

Special REPORT

IV Acetaminophen Improves Pain Management and Reduces Opioid Requirements in Surgical Patients:

A Review of the Clinical Data and Case-based Presentations

Acute pain is a common and suboptimally managed occurrence in the postoperative setting. In a survey of adults who had undergone surgical procedures in the United States, Warfield and colleagues noted that 77% reported pain after surgery, with 80% of affected individuals experiencing moderate to severe pain.¹ Furthermore, postoperative pain is associated with various complications and poor

outcomes, including longer times to ambulation, longer hospital lengths of stay (LOS),² higher rates of medical complications (eg, venous thromboembolic disease from reduced activity), and decreased patient satisfaction.^{3,4} Long-term complications also can arise from undertreated postoperative pain, including worse functional outcomes and a higher prevalence of chronic pain syndromes.^{2,4,5}

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Although monotherapy with opioids has been the mainstay of treatment for postoperative pain, these agents are associated with various adverse events (AEs)—nausea and vomiting, constipation, and ileus—that can occur even at low doses of opioids and can result in significant discomfort and longer hospital LOS.⁶ Some of the more severe AEs include respiratory depression and sedation, both of which increase the risk for respiratory failure, aspiration, decreased mobility, and falls.^{6,7} Thus, opioid monotherapy is not an adequate or appropriate strategy to improve pain management in postoperative patients.

Over the past decade, multimodal analgesia has gained recognition for being an effective strategy in managing postoperative pain.⁸⁻¹⁰ Using different classes of analgesics each with different pathways and receptors, multimodal analgesia optimizes analgesic efficacy using lower doses of each of the respective agents, thus limiting the risk for dose-related AEs.¹⁰ Clinicians find this approach beneficial, particularly when using regimens that allow lower doses of opioids. Consequently, multimodal analgesia can improve recovery after surgery and ensure rehabilitation and transfer to the outpatient setting, while reducing overall costs.^{11,12}

Agents with potency for modulating one or more discrete mechanisms of pain transmission and that have a good safety profile are favorable for multimodal analgesia.⁴ Additionally, analgesics that can be given intravenously can enhance bioavailability and earlier onset of analgesic effect in the immediate postoperative period, as surgical patients may experience postoperative nausea and vomiting or because the enteral route may not be an option based on the procedure.¹³ In fact, both parenteral opioids and major surgery have been shown to cause profound delays in gastric absorption, which have implications regarding optimal route of drug delivery during the perioperative period.^{14,15}

IV acetaminophen (OFIRMEV™) can be integrated into a multimodal approach to optimize pain management effectively. In November 2010, the FDA approved the use of IV acetaminophen for the management of mild to moderate pain, the management of moderate to severe pain with adjunctive opioid analgesics, and the reduction of fever.¹⁶ The following material will discuss the use of IV acetaminophen as a component of multimodal analgesia

in postoperative patients. A review of the pharmacokinetics and pharmacodynamics will be followed by a discussion of data from clinical studies and case-based presentations.

IV Acetaminophen: Pharmacokinetics and Pharmacodynamics

Although acetaminophen (paracetamol or *N*-acetyl-*p*-aminophenol [APAP]) produces a central analgesic effect, its precise mechanism(s) remain unknown. Postulated targets include cyclooxygenase isoenzymes, endogenous opioid or serotoninergic bulbospina pathways, and/or cannabinoid/vanilloid tone.¹⁷ More recently, evidence suggests that acetaminophen is a TRPV-1 agonist that mediates response to pain.¹⁸ It also has an antipyretic effect, which may be mediated by inhibition of prostaglandin formation that otherwise acts to increase the temperature “set point” within the hypothalamus.¹⁹ This agent is available in oral and rectal formulations in the United States and also has been available as an IV formulation in Europe since 2002 and in the United States since 2010.

