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The Role of Intravenous Acetaminophen in Acute Pain Management

A Case-Illustrated Review

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Abstract and Introduction

Abstract

For more than a century, acetaminophen has been recognized worldwide as a safe and effective agent for relieving pain and reducing fever in a wide range of patients. However, until recently, acetaminophen was available in the United States only in oral and rectal suppository formulations. In November 2010, the United States Food and Drug Administration granted approval for the use of a new intravenous (IV) formulation of acetaminophen for: 1) the management of mild to moderate pain; 2) the management of moderate to severe pain with adjunctive opioid analgesics; and 3) the reduction of fever in adults and children (age ≥2 years). This case-illustrated review of IV acetaminophen begins with a discussion of the rationale for the drug's development and proceeds to analyze the clinical pharmacology, efficacy, safety, and nursing implications of its use, both as monotherapy and in combination with other agents as part of a multimodal pain therapy strategy.

Introduction

For more than a century, acetaminophen (N-acetyl-*p*-aminophenol; known internationally as paracetamol) has been recognized worldwide as a safe and effective agent for relieving pain and reducing fever in a wide range of patients (Malaise, Bruyere, & Reginster, 2007). Synthesized in 1878 and first used clinically in 1887, the drug was not widely marketed in the United States (U.S.) until the 1950s (Bertolini, Ferrari, Ottani, Guerzoni, Tacchi, & Leone, 2006). It has since become one of the mostly widely used analgesic and antipyretic agents (Bertolini et al., 2006; Kaufman, Kelly, Rosenberg, Anderson, & Mitchell, 2002; Malaise et al., 2007) and is often the first-line therapy of choice for children (Cranswick & Coghlan, 2000).

Outside the U.S., intravenous (IV) acetaminophen has been available since 2001 in Europe under the trade name Perfalgan (Bristol-Myers Squibb, Anagni, Italy) and is now available in approximately 80 countries (Fang, 2009). Until recently, acetaminophen was available in the U.S. only in oral and rectal suppository formulations (Pasero, Portenoy, & McCaffery, 2011). However, oral and rectal acetaminophen formulations are associated with a slower onset of action and more variable analgesic activity than IV acetaminophen, making them less useful in perioperative, postoperative, and acute care settings (Holmér Pettersson, Jakobsson, & Owall, 2005, 2006). In November 2010, the U.S. Food and Drug Administration (FDA) approved Ofirmev (acetaminophen for injection; Cadence Pharmaceuticals; San Diego, CA) for: 1) the management of mild to moderate pain; 2) the management of moderate to severe pain with adjunctive opioid analgesics; and 3) the reduction of fever in adults and children (age ≥2 years) (Cadence, 2010).

The present case-illustrated review of IV acetaminophen begins with a discussion of the rationale for the drug's development and proceeds to analyze the clinical pharmacology, efficacy, safety, and nursing implications of its use, both as monotherapy and in combination with other agents as part of a multimodal pain therapy strategy.

The Need for Improved Acute Pain Management

Effective treatment for pain is essential to achieve and maintain patient comfort and good clinical outcomes (Pasero, Quinn, Portenoy, McCaffery, & Rizos, 2011). Inadequate acute pain management can result in shortened or missed rehabilitation sessions and delayed mobilization (Morrison, Magaziner, McLaughlin, Orosz, Silberzweig, Koval, & Sui, 2003), and delayed ambulation can increase the risk for venous thromboembolism (Agnelli, Bolis, Capussotti, Scarpa, Tonelli, Bonizzoni, … Gussoni, 2006; Geerts, Bergqvist, Pineo, Heit, Samama, Lassen, … American College of Chest Physicians, 2008; Pasero & Portenoy, 2011). The psychologic effects of uncontrolled

pain, such as insomnia, depression, and anxiety, may contribute to decreased quality of life, poor patient outcomes, and decreased patient satisfaction (Joshi & Ogunnaike 2005; Pasero & Portenoy, 2011; Wu, Naqibuddin, Rowlingson, Lietman, Jermyn, & Fleisher, 2003). Ineffective pain management also results in increased health care costs. In one study of patients undergoing surgical repair of a hip fracture, patients with higher postoperative pain scores had significantly longer hospital stays (Morrison et al., 2003). Another study found that the primary reason for unanticipated postoperative hospital admissions or readmissions was not due to surgical complications, medical complications, or bleeding, but was due to poorly controlled pain (Coley, Williams, DaPos, Chen, & Smith, 2002).

Despite improvements in analgesic delivery, including new analgesic options and the use of patient-controlled analgesia (PCA) by a variety of routes of administration (Pasero 2011), postoperative pain remains undertreated (Wu & Raja, 2011). The continued undertreatment of acute pain worldwide led the International Association for the Study of Pain (IASP) to designate 2011 as the Global Year Against Acute Pain (Vijayan, 2011). A comparison of two studies investigating the epidemiology of acute pain in postoperative patients—one conducted in 1995 and another in 2003—illustrates that pain control did not improve during that period. Warfield and Kahn (1995) reported the results of a study using telephone surveys of patients who had undergone surgery in teaching or community hospitals. They found that ~77% of patients reported experiencing postsurgical pain, and 80% of those patients rated their postsurgical pain as moderate to extreme (Warfield & Kahn, 1995). Apfelbaum, Chen, Mehta, & Gan (2003) reported similar results from their study using telephone surveys of 250 adults who had had recent surgical procedures. They found that ~80% of patients reported having acute postsurgical pain, and 86% of those patients reported that the pain was moderate, severe, or extreme (Apfelbaum et al., 2003).

Undertreatment of acute postoperative pain also increases the risk of progression from acute to chronic (persistent) pain (Joshi & Ogunnaike, 2005; Pasero, 2011). Kehlet, Jensen, and Woolf (2006) examined the incidence of persistent pain after common surgical procedures, such as coronary artery bypass surgery, breast and thoracic surgery, groin hernia repair, and leg amputation, and found that chronic (often disabling) pain can persist for months or years after the surgical wound has healed (Kehlet, Jensen, & Woolf, 2006).

Disadvantages of Opioid Monotherapy

Opioids have been used as analgesics for more than 2,000 years and continue to be a key element in moderate to severe acute postoperative pain management. However, opioid-only treatment plans can result in intolerable and dangerous adverse effects, including constipation, nausea and vomiting, excessive sedation, and respiratory depression (Jarzyna Jungquist, Pasero, Willens, Nisbet, Oakes, … Polomano, 2011; Pasero, 2009). Concerns are also being raised about a possible link between opioid-only treatment plans and a paradoxic clinical situation in which increasing doses of opioid result in increasing sensitivity to pain, a condition referred to as opioid-induced hyperalgesia (Angst & Clark, 2006; Lee, Silverman, Hansen, Patel, & Manchikanti, 2011; Pasero & McCaffery, 2012; Pasero 2011).

