Analgesics In The Initial Management Of Acute Abdominal Pain

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Abstract

Introduction: Acute abdominal pain is one of the most common chief complaints of patients presenting to emergency departments. Historically, physicians have been reluctant to treat this pain with analgesics because of fear of obscuring physical findings, which were often critical to proper diagnosis and treatment.

Methods: Articles highlighting the role of analgesics in acute abdominal pain were reviewed, with particular emphasis on the practice of Oligoanalgesia (undertreating pain), effects of unrelieved pain, the beneficial or detrimental effects of analgesics, and methods of analgesic administration.

Results and conclusions: Studies indicate that unrelieved pain has serious adverse physiologic, psychologic and economic consequences. Providing immediate pain relief after stabilizing patients may not impact diagnostic ability or subsequent surgical decision-making capacity, and indeed may be beneficial in making a diagnosis. Many practical suggestions exist for how to best provide analgesia in abdominal pain. Given this evidence, appropriate and aggressive treatment resulting in prompt relief of acute abdominal pain is the desirable standard of care. A protocol to alert other involved physicians of analgesic administration is important.

INTRODUCTION

Acute abdominal pain is one of the most common chief patient complaints in emergency departments (ED), and constitutes 6.4% of the 100 million ED patient visits each year.[1,2] Twenty five percent of general surgical admissions present primarily with acute abdominal pain.[3] In 25 percent of patients presenting with pain to the ED as the chief complaint, the pain is abdominal.[4] In many acute care settings, analgesics are often withheld in patients with acute abdominal pain for fear that it may change physical examination findings, delaying diagnosis and treatment. The medical community's interest and understanding of pain is evolving and to many, it is now the fifth vital sign. Advances in the management of chronic pain and end-of-life issues have also focused attention on the adverse effects of unrelieved pain. The purpose of this paper is to explore the historical reasons for withholding analgesia, the drawbacks of this strategy, the evidence for a new paradigm and some practical tools to help in providing analgesia for acute abdominal pain.

METHODS

Search terms used to review the literature in the English language included “Oligoanalgesia”, “Analgesia in abdominal pain” and “Opioids in abdominal pain”. Other articles were identified using the bibliographies of publications found through the initial search. The literature chosen for more careful review was limited to publications, including clinical trials and case reports, which described the adverse effects of pain, outlined the role of analgesics in managing acute abdominal pain, addressed analgesic choice and administration, or highlighted the complications associated with its use.

DISCUSSION

HISTORY OF “OLIGOANALGESIA”

Wilson and Pendleton coined the word “oligoanalgesia,” to represent the failure to recognize or properly treat pain.[5] Sir. Zachary Cope, one of the doyens of surgery, in his book Early Diagnosis of the Acute Abdomen suggested that “Though it may appear cruel, it is really kind to withhold

morphine until one is certain or not that surgical interference is necessary, i.e. until a reasonable diagnosis has been made."[6] This sentiment has pervaded medical practice until recent times. Historically, and to some extent today, abdominal pain is a clinical diagnosis; a definite cause is often obscure in over 40 percent of cases.[7] Analgesics were thought to hinder the ability to reach a diagnosis, leading to large numbers of negative work-ups and unnecessary surgeries. Withholding analgesics was thought to minimize the increased burden on patient and hospital resources, resulting from delay in diagnosis and inappropriate treatment. As recently as 1996, a majority of surgeons considered that analgesics interfered with patient's signing a valid informed consent and impacted diagnostic accuracy, thus influencing their decision to withhold pain relief.[8]

The attitudes regarding treatment of pain are shifting, nevertheless slowly. A prospective study of 100 emergency admissions for acute abdominal pain by Tait et al showed that most of the trained surgical staff (88%) favored early administration of analgesia in the ED and a majority (79%) would administer analgesia in the absence of a firm diagnosis.[9] The Tait study, however, also showed that the mean "door to analgesia" time in the ED was 2.3 hours for patients with severe pain and 6.3 hours for moderate pain, even though all patients were assessed almost immediately (within 20 minutes) by a trainee physician. Nearly half of the patients in the study were transferred to the floor without analgesia having been given (mean wait 5.7 hours).[9] Clinical diagnosis did not influence the speed or urgency with which patients received analgesia. In the study, almost half the surgical trainees believed that analgesics would mask the diagnostic features and delay appropriate management. This discrepancy between the opinions of the surgeons and the trainees explained the discordance between surgical staff sentiment and actual practice.[9]