One important advantage of acetaminophen over other analgesic agents used for the treatment of postoperative pain is its safety and tolerability profile.²⁰ In contrast to opioids, acetaminophen does not produce sedation, respiratory depression, or ileus and constipation, nor is it associated with a risk for substance abuse or misuse.¹⁶ Nonsteroidal anti-inflammatory drugs (NSAIDs) also are commonly used in the postoperative setting, but can compromise renal function and increase the risk for cardiovascular events.²¹ Furthermore, the adverse effects of NSAIDs on mucosal integrity and platelet function are associated with an increased risk for bleeding, a complication that can be particularly problematic in the postoperative setting.²²

The pharmacokinetics and pharmacodynamics of IV acetaminophen have been well characterized (Table 1).¹⁶ IV infusion of acetaminophen results in a rapid elevation in plasma concentrations and higher peak levels compared with

Table 1. Mean Pharmacokinetic Data After First Dose in Healthy Adults

Parameter	OFIRMEV 1 g (n=34)	Oral acetaminophen 1 g (n=33)
C _{max}	28.4 mcg/mL	15.1 mcg/mL
T _{max}	0.28 h	0.72 h
t _{1/2}	2.39 h	2.66 h
Area under the curve	47.0 mcg • h/mL	42.4 mcg • h/mL
Hepatic first-pass exposure	No	Yes

C_{max}, peak concentration; t_{1/2}, half-life; T_{max}, maximum plasma concentration

Based on reference 16.

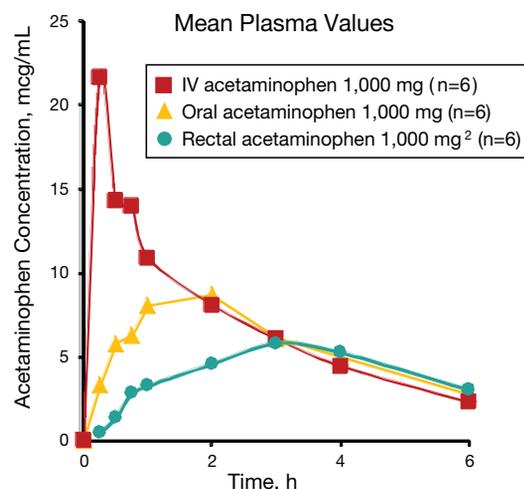


Figure 1. Acetaminophen plasma concentration over time.

Based on reference 23.

oral acetaminophen (Figure 1),²³ sustained pharmacokinetic differences from oral acetaminophen over repeated doses, with a clinical analgesic effect that occurs within 5 to 15 minutes of administration.²⁴ The clinical analgesic effect peaks within 1 hour and lasts for approximately 4 to 6 hours.¹⁶

These characteristics are favorable when compared with either oral or rectal formulations of acetaminophen. Specifically, the mean peak concentration after infusion of IV acetaminophen is approximately 70% higher than the mean peak concentration observed at an equivalent oral dose.¹⁶ Additionally, the higher peak concentration with IV acetaminophen remains far below the concentration considered the threshold for potential hepatotoxicity (150 mcg/mL at 4 hours post-administration).²⁵⁻²⁷ The median time to reach maximum plasma concentration (T_{max}) for IV acetaminophen, is 15 minutes (at the end of infusion), whereas the T_{max} for oral or rectal routes of administration is 45 to 75 minutes (depending on the formulation) or 3 to 4 hours, respectively.^{28,29} Pharmacokinetic parameter estimates for IV acetaminophen are similar in children, adolescents, and adults, when normalized for body weight.¹⁶ IV acetaminophen is not approved for patients under the age of 2.¹⁶

Acetaminophen readily penetrates the blood-brain barrier, and its analgesic and antipyretic effects correlate well with cerebrospinal fluid (CSF) levels.^{23,25,30} In fact, the rapid CSF penetration, combined with the earlier and higher peak concentration observed with IV acetaminophen, may be responsible for its more rapid onset of action and peak efficacy compared with oral or rectal acetaminophen (Figure 2).^{23,25,31}

