Pain management among patients undergoing orthopedic surgery is often a challenge. Regional anesthesia has become a popular anesthetic technique providing optimal pain control during the intraoperative and postoperative periods. A 61-year-old woman presented for an open reduction and internal fixation of bilateral distal radius fractures. The patient underwent general anesthesia and received bilateral axillary nerve blocks. A single 8-mg dose of dexamethasone was given intravenously to prolong the analgesic effect of the axillary nerve blocks. The patient did not receive opioids in the immediate postoperative setting and received only one dose of intravenous morphine during her hospital stay.

Current research has shown prolonged analgesic effects when dexamethasone is administered either intravenously or perineurally. However, the Food and Drug Administration has not approved perineural administration of dexamethasone. Intravenous administration of dexamethasone prolongs analgesic effects equivalently. This case study supports previous findings suggesting that dexamethasone, 8 mg, administered intravenously prolongs the duration of analgesia when used in conjunction with bupivacaine in a peripheral nerve block.

Keywords: Analgesics, anti-inflammatory, dexamethasone, regional anesthesia, steroid.

Peripheral nerve blocks provide several benefits for patients undergoing orthopedic surgery, most notably, analgesia with decreased opioid consumption leading to more timely discharge and shortened hospital stay.1 As value-based healthcare delivery systems have become popular in an evolving healthcare economy, improved outcomes, timeliness, efficiency, and patient satisfaction are critical elements to achieve.2 Peripheral nerve blocks with local anesthetics alone provide between 4 and 8 hours of analgesia, but pain control becomes a concern after the nerve block has worn off.3 Several studies confirm the prolonged duration of analgesia when dexamethasone is used as an adjunct to local anesthetics administered perineurally via single-shot nerve block.3-5 Recent randomized controlled trials show equivalent duration of analgesia when dexamethasone is given intravenously (IV).6,7 With a lack of US Food and Drug Administration (FDA) approval for the perineural administration of adjunctive medications and their potential for histologic nerve damage, the IV administration of dexamethasone in conjunction with peripheral nerve blocks should be considered. In this case report, IV dexamethasone was administered with bilateral axillary nerve blocks to prolong the duration of analgesia for repair of bilateral distal radius fractures.

Case Summary
A 61-year-old English-speaking woman (height of 142 cm, weight of 47 kg) presented for an open reduction and internal fixation of bilateral distal radius fractures resulting from a ground-level fall. The patient's medical history was remarkable for eczema and lung cancer. Her lung cancer had been in remission for the past 8 years after she underwent a lobectomy, and there was no respiratory compromise. The patient was not receiving medications long term. She was given a single dose of morphine, 4 mg IV, 4 hours before surgery, and no other medications were consumed before her preoperative assessment. A pain score of 8 of 10 on the visual analog scale (VAS) was reported during the preoperative assessment. Preoperative vital signs were as follows: heart rate of 63/min, blood pressure of 144/52 mm Hg, respiratory rate of 20/min, oxygen saturation of 98%, and temperature of 36.7°C.

The patient consented to general anesthesia supplemented with bilateral axillary nerve blocks; the first nerve block was placed in the preoperative holding area. Because of substantial discomfort and anxiety, the patient requested that the second axillary nerve block be done after general anesthesia. Standard monitors were applied, and oxygen was given at 6 L/min via face mask. The left axillary region was prepared in a sterile manner, and an ultrasound probe was draped and used to identify the brachial plexus anatomy. After visualization of the axillary vasculature and nerves, a 21-gauge peripheral nerve block needle (Arrow StimuQuik, Teleflex Inc), through an in-plane approach, was used to place the axillary block. On appropriate placement of the needle and no aspiration, 0.5% bupivacaine was injected in 5-mL increments (total dose of 50 mg) for a total of 10
mL surrounding the median, ulnar, radial, and musculocutaneous branches of the brachial plexus. No changes occurred in heart rate, blood pressure, or the electrocardiogram. There was minimal resistance with injection, and the patient had no complaints of paresthesia or pain. The spread of bupivacaine around the axillary artery and nerves was visualized under ultrasound guidance. The patient reported a relief of pain to a score of 4 of 10 approximately 10 minutes after the block was completed. In the preoperative setting, the patient reported progressing loss of sensation to the distal left forearm.