ADVERSE EFFECTS OF UNREQUITED ACUTE PAIN

Pain is a fundamentally noxious sensation. Unrelieved acute pain has adverse physical, psychological and economic consequences. It causes voluntary or involuntary splinting of respiratory muscles resulting in pooling of secretions, promoting the development of pneumonia, atelectasis, and ventilation-perfusion abnormalities. Increased serum levels of neuroendocrine hormones cause hyperalgesia, promote glycogenolysis, oxidation of free fatty acids, protein catabolism, sodium and water retention and kaliuresis (causing hypertension, tachycardia and aggravating congestive heart failure), and modify coagulation and fibrinolytic activity.[10,11] Pain and anxiety also cause anorexia, insomnia, depression and feelings of hopelessness and helplessness. This combination of pain and emotional stress is termed suffering. Perception of pain by the patient may be higher if subjected to the same noxious stimulus the second time around.[12] Unrelieved pain results in longer hospital stays, increased rate of re-hospitalization, increased outpatient visits and decreased level of function, leading to loss of income and insurance coverage.[13]

THE EVIDENCE FOR ANALGESIA (TABLE 1)

Evidence from multiple studies suggests that analgesic administration does not hinder accurate diagnosis and treatment, and that it may even be helpful (Table 1).

Figure 1

Table 1: Controlled trials of analgesia in acute abdominal pain

Study	Study Type	Patient number	Level of evidence	Intervention	Result
Attard et al 1992	Prospective, randomized placebo-controlled trial	100	1b	IM Papaveratum	Significant pain improvement. Reduction in tenderness thought to facilitate diagnosis. No diagnostic impact
Mahadevan and Graff 2000	Prospective, randomized placebo-controlled trial	68	1b	Tramadol IM	Significant levels of pain reduction without concurrent normalization of abdominal examination findings
Pace and Burke 1996	Prospective, randomized, double-blind, placebo-controlled	75	1b	IV morphine vs. Normal saline	Effective pain relief with morphine. No difference in diagnostic accuracy, management errors
Kim et al 2002 (children)	Prospective, randomized, double-blind, placebo-controlled	60	1b	IV Morphine vs. Normal saline	Significant pain reduction No change in objective examination No impact on diagnostic ability, no complications
LoVecchio et al 1997	Prospective, randomized placebo-controlled.	48	1b	IV morphine vs. placebo	Significant subjective and objective improvement of pain following morphine Change in physical findings did not cause adverse events or delays in diagnosis
Vermeulen et al 1999	Prospective randomized, double-blind placebo-controlled	340	1b	IV morphine vs. placebo	Significant pain reduction with morphine. No improvement in the diagnostic performance of ultrasound. Did not result in delayed or missed diagnosis of appendicitis and did not influence the rate of unnecessary laparotomy
Wolfe et al 2004	Prospective randomized, double-blind cross-over	34	1b	IV morphine vs. placebo in patients scheduled for appendectomy	Significant pain reduction. No change in physical findings.
Thomas Silen 2003	Review of 8 randomized controlled trials	> 600	2a	Various analgesics administered in acute abdominal pain	Reduction in pain after analgesics without significant side effects, including respiratory depression or cardiovascular compromise. No compromise in diagnostic end-points, operative decision making, and no untoward outcomes post-analgesic administration.

Levels of evidence- as per the Center for Evidence-based Medicine (http://www.cebm.net/levels_of_evidence.asp)

Wolfe and associates examined the current practice patterns of administering analgesics for acute abdominal pain among ED physicians. Of those who responded 85 percent felt that opiate pain medication did not change important clinical findings.[14] However, the same number of respondents chose to administer the analgesic only after surgical evaluation was completed.

Prospective, double-blind, placebo-controlled studies, conducted to determine whether morphine administration affected evaluation or outcome in adult patients with undifferentiated acute abdominal pain, showed that morphine administration did not impact diagnostic ability, and relieved pain without altering the ability of physicians to accurately evaluate and treat patients (LOE- 1b).[15,16,17]

Wolfe et al showed that patients with features suggesting appendicitis experienced significant pain relief after morphine administration without changes on examination findings.[18] A similar clinical trial in children showed that intravenous morphine provided significant pain reduction without adversely affecting examination findings, or the ability to identify children requiring surgery.[19] (LOE-1b)