Regardless of route of administration, acetaminophen is metabolized by the liver via 3 primary pathways: glucuronidation (85%), sulfation, and oxidation.^{25,32} The latter pathway metabolizes acetaminophen into the hepatotoxic compound, *N*-acetyl-*p*-benzoquinone imine, which is subsequently metabolized to non-hepatotoxic compounds by glutathione.³³ Thus, hepatotoxicity may occur in the setting of elevated hepatic levels of acetaminophen that overcome hepatic glutathione stores.²⁵

This mechanism of hepatotoxicity becomes especially relevant when considering that absorption of drugs via the enteral route may result in locally high drug levels in the portohepatic circulation (ie, "first-pass" effect).²⁵ By contrast, IV infusion of drugs results in rapid elevations of plasma levels while avoiding this first-pass effect. Indeed, first-pass pharmacokinetic models have shown that the IV route of administration reduced initial hepatic acetaminophen exposure by approximately 2-fold when compared with the oral route.^{25,34} In adults weighing more than 50 kg, a maximum dose of 4 g per day, in repeated doses, has been shown to be safe and well tolerated.¹⁶

The American Society of Anesthesiologists (ASA) Task Force on Acute Pain Management has endorsed the use of acetaminophen as a component of multimodal analgesia for the purposes of reducing reliance on opioids.³⁵ The availability of this agent as an IV formulation furthers the ability to deliver acetaminophen in the postoperative setting. The ASA guidelines specifically advocate the use of nonopioid analgesics administered as first-line agents around the clock and for opioids to be used as adjunctive agents.³⁵

Clinical Studies of IV Acetaminophen

Two pivotal trials investigated the use of IV acetaminophen for the treatment of postoperative pain. In the first study, 101 patients with moderate to severe pain following orthopedic surgery were given either 1 g IV acetaminophen or placebo

at 6-hour intervals for 24 hours.²⁴ Supplemental IV patient-controlled analgesia (IV-PCA) morphine was available to all patients if needed. IV acetaminophen was significantly better than placebo in terms of pain relief from 15 minutes to 6 hours postoperatively, median time to morphine rescue (IV acetaminophen: 3 hours; placebo: 0.8 hours), and morphine consumption over 24 hours (38.3 vs 57.4 mg for placebo; 33% decrease in morphine consumption with IV acetaminophen) (Figure 3).²⁴ An expanded analysis of these study data was recently published and demonstrated that the sum of pain intensity differences over 24 hours (SPID24) using a 0- to 100-mm visual analog scale (VAS) was significantly improved with IV acetaminophen when compared with placebo.³⁶ Rescue medication consumption, requests, and actual administration were all lower in the IV acetaminophen group when compared with placebo for each 6-hour dosing interval.³⁶

The other pivotal trial of IV acetaminophen was a double-blind, placebo-controlled, parallel-group study in which 244 patients with moderate to severe pain after abdominal laparoscopic surgery were randomized to receive either IV acetaminophen (1,000 mg every 6 hours or 650 mg every 4 hours) or IV placebo (100 mL every 6 hours or 65 mL every 4 hours) over 24 hours.³⁷ Results showed that the primary end point, SPID24, was statistically more favorable than placebo (-194.1 vs -45.2 mm; $P < 0.007$),³⁷ and the time to meaningful pain relief was significantly shorter in patients receiving IV acetaminophen 1,000 mg compared with placebo (24.9 vs 53.9 minutes, $P < 0.003$).³⁷ Furthermore, IV acetaminophen was associated with a longer median time to first rescue medication, a lower proportion of patients requiring rescue medications, and significantly better

