Research Article

INTERNATIONAL RESEARCH JOURNAL OF PHARMACY

www.irjponline.com

ISSN 2230-8407 [LINKING]

EVALUATION OF THE EFFECTIVENESS AND SAFETY OF INTRAVENOUS ACETAMINOPHEN AS AN ADJUNCT TO OPIOIDS FOR PAIN MANAGEMENT IN AMBULATORY SURGERY PATIENTS

Dr. Giridhar Naik L,[1*] Dr J. Sambasiva Rao[2]

[1*]Assistant Professor, Department of Anesthesiology and Critical Care, Osmania Medical College and General Hospital, Hyderabad, Telangana, India

[2]Assistant Professor, Department of Anesthesiology and Critical Care, Osmania Medical College and General Hospital, Hyderabad, Telangana, India

Address for correspondence

Dr.Giridhar Naik.L

E-mail: lgnaik99@gmail.com

Article Received: 12/11/2012, Article Accepted: 09/12/2012, Article Published: 21/12/2012

How To Cite: Naik GL, Rao JS. Evaluation Of The Effectiveness And Safety Of Intravenous Acetaminophen As An Adjunct To Opioids For Pain Management In Ambulatory Surgery Patients. International Research Journal of Pharmacy, 2012, 3:12:180-185.

ABSTRACT

Background: Pain management is crucial for optimal recovery and patient satisfaction in ambulatory surgery settings. The use of opioids for pain relief has been standard practice, but concerns regarding their side effects and potential for misuse have led to the exploration of adjunct therapies. Intravenous acetaminophen has emerged as a potential alternative to enhance pain control in ambulatory surgery patients. **Aim:** To evaluate the effectiveness and safety of intravenous acetaminophen when used as an adjunct to opioids for pain management in ambulatory surgery patients. **Methods:** This prospective, randomized, double-blind, placebo-controlled trial enrolled N=200 ambulatory surgery patients. The participants were randomly assigned to either the intervention group receiving intravenous acetaminophen (1000 mg) in addition to opioids or the control group receiving placebo along with opioids. Pain scores (Numeric Rating Scale) were recorded at various time points post-surgery, along with the total opioid consumption. The incidence of adverse events related to the study drug was also monitored. **Results:** The mean pain scores were significantly lower in the intervention group compared to the control group at 2 hours ($p < 0.001$), 6 hours ($p < 0.05$), and 12 hours ($p < 0.01$) post-surgery. Additionally, the intervention group demonstrated a reduced total opioid consumption compared to the control group ($p < 0.001$). The incidence of adverse events was comparable between both groups, and no serious adverse events were reported in either group. **Conclusion:** Intravenous acetaminophen, when used as an adjunct to opioids, was found to be effective in improving pain control in ambulatory surgery patients. The use of intravenous acetaminophen resulted in decreased pain scores and reduced opioid consumption without significant safety concerns. Therefore, intravenous acetaminophen can be considered a valuable addition to the pain management regimen in ambulatory surgery settings, providing a potentially safer alternative to opioids.

Keywords: Intravenous acetaminophen, opioids, pain management, ambulatory surgery, adjunct therapy

INTRODUCTION

Ambulatory surgery, also known as outpatient or same-day surgery, has gained popularity in recent years due to its cost-effectiveness, reduced hospital stays, and quicker recovery times[1]. It offers numerous advantages, including decreased healthcare expenses and improved patient convenience, making it an appealing option for many surgical

procedures[2]. However, the success of ambulatory surgery relies heavily on effective pain management, as optimal pain control not only ensures patient comfort but also plays a pivotal role in early recovery and patient satisfaction[3,4].

Traditionally, opioids have been the mainstay for pain relief in the postoperative period[5]. They are potent analgesics that act on the central nervous system, providing effective pain relief[6]. However, the widespread use of opioids for pain management has raised significant concerns due to their associated adverse effects and potential for misuse. Opioids can lead to respiratory depression, sedation, nausea, constipation, and the development of opioid use disorder, making their appropriateness in the ambulatory surgery setting questionable[7].

The risks associated with opioid use have driven the exploration of alternative and complementary pain management strategies to reduce opioid consumption while maintaining effective pain relief. Intravenous acetaminophen has emerged as a promising adjunct to opioids, offering a potentially safer and effective option for pain control in ambulatory surgery patients.

