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The impact of intravenous acetaminophen on pain after abdominal surgery on pain: a meta-analysis

Jacqueline J. Blank, MD,[a] *Nicholas G. Berger, MD,*[a] *Justin P. Dux, MD,*[a] *Fadwa Ali, MD,*[a] *Kirk A. Ludwig, MD,*[b] *and Carrie Y. Peterson, MD, MS*[b,*]

[a] *Department of Surgery, Medical College of Wisconsin, Milwaukee, Wisconsin*
[b] *Division of Colorectal Surgery, Medical College of Wisconsin, Milwaukee, Wisconsin*

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ABSTRACT

Background: Pain after surgery is commonly controlled with opioid pain medications. A multi-modal pain strategy that involves acetaminophen may help minimize the negative consequences of opioids, such as ileus, respiratory depression, and addictive potential. There are limited data on the effectiveness of intravenous (IV) acetaminophen in comparison with other nonopioid pain medications.

Materials and methods: Four databases were queried for the keywords "acetaminophen," "intravenous," and "postoperative". Prospective studies of adult patients receiving at least 24 h of IV acetaminophen after intraabdominal surgery were analyzed for 12- and 24-h pain scores and 24-h narcotic consumption. A random effects model was performed using mean differences and 95% confidence intervals to assess the effect of IV acetaminophen on outcomes. Heterogeneity was assessed using χ^2 and the I^2 statistics.

Results: Seventeen articles were identified that complied with inclusion and exclusion criteria. There was no significant difference in 24-h pain scores between IV acetaminophen and any other comparator, or in secondary endpoints of 12-h pain scores and 24-h narcotic consumption. Subgroup analysis demonstrated significant benefit for IV acetaminophen in open surgeries for decreased 24-h narcotic consumption. When analyzing individual medications, non-steroidal anti-inflammatory drugs demonstrated the largest reduction in 24-h narcotic consumption. Data were of moderate quality and demonstrated significant heterogeneity between studies.

Conclusions: The lack of significant differences in primary endpoints may be explained by the heterogeneous, moderate-quality data. However, subgroup analyses suggested IV acetaminophen may be advantageous in open surgeries, and non-steroidal anti-inflammatory drugs may lower the 24-h narcotic requirement.

* *Corresponding author*. Division of Colorectal Surgery, Department of Surgery, Medical College of Wisconsin, 9200 W Wisconsin Avenue, Milwaukee, WI 53226. Tel.: +1 414 805 5783; fax: +1 414 805 8115.
E-mail address: cypeterson@mcw.edu (C.Y. Peterson).

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Introduction

Opioid pain medications are typically the cornerstone of pain management after surgery, with various modifications depending on a patient's age, comorbidities, and surgical procedure. However, opioids are known to have multiple negative effects, including ileus, decreased respiratory drive, and addictive potential. Acetaminophen is a viable alternative to opioids for use in postoperative pain control due to its benign side-effect profile, ease of administration, limited allergic reactions, and excellent efficacy. Currently, intravenous (IV) acetaminophen is approved by the U.S. Food and Drug Administration for postoperative analgesia; however, its cost is higher than other medications, specifically oral acetaminophen. The efficacy of IV acetaminophen, as opposed to other nonopioids, has not been well-studied for intraabdominal surgery.

For patients requiring abdominal surgery, some level of postoperative bowel dysfunction following surgery is expected. In one study by Gelpi *et al.*,[1] oral acetaminophen was given to both laparoscopic and open colectomy patients in the immediate postoperative period and serum levels were measured at 24 and 48 h. Both groups showed significantly reduced absorption of acetaminophen at all time-points in comparison to nonopioid controls, suggesting that intestinal dysfunction is present even in an ideal setting and supporting the use of parenteral medications whose absorption and distribution is easily predictable.[1] Intravenous acetaminophen is also preferable to its oral and rectal counterparts due to its pharmacokinetics. The IV formulation has been shown to reach higher peak central nervous system concentrations and reaches these concentrations more quickly than oral or rectal formulations.[2,3]

In addition to surgical manipulation of the bowel and the physiologic stress response to surgery, mu-opioid receptor activation by opioid pain medications in the small and large intestine also decreases gastrointestinal (GI) motility. Postoperative ileus, a disruption in normal intestinal peristalsis, can result in longer hospital stays, increased incidence of complications, and decreased patient satisfaction.[4] Minimizing these consequences through optimal medication management can improve patient outcomes, satisfaction, and health-care costs.