The patient was brought to the operating room and standard monitors were applied. Before induction of general anesthesia, the axillary nerve block was assessed, again revealing sensory loss to temperature because there was no response to an alcohol swab to the distal digits. Because of the progression of motor loss, the patient required assistance with transfer onto the operating room table. She was placed in the supine position on the operating table and preoxygenated for 5 minutes. General anesthesia was induced with propofol, 150 mg, and a size 3 laryngeal mask airway (Teleflex Inc) was placed in the supraglottic region. General anesthesia was maintained with a propofol infusion at 100 µg/kg/min, and 8 mg of dexamethasone was given IV after induction. Once the patient was stable under anesthesia and surgery had begun on the left distal radius, a right axillary nerve block was performed in the same manner in anticipation of the right distal radius surgery. This block was done at this time per the surgeon’s request to decrease delay. An equivalent dose of 0.5% bupivacaine (50 mg) was administered for a total of 10 mL to the branches of the right brachial plexus. The patient’s vital signs remained within 20% of preoperative measurements throughout the case.

The surgery began at midnight, lasted approximately 4 hours, and was uneventful. On the patient’s arrival to the postanesthesia care unit, a pain score of 1 of 10 was reported, vital signs remained within 20% of baseline, and no opioids were administered during this time. The first dose of opioid administration was given on the ward 16 hours after placement of the peripheral nerve block, still considered postoperative day 0. Morphine, 4 mg IV, was given for a VAS pain score of 5 of 10 targeted in the left wrist. The patient was able to participate in physical and occupational therapy after the block had worn off because her surgery had been completed in the early morning. On postoperative day 1 the patient was given 10/325 mg of hydrocodone-acetaminophen for relief of pain (score of 4/10) at the right wrist. No additional analgesics were administered throughout the patient’s hospital stay. The patient was discharged home on postoperative day 2.

Discussion

Pain management continues to be a challenge for health-care providers. Patients with poor pain management are at higher risk of extended hospital stays and readmission. They are also at higher risk of development of hospital-related complications, which can increase the overall cost of healthcare. The Joint Commission has incorporated pain management as a standard of care, and the Hospital Consumer Assessment of Healthcare Providers and Systems has incorporated a 2-question patient satisfaction survey for evaluating pain management. Failure to maintain adequate pain management may negatively affect reimbursement rates to healthcare facilities from the Centers for Medicare and Medicaid Services.

Opioids are known to have several adverse effects, including nausea, vomiting, constipation, pruritus, somnolence, dizziness, oversedation, and respiratory depression. These adverse events are associated with extended hospital stays and increased healthcare costs. Liu and Wu published a systematic review investigating analgesia, health-related quality of life, quality of postoperative recovery, and patient satisfaction. The authors reviewed the use of epidural analgesia, single-shot peripheral nerve blocks, and continuous perineural analgesia compared with outcomes using IV opioids for analgesia. The review concluded that regional analgesic techniques were superior to the administration of systemic opioids in providing analgesia. The use of regional anesthesia was shown to decrease overall opioid consumption and the need for intraoperative opioids, and to control pain throughout the postoperative period. This discussion will include a brief review of the action of local anesthetics, a postulated mechanism of action of dexamethasone as an adjunct in regional anesthesia, perineural vs IV administration of dexamethasone with regional anesthesia, and dexamethasone given IV in the absence of regional anesthesia in providing analgesia.

Clinical Pharmacology. Local anesthetic drugs block the conduction of electrical impulses to nerve fibers and are commonly used to treat acute and chronic pain in regional anesthesia. These drugs bind to voltage-gated sodium channels (Na+) and prevent the initiation of an action potential. The nonionized local anesthetic molecules are lipid soluble and gain access across the cell membrane by diffusion. Beyond the cell membrane, the chemical equilibrium results in ionized local anesthetic molecules to bind to the sodium channel and block nerve conduction (Figure). Local anesthetics will target nerve fibers, specifically C-fibers, with early onset of nerve block and high sensitivity.