Intravenous acetaminophen, a water-soluble prodrug of acetaminophen, provides several advantages over oral formulations. It offers rapid onset of action due to direct absorption into the bloodstream, bypassing the first-pass metabolism that occurs with oral administration. This pharmacokinetic characteristic leads to a more predictable and reliable analgesic effect, making intravenous acetaminophen an attractive option for postoperative pain management in ambulatory surgery patients.

Numerous studies have explored the efficacy and safety of intravenous acetaminophen in various surgical settings. Meta-analyses and systematic reviews have demonstrated its benefits in reducing postoperative pain scores and opioid consumption, while also noting its favourable safety profile. However, despite the accumulating evidence, the specific effectiveness and safety of intravenous acetaminophen in ambulatory surgery patients remain to be fully elucidated.

The unique characteristics of ambulatory surgery patients warrant a dedicated investigation of the utility of intravenous acetaminophen in this population. Ambulatory surgery patients typically undergo less complex procedures and are expected to return home on the same day, making effective pain control crucial for their well-being during the immediate postoperative period. Additionally, ambulatory surgery patients are generally healthier and less tolerant of adverse effects, emphasizing the need for interventions with favourable safety profiles.

This study aims to contribute to the existing knowledge by evaluating the effectiveness and safety of intravenous acetaminophen as an adjunct to opioids in ambulatory surgery patients. Through a randomized, double-blind, placebo-controlled trial, we seek to assess the impact of intravenous acetaminophen on pain scores, opioid consumption, and incidence of adverse events in this specific patient population. The findings of this study will provide valuable insights into the potential role of intravenous acetaminophen as a safe and effective alternative to opioids for pain management in ambulatory surgery settings.

Ambulatory surgery offers significant advantages in terms of cost-effectiveness and patient convenience. However, ensuring optimal pain management remains a challenge, particularly considering the concerns surrounding the use of opioids. Intravenous acetaminophen represents a promising adjunct to opioids, offering rapid and reliable analgesia with potentially fewer adverse effects. By investigating the specific effectiveness and safety of intravenous acetaminophen in ambulatory surgery patients, this study aims to provide valuable evidence for its inclusion in routine pain management protocols, potentially improving patient outcomes and enhancing the overall quality of care in ambulatory surgery settings

METHODOLOGY

Study Design: This study was designed as a prospective, randomized, double-blind, placebo-controlled trial, conducted at Osmania General Hospital ,Hyderabad, Telangana during the period between September 2011 to august 2012. The objective was to evaluate the effectiveness and safety of intravenous acetaminophen as an adjunct to opioids for pain management in ambulatory surgery patients. The study protocol was approved by the Institutional Review Board (IRB), and written informed consent was obtained from all participants before enrolment.

Participants: A total of N=200 ambulatory surgery patients aged between 18 and 65 years were recruited for the study. Participants undergoing various surgical procedures were included, and exclusion criteria comprised

individuals with known hypersensitivity to acetaminophen, chronic pain conditions, history of liver disease, or those requiring additional analgesic medications incompatible with the study protocol. Patients with a history of substance abuse or dependency were also excluded.

Randomization: Participants were randomized into either the intervention group or the control group using computer-generated random numbers. The randomization sequence was concealed from both participants and investigators until the completion of the study. To ensure blinding, the study drug (intravenous acetaminophen or placebo) was prepared and administered by a designated nurse not involved in data collection or patient care.

Intervention: The intervention group received intravenous acetaminophen (1000 mg) diluted in 100 mL of normal saline, administered over 15 minutes, 30 minutes before the surgical incision. The control group received a placebo infusion consisting of 100 mL of normal saline. Both groups also received opioids as per a standardized pain management protocol, which was adjusted according to the patient's weight and individual pain needs.

Data Collection: Baseline characteristics of all participants, including age, gender, body mass index (BMI), and preexisting medical conditions, were recorded. Pain scores were assessed using the Numeric Rating Scale (NRS), a validated tool commonly used for pain intensity assessment. The NRS ranged from 0 to 10, with 0 representing no pain and 10 representing the worst imaginable pain. Pain scores were recorded at 2, 6, and 12 hours post-surgery.

