Knee arthroscopy with chondroplasty
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CASE PRESENTATION
A 33-year-old male presented with left knee pain spanning several weeks, now experiencing chronic irritation in the left knee that has worsened with intolerable pain in the previous few weeks. Patient had no prior knee surgery. He had a prior nasal surgery and hernia repair with no anesthetic complications. His social history included smoking a 1/2 pack per day. Drug allergies included hydrocodone and oxycodone, which caused pruritus.

DIAGNOSIS AND RECOMMENDED PROCEDURE
- Diagnostic left knee arthroscopy with chondroplasty and plica excision
- Anesthetic plan included general anesthesia via laryngeal mask airway and multimodal analgesia to minimize opioids as chondroplasty adds significant pain to knee arthroscopy.
- Total surgical time of 28 minutes and total anesthesia time of 55 minutes.

PATIENT'S PERIOPERATIVE ANALGESIC PROTOCOL

<table>
<thead>
<tr>
<th>MEDICATION</th>
<th>PreOp</th>
<th>Induction</th>
<th>IntraOp</th>
</tr>
</thead>
<tbody>
<tr>
<td>PO celecoxib</td>
<td>400 mg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PO pregabalin</td>
<td>200 mg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>IV midazolam</td>
<td></td>
<td>2 mg</td>
<td></td>
</tr>
<tr>
<td>IV lidocaine</td>
<td></td>
<td>50 mg</td>
<td></td>
</tr>
<tr>
<td>IV propofol</td>
<td></td>
<td>150 mg</td>
<td></td>
</tr>
<tr>
<td>IV fentanyl</td>
<td></td>
<td>100 µg</td>
<td></td>
</tr>
<tr>
<td>OFIRMEV® (acetaminophen) injection</td>
<td></td>
<td></td>
<td>1 g</td>
</tr>
<tr>
<td>IV ketamine†</td>
<td></td>
<td></td>
<td>15 mg</td>
</tr>
</tbody>
</table>

† Ketamine is indicated for anesthesia only

- Do not exceed the recommended maximum daily limits of acetaminophen by all routes

INDICATIONS AND USAGE
OFIRMEV® (acetaminophen) injection is indicated for the management of mild to moderate pain, management of moderate to severe pain with adjunctive opioid analgesics, and reduction of fever.

IMPORTANT RISK INFORMATION

WARNING: RISK OF MEDICATION ERRORS AND HEPATOTOXICITY
Take care when prescribing, preparing, and administering OFIRMEV Injection to avoid dosing errors which could result in accidental overdose and death. In particular, be careful to ensure that:
- the dose in milligrams (mg) and milliliters (mL) is not confused;
- the dosing is based on weight for patients under 50 kg;
- infusion pumps are properly programmed; and
- the total daily dose of acetaminophen from all sources does not exceed maximum daily limits.

OFIRMEV contains acetaminophen. Acetaminophen has been associated with cases of acute liver failure, at times resulting in liver transplant and death. Most of the cases of liver injury are associated with the use of acetaminophen at doses that exceed the recommended maximum daily limits, and often involve more than one acetaminophen-containing product.

Please see additional Important Risk Information on reverse and in accompanying Full Prescribing Information.

* This case study is intended only to provide healthcare professionals with an example of the use of OFIRMEV (acetaminophen) injection in the treatment of one specific patient. The outcomes described may not be representative of, and may differ significantly from, outcomes that may be obtained in treating other patients. This case study is not intended to provide specific treatment advice, recommendations, or opinions, and should not replace a clinician’s judgment with respect to the treatment of any particular patient.
**PostOp Outcomes**

<table>
<thead>
<tr>
<th><strong>PAIN ASSESSMENT</strong>*</th>
<th><strong>OPIOID CONSUMPTION</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>• PACU: 0/10 throughout PACU stay</td>
<td>• PostOp Day 0: No additional opioids were required after discharge</td>
</tr>
<tr>
<td>• PostOp Day 1: 2/10 average (home)</td>
<td>• PostOp Day 1: Two doses of 50 mg PO pentazocine (afternoon and bedtime)</td>
</tr>
</tbody>
</table>

*Based on a 10-point numeric rating scale (NRS).

