1-1-2013

The Relationship Between The Use Of Intravenous Acetaminophen During Laparoscopic Cholecystectomy And Appendectomy Surgery And The Use Of Intravenous Opioids After Surgery

Linda M. Green
Rhode Island College

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A Major Paper Presented

By

Linda Green, RN, BSN

Approved:

Committee Chairperson	_____	_____ (Date)
Committee Members	_____	_____ (Date)
	_____	_____ (Date)
Director of Master's Program	_____	_____ (Date)
Dean, School of Nursing	_____	_____ (Date)

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A Major Paper Submitted in Partial Fulfillment

of the Requirements for the Degree of

Master of Science in Nursing

in

The School of Nursing

Rhode Island College

2013

Abstract

Multimodal pain management is the use of combinations of medications from different classes or medications with different routes of delivery to optimize pain relief. The adjunctive use of multiple analgesic agents is associated with better pain relief and fewer adverse effects. Intravenous acetaminophen offers a relatively low risk, safe adjunct to multimodal therapy. A comparative retrospective chart review showed that adult patients undergoing laparoscopic appendectomy or cholecystectomy surgery who received intravenous acetaminophen in the operating room had a reduced opioid requirement directly after surgery, in the post anesthesia care unit. A total of 34 doses of opioids (Fentanyl and Dilaudid) were given to the group who received the intravenous acetaminophen as compared to 65 doses of the same opioids given to the group that did not. Since only two surgical procedures were studied, the results may not be applicable to other surgical procedures. Additionally, the small sample size (60 patient charts) was a noted limitation. Data is consistent with previous studies supporting the use of intravenous acetaminophen to help reduce the amount of opioid use postoperatively Because of its relatively safe profile, intravenous acetaminophen should be thoughtfully considered when addressing pain management in the operative setting.

Keywords: postoperative pain, acetaminophen injection, acetaminophen IV, intravenous paracetamol, laparoscopic surgery and IV acetaminophen.

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Statement of Problem

Ambulatory surgical procedures now make up 70% of the total volume of hospital-based elective surgical procedures. Postoperative pain, nausea, and vomiting are the most common factors leading to delays in outpatient discharge and admissions to the hospital following ambulatory surgery.[1] Multimodal pain management, also known as balanced analgesia, is defined as using combinations of medications from different classes or medications with different routes of delivery to optimize pain relief and minimize adverse effects.[2] It is fast replacing traditional pain treatment options.[3] Pain control regimens should not be standardized but tailored to the needs of the individual patient, taking into account medical, psychological, and physical condition, age, level of fear or anxiety, surgical procedure, personal preference and response to agents given.[4] The adjunctive use of multiple analgesic agents is associated with better pain relief, fewer significant adverse effects, facilitation of earlier recovery and improved patient outcomes and satisfaction.[5]

Literature Review

Opioids have long been the mainstay of postoperative pain, but the long list of associated adverse effects has given support to the multimodal approach to pain management. Treatment plans that use only opioids run the risk of intolerable and dangerous adverse effects. Common side effects of opioid administration include sedation, dizziness, nausea, vomiting, constipation, physical dependence, tolerance and respiratory depression.[6] The financial burden of these side effects can be seen in increased lengths of hospitalization stay, unexpected admission to the hospital,

administration of additional medications to treat the side effects, the potential for unexpected intubation to protect the airway in the event of over-sedation, and an abundance of additional burdens should the patient become opioid dependent. Additionally, opioid-induced hyperalgesia, a condition in which increasing dosages of opioid consumption result in an increased sensitivity to pain, can result.[7]

Multimodal analgesia, utilizing regional analgesic techniques, where possible, and non-opioid analgesics, appears to represent a viable strategy to decrease systemic opioid consumption and improve postoperative analgesia.[8] In the United States (US), there are a number of nonopioid oral analgesics that, given alone or in combination with opioids, are approved and frequently used for acute pain management. While these agents are typically not sufficient to treat moderate-to-severe pain by themselves, they are useful adjuncts to opioids.[9] The American Society of Anesthesiologists recommended that, unless contraindicated, all post surgical patients should receive an around-the-clock regimen of a non-opioid agent.[10]