Adverse effects associated with opioids commonly occur and can prevent patients from experiencing satisfactory analgesia (Oderda, Said, Evans, Stoddard, Lloyd, Jackson, … Samore, 2007; Wheeler, Oderda, Ashburn, & Lipman, 2002). In a systematic review analyzing opioid-induced adverse effects among postoperative patients in 45 randomized-controlled studies, 31% of patients experienced an adverse gastrointestinal (GI) event (ileus, nausea, vomiting, constipation), 30.3% of patients reported an adverse central nervous system (CNS) event (somnolence, sedation), 18.3% of patients reported pruritus, 17.5% of patients experienced urinary retention, and 2.8% of patients had respiratory depression (Wheeler et al., 2002). These adverse effects, especially nausea and vomiting, can be so unpleasant that some patients are willing to accept less-than-adequate pain relief to avoid them (Eberhart, Morin, Wulf, & Geldner, 2002; Gan, Lubarsky, Flood, Thanh, Mauskopf, Mayne, & Chen, 2004). CNS effects associated with opioids also increase the risk for major postoperative complications, such as aspiration, respiratory failure, decreased mobility, and falls (Jarzyna et al., 2011; Oderda et al., 2007; Wheeler et al., 2002).

Multimodal Pain Management

To address the undertreatment of postoperative pain and the limitations of opioid monotherapy, a strategy known as multimodal pain management was introduced in the early 1990s (Kehlet & Dahl, 1993; White, 2008). This approach simultaneously administers two or more analgesic agents with different mechanisms of action.

Combination therapy using drugs with distinct mechanisms of action may add analgesia or have a synergistic effect and allow for better analgesia with the use of lower doses of a given medication than if the drug were used alone (Pasero 2011). For example, postoperative multimodal analgesia may consist of the use of opioid and nonopioid pharmacologic agents, as well as regional anesthesia and continuous peripheral neural blockade. The multimodal approach has been endorsed by many professional organizations, including the American Society of Anesthesiologists (ASA) (ASA Task Force, 2012), the American Pain Society (APS) (APS, 2008), and the American Society for Pain Management Nursing (ASPMN) (Jarzyna et al., 2011).

The ASA acute pain management practice guidelines state that clinicians should use multimodal analgesia whenever possible in the perioperative setting (ASA Task Force, 2012). The ASA recommends that all surgical patients receive an around-the-clock (ATC) regimen of acetaminophen and a nonsteroidal antiinflammatory drug (NSAID) unless contraindicated, and that the dosages and duration of therapy should be individualized, balancing efficacy with the risk of adverse events. In addition, regional anesthesia should be considered (ASA Task Force, 2012). Numerous studies have shown this type of multimodal treatment plan can produce a significant opioid dose-sparing effect (ASA Task Force, 2012; Pasero et al., 2011). Most recently, anticonvulsants, such as gabapentin and pregabalin, have also been added to postoperative pain treatment plans in an attempt to produce a dose-sparing effect and to prevent persistent postsurgical pain syndromes (Pasero, 2011; Pasero, Polomano, Portenoy, & McCaffery, 2011). In addition to reducing opioid consumption and minimizing the incidence of opioid-related adverse events, a multimodal approach can improve postoperative pain relief, increase patient satisfaction, expedite mobilization and rehabilitation, and reduce health care costs (Buvanendran & Kroin, 2009; White et al., 2007).

The ASPMN guidelines on monitoring for opioid-induced sedation and respiratory depression state that nurses should advocate for opioid-sparing pain management strategies before, during, and after surgery (Jarzyna et al., 2011). The ASPMN guidelines also appropriately point out that, despite the evidence that multimodal pain management plans may have opioid dose–sparing effects, sedation and respiratory status must still be carefully monitored when opioid analgesics are given concomitantly with nonopioids (Jarzyna et al., 2011).

One multimodal strategy for the management of postoperative pain involves a stepwise approach (). In this approach, for mild postoperative pain, nonopioid analgesics (acetaminophen and an NSAID) are administered in a scheduled ATC dosing regimen along with local anesthetic infiltration of the surgical site before the incision is made. Then, analgesics with different modes of action are added in subsequent steps based on increased or anticipated increased pain intensity. For moderate postoperative pain, in addition to the nonopioid analgesics, an opioid analgesic may be administered on an as-needed basis for breakthrough pain. For continuous severe pain, a modified-release opioid may be administered ATC or a continuous local anesthetic peripheral nerve blockade might be added (Crews, 2002). The rationale for this strategy is based on the known additive or synergistic effects between different classes of analgesics, which allow a reduction in any one individual drug dose, thus potentially lowering the incidence of that medication's adverse effects (White, 2008).

Table 1. Stepwise Multimodal Pain Therapy

Step 1	Mild postoperative pain	Nonopioid analgesics (acetaminophen, NSAID) *and* Local anesthetic infiltration
Step 2	Moderate postoperative pain	Nonopioid analgesics (acetaminophen, NSAID) *and* Local anesthetic infiltration *and* Intermittent doses of opioid analgesics
Step	Severe postoperative	Nonopioid analgesics (acetaminophen and NSAID) *and* Local anesthetic infiltration *and* Intermittent doses of opioid analgesics for breakthrough pain

3	pain	*and* Local anesthetic peripheral nerve block (with or without catheter) for continuous severe pain *or* Modified-release opioid analgesics for continuous pain

Modified from: Crews, J. C. (2002). Multimodal pain management strategies for office-based and ambulatory procedures.

Delivery of Analgesics

Opioids are available for delivery by a number of different routes, including oral, rectal, IV, subcutaneous, transdermal, intraspinal, transmucosal, intranasal, and topical (Pasero et al., 2011). Commonly used oral opioids include hydrocodone and oxycodone. In the U.S., a number of oral nonopioid analgesics, including acetaminophen, nonselective NSAIDs, such as naproxen (Naprosyn) and ibuprofen (Advil, Motrin), and the COX-2–selective NSAID celecoxib (Celebrex), are approved and frequently used for acute pain treatment, either as monotherapy or in combination with opioids.

NSAIDs are considered to be appropriate for mild- to some moderate-intensity acute pain and as adjuncts to opioids for the relief of more severe acute pain (Pasero, Portenoy, & McCaffery, 2011). They do not produce respiratory depression or impair GI motility so are considered an important component with acetaminophen in a multimodal treatment plan for acute pain (Pasero, Portenoy, & McCaffery, 2011). However, the use of NSAIDs may be limited in some patients, and an understanding of their underlying mechanisms of action is important to ensuring their safe use. NSAIDs exert their analgesic and antiinflammatory effects by blocking the production of prostaglandins, which are compounds that facilitate the transmission of pain following tissue damage (e.g., surgical incision) (Pasero & Portenoy, 2011). Prostaglandins are formed when the enzyme phospholipase breaks down phospholipids into arachidonic acid. In turn, the enzyme cyclooxygenase (COX) breaks down arachidonic acid. Cyclooxygenase is a small family of enzymes, each of which is known as an isoenzyme. The best characterized isoenzymes are COX-1 and COX-2 (Pasero & Portenoy, 2011). COX-1 mediates primarily beneficial processes and is present in practically all tissues. COX-2 is found mainly at sites of injury and in the brain and mediates harmful processes. Nonselective NSAIDS, such as naproxen, ibuprofen, and ketorolac (Toradol), inhibit both COX-1 and COX-2. COX-2 selective NSAIDs, such as celecoxib, inhibit just COX-2.