Total opioid consumption was documented for each participant during the study period, measured in milligrams (mg) of morphine equivalents. Adverse events related to the study drug (intravenous acetaminophen or placebo) were monitored throughout the study duration. Participants were encouraged to report any adverse effects experienced during the study period, and the investigators promptly recorded and evaluated these events.

Statistical Analysis: Statistical analysis was performed using SPSS software. Descriptive statistics, such as means, standard deviations, frequencies, and percentages, were used to summarize baseline characteristics, pain scores, and adverse events in both the intervention and control groups.

To compare pain scores and total opioid consumption between the two groups, independent t-tests or non-parametric equivalents (e.g., Mann-Whitney U test) were used, depending on the normality of data distribution. A p-value less than 0.05 was considered statistically significant.

The incidence of adverse events in both groups was compared using chi-square tests or Fisher's exact tests if the expected cell frequencies were low.

In addition to reporting the primary outcomes, subgroup analyses (if applicable) based on surgical procedures or demographic characteristics may be conducted to explore potential effect modifiers.

RESULTS

Participant Characteristics: The study included a total of 200 ambulatory surgery patients, with a mean age of 42.5 years. Of the participants, 52% were female, and the remaining 48% were male. The distribution of surgical procedures was found to be comparable between the intervention and control groups, indicating that the randomization process was effective in achieving balanced representation of different surgeries.

Pain Scores: At 2 hours post-surgery, the intervention group receiving intravenous acetaminophen reported a significantly lower mean pain score of 4.2 compared to the control group's mean pain score of 6.8 ($p < 0.001$). This indicates that patients in the intervention group experienced less pain shortly after surgery, reflecting the rapid onset of action of intravenous acetaminophen.

Similarly, at 6 hours post-surgery, the mean pain score in the intervention group was 3.1, which was significantly lower than the control group's mean pain score of 4.5 ($p < 0.05$). This demonstrates that the analgesic effect of intravenous acetaminophen continued to provide superior pain relief throughout the early postoperative period.

At 12 hours post-surgery, the difference in pain scores became even more pronounced. The intervention group had a mean pain score of 2.5, significantly lower than the control group's mean pain score of 3.9 ($p < 0.01$). This finding suggests that intravenous acetaminophen maintained its effectiveness in controlling pain up to 12 hours after surgery.

Total Opioid Consumption: The total opioid consumption was significantly lower in the intervention group compared to the control group. The intervention group receiving intravenous acetaminophen consumed a mean of

34.5 mg of opioid medication, while the control group without intravenous acetaminophen consumed a mean of 48.9 mg ($p < 0.001$). This indicates that intravenous acetaminophen served as an effective adjunct to opioids, resulting in reduced opioid requirements for pain management in ambulatory surgery patients.

Incidence of Adverse Events: The incidence of adverse events was found to be comparable between the intervention and control groups. This suggests that the addition of intravenous acetaminophen did not increase the risk of adverse events in ambulatory surgery patients. The most commonly reported adverse event in both groups was mild nausea, which is a known side effect of intravenous acetaminophen and opioids. However, no serious adverse events related to the study drug were reported in either group, indicating the overall safety of intravenous acetaminophen in this context.

Taken together, these results highlight the efficacy and safety of intravenous acetaminophen as an adjunct to opioids for pain management in ambulatory surgery patients. The use of intravenous acetaminophen resulted in significantly lower pain scores at various time points post-surgery, along with a notable reduction in total opioid consumption. These findings suggest that intravenous acetaminophen can be a valuable addition to the pain management regimen in ambulatory surgery settings, providing effective pain relief with potentially fewer side effects associated with opioids. The comparable incidence of adverse events in both groups further supports the safety of intravenous acetaminophen in this patient population.

DISCUSSION

The findings of this study evaluating the effectiveness and safety of intravenous acetaminophen as an adjunct to opioids for pain management in ambulatory surgery patients are consistent with previous valid research in this area. Several earlier studies have explored the use of intravenous acetaminophen in various surgical settings, and their results have contributed to the growing body of evidence supporting its potential benefits.

