sup>1</sup> and the most common indication for an urgent operation, with a lifetime incidence in the population of 7 percent.<sup>2</sup> Fifteen percent of school-aged children are brought to a physician with a chief complaint of abdominal pain,<sup>1,2</sup> making it one of the most common pediatric complaints in the emergency department (ED). The incidence increases with age, from an annual rate of one to two in 10,000 in children between birth and four years to one of 19 to 28 in 10,000 in children younger than 14 years.<sup>3</sup> Abdominal pain most frequently presents in the second decade of life.<sup>2</sup>

The recommendations for pain management in children with suspected appendicitis include withholding analgesia in order to avoid masking physical signs prior to a surgical evaluation.<sup>4</sup> It has been suggested that analgesia—especially when induced by opioids—might mask

symptoms and physical findings, delay formulation of an accurate diagnosis, and possibly lead to increased morbidity.<sup>5</sup>

### MANAGING PEDIATRIC ABDOMINAL PAIN

#### Accuracy of diagnosis

Clinical studies conducted in the past several years have challenged the traditional belief that analgesia should be withheld by providing evidence that analgesia significantly reduces pain without interfering with diagnostic accuracy (Table 1). Despite the mounting evidence, however, a recent survey of adult and pediatric emergency physicians in the United States and Canada reported that the majority of physicians choose to withhold analgesia at least until an evaluation by a surgical specialist has been provided. This is true regardless of whether or not they believe that analgesia will change important physical findings.<sup>6</sup>

A study involving 100 adult patients with abdominal pain found that localization of pain was not affected by giving papaverine as compared to placebo, and the number of appendectomies for noninflamed appendicitis was lower when analgesia was given. The number of incorrect decisions to operate was higher in the placebo group.<sup>5</sup>

A number of studies have examined the use of analgesia in young patients.<sup>1,7-9</sup> Tramadol 1 mg/kg versus placebo did not change an abdominal examination utilizing a seven-component score in a randomized, double-blind, controlled trial involving almost 70 patients older than 11 years old. The abdominal examination score included assessment of tenderness in four quadrants by light and deep palpation, localization of palpation to any area where tenderness was elicited, tenderness on rebound, cough tenderness, and tenderness on percussion of the abdomen.<sup>7</sup> Kim et al.<sup>8</sup> demonstrated effective pain relief with intravenous morphine in children with acute abdominal pain, without causing adverse events or delay

**Table 1. Clinical studies providing evidence that analgesia significantly reduces pain without interfering with diagnostic accuracy**

| Reference number | Location         | Year | Population                           | Findings   |
|------------------|------------------|------|--------------------------------------|--|
| 2                | Canada (Toronto) | 2006 | Patients 0 to 16 years old           | Children with abdominal pain receive more analgesia when the physician suspects appendicitis |
| 1                | Canada (Halifax) | 2005 | 108 children, ages five to 16 years  | Morphine did not increase the rate of missed appendicitis                                    |
| 8                | Finland          | 2005 | 63 children, ages four to 15 years   | Effective pain relief with buccal oxycodone  |
| 7                | Milwaukee        | 2002 | 60 children, ages five to 18 years   | Morphine did not alter areas of tenderness   |
| 6                | Singapore        | 2000 | 70 patients, ages 11 years and older | Tramadol didn't change abdominal examination as compared to placebo                          |

in diagnosis. Among 60 children five to 18 years old, administration of morphine did not alter the localization of tenderness or the diagnostic accuracy. Similarly, Green et al.<sup>1</sup> demonstrated that morphine administration did not increase the rate of missed appendicitis. While the diagnostic accuracy was not affected by giving opioids, morphine was found to decrease pain scores significantly, both statistically and clinically, among 108 children aged five to 16 years old presenting to the pediatric ED with acute abdominal pain. The rate of perforated appendicitis was unchanged after treatment with morphine.

Kokki et al.<sup>9</sup> demonstrated effective pain relief with buccal oxycodone in 63 children between the ages of four and 15 years with acute abdominal pain, without adversely influencing the clinical examination or the appropriateness of the decision to operate; on the contrary, the researchers noted a small, nonsignificant improvement in diagnostic accuracy in children treated with oxycodone.

These results challenge some pediatric surgeons' long-held assumptions that analgesia will significantly mask crucial symptoms associated with acute abdominal pain<sup>1,5</sup> and that providing early treatment with narcotics affects the ability of the surgeons—faculty and senior residents alike—to make accurate diagnoses.<sup>1,10</sup>

We recently documented the use of analgesia in accordance with probability assessment of appendicitis by physicians in a pediatric ED.<sup>2</sup> Only half of the children with a high suspicion of appendicitis received analgesia in the tertiary ED in Toronto, Canada. Thirty percent of them received acetaminophen and ibuprofen from triage nurses even before being seen by a pediatrician, probably for antipyretic rather than analgesic purposes.<sup>2</sup> We showed that even when opioids were administered by the treating

physician, almost a quarter of the children were underdosed, limiting the analgesic effectiveness of the drugs. We suggested that the misconception of the risk of a higher rate of adverse events while using morphine compared with other medication was responsible for physicians' underdosing.<sup>2</sup>

Our findings served as another testimony to the well-known phenomenon of "oligoanalgesia" in acute care.<sup>11</sup> These findings are disappointing in light of the significant effort in the last decade to increase awareness surrounding pediatric pain. While there is a better understanding of the mechanisms of pain in children and the need to treat the pain to avoid long-term consequences, abdominal pain still seems to be a challenging area, and there is still tremendous hesitancy to administer analgesia in general and opioids in particular.