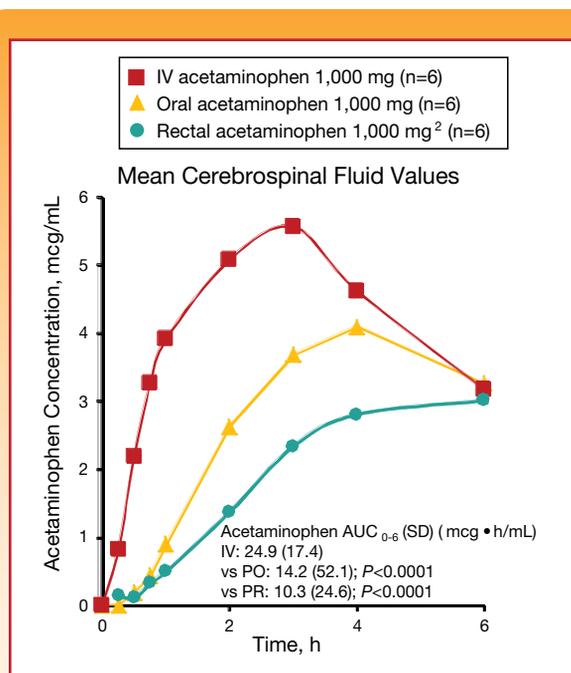


Figure 2. Mean (SD) CSF acetaminophen concentration-time curves after IV, PO, and PR administration of 1,000 mg (N=6).

AUC, area under the curve; CSF, cerebrospinal fluid; PO, oral; PR, rectal; SD, standard deviation

Based on reference 23.

patient satisfaction with pain control when compared with placebo.³⁷ Although both IV acetaminophen regimens, 1,000 mg every 6 hours or 650 mg every 4 hours, are efficacious, only the 1,000-mg dose produced a statistically significant difference in time to meaningful pain relief and total pain relief over the first dosing interval compared with placebo.³⁷

IV acetaminophen also has been studied in other surgical populations. For example, Cakan and colleagues performed a prospective, double-blind, randomized placebo-controlled study of IV acetaminophen (1 g every 6 hours for 24 hours) in 40 patients undergoing lumbar laminectomy and discectomy.³⁸ Pain scores at rest and on movement at multiple time points (12, 18, and 24 hours) were significantly lower with IV acetaminophen than with placebo.³⁸ Furthermore, patients receiving IV acetaminophen had greater satisfaction with pain control (“excellent” rating: 45% vs 5%, $P<0.05$), lower morphine consumption at all evaluation times, and a decreased incidence of vomiting ($P<0.05$).³⁸

The efficacy and safety of IV acetaminophen versus placebo has been investigated in patients following major abdominal and pelvic surgery requiring a planned admission to the intensive care unit (ICU). Memis and colleagues studied the efficacy of IV acetaminophen (1 g every 6 hours for 24 hours) or placebo (100 mL saline every 6 hours for 24 hours).³⁹ Use of IV acetaminophen was associated with significantly lower pain scores and lower postoperative opioid consumption (61% reduction, $P<0.05$) and lower nausea and vomiting ($P<0.05$) and sedation scores ($P<0.05$) when compared with placebo. Patients were sent to the ICU still intubated, and those receiving IV acetaminophen demonstrated a shorter time to extubation compared with placebo (64.3 vs 204.5 minutes; $P<0.05$).³⁹

In addition to these studies, IV acetaminophen has been

shown to exert similar benefits in the postoperative setting in adults undergoing a variety of other types of surgical procedures, including open abdominal, gynecologic, cardiac surgery, and thyroidectomy.⁴⁰ Several studies have shown that these postoperative benefits also occurred in pediatric patients undergoing hernia repair, tonsillectomy, strabismus surgery, or dental procedures.⁴¹⁻⁴⁴

Another benefit associated with the use of IV acetaminophen in the postoperative setting is its antipyretic properties. Peacock and colleagues reported that IV acetaminophen was as effective as oral acetaminophen in reducing fever.⁴⁵ The significance of this effect is underscored by the fact that fever can adversely affect the patient’s metabolism and cardiovascular system, especially during the “temperature spike” phase with its shivering-induced increase in metabolic rate, norepinephrine-mediated peripheral vasoconstriction, and increased arterial blood pressure.⁴⁶ Additionally, antipyretic therapy may enhance patient comfort in the postoperative setting and could potentially reduce the risk for fever-associated delirium in the elderly or febrile seizures in the pediatric population.^{47,48} However, the role of postoperative fever or the use of antipyretics as independent predictors of outcomes has not been definitively studied in the postoperative setting.