The analgesia and antiinflammatory effects induced by NSAIDs are the result of COX-2 inhibition, while the adverse effects of NSAIDs are generally the result of COX-1 inhibition. For example, an adverse effect of COX-1 inhibition is reduced platelet aggregation, which helps to explain why many surgeons tell their patients to withhold nonselective NSAIDs before surgery to avoid excessive incisional site bleeding. The most common adverse effect of NSAIDs is gastric toxicity, and older adults and individuals with a history of peptic ulcer disease are among the highest risk for this adverse effect. NSAIDs can also induce acute renal failure, particularly in patients with acute or chronic volume depletion, cardiac failure, liver cirrhosis, ascites, diabetes, or preexisting hypertension (Pasero, Portenoy, & McCaffery, 2011). Shortly after the release of the COX-2–selective NSAIDs (e.g., rofecoxib [Vioxx] and valdecoxib [Bextra]), research revealed an association between their perioperative use and an increase in renal dysfunction and adverse cardiovascular events, such as myocardial infarction and stroke, in patients who had undergone high-risk cardiac surgery (Nussmeier Whelton, Brown, Langford, Hoeft, Parlow, … Verburg, 2005; Ott, Nussmeier, Duke, Feneck, Alston, Snabes, … Multicenter Study of Perioperative Ischemia Research Group, Ischemia Research and Education Foundation Investigators, 2003). The underlying mechanism for this is not entirely clear (Pasero, Portenoy, & McCaffery, 2011). All NSAIDs now carry boxed warnings for both cardiovascular and GI adverse effects (Cumberland, 2009; U.S. Food and Drug Administration, 2005).

Oral analgesics have a relatively slow onset of action due to the time required to absorb the medication from the GI tract. In addition, many hospitalized patients may not be able to take oral medications owing to nothing-by-mouth status, nausea and vomiting, reduced GI motility or function, endotracheal intubation, or the effects of anesthesia and sedation (Pasero et al., 2011). The enteral route may also be compromised by the nature of the surgery, thereby precluding oral drug administration (Joshi & Ogunnaike, 2005; White, 2008).

The use of an analgesic in an IV formulation during the immediate postoperative period provides a number of

advantages, including improved bioavailability and earlier onset of action compared with oral and rectal formulations (Holmér Pettersson, Jakobsson, & Owall, 2006; Malaise et al., 2007). Most of the first-line opioids are available in IV formulation; however, until recently, the only nonopioid IV analgesics approved for use in the U.S. were in the NSAID family: ketorolac and ibuprofen (Caldolor). Ketorolac is a generic drug available in the U.S. from a number of manufacturers. Intravenous ibuprofen was approved by the FDA in mid-2009 for the management of mild to moderate pain, management of moderate to severe pain as an adjunct to opioid analgesics, and reduction of fever (Cumberland, 2009). Neither of these IV NSAIDs is currently FDA approved for use in pediatric patients.

IV Acetaminophen

Intravenous acetaminophen differs in many ways from the available IV opioids and NSAIDs. It is the only approved IV nonopioid analgesic that does not include a boxed warning on the label and that is indicated for use in pediatric patients. The drug is not associated with the increased incidence of nausea, vomiting, and respiratory depression that can occur with opioids, or the platelet dysfunction, gastritis, and renal toxicity that are sometimes associated with NSAIDs (Haas, 2002; Silvanto, Munsterhjelm, Savolainen, Tiainen, Niemi, Ylikorkala, … Olkkola, 2007).

Intravenous acetaminophen has a faster onset and results in more predictable pharmacokinetics than oral or rectal acetaminophen formulations (Bertolini et al., 2006, Malaise et al., 2007). In a recent study, in which six adult volunteers were given IV, oral, or rectal acetaminophen, the mean IV C_{max} (maximum plasma concentration of drug) was nearly twice that observed with oral administration and nearly four times that observed with rectal administration (Singla, Parulan, Samson, Hutchinson, Bushnell, Beja, & Royal, 2011). The IV group showed consistently earlier and higher peak plasma and cerebrospinal fluid (CSF) maximum concentration values than after either oral or rectal delivery. The variability in plasma and CSF results was much higher in the oral and rectal groups than in the group that received IV acetaminophen.

A major benefit is that IV acetaminophen may be administered before or during surgery, permitting the initiation of effective analgesic therapy in the early phase of the postoperative period (Dahl & Møiniche, 2004; Ong, Lirk, Seymour, & Jenkins, 2005). When patients are able to tolerate oral intake, they may be switched from IV to oral acetaminophen to maintain the predictable analgesia established by the IV route (Pergolizzi, Raffa, Tallarida, Taylor, & Labhsetwar, 2011).

Intravenous acetaminophen appears to avoid first-pass hepatic exposure and metabolism via portal circulation, which may reduce the potential for hepatic injury (Jahr & Lee, 2010). With therapeutic dosing (up to 4,000 mg daily) (Gregoire, Hovsepian, Gualano, Evene, Dufour, & Gendron, 2007), IV acetaminophen is rarely associated with hepatotoxicity, and it has been shown to be safe for use in some patients with underlying liver conditions (Benson, Koff, & Tolman, 2005; Rumack, 2002). Nonetheless, according to its prescribing information, IV acetaminophen is contraindicated in patients with severe hepatic impairment or severe active liver disease (Cadence, 2010).

Because of its efficacy, safety, lack of clinically significant drug interactions, and lack of the adverse effects associated with other analgesics, IV acetaminophen is an attractive component of a multimodal analgesic treatment plan (Groudine & Fossum, 2011).

Clinical Pharmacology

Mechanism of Action. Acetaminophen has both analgesic and antipyretic effects. Although the exact mechanisms of action of acetaminophen are still unclear, it is thought to exert its analgesic activity by inhibiting the synthesis of prostaglandins in the CNS (central acting) and peripherally blocking pain impulse generation (Aronoff, Oates, & Boutaud, 2006; Graham & Scott, 2005). Unlike NSAIDs, acetaminophen is not a peripheral COX inhibitor (Aronoff et al., 2006, Groudine & Fossum, 2011). In addition, it has been proposed that acetaminophen has a serotonergic (5-HT) mechanism and a cannabinoid agonism mechanism, which may contribute to its analgesic effect (Smith, 2009). The antipyretic effect of acetaminophen is thought to involve inhibition of the hypothalamic heat-regulating center, prostaglandin inhibition, and cannabinoid agonism (Malaise et al., 2007). The differences in mechanisms of action between acetaminophen and NSAIDs are likely responsible not only for the synergistic effect they have when used in combination, but also for the differences in safety profiles observed with the drugs (Groudine & Fossum, 2011).

