

Improved Outcomes Associated with the Use of Intravenous Acetaminophen for Management of Acute Post-Surgical Pain

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ABSTRACT:

Background: The provision of safe, efficient, and cost-effective acute pain management during surgery for inpatient patients is a major problem for clinicians and healthcare administrators. Post-surgical pain affects a lot of patient outcomes. Acetaminophen (APAP) plays a major role in multimodal analgesia regimens, which are becoming more and more necessary for effective pain treatment.

Objective: The aim of this study is to evaluate the outcomes associated with the use of intravenous acetaminophen for management of acute post-surgical pain.

Methods: The cross-sectional observational study was conducted in the department of Surgery, BSMMU, Dhaka, from July 2022 to June 2023. A total of 52 patients were enrolled and analyzed in this study. All of them were underwent different surgery. The questionnaire was pretested, corrected and finalized. Data were collected by face-to-face interview and analyzed by appropriate computer based programmed software Statistical Package for the Social Sciences (SPSS), version 24.

Results: In this study, majority 30 (46.9%) of the patients were in 41 - 50 years age group and 21 (32.8%) patients were in 31 - 40 years age group, Mean \pm SD of age was 45 \pm 4 years and most of the patients 42 (65.60%) were male and 22 (34.40%) patients were female. Meajority of the patients 34 (53.1%) were from the department of Gynae & obs, Orthopedic 9 (14.1%) patients, General surgery 8 (12.5%) patients, Cardiovascular 5 (7.8%), Colorectal and Spine surgery 8 (12.5%) patients. About 32 (50.0%) patients were admitted in emergency basis, 12 (18.8%) patients were admitted through non-healthcare facility. Elective type of admission was in 26 (40.6%) patients and 23 (35.9%) patients were admitted in emergency. Average length of stay in the hospital was shorter in case of IV APAP than Oral APAP, less morphine consumption was needed in case of IV APAP than Oral APAP, total pharmacy costs were lower in case of IV APAP than Oral APAP and in IV APAP had lower risk of developing an Opioid related adverse events (ORADEs).

Conclusion: When patients receiving IV APAP for post-surgical pain were compared to those receiving oral APAP, there was a decrease in opiate consumption, a shorter length of stay after surgery, and a lower risk of ORADEs. These effects were observed without having a negative effect on overall pharmacy expenditures.

Keywords: IV acetaminophen, Multimodal analgesia, Opioid, Post-surgical pain, Acute pain, Health outcomes.

I. INTRODUCTION:

Effective pain management following surgery is essential for a good surgical recovery [1]. Both short- and long-term post-surgical outcomes are impacted by acute pain because poor pain management can lead to longer hospital stays and a higher chance of acquiring chronic pain [2, 3]. Women are more prone than males to suffer from chronic pain syndromes, according to population-based research, and they also have obstetric and gynecologic operations more frequently than men [4-6].

When treating post-surgical pain, intravenous (IV) and oral opioids are the most often utilized analgesics. Opioids are useful for treating pain, but they also come with a number of expensive side effects called opioid-related adverse events (ORADEs) [7, 8]. The overprescription of opioids following surgery is one

factor contributing to the opioid epidemic in the United States [10], and the usage of opioids can result in addiction and misuse [9]. Men and women have been found to differ in the effectiveness of opioids [11, 12], and after cesarean deliveries, there are further worries about the management of postoperative pain. For instance, while it is generally acceptable to breastfeed while taking opioid medications [13, 14], breastfeeding, infant care, and mother-infant bonding can be disrupted [15] by the sedation associated with opioid-based analgesia after cesarean sections; additionally, inadequate pain management or increased sedation may impair the mother's ambulation, which raises the risk of thromboembolic disease [16].

The American Pain Society (APS), American Society of Anesthesiologists (ASA), American Society of Regional Anesthesia and Pain Medicine (ASRA), and other professional societies have released new guidelines that strongly advocate the use of multimodal therapies, with non-opioid analgesics serving as the cornerstone of care for postoperative pain [17]. The use of multi-modal non-opioid analgesics, such as acetaminophen (APAP) and non-steroidal anti-inflammatory drugs (NSAIDs), should be maximized by breastfeeding mothers, according to specific guidelines and recommendations from the American College of Obstetricians and Gynecologists (ACOG), the Society for Maternal-Fetal Medicine (SMFM), and the Academy of Breastfeeding Medicine (ABM) [18].