Until the Federal Drug Administration (FDA) approved intravenous acetaminophen in 2010, there were only two approved intravenous non-opioid analgesics available for use for multimodal pain management: *ketorolac* and *ibuprofen*, both of which are NSAIDs. Intravenous (IV) NSAIDs have potential adverse events as well, including bleeding and renal toxicity, which limits their use in the perioperative setting.[11] Acetaminophen is the most widely used analgesic and antipyretic in the US, and is considered the first line drug of choice by the World Health Organization (WHO). It has been used in Europe for many years under the generic name *paracetamol.* Intravenous

acetaminophen represents a relatively new drug for the short-term treatment of mild to moderate pain, and moderate to severe pain with adjunctive opioid use. Acetaminophen injection, which is marketed in the US as *Ofirmev,* provides a significant level of analgesia after a 15 minute infusion.[12] Acetaminophen IV now provides another therapeutic option for hospitalized patients unable to take oral medications, particularly in the peri-operative setting.[13]

Intravenous acetaminophen is administered as a 15 minute infusion. The recommended dosage in adults and adolescents weighing more than fifty kilograms is one gram, up to four times per day, with a minimum interval of four hours between doses and a maximum daily dose of four grams.[14] The advantage of using IV acetaminophen in a multimodal approach is that it is safe to use in conjunction with other drugs, and has few clinically significant drug interactions.[15] Its efficacy and tolerability are well established and in contrast with opioid analgesics, it has a favorable safety profile.[16] Unlike NSAIDs, it does not produce gastrointestinal damage. It should be used with caution in patients with hepatic impairment or active hepatic disease, alcoholism, chronic malnutrition, severe hypovolemia or severe renal impairment, and it should not be used in patients with acetaminophen allergy.[17]While the mechanism of acetaminophen-mediated pain relief is still not completely understood, it has been shown that it rapidly enters the intact central nervous system (CNS) and the majority of the mechanisms involved in analgesia occur in the CNS.[18]

Wininger and associates (2010) conducted a randomized, double-blind, placebo-controlled, parallel-group study at 17 US sites to evaluate the analgesic efficacy and

safety of repeated doses of two dosing regimens of IV acetaminophen compared with placebo over 24 hours in subjects with moderate to severe pain after abdominal laparoscopic surgery. A total of 244 subjects were randomized. Both regimens of IV acetaminophen (1000 milligrams every six hours vs. 650 milligrams every four hours) were associated with statistically significant analgesic efficacy compared with placebo and were well tolerated. These results are consistent with those of previously published studies in which IV acetaminophen was reported to be more effective than placebo and comparable to several nonopioid and opioid analgesics in the treatment of postoperative acute pain in a wide variety of surgical settings, ranging from tonsillectomy and endoscopic sinus surgery to spine and cardiac surgery.

Marcario and Royal (2010) performed a literature review of randomized clinical trials of IV acetaminophen for acute postoperative pain.

Sixteen articles from nine countries published between 2005 and 2010 met inclusion criteria and had a total of 1,464 patients. In seven of the eight studies where IV acetaminophen was compared with an active comparative medication, IV acetaminophen was found to have similar analgesic outcomes. Three of the eight studies also found IV acetaminophen resulted in a significant reduction in mean opioid consumption. Twelve of 14 placebo-controlled studies found that IV acetaminophen patients had improved pain relief. The limitations of the studies reviewed were small sample size (only 5 of the 16 studies included more than 40 patients in the acetaminophen group). Additionally, because the best analgesic approach needs to be individualized to the specific surgical procedure, results from a specific study may not be applicable to other surgery types or

when other analgesic interventions such as nerve blocks are added to a multimodal approach.[19]

Clinically, the goal is to advance simple, safe, effective therapies that will reduce postoperative pain. Reduction of pain and reduction of adverse side effects ultimately leads to safe, effective patient outcomes. The purpose of this project was to investigate the relationship between the use of IV acetaminophen in the operating room (OR) and the opioid requirement in the post anesthesia care unit (PACU) in patients undergoing laparoscopic appendectomies and laparoscopic cholecystectomies.