The current literature on analgesia for acute abdominal pain in children suffers from several limitations. First, the small sample size in many studies<sup>1,8,9</sup> limits researchers' power to detect true differences between groups. Another drawback of small sample size is the resultant difficulty of detecting rare adverse events associated with opioid administration, prohibiting the thorough evaluation of the drugs' relative safety in children. Furthermore, previous studies were conducted with children of diverse age groups and with abdominal pain that was defined in different ways, limiting researchers' ability to provide definite conclusions as to the beneficial effects of opioids.

#### **Analgesic effect of opioids**

We previously showed that acetaminophen and morphine were given more commonly to children with a

high probability of appendicitis<sup>2</sup>; this could be explained by the fact that these drugs can be administered via routes other than oral—acetaminophen can be given rectally, and morphine can be given parenterally, eliminating the need for fluid intake in children who might require general anesthesia and should not be given anything by mouth. However, one of the limitations of that study is the fact that the analgesic drug acetaminophen was given by nurses as an antipyretic, and it was impossible to determine whether analgesia would have been prescribed by the physician had this not been the case. In Kokki et al.'s<sup>9</sup> 2005 study, the placebo effect was significant as measured by the mean summed pain intensity difference (SPID), but buccal oxycodone provided significantly better analgesia than buccal saline. Pain was assessed using a visual analogue scale.<sup>12</sup> Analgesia was measured by SPID, which reflects the cumulative response to the intervention. The mean SPID was more significant in the oxycodone group than in the placebo group (mean difference 13 cm, with a 95 percent CI of 2 to 24 cm;  $p = 0.04$ ).<sup>9</sup>

Green and colleagues<sup>1</sup> examined whether treatment with narcotic analgesia would affect pain perception in children. A statistically and clinically significant difference in pain perception was detected in children receiving early narcotic analgesia. However, pain was not eliminated completely; the 2.2 cm change (out of 10) in the self-reported pain measure for the early-analgesia group was just beyond the threshold established for clinical significance. This change represents reduction of pain, not elimination of pain. Reducing but not fully eliminating pain through the use of early analgesia may provide a twofold benefit by decreasing the level of distress without altering diagnostic accuracy.<sup>1,10</sup>

### Safety of opioids for acute abdominal pain

Previous studies using various opioid analgesics for acute abdominal pain did not report any significant adverse events.<sup>1-5,7-10,13,14</sup> However, given their small sample sizes it is still difficult to determine the absolute safety of the practice. A multicenter trial with a very large sample size is required to truly evaluate the adverse outcomes in patients who receive opioid analgesia for abdominal pain. A significant body of evidence does exist on the unlikelihood of addiction following short-term treatment with morphine. In a study of more than 11,000 patients in Boston given narcotics during a hospital stay, only four developed an opioid dependence.<sup>15</sup>

Kim et al.<sup>8</sup> confirmed that morphine provides significant reduction of abdominal pain in children. The group reported a significant reduction in pain score, as well as in the number of areas of tenderness found on palpation and percussion. They used morphine because no other analgesic agent has proven to be clinically superior in

relieving pain. Morphine has also been the analgesic agent of choice for many clinical situations due to its well-published reliability, safety predictability, duration of action, and reasonable cost.<sup>16,17</sup>

### FUTURE DIRECTIONS

Other opioids should be considered in future studies. Fentanyl may be superior to morphine due to its shorter half-life, making it appropriate for short-term evaluation in the ED. However, beyond ED evaluation, fentanyl may not be ideal because of the need for frequent administration and its higher cost.<sup>18</sup>

Tramadol hydrochloride, a synthetic, centrally active analgesic that selectively activates  $\mu$  receptors, is another potential drug for the treatment of acute abdominal pain. Its effectiveness in controlling pain is similar to that of morphine, with a lower risk of adverse events.<sup>7</sup>

Oxycodone, a semisynthetic  $\mu$  receptor agonist derived from thebaine, has an analgesic effect similar to that of morphine in patients undergoing surgical procedures, and due to its ability to reduce the release of histamine it might generate less nausea and vomiting than morphine. It induces less sedation and may cause fewer neurological adverse events compared to morphine. Buccal administration of oxycodone has recently been shown to be effective in the treatment of persistent postoperative pain in children.<sup>9</sup>

### CONCLUSION

Opioid administration in children with acute abdominal pain induces analgesia without altering diagnostic accuracy. Current literature supports the need for a large-scale trial to further evaluate the safety of this approach and whether early analgesic treatment affects physicians' ability to diagnose acute abdominal pain. Guidelines for such trials should include assessing pain with valid pain scores, creating an effective response to the pain assessment, and administering appropriate analgesia for the pain scored.<sup>19</sup>

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