IV acetaminophen may be preferable for some surgical patients because, unlike other analgesics, it does not affect mental status, rates of bleeding, respiratory drive, gastric mucosal integrity, or renal function.²¹ However, acetaminophen doses in excess of 4 g daily have been associated with hepatic injury, and therapeutic doses have been associated with injury in patients who are at an increased risk for hepatotoxicity (eg, the elderly, alcoholics, and those who have preexisting liver disease or who are severely malnourished)¹⁶; thus, clinicians are encouraged to follow the recommended doses based on the patient’s weight and the appropriate time intervals when administering repeat doses (Table 2).¹⁶ Clinicians should be cautious to ensure that patients are not receiving more than one form of acetaminophen at a given time as overdoses have been associated with accidental administration of multiple drugs containing acetaminophen.

In a study of 213 patients, the safety of IV acetaminophen was compared with standard of care, with results showing a numerically lower proportion of patients with elevated liver function tests in the IV acetaminophen group.⁴⁹ Furthermore, in a meta-analysis of 36 studies involving the use of IV acetaminophen in the postoperative setting, there was no statistical difference in the rates of AEs, including liver function abnormalities, when comparing IV acetaminophen with placebo.⁵⁰

Conclusion

Postoperative pain is a common problem with serious implications in terms of patient outcomes and health care costs. Opioid monotherapy is inadequate for postoperative pain management, and opioids and NSAIDs are associated with various common AEs that limit their overall utility.

IV acetaminophen has properties well suited for use within a multimodal analgesia paradigm, including delivery by a non-oral route, fast onset, proven safety, and reduction in pain and fever as demonstrated by multiple clinical studies. When used as a component of multimodal analgesia, IV acetaminophen also can improve outcomes by reducing the amount of opioids required for pain control in the postoperative setting among a wide variety of surgical patients.

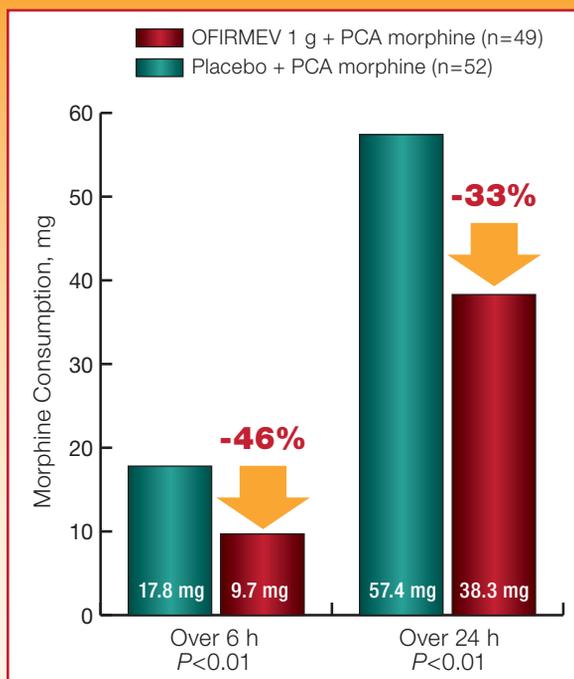


Figure 3. Morphine consumption following orthopedic surgery.

PCA, patient-controlled analgesia
Based on reference 24.

Table 2 . Recommended Dosing of IV Acetaminophen

Age Group	Dose Given Every 4 h	Dose Given Every 6 h	Maximum Single Dose	Maximum Total Daily Dose of Acetaminophen (Any Route)
Adults and adolescents (≥13 y) weighing ≥50 kg	650 mg	1,000 mg	1,000 mg	4,000 mg in 24 h
Adults and adolescents (≥13 y) weighing <50 kg	12.5 mg	15 mg/kg	15 mg/kg (up to 750 mg)	75 mg/kg in 24 h (up to 3,750 mg)
Children (2-12 y)	12.5 mg	15 mg/kg	15 mg/kg	75 mg/kg

Based on reference 16.

Case Study 1

A 47-year-old woman undergoing an anterior-posterior cervical spine procedure.