In addition, the current opioid epidemic in the United States emphasizes the importance of nonopioid analgesia after surgery. In 2014, 1.9 million Americans had a substance abuse disorder involving prescription pain relievers, with nearly 19,000 deaths related to overdoses of these drugs.[5,6] In the past decade, prescriptions of opioid pain medications in the United States have increased dramatically.[7] Prescription pain medication use may lead to addiction to more dangerous substances: according to the American Society of Addiction Medicine, four of five new heroin users were initially misusing prescription painkillers.[8]

IV acetaminophen has incredible potential as part of a multi-modal pain strategy after surgery. Benefits include improved analgesia and decreased opioid use, the latter of which could significantly improve postoperative complications, accelerate intestinal recovery from surgery, and shorten hospital stays. It also has a favorable side-effect profile with a very low risk of adverse events, making it ideal for use in many patients. Its routine use for postoperative pain control may also help alleviate the nationwide opioid crisis and improve the overall societal impact of narcotic medications. Unfortunately, the data comparing IV acetaminophen to other alternatives are limited and incredibly heterogeneous. A focused, directed investigation into the existing literature to understand the potential impact and benefit is warranted. The results could help guide clinicians when making choices about postoperative pain regimens for their patients.

The aim of the present study was to evaluate the efficacy of IV acetaminophen compared with other nonopioid analgesics for postoperative pain control using meta-analysis techniques. We hypothesized that IV acetaminophen would be more effective than other nonopioid counterparts for pain control after abdominal surgery leading to improved pain scores and decreased narcotic use. We also hypothesized that such benefits could translate into early return of bowel function and reduced hospital stays.

Methods

Literature search and study selection

PRISMA guidelines were followed in the conduct of the systematic review and meta-analysis.[9] As this was non-human subject research, IRB approval was not indicated. A query of PubMed, Scopus, Cochrane Reviews and Trials, and Google Scholar databases was performed using the following keywords: acetaminophen (apap, acamol, acephen, acetaco, acetamidophenol, acetaminophen, acetaminophen, algotropyl, anacin 3, anacin-3, anacin3, datril, hydroxyacetanilide, "n-4-hydroxyphenyl acetanilide," n-acetyl-p-aminophenol, panadol, paracetamol, Tylenol, p-acetamidophenol, or p-hydroxyacetanilide), intravenous (intravenous, iv, intra-venous, infusion*, or inject*), postoperative (postoperativ*, post-operativ*, "post operativ*," "post op," "post-op," postop, postoperative, surgical*, surger*, or surgery). In addition, gray literature sources were queried with similar keywords and the references of the included studies were hand searched to identify other relevant articles.

Inclusion and exclusion criteria

Studies that met the following criteria were included for analysis: prospective comparison study with at least two arms (either cohort or randomized), use of intravenous acetaminophen or paracetamol in one study arm for at least 24 h or three doses during the postoperative period, comparison group receiving an alternative medication or placebo, adult patients undergoing a trans-abdominal surgery, and reporting of pain outcomes at 24 h after surgery.

Studies were excluded if one or both arms were retrospective or historical patients, if there was no comparison group, if patients had non-abdominal surgery (including retroperitoneal surgeries or extra-peritoneal dissections only), or if pediatric patients were included. In addition, studies with missing pain data at 24 h were excluded along with those studies that were published in languages other than English and could not be translated freely. Studies were screened first by title, then abstract, followed by full-article review to determine eligibility.