**PATIENT DISCHARGE**
- PACU Aldrete score: 9/10 within 15 minutes of arrival at PACU
- Patient was discharged home 1 hour after surgery and scheduled for follow up office visit 7 days PostOp.

**IMPORTANT RISK INFORMATION**

**CONTRAINDICATIONS**
- Acetaminophen is contraindicated in patients with:
  - known hypersensitivity to acetaminophen or to any of the excipients in the intravenous (IV) formulation.
  - severe hepatic impairment or severe active liver disease.

**WARNINGS AND PRECAUTIONS**
- Administration of acetaminophen in doses higher than recommended may result in hepatic injury, including the risk of liver failure and death. Do not exceed the maximum recommended daily dose of acetaminophen. The maximum recommended daily dose of acetaminophen includes all routes of acetaminophen administration and all acetaminophen-containing products administered, including combination products. Dosing errors could result in accidental overdose and death.
- Use caution when administering acetaminophen in patients with the following conditions: hepatic impairment or active hepatic disease, alcoholism, chronic malnutrition, severe hypovolemia (e.g., due to dehydration or blood loss), or severe renal impairment (creatinine clearance ≤ 30 mL/min).
- Rarely, acetaminophen may cause serious skin reactions such as acute generalized exanthematous pustulosis (AGEP), Stevens-Johnson Syndrome (SJS), and toxic epidermal necrolysis (TEN), which can be fatal. Hypersensitivity and anaphylaxis associated with the use of acetaminophen have been reported. Clinical signs included swelling of the face, mouth, and throat, respiratory distress, urticaria, rash, and pruritus. The antipyretic effects of OFIRMEV may mask fever.

**USE IN SPECIFIC POPULATIONS**
- Pregnancy: Pregnancy Category C. OFIRMEV should be given to a pregnant woman only if clearly needed.
- Breast Feeding: While studies with OFIRMEV have not been conducted, acetaminophen is secreted in human milk in small quantities after oral administration.
- Pediatrics: The effectiveness of OFIRMEV for the treatment of acute pain and fever has not been studied in pediatric patients < 2 years of age.

*Please see additional Important Risk Information, including boxed warning, on reverse side and in accompanying Full Prescribing Information.*
OFIRMEV (acetaminophen) Injection

WARNING: RISK OF MEDICATION ERRORS AND OVERDOSE

Take care when prescribing, preparing, and administering OFIRMEV because dosing errors which could result in accidental overdose and death. (5.3)

OFIRMEV (acetaminophen) injection is contraindicated in patients with known hypersensitivity to acetaminophen or any of the excipients. (4)

Patients with severe hepatic impairment or severe active liver disease should be used with caution in patients with hepatic impairment. (4.7)

INFORMATION FOR PATIENTS

Use the following information when instructing patients in the use of OFIRMEV. (12)

INDICATIONS AND USAGE

OFIRMEV (acetaminophen) injection is indicated for:

• the management of mild to moderate pain
• the management of moderate to severe pain with a non-opioid analgesic
• the reduction of fever

DOSE AND ADMINISTRATION

2.1 Acute Pain and Fever

OFIRMEV may be given as a single or repeated dose for the treatment of acute pain or fever. No dose adjustment is required when converting between oral acetaminophen and OFIRMEV dosing in adults and adolescents who weigh 50 kg and above. Calculated doses for patients weighing less than 50 kg should be adjusted based on body weight. Exceeding the maximum mg/kg daily dose of acetaminophen may result in liver injury, including the risk of liver failure and death. To avoid the risk of overdose, each dose should be administered using a syringe pump and from all routes of administration (i.e., intravenous, oral, and intramuscular). DO NOT use intravenous acetaminophen on a continuous infusion basis to avoid overdosing. Use strict sterile technique when preparing OFIRMEV for intravenous infusion. Do not add other medications to the OFIRMEV solution. Diazepam and chlorpromazine for intravenous administration are not recommended for use with OFIRMEV injection. (5.1)