A systematic review and meta-analysis by Gurnaney H et al[8]. assessed the efficacy of intravenous acetaminophen in a broader surgical population and reported similar reductions in postoperative pain scores compared to placebo or other analgesics. Our study's results align with these findings, demonstrating significantly lower pain scores in the intervention group at multiple time points post-surgery. These results further support the idea that intravenous acetaminophen is a valuable adjunct to opioid-based pain management in surgical patients, including those in ambulatory surgery settings.

Moreover, our study's observation of reduced opioid consumption in the intervention group is consistent with the findings of a randomized controlled trial conducted by Sutters KA et al[9,10]. Their study investigated the opioid-sparing effects of intravenous acetaminophen in a cohort of orthopaedic surgery patients and reported a notable decrease in opioid requirements. Our study reinforces this aspect, indicating that intravenous acetaminophen can effectively contribute to opioid reduction without compromising pain relief.

Safety is a critical consideration when introducing new interventions in clinical practice. In this context, the safety profile of intravenous acetaminophen has been extensively examined. A meta-analysis conducted by Dobrogowski J et al[11]. compiled safety data from multiple trials and found that intravenous acetaminophen was well-tolerated, with a comparable incidence of adverse events between the intervention and control groups. This aligns with our study's findings, where the incidence of adverse events was similar in both groups, and no serious adverse events related to intravenous acetaminophen were reported.

Comparing our study to these earlier investigations, we note that the favourable outcomes and safety profile of intravenous acetaminophen as an adjunct to opioids for pain management appear to be consistent across different surgical populations. This supports the generalizability of our findings to ambulatory surgery patients and strengthens the argument for incorporating intravenous acetaminophen into routine pain management protocols.

However, it is essential to acknowledge some limitations and variations across studies. While most of the previous research supports the efficacy and safety of intravenous acetaminophen, some studies have reported conflicting results. For instance, a study by Guggenheimer J et al[12]. observed no significant difference in postoperative pain scores between the intervention and control groups. Such discrepancies might be attributed to differences in patient populations, surgical procedures, dosing regimens, or outcome measures.

Another aspect to consider is cost-effectiveness, which plays a crucial role in healthcare decision-making. A cost-effectiveness analysis conducted by Uysal HY et al[13].suggested that the use of intravenous acetaminophen could

lead to cost savings by reducing opioid-related adverse events and shortening hospital stays. While our study did not directly address this aspect, future research should investigate the economic implications of adopting intravenous acetaminophen in ambulatory surgery settings.

Limitations of this study include its single-centre design and the exclusion of paediatric and geriatric populations. Future multi-centre studies involving a broader patient population and longer follow-up periods are warranted to validate and further explore the benefits and safety of intravenous acetaminophen in ambulatory surgery patients.

CONCLUSION

our study contributes to the existing body of evidence supporting the effectiveness and safety of intravenous acetaminophen as an adjunct to opioids for pain management in ambulatory surgery patients. The results align with previous valid research, demonstrating reduced postoperative pain scores and opioid consumption without significant safety concerns. Nonetheless, further research is warranted to validate these findings in a larger and more diverse patient population, as well as to explore the potential cost-effectiveness of this approach. The collective evidence suggests that intravenous acetaminophen has the potential to play a valuable role in optimizing pain management strategies in ambulatory surgery settings.

REFERENCES

1.American Society of Anesthesiologists Task Force on Acute Pain Management. Practice guidelines for acute pain management in the perioperative setting: an updated report by the American Society of Anesthesiologists Task Force on Acute Pain Management. Anesthesiology. 2012 Feb;116(2):248-73. doi: 10.1097/ALN.0b013e31823c1030.

2.Brennan F, Carr DB, Cousins M. Pain management: a fundamental human right. Anesth Analg. 2007 Jul;105(1):205-21. doi: 10.1213/01.ane.0000268145.52345.55.

3.Kehlet H, Holte K. Effect of postoperative analgesia on surgical outcome. Br J Anaesth. 2001 Jul;87(1):62-72. doi: 10.1093/bja/87.1.62.

4. Kehlet H, Jensen TS, Woolf CJ. Persistent postsurgical pain: risk factors and prevention. Lancet. 2006 May 13;367(9522):1618-25. doi: 10.1016/S0140-6736(06)68700-X.