Pharmacokinetics and Pharmacodynamics. The pharmacokinetics of IV acetaminophen has been studied in patients and healthy volunteers in a wide range of ages, from premature neonates to adults 60 years old (Cadence, 2010). IV acetaminophen achieves a higher C_{max} and an earlier time to maximum concentration (T_{max}), with less intrasubject variability than bioequivalent oral or rectal formulations (Bertolini et al., 2006; Malaise et al., 2007; Holmér Pettersson, Owall, & Jakobsson, 2004). A major advantage of IV acetaminophen is that the median time to reach T_{max} for IV acetaminophen is much faster than typically reported for oral or rectal formulations (>45 minutes) (Bertolini et al., 2006). C_{max}, which occurs at the end of the 15-minute infusion of IV acetaminophen, is up to 70% higher than that observed with the same dose of oral acetaminophen, although the overall exposure (area under the concentration time curve) is very similar (Cadence, 2010). The higher C_{max} with IV acetaminophen compared with oral acetaminophen does not seem to compromise the drug's safety profile, because the C_{max} at this dose remains far below the 150 mg/L concentration considered to be the threshold for potential hepatotoxicity (Gregoire et al., 2007).

Acetaminophen is detectable in the CSF within minutes after IV administration (Jahr & Lee, 2010; Kumpulainen, Kokki, Halonen, Heikkinen, Savolainen, & Laisalmi, 2007). The rapid CSF penetration and earlier and higher C_{max} observed with IV acetaminophen seem to be responsible for its more rapid onset and peak efficacy compared with oral or rectal acetaminophen (Jahr & Lee, 2010). The drug's duration of effect is predictable, from 4 to 6 hours (Moller, Juhl, Payen-Champenois, & Skoglund, 2005).

Metabolism. Acetaminophen undergoes metabolism by the liver via three pathways: 1) conjugation with glucuronide; 2) conjugation with sulfate; and 3) oxidation via the cytochrome P450 enzyme pathway (primarily CYP2E1) (Bertolini et al., 2006; Cadence, 2010; Gelotte, Auiler, Lynch, Temple, & Slattery, 2007; Manyike, Kharasch, Kalhorn, & Slattery, 2000).

When delivered orally, acetaminophen undergoes first-pass metabolism in the liver; however, IV administration bypasses first-pass liver metabolism (Jahr & Lee, 2010). Compared with the oral route, the IV route of administration reduces initial hepatic acetaminophen exposure by approximately twofold (Jahr & Lee, 2010).

Dosing and Administration

Intravenous acetaminophen may be given as a single dose or as repeated doses. The maximum daily dose of acetaminophen is based on all routes of administration (i.e., IV, oral, and rectal) and all products (prescription and nonprescription) containing acetaminophen. The recommended dosing for IV acetaminophen is presented in (Cadence, 2010). It is not necessary to adjust the dose when converting between oral and IV acetaminophen in adults and adolescents (Cadence, 2010).

Table 2. Dosing for IV Acetaminophen

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

Reference: Cadence, 2010.

Intravenous acetaminophen is supplied in a 100-mL glass vial containing 1,000 mg (10 mg/mL) ready-to-use acetaminophen (i.e., no reconstitution or dilution is required) (Cadence, 2010). The entire dose of IV acetaminophen is administered over 15 minutes, and the infusion must be vented for proper delivery.

Patients who weigh <50 kg should not receive the entire 100-mL vial of IV acetaminophen. Therefore, to avoid the inadvertent delivery of the total volume of the vial to these patients, the appropriate dose must be aseptically withdrawn and placed into a separate empty sterile container (e.g., glass bottle, plastic IV container, or syringe) before administration.

Once the vacuum seal of the glass vial has been penetrated, the dose of IV acetaminophen must be administered within 6 hours. IV acetaminophen is a single-use vial, and the unused portion must be discarded (Cadence, 2010).

Other medications should not be added to the IV acetaminophen solution. Diazepam and chlorpromazine hydrochloride are physically incompatible with IV acetaminophen, so simultaneous IV administration of these drugs should be avoided (Cadence, 2010). To prevent the possibility of an air embolism, it is important to observe the end of the infusion (Cadence, 2010).

Clinical Research on the Use of IV Acetaminophen

Preemptive Analgesia. An IV formulation of acetaminophen may have important implications for implementation of a preemptive approach to the management of postoperative pain (i.e., dosing an analgesic before a pain stimulus, such as a surgical incision, with the intent to reduce subsequent pain), a concept introduced in the clinical setting decades ago (Dahl & Kehlet, 1993; Woolf & Chong, 1993). One goal of preemptive analgesia is to decrease pain by timing the analgesic's peak pharmacodynamic effect with the anticipated onset of pain or peak pain response (Dahl & Moiniche, 2004).

Two studies demonstrated a preemptive effect with the administration of IV acetaminophen before surgical incision (Arici, Gurbet, Türker, Yavaşcaoğlu, & Sahin, 2009; Prasanna & Sharma, 2010). In one of these studies (Arici et al., 2009), 82 patients undergoing total abdominal hysterectomy were randomized to receive either 1,000 mg IV acetaminophen preemptively 30 minutes before anesthesia induction (group 1; n = 28), 1,000 mg IV acetaminophen at the end of surgery before skin closure (group 2; n = 27), or placebo (group 3; n = 27). No statistically significant differences were found between the operation times among the three groups (group 1, 121.6 min; group 2, 114.3 min; group 3, 118.3 min). Postoperatively, all patients received IV PCA morphine rescue as needed. Total morphine consumption in both IV acetaminophen groups (group 1, 25.93 mg; group 2, 35.73 mg; $p <$ .05 for both) was significantly lower than in the placebo group (62.93 mg), and the preinduction acetaminophen group used less morphine than the end-of-surgery acetaminophen group ($p <$ .05). Another important finding was that, compared with both IV acetaminophen groups, the placebo group had a statistically significantly higher incidence of postoperative nausea, vomiting, and itching ($p <$ .05 for each). Patients in group 1 experienced the lowest incidences of all of these adverse effects and the shortest length of hospital stay (group 1, 5.03 days; group 2, 5.20 days; group 3, 6.43 days).