Method

Study Design

This study used a two group design. Group One included subjects who received the standard dose of IV acetaminophen in the OR during an appendectomy or cholecystectomy and Group Two were subjects who did not receive the IV acetaminophen.

Site and Sample

This research study was conducted at a 350 bed acute care hospital in Rhode Island. The sample was selected from subjects over the age of 18 who had undergone laparoscopic appendectomies and laparoscopic cholecystectomies and who met the inclusion criteria. Inclusion criteria included adult patients who received IVacetaminophen during the course of laparoscopic appendectomy or laparoscopic cholecystectomy surgery and who were able to verbally enumerate their level of pain in

the post-operative care unit (PACU). The numeric pain scale 0-10, where 0 equals no pain and 10 equals intolerable pain, was used. Exclusion criteria included patients who were opioid dependent prior to surgery, those that used analgesics or alcohol chronically, those with chronic hepatic failure, and those with an allergy to acetaminophen as noted on the pre-operative interview by the anesthesiologist. Patients receiving nerve blocks or those that have any pain control devices, such as a patient-controlled analgesia (PCA) pump or opioid medication patches were also excluded. Additionally, patients whose pain level was documented in a scale other than the numeric pain scale were excluded.

Procedures

Approval was obtained from the institutional and RIC IRB. The student researcher developed a data collection tool derived from the review of the literature and clinical experience. The written anesthesia record was used to review the pre-operative interview data obtained by the anesthesiologist in order to identify potential exclusions. The intraoperative record was reviewed to ascertain whether the patient received IV acetaminophen in the operating room. The patient electronic record was surveyed to obtain the pain scale and medication interventions used in the post anesthesia care unit (PACU). including IV acetaminophen and other analgesics. Pain scores were recorded from PACU admission, at 15 minutes, 30 minutes, and every 15 minutes thereafter until transfer from PACU to the outpatient area (for those patients going home) or admission to a hospital bed (for those patients being admitted). The total amount of opioid analgesia use was collected and compared between the two groups.

Data analysis included a comparison of the number of patients reporting pain between the two groups as well as the number of doses of IV Fentanyl and IV Dilaudid given to patients in each group.

Results

A total of 94 charts were reviewed. Of those, 60 who met eligibility criteria were included: 30 who received IV acetaminophen (Group One) and 30 who did not receive IV acetaminophen (Group Two). Table 1 illustrates the number of patients reporting pain in each group from arrival to PACU and in 15 minute increments thereafter. Of the 30 patients who did NOT receive IV acetaminophen in the OR (Group Two), 23 reported pain levels during their stay in the PACU sufficient to require IV opioid administration while 7 did not report pain levels requiring opioids. Of the 30 patients who did receive the IV acetaminophen (Group One), 16 reported pain levels sufficient to require IV opioids, and 14 did not require IV opioids. Only one patient in Group One required an opioid on arrival to PACU, while three patients in Group Two had a pain level requiring the use of an IV opioid. At every time increment, with the exception of the 15 minute time period, more patients in Group Two experienced pain compared to Group One. Additionally, over time, Group One had a higher percentage of reduction in the number of patients reporting pain compared to Group Two.