Different drugs have been added to local anesthetics to alter their effects. Sodium bicarbonate and epinephrine are common adjuncts that aid in accelerating onset and prolonging block duration, respectively. Tramadol, buprenorphine, clonidine, dexmedetomidine, and magnesium are also adjuncts that have been investigated. Dexamethasone is a glucocorticoid commonly
used during surgery and anesthesia as prophylaxis for postoperative nausea and vomiting. Its off-label use to prolong analgesia in regional nerve blocks has become popular; however, the exact mechanism of action remains unclear. Theories suggest its analgesic benefit is related to the interruption of nociceptive C-fiber transmission. Johansson et al found a reduced transmission in unmyelinated C-fibers on application of corticosteroid in rats. On removal of the corticosteroid solution, nerve transmission returned to baseline, possibly indicating a relationship. Other speculations on dexamethasone’s mechanism of action include the reduction of inflammatory mediators, ectopic neuronal discharges, and inhibition of potassium channels on C-fibers. Table 1 summarizes the known and putative mechanisms of action of local anesthetics and dexamethasone.

- Clinical Impact. Dexamethasone has been demonstrated to be an effective adjuvant when administered perineurally with local anesthetics. Cummings et al concluded that dexamethasone prolonged the duration of interscalene blocks when given perineurally with 0.5% ropivacaine or 0.5% bupivacaine. The analgesic duration of 0.5% ropivacaine was approximately 12 hours; however, dexamethasone extended the analgesic effects to 22 hours ($P < .001$). Similarly, the action of 0.5% bupivacaine was prolonged when dexamethasone was added (15 hours vs 22 hours; $P < .001$). This trial was included in a meta-analysis of randomized trials conducted by Choi et al, which determined that the perineural administration of dexamethasone with local anesthetics in brachial plexus blocks prolonged the duration of analgesia. The meta-analysis included 9 trials for a total of 801 patients. Perineural dexamethasone added to long-acting local anesthetics prolonged sensory blocks by an additional 576 minutes (nearly 10 hours; 95% confidence interval [CI], 515-625 minutes; $P < .00001$) with low heterogeneity and by 175 minutes (nearly 3 hours; 95% CI, 73-277 minutes; $P < .00001$) with significant heterogeneity when added to intermediate-acting local anesthetic. Overall results did not show any incidence of persistent nerve palsy or dexamethasone-related complications. They did find that perioperative measurements of blood glucose were elevated, but the elevations were not clinically relevant.

Prolongation of analgesia and motor blockade with injection of perineural dexamethasone and local anesthetics was also identified in a meta-analysis conducted by Albrecht et al involving 1,695 participants in 29 controlled trials. The evidence demonstrated decreased pain scores in both the early and late postoperative periods, resulting in decreased opioid consumption. In this analysis of multiple randomized controlled trials, serum glucose concentrations were evaluated and found to be elevated (1.2 mg/dL−1), and in one randomized controlled trial, a superficial wound infection was reported. Research conducted in animal studies has not ruled out histologic damage to nerves with perineural administration of adjunctive medications. Although no known study results show neurotoxicity with dexamethasone, the possibility should be considered.

Research supports the analgesic effects of dexamethasone given IV along with a peripheral nerve block. Although at least 9 studies in more than 800 surgical patients examine the perineural use of dexamethasone, only 2 studies in 225 surgical patients directly compare the perineural administration and IV administration of dexamethasone to the brachial plexus, aiming to establish the administration route that provided the longest duration of analgesia. A prospective, double-blind, randomized placebo-controlled study by Desmet et al compared the analgesic duration of a single-shot interscalene block when dexamethasone was given IV vs perineurally. A total of 144 patients were randomly as-