Eugene R. Viscusi, MD

The patient had a 2-month history of severe, burning neck pain radiating to her arms and numbness and weakness of the upper extremities. Magnetic resonance imaging confirmed discogenic cord impingement at C 4-5-6 levels. She had had moderate control of her pain with oxycodone 10 mg every 4 hours over the past month. Otherwise, she was generally healthy. She required a general anesthetic with electrodiagnostic monitoring of her spinal cord and hence needed total IV anesthetic. The surgeon cautioned that NSAIDs would be contraindicated because of concerns for bone healing. A multimodal perioperative analgesic approach was planned. Because she used 40 to 60 mg of oxycodone per day, she was considered opioid-tolerant and special care would be taken to meet her opioid requirements and avoid opioid withdrawal.

Approximately 1 hour before induction, 1 g IV acetaminophen was administered. Her surgery concluded in approximately 5 hours. Upon arrival to the postanesthesia care unit (PACU), she was awake, responsive, and complaining of pain. Because more than 4 hours had elapsed since her last dose of IV acetaminophen, 1 g was administered and her pain improved. IV-PCA with hydromorphone was initiated in the PACU. Because she was opioid-tolerant, the patient-administered dose was set at 0.3 mg with a 6-minute lock-out. Supplemental nursing doses were 0.6 mg as needed every 2 hours. IV acetaminophen was continued for 24 hours, 1 g every 6 hours to a maximum of 4 g every 24 hours. Oral pregabalin

150 mg was continued twice daily throughout the inpatient stay. Throughout the remainder of her operative day, she was able to titrate to comfort with supplemental IV-PCA.

At 24 hours following surgery, the patient was awake, alert, comfortable, and had advanced to solid food. She described her pain as “aching now but the burning was much less than before surgery.” She said she was able to maintain reasonable comfort with her PCA but noticed improvement when IV acetaminophen was administered. She said the IV acetaminophen did not make her sleepy. She used approximately 20 mg of hydromorphone via IV-PCA over 24 hours. Oral conversion was requested with intent to discharge by postoperative day (POD) 3. She was placed on oxycodone extended release (ER) 20 mg twice daily, oxycodone immediate release (IR) 10 mg as needed every 4 to 6 hours, and IV acetaminophen was continued for an additional 24 hours. She remained comfortable throughout the next day. On POD 3, she was discharged home on oxycodone ER 20 mg, oxycodone IR 10 mg every 4 hours as needed, pregabalin 75 mg twice daily, and oral acetaminophen 975 mg (ie, 325 g x 3) every 6 hours with follow-up in 2 weeks.

At 2 weeks, her pain was much improved and she was using her oxycodone IR 10 mg only 2 to 3 times per day. At this point, oxycodone ER and pregabalin were discontinued. She was maintained on oxycodone IR 10 mg every 4 to 6 hours as needed and acetaminophen 650 mg every 4 to 6 hours as needed.

Case Study 2

A 60-year-old woman undergoing total left knee revision.

Jeffrey Stepanian, PA-C

The patient presented with a history of uncomplicated left knee total joint arthroplasty 2 years prior and an 18-month complaint of severe pain in her left knee causing significant mobility issues and requiring a walker. X-rays showed a loose tibial component, with no signs of infection. She was diagnosed

with aseptic loosening and a total left knee revision was planned. At the time of surgery, she had been taking oral oxycodone/acetaminophen as her primary analgesic for the past 8 months, normally a total of 30 mg oxycodone and 2 g acetaminophen per day. Despite this, she complained of persistent, constant,

and severe pain at an 8 on a 10-point pain intensity scale. No other significant comorbidities were noted.

The patient underwent a left total knee revision under general anesthesia. A regional nerve block was not performed. Prior to the skin incision at 7:30 AM, 1,000 mg IV acetaminophen was administered simultaneously with 2 g of cefazolin.

Following the surgery, which lasted 181 minutes, the patient was taken to the PACU in stable condition. A Polar Care cryotherapy bladder was applied to the patient's left knee. While in the PACU, the patient complained of pain at a level of 6 to 9/10. A bolus of 100 mcg IV fentanyl was administered, but failed to be effective. The patient was then administered boluses of 0.2 mg IV hydromorphone, and she required 4 doses while in the PACU still with a pain intensity reading of 7.