Table 1

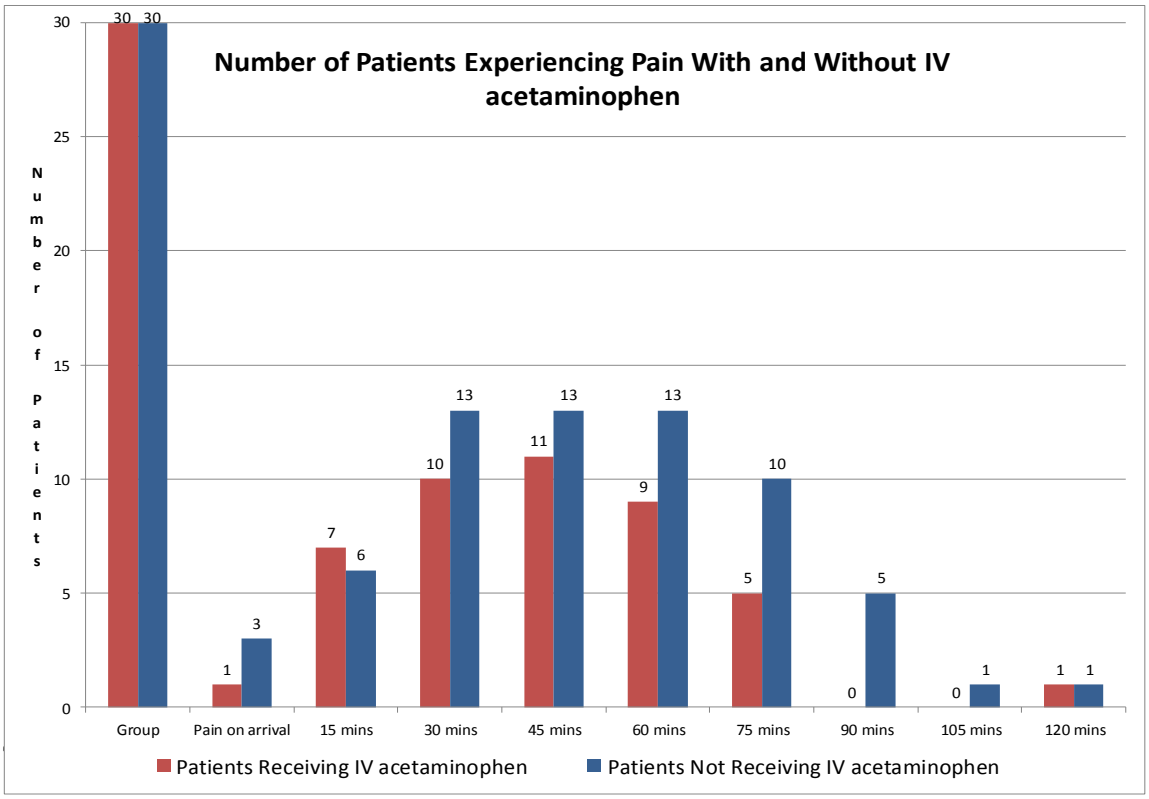

Number of Patients Experiencing Pain With and Without IV acetaminophen
Number of Patients
30
25
20
15
10
5
0
30 30
1 3
7 6
10 13
11 13
9 13
5 10
0 5
0 1
1 1
Group
Pain on arrival
15 mins
30 mins
45 mins
60 mins
75 mins
90 mins
105 mins
120 mins
Patients Receiving IV acetaminophen
Patients Not Receiving IV acetaminophen

Table Two illustrates the number of doses of IV Fentanyl that were given between the two groups. The standard dose of Fentanyl was 50 mcg IV, which could be repeated in five minutes, for a total of 100 mcg of Fentanyl. A total of 27 doses of IV Fentanyl (50 mcg) was given to patients who received IV acetaminophen in the OR, as compared to 41 doses given to the patients who did not. Additionally, on arrival, at 30 minutes, 60 minutes and 75 minutes, at least twice as many doses of Fentanyl were given to the group not receiving acetaminophen.