In the second study of preemptive analgesia (Prasanna & Sharma, 2010), 80 patients undergoing cesarean section were randomized to receive either 1,000 mg IV acetaminophen plus 75 mg intramuscular (IM) diclofenac preemptively before surgical incision but after induction of anesthesia (n = 40) or 1,000 mg IV acetaminophen plus 75 mg IM diclofenac at the end of surgery before skin closure (n = 40). The exact time of analgesic administration was not reported, although the authors mentioned consideration of a 45-minute peak time for IM diclofenac. All patients were given 3 µg/kg IV fentanyl immediately after delivery, and postoperatively, all patients could receive as-needed rescue opioid analgesia (opioid was not named in the report). The need for rescue analgesia for treatment of breakthrough pain was recorded during cleaning after surgery, transfer from the operating room table to the stretcher, and during transport from the operating room to the PACU. Patients in the group receiving the study treatment before surgery reported significantly fewer total instances of breakthrough pain compared with patients in the group receiving study treatment at the end of surgery (45 vs. 90; $p <$ .001). In the group receiving study treatment before surgery, seven patients required rescue opioid before transfer to the PACU and 14 patients required rescue opioid during transfer. In the group receiving study treatment at the end of surgery, 14 patients required rescue opioid before transfer to the PACU and the balance of patients (26) required rescue opioid immediately in the PACU. No other patient outcomes were reported.

Intravenous acetaminophen has been given prophylactically as a component of multimodal treatment plans for patients undergoing fast-track surgical procedures. A randomized controlled trial of 160 patients who underwent

laparascopic cholecystectomy found that those who received IV acetaminophen during surgery and oral acetaminophen after surgery experienced similar pain relief and adverse effects but required less rescue medication on the first postoperative day compared with those who were given an IV COX-2–selective NSAID (parecoxib, not available in the U.S.) during surgery and an oral COX-2–selective NSAID (valdecoxib) after surgery (Tiippana, Bachman, Kalso, & Pere, 2008). A report of 500 consecutive patients who were given IV acetaminophen, parecoxib, and bupivacaine surgical site infiltration before fast-track bariatric surgery described a significant reduction in hospital stay from 3 to 2 days (Bergland, Gislason, & Raeder, 2008).

Acute Postoperative Pain in Adults. The efficacy of IV acetaminophen for the management of postoperative pain in adult patients has been studied in several randomized placebo-controlled trials around the world demonstrating effective pain relief and opioid dose–sparing effects () (Atef & Fawaz, 2008; Juhl, Norholt, Tonnesen, Hiesse-Provost, & Jensen, 2006; Memis, Inal, Kavalci, Sezer, & Sut, 2010; Moller et al., 2005; Sinatra, Jahr, Reynolds, Viscusi, Groudine, & Payen-Champenois, 2005; Wininger, Miller, Minkowitz, Royal, Ang, Breitmeyer, & Singla,). Macario and Royal (2011) conducted a systematic literature review of 16 prospective randomized-controlled trials (1,464 patients, with 780 receiving IV acetaminophen) that compared IV acetaminophen with either placebo or an active comparator in patients undergoing a wide variety of surgical procedures. The active comparators in these studies were parecoxib, IV metamizol (an NSAID removed from the U.S. market in the 1970s because of its adverse effect profile), and oral ibuprofen. In seven of the eight active-comparator studies, patients receiving IV acetaminophen experienced similar pain relief as those who received the comparative agent. Of these eight, three reported significant reductions in opioid consumption, fewer patients requiring rescue analgesia, or longer time to request for rescue analgesia. In 12 of the 14 placebo-controlled trials, patients who were given IV acetaminophen experienced improved pain relief. In 10 of the 14 trials, the IV acetaminophen group had reduced opioid consumption, the duration of analgesia was longer, and fewer patients required rescue analgesics.

Table 3. Clinical Studies of Postsurgical IV Acetaminophen in Adult Patients

Authors/Year Published	Surgical Procedure	No. of Patients	Comparators	Results
Sinatra et al., 2005	Total hip or knee arthroplasty	101	•IV acetaminophen (1,000 mg) •Placebo	•IV acetaminophen plus PCA morphine improved pain relief compared with placebo plus PCA morphine over 24 hours •IV acetaminophen reduced morphine consumption •Duration of analgesia (time to first rescue medication) was longer with IV acetaminophen •Patients' global evaluations of satisfaction were higher with IV acetaminophen
Wininger et al., 2010	Abdominal laparoscopic surgery	244	•IV acetaminophen (1,000 mg) •Placebo	IV acetaminophen produced greater reduction in pain intensity over 24 hours
Memis et al., 2010	Major abdominal or pelvic surgery	40	•IV acetaminophen (1,000 mg)	•Postoperative meperidine consumption was significantly less with IV acetaminophen •Time to extubation was ~3 hours shorter for the IV acetaminophen group

			•Placebo	•Postoperative nausea and vomiting and sedation scores were significantly lower with IV acetaminophen
Atef & Fawaz, 2008	Tonsillectomy	76	•IV acetaminophen (1,000 mg) •Placebo	•Postoperative meperidine consumption was lower with IV acetaminophen (18 mg) than with placebo (82 mg) •Patients in the IV acetaminophen group experienced significantly less pain •The occurrence of insufficient pain relief was less with IV acetaminophen •No significant difference between groups in the incidence of adverse effects
Moller et al., 2005	Third molar extraction	101	•IV acetaminophen (1,000 mg) •Placebo	•IV acetaminophen provided significantly more effective pain relief than placebo •Duration of analgesia was longer with IV acetaminophen •Patients' global satisfaction was higher with IV acetaminophen
Juhl et al., 2006	Third molar extraction	297	•IV acetaminophen (1,000 mg) •IV acetaminophen (2,000 mg) •Placebo	•Pain relief and duration of analgesia with the 2,000 mg dose were improved compared with those seen with either the recommended 1,000 mg dose or placebo •No difference in adverse effects between the groups

Total Hip or Knee Arthroplasty. Sinatra et al. (2005, 2011) reported the results of a randomized double-blind placebo-controlled clinical trial that evaluated the analgesic efficacy of single and repeated doses (every 6 hours) of 1,000 mg IV acetaminophen plus PCA morphine versus placebo plus PCA morphine for 24 hours in 101 patients with moderate to severe pain after total hip or knee arthroplasty. Treatment was initiated the morning after surgery. The primary end point of this study was pain relief measured on a 4-point scale (0 = no pain; 1 = mild pain; 2 = moderate pain; 3 = severe pain) over 6 hours. Patients who received IV acetaminophen experienced better pain relief and significant reductions in morphine consumption (46% reduction over 6 hours and 33% reduction over 24 hours) compared with those who received placebo. Furthermore, a significant improvement in median time to first rescue medication was seen with IV acetaminophen (3 hours) compared with placebo (0.8 hours). Other important findings were that adverse effects were similar between the patients treated with IV acetaminophen and those receiving placebo, and that patients' global evaluations of satisfaction with study treatment at 24 hours were significantly higher among those treated with IV acetaminophen: 79.6% of patients in the IV acetaminophen group rated their satisfaction as fair to excellent, compared with 65.4% of those in the placebo group.