### Table 1. Known and Putative Mechanisms of Action

<table>
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<th>Abbreviations: K, potassium; Na, sodium.</th>
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<tr>
<td><strong>Local anesthetic</strong></td>
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<tr>
<td>Na+ channel blockade</td>
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<tr>
<td>Penetration of C-fibers</td>
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<td>Anti-inflammatory effect</td>
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**Figure.** A: Sodium (Na+) channel in resting state. B: Activation opens Na+ channel and allows sodium ions intracellularly. C: Binding site of local anesthetics in the pore of Na+ channels. D: Na+ channel is closed from intracellular side by inactivation gate.
signed into 3 groups: 0.5% ropivacaine (control); 0.5% ropivacaine and perineural dexamethasone, 10 mg; and 0.5% ropivacaine with IV dexamethasone, 10 mg. There was clinical significance in the duration of sensory block in a comparison of the control with 0.5% ropivacaine and dexamethasone as an adjunct given perineurally or IV. Analgesia in the control group lasted 757 minutes (12.6 hours), whereas analgesia lasted 1,405 minutes (23.4 hours) and 1,275 minutes (21.25 hours) in 0.5% ropivacaine with perineural dexamethasone, 10 mg, and 0.5% ropivacaine with IV dexamethasone, 10 mg, respectively.

In another trial comparing IV and perineural dexamethasone administration, the researchers found similar results using 0.5% bupivacaine. This study randomly assigned 75 patients into 3 groups: 0.5% bupivacaine; 0.5% bupivacaine with IV dexamethasone, 8 mg; and 0.5% bupivacaine with perineural dexamethasone, 8 mg. The results showed that analgesia was prolonged by 25 hours in both groups that included dexamethasone, whereas the control group had analgesia for 13 hours (P < .001). A summary of the extended analgesia in the 2 studies is included in Table 2.

As further support of the analgesic efficacy of dexamethasone administered IV (without regional anesthesia), its effects include a decrease in VAS pain scores and total opioid consumption, and prolonged analgesia in the postoperative period. Waldron et al performed a systematic review and meta-analysis, including 45 studies, to investigate the impact of IV dexamethasone on postoperative analgesia and side effects in patients undergoing laparoscopic surgery, open abdominal surgery, and middle ear surgery. They calculated mean differences with 95% CI. Although they had some statistical heterogeneity, the results concluded that patients experienced less postoperative pain, consumed less postoperative opioids, had extended times to first analgesic dose, required less rescue analgesia, and spent less time in the recovery unit. Nineteen studies measured VAS pain scores 2 hours postoperatively, and 28 studies measured VAS pain scores 24 hours postoperatively. Results showed that patients receiving IV dexamethasone had significantly lower VAS pain scores (mean difference, −0.49; 95% CI, −0.83 to −0.15; P = .005; and mean difference, −0.48; 95% CI, −0.62 to −0.35; P < .00001, respectively). Furthermore, patients receiving IV dexamethasone consumed significantly less opioids (in morphine equivalents) at 2 hours and 24 hours after surgery (mean difference, −0.87; 95% CI, −1.40 to −0.33; P = .002; and −2.33 mean difference; 95% CI, −4.39 to −0.26; P = .03, respectively). Compared with the control group, there was a 13% and 10% reduction in opioid consumption, respectively. Seven studies (947 patients) measured time to first analgesic dose, and results revealed an extended time to the first dose of opioid (P = .04). This analysis yielded small positive outcomes on reductions in postoperative pain, postoperative opioid consumption, and longer times to first opioid dose while producing statistically significant results. This systematic review did have limitations; 5 of the studies included various doses of dexamethasone, 7 studies examined pain as a primary outcome, and 35 studies examined postoperative nausea and vomiting as a primary outcome.

An additional meta-analysis by De Oliveira and colleagues investigated a single dose of IV dexamethasone on postoperative pain and concluded that the use of IV dexamethasone decreased opioid consumption, with a mean difference of −0.41 (95% CI, −0.58 to −0.24) compared with placebo. The meta-analysis included orthopedic, laparoscopic, and ear, nose, and throat surgical procedures. This analysis stratified the dexamethasone dosage into 3 groups: low-dose (≤ 0.10 mg/kg), intermediate-dose (0.11-0.20 mg/kg), and high-dose (≥ 0.21 mg/kg). In an analysis of 2,500 patients, dexamethasone at 0.1 mg/kg or higher given systemically reduced postoperative pain and opioid consumption effectively by −0.82 (−1.22 to −0.42) compared with the placebo. Intermediate- and high-dose IV dexamethasone significantly decreased opioid consumption (P = .003 and P = .002, respectively) compared with low-dose IV dexamethasone. Table 3 reviews advantages and disadvantages to the administration of IV dexamethasone.