In general, multimodal analgesia (MMA) regimens can lower the amount of opioids used and the ensuing ORADEs [17]. Due to the physiology of pain transmission, the majority of pain is multifactorial in character. Therefore, using analgesic combinations with different modes of action may also have additive or synergistic effects on pain relief [19–22].

Surgery standards have well-established MMA protocols. MMA has been linked to lower hospital readmission rates and a decrease in the usage of opioids in both surgery types [23–26]. MMA regimens use a wide range of drugs, such as GABA analogs (pregabalin, gabapentin), non-NSAIDs (such APAP), and NSAIDs. Nonetheless, in cases where specific comorbidities exist, NSAIDs may not be recommended [27].

Over 50 years have seen a widespread use of oral APAP. 2010 saw the release of an intravenous (IV) APAP formulation suitable for post-surgical patients who are sedentary, have nausea or vomiting, or are recovering slowly from gastrointestinal (GI) surgery and are unable to take oral medications. The use of IV APAP has increased in a number of medical specialties, such as orthopedic and spine operations, but little is known about how IV APAP generally affects post-surgical pain in real-world, non-clinical settings [28, 29].

Intravenous (IV) opioid agonists, including morphine, hydromorphone, and fentanyl, have long been used as crucial analgesics in critical care and early postoperative settings in the United States. Over 70% of surgical inpatients and outpatients in the US were treated for acute pain with opioid monotherapy in the first half of 2015 [14]. In the context of inpatient healthcare, an overreliance on opioid monotherapy increases patient health risks and drives up healthcare expenditures due to avoidable adverse events.

Multimodal analgesia (MMA), an alternative to opioid monotherapy, aims to reduce the negative effects of a single analgesic while maximizing the effectiveness of each agent at the appropriate concentrations [7]. The theory underlying this significant idea is that various agents with distinct mechanisms of analgesia, including opioids, nonopioids (acetaminophen and nonsteroidal anti-inflammatory drugs [NSAIDs]), local anesthetics, and anticonvulsants, may work in concert to prevent or treat acute pain [7]. With opioid analgesics increasingly playing the role of rescue analgesics for acute pain, the effectiveness of multimodal analgesic regimens is still improving [23].

II. METHODOLOGY:

The cross-sectional observational study was conducted in the department of Surgery, BSMMU, Dhaka, from July 2022 to June 2023. A total of 52 patients were enrolled and analyzed in this study. All of them were underwent different surgery. Patients who matched the inclusion and exclusion criteria were approached for participation in the study. Patients who were not willing to give consent were excluded. Purposive sampling was done according to the availability of the patients who fulfilled the selection criteria. Face to face interview was done to collect data with a semi-structured questionnaire. After collection, the data were checked and cleaned, followed by editing, compiling, coding, and categorizing according to the objectives and variable to detect errors and to maintain consistency, relevancy and quality control. Statistical evaluation of the results used to be obtained via the use of a window-based computer software program devised with Statistical Packages for Social Sciences (SPSS-24).

III. RESULT:

Table I: Distribution of the patients according to age (n = 64)

Table I shows that, majority 30 (46.9%) of the patients were in 41 - 50 years age group and 21 (32.8%) patients were in 31 - 40 years age group, Mean±SD of age was 45±4 years.

Age group	Frequency	%
20 – 30 years	7	10.9
31 - 40 years	21	32.8
41 - 50 years	30	46.9
51 - 60 years	6	9.4
Total	64	100.0
Mean + SD: 45±4 Years		

Figure I: Distribution of the patients according to sex (n=64)

Figure I show that most of the patients 42 (65.60%) were male and 22 (34.40%) patients were female.