Abdominal Laparoscopic Surgery. Wininger et al. (2010) reported the results of a randomized double-blind placebo-controlled clinical trial evaluating the analgesic efficacy of repeated doses of two dosing regimens of IV

acetaminophen (1,000 mg every 6 hours or 650 mg every 4 hours for 24 hours) versus placebo in 244 patients with moderate to severe postoperative pain after abdominal laparoscopic surgery (included hysterectomy, cholecystectomy, and hernia repair). Patients in both IV acetaminophen dosing groups experienced statistically significantly greater pain relief over 24 hours compared with placebo.

Major Abdominal or Pelvic Surgery. Memis et al. (2010) assessed the effect of adding IV acetaminophen to IV meperidine in 40 adults admitted to the intensive care unit after major surgery. Patients were randomized to receive either 1,000 mg IV acetaminophen every 6 hours and IV meperidine as needed or placebo (IV saline) every 6 hours plus IV meperidine as needed for 24 hours. While patients were sedated and mechanically ventilated, rescue IV meperidine was administered for analgesia when Behavior Pain Scale (BPS) scores (3 = no pain; 12 = maximum pain) were >4. After extubation, rescue IV meperidine was administered when visual analog scale (VAS) scores (0 = no pain; 10 = worst pain imaginable) were >4. In the group that received IV acetaminophen, BPS and VAS scores were significantly lower ($p < .01$), postoperative meperidine consumption was significantly less ($p < .05$), the time to extubation was ~3 hours shorter, and postoperative nausea and vomiting, as well as sedation scores, were significantly lower than in the group that did not receive IV acetaminophen.

Tonsillectomy. A prospective placebo-controlled study randomized 76 adult patients undergoing tonsillectomy under general anesthesia to receive either 1,000 mg IV acetaminophen or placebo at 6, 12, and 18 hours after surgery (Atef & Fawaz 2008). Patients who reported moderate to severe pain (i.e., VAS pain score >30 mm at rest) were given IM meperidine. During the first 24 hours after surgery, meperidine consumption was significantly lower among the patients who received IV acetaminophen (18 mg) than those who received placebo (82 mg). Patients in the IV acetaminophen group reported significantly less pain than those in the placebo group. Insufficient pain relief (defined as a VAS score of >30 mm at rest and >50 mm on swallowing) occurred more often in patients in the placebo group than in the IV acetaminophen group ($p < .001$). In this study, no significant difference in adverse effects was seen between the two groups.

Dental Surgery. Two randomized double-blind studies evaluated the efficacy of a single dose of IV acetaminophen versus placebo in adults with moderate to severe pain after third molar extraction. Moller et al. (2005) compared the efficacy of IV infusions of 1,000 mg acetaminophen (n = 51) and placebo (n = 50) for 6 hours after starting the 15-minute infusions and found that IV acetaminophen provided significantly more effective pain relief than placebo ($p < .01$), with a significantly longer duration of analgesia and better scores on patients' global evaluation compared with placebo. Juhl et al. (2006) conducted a similar study (n = 297); however, they included a 2,000-mg IV acetaminophen group and evaluated efficacy over 8 hours. They found that pain relief and duration of analgesia with the 2,000 mg dose were significantly superior compared with either the recommended 1,000 mg dose or placebo, with no difference in adverse effects among the groups.

Peri- and Postoperative Pain in Pediatric Patients. The efficacy of 15 mg/kg IV acetaminophen for the management of perioperative pain in pediatric patients has been studied in several randomized active comparator–controlled trials () (Alhashemi & Daghistani, 2006, 2007; Capici, Ingelmo, Davidson, Sacchi, Milan, Sperti, … Fumagalli, 2008; Murat, Baujard, Foussat, Guyot, Petel, Rod, & Ricard, 2005). Murat et al. (2005) conducted a randomized, active-controlled, double-blind, parallel-group, multicenter study in 183 children ranging in age from 1 to 12 years. Patients were randomized to receive either a single dose of IV acetaminophen (15 mg/kg) or a bioequivalent dose of IV propacetamol (the prodrug of acetaminophen, not available in the U.S.; 30 mg/kg) when their postoperative pain intensity, as rated by the investigator, was >30 on a 0–100-mm VAS. Both treatments rapidly reduced pain scores, with a steep reduction from baseline pain intensity during the first 15-minute interval after infusion. The duration of analgesia, measured as the time to first rescue dose, was >4 hours for both groups. Similarly, only ~20% of the patients in both groups required rescue medication, and global evaluations of "excellent" were reported for 76% of patients receiving IV acetaminophen.

Table 4. Clinical Studies of Peri- and Postsurgical IV Acetaminophen in Pediatric Patients

Authors/Year Published	Surgical Procedure	No. of Patients/Ages	Comparators	Results

Murat et al., 2005	Inguinal hernia repair	183 (1–12 y)	•IV acetaminophen (15 mg/kg) •Propacetamol (prodrug of acetaminophen; 30 mg/kg)	•Both treatments rapidly reduced pain scores, with a steep reduction from baseline pain intensity during the first 15-minute interval after infusion •The duration of analgesia (time to first rescue) was >4 hours for both groups •20% of patients in both groups required rescue medication •Global evaluations of "excellent" were reported for 76% of patients receiving IV acetaminophen
Alhashemi & Daghistani, 2006	Tonsillectomy	80 (3–16 y)	•IV acetaminophen (15 mg/kg) •IM meperidine (1 mg/kg)	Compared with IM meperidine, IV acetaminophen provided adequate analgesia, less sedation, and earlier readiness for PACU discharge
Alhashemi & Daghistani, 2007	Dental restoration	50 (3–16 y)	•IV acetaminophen (15 mg/kg) •IM meperidine (1 mg/kg)	Compared with IM meperidine, intraoperative IV acetaminophen resulted in slightly higher pain scores but earlier readiness for PACU discharge
Capici et al., 2008	Adenotonsillectomy	50 (2–5 y)	•IV acetaminophen (15 mg/kg) •Rectal acetaminophen (40 mg/kg)	Duration of analgesia (time to first rescue analgesia) was longer with rectal acetaminophen compared with IV acetaminophen

Alhashemi and Daghistani (2006) conducted a randomized double-blind study comparing the analgesic effects of intraoperative IV acetaminophen (15 mg/kg) and IM meperidine (1 mg/kg) in 80 pediatric patients (3–16 years old) undergoing tonsillectomy. Patients who received IV acetaminophen experienced pain relief similar to those who received IM meperidine; however, those who received IV acetaminophen experienced less sedation in the early recovery period and were ready for discharge from the recovery room earlier than those who had received meperidine. These same researchers conducted another study comparing intraoperative IV acetaminophen (15 mg/kg) and IM meperidine (1 mg/kg) in 40 pediatric patients (3–16 years old) undergoing dental restoration under general anesthesia (Alhashemi & Daghistani, 2007). All patients received 0.5 mg/kg oral midazolam 30 minutes before surgery and 1 µg/kg IV fentanyl immediately after induction. Anesthesia was induced with either sevoflurane inhalation or 2–3 mg/kg IV propofol and was maintained with sevoflurane. Patients who received IV acetaminophen had slightly higher pain scores but were ready for discharge from the recovery room earlier than those who received meperidine.