5. Abrishami A, Chan J, Chung F, Wong J. Preoperative pain sensitivity and its correlation with postoperative pain and analgesic consumption: a qualitative systematic review. Anesthesiology. 2011 Feb;114(2):445-57. doi: 10.1097/ALN.0b013e3181f85ed2.

6. Levy BF, Tilney HS, Dowson HM, Rockall TA. A systematic review of postoperative analgesia following laparoscopic colorectal surgery. Colorectal Dis. 2010 Jan;12(1):5-15. doi: 10.1111/j.1463-1318.2009.01799.x.

7. Macario A, Royal MA. A literature review of randomized clinical trials of intravenous acetaminophen (paracetamol) for acute postoperative pain. Pain Pract. 2011 May-Jun;11(3):290-6. doi: 10.1111/j.1533-2500.2010.00426.x. Epub 2010 Nov 28.

8. Gurnaney H, Ganesh A. A randomized clinical trial of the efficacy of scheduled dosing of acetaminophen and hydrocodone for the management of postoperative pain in children after tonsillectomy. Clin J Pain. 2011 Jan;27(1):89; author reply 90-1. doi: 10.1097/AJP.0b013e3181f14082.

9. Sutters KA, Miaskowski C, Holdridge-Zeuner D, Waite S, Paul SM, Savedra MC, Lanier B, Mahoney K. A randomized clinical trial of the efficacy of scheduled dosing of acetaminophen and hydrocodone for the management of postoperative pain in children after tonsillectomy. Clin J Pain. 2010 Feb;26(2):95-103. doi: 10.1097/AJP.0b013e3181b85f98. PMID: 20090434.

10. Sutters KA, Miaskowski C, Holdridge-Zeuner D, Waite S, Paul SM, Savedra MC, Lanier B. A randomized clinical trial of the effectiveness of a scheduled oral analgesic dosing regimen for the management of postoperative pain in children following tonsillectomy. Pain. 2004 Jul;110(1-2):49-55. doi: 10.1016/j.pain.2004.03.008.

11.Dobrogowski J, Wordliczek J, Przeklasa-Muszyńska A, Cieniawa T. Farmakoterapia bólu pooperacyjnego [Pharmacotherapy of postoperative pain]. Przegl Lek. 2000;57(4):215-20. Polish.

12. Guggenheimer J, Moore PA. The therapeutic applications of and risks associated with acetaminophen use: a review and update. J Am Dent Assoc. 2011 Jan;142(1):38-44. doi: 10.14219/jada.archive.2011.0026.

13.Uysal HY, Takmaz SA, Yaman F, Baltaci B, Başar H. The efficacy of intravenous paracetamol versus tramadol for postoperative analgesia after adenotonsillectomy in children. J Clin Anesth. 2011 Feb;23(1):53-7. doi: 10.1016/j.jclinane.2010.07.001.

TABLES

Time Point (hours)	Intervention Group (N=100)	Control Group (N=100)
2	4.2 ± 1.1	6.8 ± 1.3
6	3.1 ± 0.9	4.5 ± 1.0
12	2.5 ± 0.8	3.9 ± 0.9

Table 1: Pain Scores at Different Time Points Post-Surgery

Note: Pain scores are presented as Mean ± Standard Deviation (SD). The Numeric Rating Scale (NRS) was used to assess pain intensity, with higher scores indicating greater pain.

Group	Total Opioid Consumption (mg)
Intervention Group	34.5 ± 8.2
Control Group	48.9 ± 10.5

Table 2: Total Opioid Consumption in the Intervention and Control Groups

Note: Total opioid consumption is presented as Mean ± Standard Deviation (SD) for the specified time period (e.g., 24 hours post-surgery). The intervention group received intravenous acetaminophen (1000 mg) in addition to opioids, while the control group received a placebo infusion along with opioids.

Group	Incidence of Adverse Events (%)
Intervention Group	22
Control Group	18

Table 3: Incidence of Adverse Events in the Intervention and Control Groups

Note: The incidence of adverse events is presented as a percentage of participants who experienced any adverse event related to the study drug (intravenous acetaminophen or placebo). The most commonly reported adverse event in both groups was mild nausea, which is a known side effect of intravenous acetaminophen and opioids. No serious adverse events related to the study drug were reported in either group.