Table 2

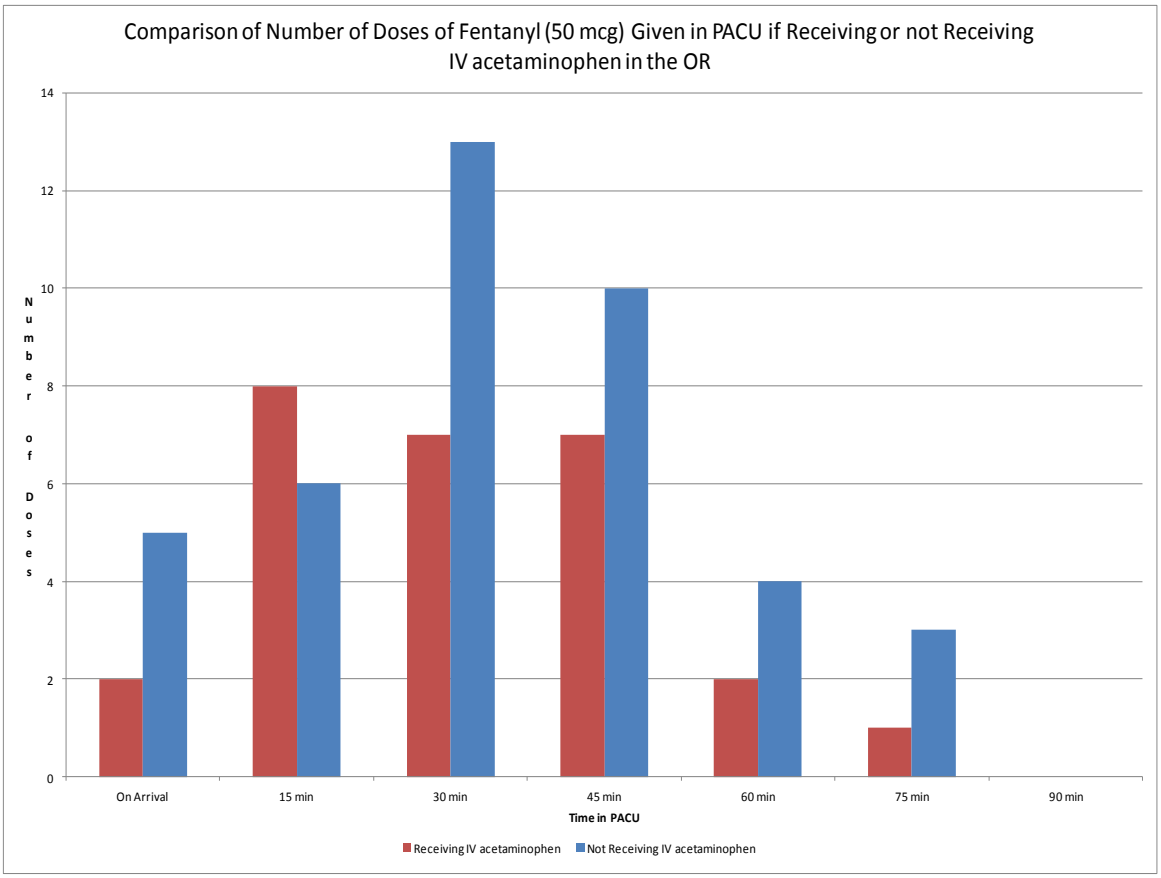
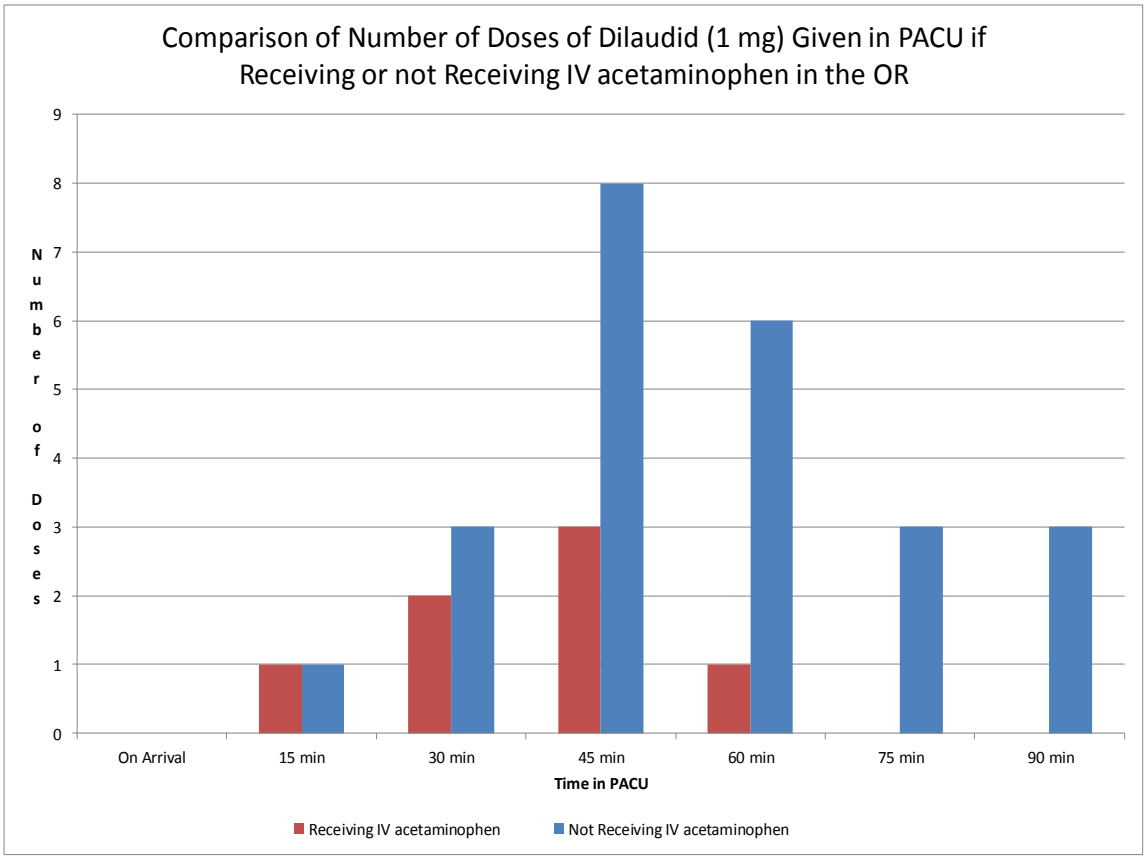