The patient arrived on the orthopedic floor at 12:05 PM still complaining of significant pain. At 12:40 PM, 0.5 mg IV hydromorphone was administered with a pain intensity rating of 6/10. Almost 2 hours later, the patient was administered 15 mg IV ketorolac with no change in pain intensity. At 2:25 PM, the patient received a second dose of 1,000 mg IV acetaminophen, and at 4:45 PM, she received 10 mg oxycodone IR. The pain intensity rating was now 5/10. The patient received a second dose of 10 mg oxycodone IR at 9:15 PM, at which time the pain intensity rating was still 5/10. Cryotherapy and rehabilitation using a continuous motion machine were continued every 4 hours. IV acetaminophen was continued at a dose of 1,000 mg every 6 hours.

At the start of POD 1, the patient's pain intensity rating was 5/10. The patient felt that her pain was controlled better

with IV acetaminophen than with oxycodone. She was given one last dose of IV acetaminophen at 7:15 AM, resulting in a pain intensity rating of 3/10. Cryotherapy and rehabilitation continued as before. The patient was able to ambulate 150 feet using a front-wheeled walker and ascend and descend a flight of stairs. With adequate pain control and good mobility, the patient was discharged home at 1:30 PM with oxycodone to use as needed.

At her postoperative visit a week later, she confirmed that she never needed to use the oxycodone following discharge. She no longer required the walker and was using a cane for ambulation.

This case describes a total knee revision where the patient was opioid-tolerant, and where the IV acetaminophen contributed to good-quality analgesia and allowed for discharge on POD 1. In addition, this facility has instituted a multimodal pre-op and post-op pain protocol for primary total knee arthroplasties that consists of a preoperative joint injection of 20 cc 2% lidocaine with epinephrine, a postoperative joint injection of 60 cc 0.25% bupivacaine with 2 mg of morphine sulfate, 15 to 30 mg IV ketorolac for 4 doses (unless medically contraindicated), continuous passive motion machine, cryotherapy, and IV/oral opiates. IV acetaminophen has now been added to the protocol commencing at time of induction and continuing every 6 hours for 24 hours. The addition of IV acetaminophen has resulted in an average hospital LOS of 1.7 days for primary total knee arthroplasties, a reduction of 0.6 days compared with the previous pain protocol.

Case Study 3

A 49-year-old woman undergoing a robotic laparoscopic sleeve gastrectomy.

Anthony Gonzalez, MD

The patient had a history of diabetes, hyperlipidemia, hypertension, back pain, shortness of breath with exertion, gastroesophageal reflux disease, diabetic neuropathy, chronic foot infections, and was morbidly obese with a body mass index (BMI) of 46 kg/m² (height: 64 inches, weight: 120 kg). She also had a past surgical history of a perforated bowel with history of exploratory laparotomy. She had failed multiple medical attempts for weight loss as prescribed by her primary care physician. These failed attempts included a grapefruit diet; low-carb diets; restricted caloric diets in combination with exercise, hypnosis, and acupuncture; and use of diet pills such as phentermine and orlistat.

She sought consultation for weight loss surgery for morbid obesity and comorbid medical problems. After a complete surgical and psychological evaluation, the patient was offered 3 procedures for consideration: adjustable gastric banding, sleeve gastrectomy, and gastric bypass. Based on her age, BMI, and comorbid medical issues, the sleeve gastrectomy was deemed the best option. After a long discussion and obtaining consent, she agreed to proceed with the bariatric procedure.