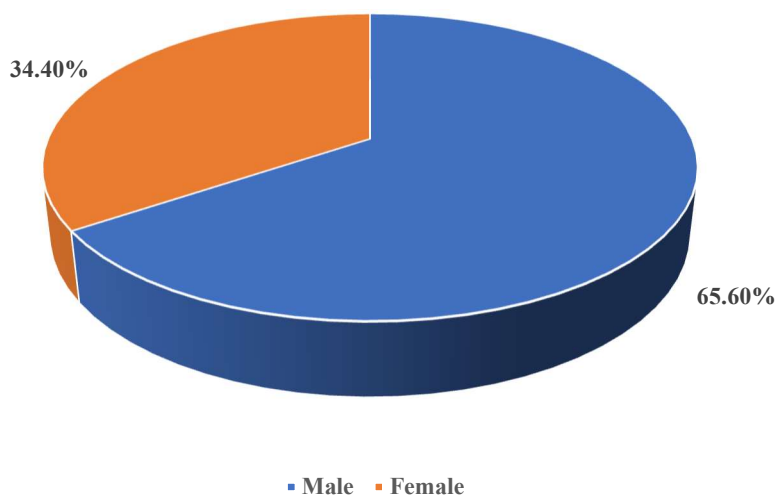


Table II: Distribution of the patients according to type of surgery (n = 64)

Table II shows that most of the patients 34 (53.1%) were from the department of Gynae & obs, Orthopedic 9 (14.1%) patients, General surgery 8 (12.5%) patients, Cardiovascular 5 (7.8%), Colorectal and Spine surgery 8 (12.5%) patients

Type of surgery	Frequency	%
Cardiovascular	5	7.8
Colorectal	4	6.3
General	8	12.5
Gynae & obs	34	53.1
Spine	4	6.3
Orthopedic	9	14.1
Total	24	100.0

Table III: Distribution of the patients according to source of admission (n = 64)

Table III shows that, 32 (50.0%) patients were admitted in emergency basis, 12 (18.8%) patients were admitted through non-healthcare facility

Admission source	Frequency	%
Emergency	32	50.0
Healthcare facility	7	10.9
Non-healthcare facility	12	18.8
Other	2	3.1
Unknown	11	17.2
Total	64	100.0

Table IV: Distribution of the patients according to type of admission (n = 64)

Table IV shows that, elective type of admission was in 26 (40.6%) patients and 23 (35.9%) patients were admitted in emergency

Admission type	Frequency	%
Emergency	23	35.9
Urgent	3	4.9
Elective	26	40.6
Other	1	1.6
Unknown	11	17.2
Total	64	100.0

Table V: Distribution of the patients according to outcomes (n = 24)

Table V shows that, length of stay in the hospital was shorter in case of IV APAP than Oral APAP, Less morphine consumption was needed in case of IV APAP than Oral APAP, total pharmacy costs were lower in case of IV APAP than Oral APAP and in IV APAP had lower risk of developing an Opioid related adverse events (ORADEs)

Outcomes	IV APAP	Oral APAP
Length of stay	Shorter	Longer
Total morphine consumption (MME) per day	Less	More
Total pharmacy costs	Lower	Higher
Opioid related adverse events (ORADEs)	Lower risk	Higher risk

IV. DISCUSSION:

Although opioid therapy is a cornerstone of postoperative pain management, there are serious safety concerns due to the possibility of adverse drug events (ADEs) and poor patient outcomes. A multimodal strategy to pain treatment is becoming more and more popular as a means of reducing postoperative opioid reliance while maintaining the highest level of pain control.

This novel method to pain management may lower the risk of ORADEs and related medical expenses due to the lower opioid dosages employed. This strategy is recommended by recent pain guidelines for critically sick patients in order to prevent ADEs. Giving balanced pain management while utilizing the lowest effective dose of opioids is a huge problem since hospitals and outpatient clinics have to operate in the present healthcare environment, where money is tight, by providing care in an efficient and cost-effective manner. Specifically, two questions on pain management are connected to HCAHPS scores, which are linked to payment.

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In another study, using a large, multi-center, retrospective database, we demonstrated that IV APAP use is associated with significantly shorter LOS (by approximately 12%) in Cesarean section and hysterectomy patients when compared to oral APAP. This analysis is one of the first to assess the clinical outcomes and costs of oral APAP versus IV APAP from EHRs, from a robust database of over 600 hospitals and over 62 million patients. Our study focused on Cesarean sections and hysterectomies, where reductions in LOS may be most impactful for hospital costs and resources, given that these patients generally have consistent LOS, with less variation when compared to other surgeries requiring hospitalization. Additionally, research indicates that pain management may differ by gender [5], but the potential for confounding by sex is eliminated by focusing on Cesarean sections and hysterectomies.