Table 3 compares the number of doses of IV Dilaudid (1 mg) given between the two groups. After the 100 mcg of IV Fentanyl had been administered, the standard was to give one milligram of IV Dilaudid, which could be repeated after five minutes, for a total of two mgs. A total of seven doses were administered to the group receiving IV acetaminophen as compared to 24 doses given to the group not receiving it.

Table 3



Discussion

The data presented in this study is consistent with previous studies that supported the use of IV acetaminophen intra-operatively to reduce the amount of opioids used postoperatively in these two surgical procedures. In the hospital where the data were collected, the standard for pain management is to medicate for pain levels greater than three on a zero to 10 numeric scale. The data collected and presented in this study suggests that patients who receive IV acetaminophen in the OR report less pain in the recovery room and, therefore, require less opioid pain medication in these two surgical procedures.

This study was a retrospective chart audit, so was limited by the data that was documented. The sample size was small and data were collected at one institution; further study is indicated. The author did not examine individual pain levels with each reported pain experience, so there is no way of knowing at what reported pain level individual patients were medicated. Anecdotally, some surgeons were found to be resistant to using IV acetaminophen in the OR if their patients were going home with a prescription for pain medication that contained acetaminophen in it. These surgeons verbalized a fear that those patients might exceed the maximum recommended dose of four grams of acetaminophen a day.

Conclusions and Recommendations.

Given the relative safety of IV acetaminophen, prior research, and results of this study, the author recommends that institutions give careful consideration to the use of IV acetaminophen. The dangers of opioids are well documented, and opioids contribute to post-operative and post discharge nausea and vomiting. Dosing schedules are available that take into account the acetaminophen given in the OR and what can be given to patients upon discharge to ensure safe dosing. Safe and effective pain management is a critical patient safety goal following any surgical procedure. The use of IV acetaminophen offers a safe adjunct in the multi-modal approach to pain control in the surgical setting. The APRN can be influential in policy development, practice change, and in working across systems and within teams to promote the use of intravenous acetaminophen as an important component in assuring safe and effective pain management in the surgical setting.

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