The patient underwent a robotic laparoscopic sleeve gastrectomy uneventfully. This procedure involved the creation of 5 small (5-mm) incisions and had an operative time of nearly

1 hour. In addition to preoperative antibiotic and prophylaxis for deep vein thrombosis, she was given a preoperative dose of 1 g IV acetaminophen. She was maintained without anything to eat or drink for the first 24 hours following surgery. Postoperatively, she was prescribed IV acetaminophen 1 g every 6 hours around the clock for mild to moderate pain. She was given hydromorphone 1 to 2 mg every 3 hours as needed for severe or breakthrough pain. During the first 24 hours after surgery, the patient did not require any opioids for pain relief. She only received IV acetaminophen during the first 24 hours. Upon questioning by the nursing staff, she stated that the pain was well relieved and did not require additional medication. On POD 1, now able to eat and drink, the patient was offered acetaminophen/hydrocodone elixir. She tolerated clear liquids, but did not ask for any pain medication.

The patient was discharged on POD 2 with a prescription for acetaminophen/hydrocodone elixir. At her follow-up office visit, the patient was doing well and reported no need to use the prescribed medication for pain relief. She reported excellent pain control and was "very satisfied" with the care at the hospital. She noted that the overall experience of undergoing and recovering from this surgery was much better than her previous surgical experience.

Note: The case studies presented are composite and are not intended to identify specific patients.

Retrospective Evaluation of Postoperative IV Acetaminophen on the Consumption of Opioids at New York Methodist Hospital

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A recent retrospective medical use evaluation (MUE) survey of “real-life” postoperative analgesic practice was conducted to evaluate the effect of the addition of IV acetaminophen to currently available therapies.¹ Although retrospective and nonrandomized, this cohort of 100 patients, who underwent various surgical procedures, confirms the value of a multimodal approach to postoperative analgesia, and more specifically, the potential of nonopioid analgesics, such as IV acetaminophen, in reducing opioid consumption and opioid-related AEs, and improving patient outcomes such as hospital LOS.

A cohort of 100 patients was evaluated as part of the retrospective survey conducted from February to July 2011 after introduction of IV acetaminophen to the formulary. Fifty patients who were administered IV acetaminophen and opioids were compared with 50 who were administered only opioids. Cohorts were matched based on surgical type and basic demographics, but not on other baseline variables. The primary efficacy end point was the total amount of morphine consumption in oral morphine equivalents. Various secondary end points included the individual morphine amounts of each subcategory of opioid therapy use after conversion to oral morphine, mean daily reduction in opioid consumption, mean change from baseline in pain intensity, mean days of each subcategory of opioid therapy use, the number of patients who used PCA and/or patient-controlled epidural analgesia (PCEA), and the mean hospital LOS.

The top 3 surgical types were gynecology, orthopedic, and general. Pain scores were similar with the combination group experiencing a change from a baseline pain intensity score of 5.5 compared with 5.2 in the opioid-only group. Patients in the IV acetaminophen and opioid groups consumed 3.7% less

morphine overall across the entire LOS when IV acetaminophen was used concomitantly with opioids. However, the mean daily reduction in opioid use in the multimodal analgesia group (IV acetaminophen plus opioids) was 64 mg compared with a 20-mg reduction in the opioid-only group. The mean days of PCA use were 1.9 and 2.3 in the combination-therapy group and opioid-only group, respectively. The mean days of PCEA use was 1.8 in the combination-therapy group and 2.1 days in the opioid-only group, respectively. The mean LOS for the IV acetaminophen group was 5.4 versus 6.4 days for the opioid-only group.

There are numerous limitations of this study. As a retrospective open-label survey, the study was not intended, nor was it powered to make between-group comparisons. It was intended to evaluate whether the initial experience with IV acetaminophen was consistent with findings in the published literature regarding its efficacy and potential for reduction of opioid consumption.

Multimodal analgesic strategies for postoperative pain, including use of nonopioid analgesic medications, in conjunction with opioid therapy have been shown to decrease opioid consumption and improve postoperative analgesia. The results of this retrospective MUE suggest that the adjunctive administration of a nonopioid analgesic such as IV acetaminophen may reduce opioid consumption after surgery and improve postoperative analgesia and patient outcomes. However, no conclusions can be drawn from these results due to the open-label design and small sample size. A larger prospective, randomized controlled trial to further study the relation between IV acetaminophen and the intended decline in opioid consumption would be appropriate.

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