In a study of 46 pediatric patients (2–5 years old) who underwent adenotonsillectomy, patients were randomized to receive either rectal acetaminophen (40 mg/kg) or IV acetaminophen (15 mg/kg) after induction of anesthesia (Capici et al., 2008). Patients received a standardized anesthetic, which included 2 µg/kg fentanyl, and rescue

analgesia (IV fentanyl) was provided after surgery if pain scale scores were ≥4. Ninety-eight percent (45/46) of the children required rescue analgesia, mostly 6–10 hours after surgery. In this study, the time to first rescue analgesia was significantly longer among the children receiving rectal acetaminophen (median 10 hours) than in the group receiving IV acetaminophen (median 7 hours; p = .01).

Safety Profile

Intravenous acetaminophen has been well tolerated in 1,375 patients (1,020 adults and 355 pediatric patients) in clinical trials, establishing an impressive safety profile (Atef & Fawaz, 2008; Cadence, 2010; Memis et al., 2010; Sinatra et al., 2005, 2011; Wininger et al., 2010). Furthermore, the safety of IV acetaminophen is supported by more than 8 years of clinical postmarketing safety experience outside the U.S., as well as more than 60 years of clinical experience with oral and rectal formulations (Wininger et al., 2010).

Adult Patients. In clinical trials, 1,020 adult patients were treated with IV acetaminophen; 380 of these (37%) received at least five doses and 173 (17%) received more than ten doses. Eighty-seven percent (n = 886) of the patients received 1,000 mg IV acetaminophen every 6 hours; the remaining 134 patients were treated with 650 mg IV acetaminophen every 4 hours (Cadence, 2010). Fifteen percent of the patients treated with IV acetaminophen in clinical studies were ≥65 years old, and 5% were ≥75 years old. No overall differences in safety were observed between older and younger patients (Cadence, 2010).

The primary safety concern with acetaminophen is its potential hepatic toxicity when used at doses higher than recommended (>4,000 mg/d for adult patients) (U.S. Food and Drug Administration, 2009). According to postmarketing surveillance, hepatic toxicity associated with acetaminophen is rare—occurring in fewer than 1 in 500,000 treated patients (Sinatra et al., 2005). In a pooled analysis of eight multicenter, double-blind, randomized, placebo-controlled studies (four single-dose and four multiple-dose studies; n = 1,064) conducted in the U.S. to evaluate the hepatic safety of IV acetaminophen versus placebo, liver enzyme elevations in patients treated with IV acetaminophen were similar to those who received placebo. In one of the trials, in which patients received repeated doses over 48 hours, the placebo group demonstrated a higher rate and greater severity of liver enzyme elevations (6/165; 3.6%) than the IV acetaminophen group (3/166; 1.8%), and the placebo group had a slightly higher rate of hepatic adverse effects (26/415; 6.3%) than the IV acetaminophen group (20/649; 3.1%) (Singla, Viscusi, Candiotti, Royal, & Breitmeyer, 2008).

Nonetheless, administration of acetaminophen by any route in doses higher than recommended may result in liver injury, including the risk of severe hepatotoxicity and death. Acetaminophen is found in more than 600 different prescription and over-the-counter medicines, including not only analgesics and antipyretics, but also sleep aids and cough, cold, and allergy medications. To reduce the risk of severe liver injury from acetaminophen overdosing, the Acetaminophen Awareness Coalition created the *Know Your Dose* (www.knowyourdose.org) patient education campaign (Acetaminophen Awareness Coalition, 2011). In addition, in January 2011, the FDA asked manufacturers of prescription acetaminophen combination products to limit the maximum amount of acetaminophen in these products to 325 mg per dosage unit (e.g., tablet, capsule) (U.S. Food and Drug Administration, 2011).

Caution must be used when administering acetaminophen to patients with liver dysfunction or active liver disease, alcoholism, chronic malnutrition, severe hypovolemia (e.g., due to dehydration or blood loss), or severe kidney dysfunction (i.e., creatinine clearance ≤30 mL/min) (Cadence, 2010). IV acetaminophen is contraindicated in patients with severe hepatic impairment or severe active liver disease.

Treatment-related adverse reactions occurring in ≥3% of patients treated with IV acetaminophen in clinical trials are presented in . The most common adverse reactions in adult patients treated with IV acetaminophen are nausea, vomiting, headache, and insomnia. The pyrexia adverse reaction frequency data are included in to point out that the antipyretic effects of IV acetaminophen may mask fever (Cadence, 2010).

Table 5. Treatment-Emergent Adverse Reactions Occurring in ≥3% of Adult Patients Treated with IV Acetaminophen

System Organ Class (Preferred Term)	n (%)	

	IV Acetaminophen (n = 402)	Placebo (n = 379)
Gastrointestinal disorders		
Nausea	138 (34%)	119 (31%)
Vomiting	62 (15%)	42 (11%)
General disorders and administration site conditions		
Pyrexia*	22 (5%)	52 (14%)
Nervous system disorders		
Headache	39 (10%)	33 (9%)
Psychiatric disorders		
Insomnia	30 (7%)	21 (5%)

Reference: Cadence, 2010.
*The pyrexia adverse reaction frequency data are included to point out that the antipyretic effects of IV acetaminophen may mask fever.

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When dosed appropriately, IV acetaminophen is not associated with cardiovascular thrombotic events, cognitive impairment, platelet inhibition, postoperative ileus, renal toxicity, respiratory depression, sedation, surgical site bleeding, or upper GI bleeding. Single doses of IV acetaminophen up to 3,000 mg and repeated doses of 1,000 mg every 6 hours for 48 hours have not been shown to significantly affect platelet aggregation (Cadence, 2010). No immediate or delayed effects on small vessel hemostasis have been seen. In clinical studies in which healthy volunteers as well as patients with hemophilia received multiple doses of oral acetaminophen, no significant changes in bleeding time were observed (Cadence, 2010). Although no studies have been conducted on short-term use, long-term use of acetaminophen at maximum dose has been shown to increase international normalized ratio (INR) in individuals stabilized on sodium warfarin (Coumadin); therefore, monitoring INR in such patients after surgery is recommended (Pasero, Portenoy, & McCaffery, 2011).