Thomas and Silen, in their detailed review of the trials addressing analgesia for patients with undifferentiated acute abdominal pain, concluded that in no study was there any association between analgesia and diagnostic impairment, or dangerous masking of physical examination findings. Judicious provision of analgesia appeared safe, reasonable and in the best interests of patients in pain.[20] (LOE- 2a) Analgesic administration probably facilitates diagnosis by enhancing the cooperation offered by a pain-free patient.[21] (LOE- 1b)

LoVecchio et al found that administration of morphine changed examination findings, without causing any adverse events or delays in diagnosis attributed to its administration, and seemed to improve the appropriateness of surgical decision-making in females, though not in males.[22] (LOE-1b) Analgesia did not improve the accuracy of ultrasound (US) in diagnosing acute abdominal pathology.[23]

Lee et al, in a prospective observational study did show, on logistic regression, that receiving opioids was associated with an adverse outcome, but the authors emphasized that the study's design precluded a conclusive causal link, and did not recommend a change in clinical practice.[24] (LOE- 2c) A recent literature review on the subject by Nissman et al suggests design flaws (absence of equivalence trials and not using patient outcomes as the primary endpoint) in the studies supporting analgesic administration in abdominal pain.[25] The authors suggest that blunting of subjective and objective findings caused by analgesic administration may be dangerous, and encourage a more judicious use of analgesics in undiagnosed abdominal pain, in the setting of an existing protocol of close communication with the responsible surgeon.

PRINCIPLES OF PAIN ASSESSMENT AND CAUSES OF UNDER-TREATMENT OF ACUTE PAIN

The patient's self-report is the most reliable indicator of the presence and intensity of pain. Physicians should trust patient's subjective reports of pain unless there is evidence to the contrary. Age, sex, ethnicity, and cognitive functioning of the patient influence the assessment and treatment of pain.[26,27,28,29,30,31,32] Children, the elderly, the cognitively impaired, and those with communication problems are often more difficult to assess and require special attention to ensure adequacy of analgesia. Pain assessment tools (eg. A visual analog scale) should be available in the ED and should be utilized appropriately. The degree of pain, the suspected underlying pathology, pain response to titration of the drug, and side effects should determine the analgesic, dosing and frequency of use. The principles of the “analgesic ladder” (non-opioid analgesics for mild to moderate pain, oral opioids- oxycodone for moderate to severe pain and parenteral opioids for severe pain), may be used to guide the choice of the analgesic.[33] Some barriers to effective pain management include reluctance on the part of patients to report pain or use analgesics, state and federal policies regarding the use of opioid analgesics, limited provider knowledge about pain assessment and treatment, and underuse of analgesics because of provider misconceptions regarding addiction.[34,35,36] Under-treatment may also arise from failure to inquire about pain, discrediting reports of pain (pain judged to be less than reported), and educational or psychological barriers on the part of the physician.[37,38,39,40]

Pseudoaddiction (inadequate pain management producing the manipulative behavior on the part of the patient) may be much more common than addiction. A retrospective review of over 12,000 hospitalized patients given opioids for pain relief identified only four who were potential addicts.[41] Alcohol abuse or drug addiction does not interfere with a patient's ability to identify painful stimuli and should not bar providing adequate pain relief; these patients may benefit from carefully supervised, judicious use of analgesics. Tolerance may also dictate a greater frequency in analgesic use, though true pharmacological tolerance requiring escalating analgesic doses is uncommon.[42]

POINTERS FOR ANALGESIA IN ACUTE ABDOMINAL PAIN

INITIAL ASSESSMENT

Patients with severe pain should be triaged as a priority, ensuring rapid pain control with reduced “door-to-analgesia” time. The Canadian Association of Emergency Physicians has developed a National Triage and Acuity Scale that incorporates a pain scale into its grading of triage level.[43] Initial pain assessment should also be used as a guide to help select type and route of medication.

In administering analgesics prior to the disposition of

patients with acute abdominal pathology, the ABCs of resuscitation should not be ignored as analgesics have the potential to cause both cardiovascular and respiratory depression. The patient's airway, oxygenation and circulation must be deemed stable before pain management. Hemodynamic instability may ensue with the use of injudicious doses of analgesics (blocks life-saving pain-induced sympathetic response), until resuscitation with adequate intra-vascular volume replacement occurs.[44]

MEASURES/INTERVENTIONS AGGRAVATING PAIN

Initial emergent treatment modalities such as nasogastric (NG) tube insertion and bladder catheterization can significantly increase patient discomfort.[45,46] Diagnostic techniques (US, abdominal CT, arteriography) may be time-consuming (use of oral contrast requires several hours to transit the gut), and may involve abdominal compression.[47] Hence there may be a need to offer continued pain relief to offset these interventions.