A previous claims-based study of Cesarean section and hysterectomy surgeries showed significantly less daily opioid use and lower hospitalization costs in patients receiving IV APAP as part of MMA versus patients receiving IV opioid- only analgesia in Cesarean section and a non-significant trend towards less opioid use and lower cost in hysterectomy; however, the claims-based analysis did not show reductions in LOS in the IV APAP cohort following adjustment [24]. The other study demonstrates statistically significant reductions in LOS and opioid consumption for both Cesarean section and hysterectomy patients. The LOS reductions approached 12%, translating to a reduction of approximately 8 to 12 h, or potentially one nursing shift per day. In the Cesarean group, IV APAP patients also had lower risk of developing an ORADE. There were no statistically significant differences in total pharmacy costs between oral APAP and IV APAP, despite cost differences between these formulations.

These findings are consistent with prior studies of MMA protocols including IV APAP, demonstrating a reduced LOS in orthopedic and spine surgery patients [28, 29]. Retrospective studies in orthopedic and other surgery types have found similar associations [24, 30-32]. MMA is thought to improve surgical outcomes by reducing opioid dosing, resulting in decreased ORADEs and complications, and creating synergies that result in pain reductions. APAP exerts its effects in the central nervous system, and versus oral APAP, IV APAP has a faster T max and a higher C max, with pharmacokinetics that achieve greater concentration in cerebrospinal fluid, suggesting better analgesia from this formulation [33, 34]. Our results support these findings and suggest that IV APAP use may be cost-effective for Cesarean section and hysterectomy surgeries through the reduction of LOS, opioid consumption, and ORADEs.

Prior studies have demonstrated postoperative use of IV APAP reduces opioid consumption. In the pivotal US study of IV APAP for acute pain management, IV APAP was associated with a 46% reduction over the first 6 h and 33% reduction (vs. placebo) in total morphine consumption in the first 24 h following surgery [40]. Other randomized controlled trials (RCTs) have shown reductions in opioid consumption up to 78% [31–35]. Taken together, results from prior studies and the current analysis suggest a positive impact on overall hospital costs associated with reducing opioid consumption and adding IV APAP. Accordingly, IV APAP may be recommended as a standard of care in MMA regimens for postoperative pain management to reduce reliance on opioid monotherapy.

Postoperative use of IV APAP has been associated with a shorter average LOS (0.4–1.5 days) relative to placebo or active controls [41, 45]. In addition, a retrospective cohort study of case-matched patients who underwent total hip or knee replacement surgery [38], IV APAP used as part of an MMA strategy was associated with improved clinical outcomes in terms of fewer overall adverse events, shortened LOS, and reduced total hospital resources. A total of 22,146 cases and controls were similar in terms of age, race, sex, marital status, insurance status, and preoperative

comorbidities. Overall adverse events were significantly lower with IV APAP (24.3%) than with controls (26.3%, $P<0.001$), numerically less frequent in all subgroups, and significantly less frequent for renal, infectious, and miscellaneous adverse events (all $P<0.05$). Also, IV APAP was associated with a shorter LOS, with 1 out of 11 patients discharged 1 day earlier ($P<0.001$) and lower average hospital costs: \$16,381 for cases compared with \$16,927 for controls ($P<0.001$). Cost savings estimated by structural equation modeling of \$547 per patient were due to \$325 from direct effects and \$222 from indirect effects, the latter mediated through adverse events and reduced LOS.

The largest percentage reduction in LOS and opioid-related complications, seen in the spine category, may represent a greater benefit of adding IV APAP in more painful procedures. Specifically, spine surgery and other painful procedures generally require higher doses and/or more frequent administration of pain medications, with opioids used predominantly. Reducing the use of opioids in these patients by using IV APAP as part of an MMA strategy can reduce ORADE incidence and LOS while also reducing hospitalization costs [36].

V. CONCLUSION:

Prevention of ORADEs rather than treatment of ADEs is a more effective strategy for hospitals, given the large economic burden and negative impact on patient outcomes associated with these events. A multimodal approach is a growing strategy to minimize the frequency of ORADEs as well as associated costs. Post-surgical pain managed with IV APAP in patients undergoing surgery was associated with a decrease in opiate consumption, a shorter length of stay after surgery, and a lower risk of ORADEs. These effects were observed without having a negative effect on overall pharmacy expenditures.

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