Pediatric Patients. Intravenous acetaminophen is the only IV agent approved to treat both pain and fever in

pediatric patients aged ≥2 years. The effectiveness of IV acetaminophen for the treatment of acute pain and fever has not been studied in pediatric patients <2 years old (Cadence, 2010). The most common adverse events reported in pediatric patients treated with IV acetaminophen are nausea, vomiting, constipation, pruritus, agitation, and atelectasis (Cadence, 2010).

Conclusion and Nursing Implications

Intravenous acetaminophen is a nonopioid non-NSAID analgesic for the management of mild to moderate pain or as part of a multimodal pain treatment strategy with adjunctive opioid analgesics for moderate to severe pain. When used as recommended, IV acetaminophen is a safe addition to the current available analgesics. Before administering IV acetaminophen, however, nurses should be aware of the patient's use of both prescription and nonprescription medications that contain acetaminophen to avoid exceeding the maximum daily dose of acetaminophen. After administration of IV acetaminophen, the nurse must explain to patients the importance of not exceeding the maximum daily dose of acetaminophen with prescription and nonprescription medications that the patient may take after discharge.

Supplied as a single-dose vial with a concentration of 1,000 mg/100 mL, IV acetaminophen requires no reconstitution or dilution and is administered by 15-minute vented infusion. Simple weight-based dose calculation is necessary for children aged 2–12 years and anyone aged ≥13 years weighing ≤50 kg. IV administration provides a more rapid onset of analgesia with more predictable pharmokinetics parameters than oral or rectal acetaminophen administration. The analgesia achieved with IV acetaminophen administration can be subsequently maintained by oral delivery. No dose adjustment is necessary when converting between oral and IV acetaminophen dosing in adults and adolescents.

Intravenous acetaminophen has broad compatibility with other agents making it an excellent choice as an adjunct to other analgesics, such as NSAIDs and opioids, where synergy through complementary mechanisms of action may be clinically useful in multimodal analgesic regimens. A major advantage of IV acetaminophen is that it reaches a significantly higher (70%) maximum concentration faster (at the end of the 15-minute infusion) than when the drug is given orally or rectally (>45 minutes), and this is accomplished without compromising the safety profile of the drug. Other benefits are that the use of IV acetaminophen may reduce opioid consumption, minimize the incidence of opioid-related adverse events, improve pain relief, increase patient satisfaction, expedite mobilization and rehabilitation, and reduce health care costs. Because of its efficacy, safety, lack of clinically significant drug interactions, and lack of the adverse effects associated with other analgesics, IV acetaminophen is an attractive component of a multimodal analgesic treatment plan. When patients are able to tolerate oral intake, they may be moved from IV to oral acetaminophen to maintain the predictable analgesia established by the IV route.

Sidebar

Case #1

Jill F. is a 51-year-old high school science teacher with stage IIIA breast cancer who underwent a mastectomy of her left breast 4 months ago. The adjacent lymph nodes and chest muscles were left intact. Her postoperative pain was managed with an opioid-only treatment plan (PRN ["as needed"] boluses IV morphine), and she experienced severe pain for most of the first 48 hours after surgery. At the 6-month postoperative visit with her nurse practitioner, she reports persistent, disabling postoperative pain ("continuous burning, tingling, like an electrical shock"). She is unable to return to work full time and participate in her usual social activities.

Case #2

Peter C. is a 48-year-old businessman who underwent a laparoscopic cholecystectomy as an outpatient. He was given a total of 150 µg IV fentanyl in 25 µg doses every 10–15 minutes for severe pain in the postanesthesia care unit (PACU). His pain was reduced to moderate intensity, but he experienced intractable nausea and excessive sedation necessitating admission for an overnight stay until the adverse effects resolved.

Case #3

Josephine B. is a 72-year-old retired secretary who is 6 hours after abdominal hysterectomy. Her pain treatment plan includes oral acetaminophen given preoperatively and continued every 6 hours postoperatively; IV ketorolac, initiated on admission to the PACU and continued every 6 hours; and IV PCA hydromorphone. She is resting comfortably with pain ratings of ≤4, and her sedation levels and respiratory status, checked hourly, have been satisfactory since admission to the clinical unit.

Case #4

Jim C. is a 49-year-old architect who will undergo rectal abscess repair. The surgeon anticipates that Jim's postoperative pain will be mild to moderate in intensity and instructs Jim to take 650 mg oral acetaminophen and 200 mg celecoxib with sips of water 2 hours before surgery. The surgeon infiltrates the surgical site with the long-acting local anesthetic bupivacaine (Marcaine) before incision. On admission to the PACU, Jim rates his pain as 5 on a scale of 0 to 10. He is given 50 µg IV fentanyl twice to reduce his pain to 2. He is discharged home 45 minutes after the last dose of fentanyl with instructions to take 650 mg acetaminophen every 6 hours and 200 mg celecoxib daily. He may also take 5–10 mg oxycodone every 4 hours as needed for moderate breakthrough pain.

Case #5

Jane R., a 37-year-old woman, is given IV acetaminophen in the preoperative holding area 10 minutes before undergoing a laparascopic tubal ligation. In the PACU after surgery, her pain rating is 4 on a scale of 0 to 10 and she is given 0.3 mg IV hydromorphone. She will be discharged home with orders to take 550 mg naproxen every 12 hours and 1,000 mg oral acetaminophen every 6 hours starting 6 hours after the preoperative IV acetaminophen dose.

Case #6

Mark J. is a 47-year-old man with a body mass index of 35 kg/m^2 who will undergo a laparascopic gastric bypass and enteral bypass. His surgeon uses a fast-track protocol that focuses on prevention of pain, early discharge, and active participation in important recovery activities, such as ambulation. Mark is given 1,000 mg IV acetaminophen before surgery, bupivacaine infiltration in the surgical site before incision, and 800 mg IV ibuprofen during surgery. He experiences excellent pain control with continued doses of IV acetaminophen and IV ibuprofen for the first 24 hours after surgery. He is moved to oral formulations of the nonopioid drugs before discharge on postoperative day 2.

Case #7

Thomas D. is 82 years old and has undergone an open colon resection and colostomy placement. His pain management plan includes continuous epidural infusion of hydromorphone and ropivacaine (Naropin) initiated preoperatively and a dose of 1,000 mg IV acetaminophen intraoperatively. 1,000 mg IV acetaminophen is given every 6 hours and the epidural infusion is continued postoperatively until Thomas is able to move to oral medications.

Case #8

Tyler C. is a 6-year-old boy who presents in the emergency room with right ulnar fracture. He rates his pain as 8 on the 0–10 Wong-Baker FACES scale. Two doses of IV morphine (0.05 mg/kg), given 10 minutes apart, in addition to IV acetaminophen (15 mg/kg) by 15-minute infusion reduced Tyler's pain to 4 within 30 minutes of admission.

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