EFFECTIVE TREATMENT OPTIONS

Nonsteroidals (NSAIDs) are especially useful in patients with renal or ureteric colic. The pain of ureteral colic arises from sudden increases in ureteral smooth muscle tension caused by enhanced intraluminal pressure. This action, directly mediated by prostaglandins, can be prevented or aborted by NSAIDs (Ketorolac IM or IV every 6- to 8-hours- Table 2).[48,49] Care must be taken and the dose of Ketorolac reduced in patients over 65 years of age, weighing less than 50 kg, and in those with even moderately elevated serum creatinine levels. In addition, Ketorolac may cause bleeding, particularly when administered at higher dosages, in older patients, or for more than five days.[50]Indocin 100 mg. as a suppository aborts the pain of renal colic in 30 minutes. It can be combined with initial morphine administration for immediate and continued pain relief.[47] In patients with significant potential for renal compromise, clotting abnormalities, or stress ulcer formation, the use of NSAIDs should probably be deferred.

Figure 2

Table 2: Analgesics in acute abdominal pain

Drug	Loading Dose	IV-PCA Bolus Dose	IV-PCA Lockout interval (min)
Morphine	1 - 2 mg q 10 min up to 0.2 mg/kg IV	0.5-3.0 mg	5-20
Meperidine	25 - 50 mg q 10 min up to 3 mg/kg IV	5-15 mg	5-15
Fentanyl	25 - 50 mug q 5 min up to 8 mug/kg IV	15-75 ug	5-10
Hydromorphone	0.5 - 1 mg q 10 min up to 0.08 mg/kg IV	0.1-0.5 mg	5-10
Oxymorphone	1-1.5 mg SQ, IM q 4-6 hours 0.5 mg IV- titrate to effect	0.2-0.8 mg	5-15
Papaveratum	7.7-15.4 mg q 4 hours IV, IM or SQ. Child ~1 month 115 micrograms/kg, 1–12 months-154 micrograms/kg, 1–5 years- 1.93–3.85 mg. 6–12 years, 3.85–7.7 mg.		
Buprenorphine	200-400 ug sublingual or IV	30-200 ug	10-20
Ketorolac	15-30 mg IV/IM q 6 hours		

Figure 3

Strength of Recommendations

Key Clinical Recommendations	Label	References
Untreated acute pain results in longer hospitalization, increased rate of re-hospitalization, increased doctor visits, decreased function, lost income and insurance coverage.	C	13
Opioids may be administered in acute abdominal pain in adults and children with good pain relief, without diminishing diagnostic ability, or the ability of physicians to accurately evaluate and treat patients.	A	15-19
Diagnostic techniques (imaging studies, paracentesis) and outpatient procedures (nasogastric tube insertion, bladder catheterization) can significantly increase patient discomfort. Analgesia should be maintained to offset this.	B,C	45-47
Morphine may be safely administered in suspected cholecystitis or pancreatitis without fear of worsening the pathology	B	62-64

Strength of Recommendation as per SORT- Am Fam Physician (www.aafp.org/afp/x13554.xml)

Almost all opioids (especially morphine) can be given intravenously. A loading dose is titrated to desired analgesic effect and should remain the standard of care for severe acute pain. Nursing protocols can be established that allow for this titration without requiring repeated physician contact.[51] Hemodynamic instability, age, other medications, mental status concerns, and previous exposure to opioids, all affect dosing. In stable patients who can be adequately monitored, intravenous patient-controlled-analgesia (IV-PCA) is an option that presents a desirable alternative with numerous advantages.[52] These include stable blood drug levels with good analgesia and less sedation, less opioid consumption, increased patient satisfaction, and improved pulmonary function when compared with nurse-administered analgesics. Use of a basal infusion (adjusted every 8-24-hours), minimizes the patient's need to request a bolus dose. Barriers to using PCA include lack of availability in

emergency settings, staff unfamiliarity with the equipment, inexperience with dosing regimens and resistance to embracing new practices.[53]

Buprenorphine is an opioid partial agonist producing less euphoria and respiratory depression than other agonists, and especially beneficial in children providing safe, rapid and long-acting analgesia. Sublingual buprenorphine 200-400 mcg (bio-availability 55%; 400 µg sublingually is equivalent to 250 µg given parenterally) provides good pain relief.[54,55,56]

SUB-OPTIMAL ANALGESIC OPTIONS

Meperidine (Demerol) has a short half-life and requires frequent dosing to maintain adequate serum levels. Its use has been discouraged because repeated dosing leads to the accumulation of the metabolite normeperidine that causes neuromuscular irritation and seizures.