In the case presented here, regional anesthesia was administered to facilitate postoperative pain relief and general anesthesia used for the anticipated length of the surgery for bilateral fractures. On induction of general anesthesia, dexamethasone, 8 mg IV, was given to prolong the duration of the peripheral nerve blocks. This dose was equivalent to the intermediate dose used in the analysis by De Oliveira et al. The patient did not require opioids throughout the case, validated by unchanged vital sign parameters. The patient also did not

<table>
<thead>
<tr>
<th>Drug</th>
<th>Duration of action</th>
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<tr>
<td>Ropivacaine 0.5%</td>
<td>757 min (12.6 h)²</td>
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<tr>
<td>Ropivacaine 0.5% + dexamethasone perineurally, 10 mg</td>
<td>1,405 min (23.4 h)²</td>
</tr>
<tr>
<td>Ropivacaine 0.5% + dexamethasone IV, 10 mg</td>
<td>1,275 min (21.2 h)²</td>
</tr>
<tr>
<td>Bupivacaine 0.5%</td>
<td>13.2 h²</td>
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<tr>
<td>Bupivacaine 0.5% + dexamethasone perineurally, 8 mg</td>
<td>25 h²</td>
</tr>
<tr>
<td>Bupivacaine 0.5% + dexamethasone IV, 8 mg</td>
<td>25 h²</td>
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Table 2. Prolonged Analgesia
Abbreviation: IV, intravenously.
(From Desmet et al⁶ and Abdallah et al.⁷)
require opioids postoperatively in the recovery unit. This case was unique because 2 nerve blocks were performed compared with the literature already cited. This may have had an influence on the duration of analgesia because the usual dose of bupivacaine for a unilateral block was divided into 2 separate doses to avoid local anesthetic toxicity in this patient. The time to first dose of opioid (morphine, 4 mg IV) was 16 hours after the placement of the first peripheral nerve block, and the duration of action of bupivacaine can be up to 10 hours. The bilateral axillary blocks were successful in controlling pain for this patient, shown by minor changes in vital signs and minimal opioid consumption in the intraoperative and postoperative periods even with early mobilization.

Dexamethasone as an adjunct to peripheral nerve block has been shown to be effective in prolonging the duration of analgesia when given either IV or perineurally. Several studies have reported no neuronal cell death or damage when used perineurally. However, concerns remain regarding the use of perineural dexamethasone because of its lack of FDA approval as adverse effects continue to be investigated. The 2 meta-analyses that examined IV dexamethasone reported no findings of complications. Although the patient in this case report represented an extended duration of peripheral nerve block with IV dexamethasone administration, it cannot be concluded that IV dexamethasone in conjunction with a brachial plexus nerve block was solely responsible for prolonged analgesia. The use of dexamethasone either perineurally or IV has clinical significance in its impact of prolonged duration of sensory block. To date, the authors are aware of only 2 studies with small sample sizes that have been published in this regard. Therefore, further studies should be implemented to evaluate the safety and efficacy of this drug and the routes for delivery.

REFERENCES

19. De Oliveira GS Jr, Almeida MD, Benzon HT, McCarthy RJ. Periop-

Table 3. Benefits vs Disadvantages of Intravenous Dexamethasone

<table>
<thead>
<tr>
<th>Benefit</th>
<th>Disadvantage</th>
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<tr>
<td>Decreased opioid consumption</td>
<td>Potential for perineal discomfort in awake patient</td>
</tr>
<tr>
<td>Decreased pain scores 24 hours postoperatively</td>
<td>Increased blood glucose postoperatively</td>
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<tr>
<td>Shorter PACU stays</td>
<td></td>
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<tr>
<td>Decreased incidence of postoperative nausea and vomiting</td>
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<tr>
<td>Decreased time to hospital discharge</td>
<td></td>
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<tr>
<td>May replace need for placement of continuous nerve block catheter</td>
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Abbreviation: PACU, postanesthesia care unit.


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DISCLOSURES
The authors declare they have no financial relationships with any commercial entity related to the content of this article. The authors did discuss off-label use within the article.

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