Intra-muscular or subcutaneous routes offer erratic absorption and do not allow accurate opioid titration.[57] There is no evidence to support that they are any safer. Onset of action is approximately the same as with oral administration. If patients cannot tolerate oral medications or if the pain is severe, they probably require intravenous dosing and titration. Acute abdominal pathology is frequently associated with gastric stasis, nausea and/or vomiting. These associated problems and the need for immediate pain relief mean that the oral route is unacceptable. One study, however, found that intra-muscular injection of up to 20 mg papaveretum to be both safe and effective when administered early to patients presenting with acute abdominal pain.[20] Trans-dermal administration of analgesics is not indicated for acute pain relief. Opioids can be delivered successfully by suppository but it is not ideal for immediate relief of acute pain because of the slow and sometimes erratic absorption. Rectal doses for most strong opioids are about half those needed by the oral route.[58]

SIDE EFFECTS OF ANALGESIC ADMINISTRATION AND MANAGEMENT

Sedation caused by analgesics may interfere with diagnostic evaluation related to central nervous system function. In order to treat pain, while at the same time maintaining physiological stability, the administration of small, but frequently repeated doses, titrated to the desired analgesic and physiological effect, is the primary treatment option.[44]

Parenteral opioids can cause hypotension in several ways: direct vascular dilatation, decreasing sympathetic outflow, and by blunting postural cardiovascular reflexes with consequent reduced venous return.[44] Opioids inhibit gastrointestinal motility, causing ileus and delayed enteral nutritional support. They also produce nausea and sedation, and may blur mental status evaluation. Opioid-induced emesis related to short-lived histamine release or gastroparesis, occurs in approximately 20 percent of patients.[59] Acting at brainstem sites, opioids decrease minute ventilation, sometimes leading to hypoxemia and excessive carbon dioxide retention.

Antihistamines or Ondansetron (Zofran) usually reverse opioid-associated emesis.[60] Persistent emesis caused by gastroparesis associated with abdominal pathology may be controlled with a gastric pro-motility agent (metoclopramide). Routine prophylaxis with metoclopramide should however, be avoided in patients receiving parenteral morphine or meperidine, because of a high incidence of side effects.[61] Phenothiazines (prochlorperazine, trimethobenzamide, and promethazine), through dopamine antagonism, also control gastroparesis, but associated sedation and extra-pyramidal side effects dictate that they should probably be used only when other measures fail.

CONVENTIONAL WISDOM REGARDING CHOICE OF ANALGESIC IN GALL BLADDER DISEASE/PANCREATITIS.

Although human studies show that morphine increases sphincter of Oddi pressure, clinical evidence does not link morphine with increased risk over other opioids in causing or aggravating pancreatitis or cholecystitis.[62] In a study comparing equianalgesic doses of morphine and meperidine in 40 patients undergoing cholecystectomy, meperidine raised the common bile duct pressure 14 percent more than morphine.[63,64]

CONCLUSION

It is well established that “oligoanalgesia” leads to unnecessary and adverse consequences. The reluctance to provide adequate pain relief in acute abdominal pain originated in an era of relative medical underdevelopment, when the abdomen was still considered a “Pandora's Box”. The availability of computerized patient monitoring, recent advances in patient imaging techniques and the increasing recognition that continued observation will minimize unnecessary surgical intervention, has resulted in a greater readiness on the part of first responders to provide adequate pain relief. Multiple studies have shown that analgesic administration in stable patients with abdominal pain is safe,

and has minimal impact on either diagnostic ability or surgical decision-making. It is probably best done with the knowledge and approval of subsequent treating physicians to minimize any potential misdiagnosis or mismanagement, though this creates a potential for delaying pain relief. Assessment and resuscitation steps such as urinary catheterization, insertion of naso-gastric tubes, imaging and venous access can all cause or aggravate pain, and steps should be taken to minimize this.

This article has explained the historical reluctance to treat pain, the adverse effects of this pain, the evidence favoring analgesic administration and some practical suggestions for providing pain relief. Hopefully this perspective on the treatment of acute abdominal pain will aid physicians in safely minimizing patient suffering.

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