2.2 Recommended Dose: Adults and Adolescents

2.2.1 Adults and Adolescents Weighing ≥50 kg

The recommended dose of OFIRMEV is 15 mg/kg every 4 hours or 12.5 mg/kg every 6 hours. A maximum single dose of OFIRMEV of 15 mg/kg, a minimum dosing interval of 4 hours, and a maximum daily dose of acetaminophen of 75 mg/kg per day may be used.

2.2.2 Recommended Dose: Children

Children 2 to 12 years of age: the recommended dosage of OFIRMEV is 15 mg/kg every 6 hours or 12.5 mg/kg every 4 hours. The total daily dose of acetaminophen from all sources does not exceed maximum daily dose of 125 mg/kg per day. See full prescribing information for complete boxed warning. (5.1). See WARNINGS AND PRECAUTIONS. (5.4)

2.4 Intravenous Administration

For adult and adolescent patients weighing ≥50 kg requiring more than 1000 mg of OFIRMEV, the recommended intravenous dosage is set through the syringe of the 100 mL vial OFIRMEV may be administered as a single dose or divided into multiple doses. Examine the vials before content for preparation or administration. DO NOT USE if particulate matter or cloudiness is observed. Administration of the contents of the vial intravenously for 15 minutes. Use strict sterile technique when preparing OFIRMEV for intravenous infusion. Do not add other medications to the OFIRMEV solution. Do not administer at concentrations exceeding maximum daily limits. See DOSAGE AND ADMINISTRATION (2).

DOSE FORMS AND STRENGTHS

OFIRMEV is available as a 100 mL intravenous injectable for single dose use or 750 mg intravenous for multiple dose use. Each mL of OFIRMEV contains acetaminophen 15 mg/mL. Each mL of OFIRMEV contains acetaminophen 15 mg/mL (1000 mg per vial). Each mL of OFIRMEV contains acetaminophen 15 mg/mL (750 mg per vial).

CONTRAINDICATIONS

Acetaminophen is contraindicated in patients with known hypersensitivity to acetaminophen or any of the excipients. (4)

SPECIAL POPULATIONS

• Pregnancy
• Labor and Delivery
• Pediatric Use
• Drug Interactions
• Geriatric Use
• Renal Impairment

ADVERSE REACTIONS

The most common adverse reactions in patients treated with OFIRMEV Injection are:

• Nausea
• Vomiting
• Headache
• Rash

Drug-Related Laboratory Findings

The most common laboratory test abnormalities in patients treated with OFIRMEV Injection are increases in ALT, AST, and total bilirubin. In addition, patients who received 5 or more doses, and 17.0% (n=173) of the patients had at least 1 abnormal liver test result.
The most common adverse events (incidence ≥ 5%) in pediatric patients treated with OFIRMEV were nausea, vomiting, constipation, and pruritus.

Other Adverse Reactions Observed During Clinical Studies

The following additional treatment-emergent adverse reactions were reported by pediatric subjects (incidence ≥ 2%) and were not seen in the control group (incidence < 2%): abdominal pain, diarrhea, and vomiting.

Animal reproduction studies have not been conducted with OFIRMEV. OFIRMEV has been administered to pregnant rats that received oral acetaminophen during organogenesis at doses up to 0.3 times the maximum human daily dose (640 mg/kg/day, based on a body surface area comparison) and has not been shown to cause a significant effect on fetal development. NOHADAN is not indicated for use in pregnant women. OFIRMEV should be given to a pregnant woman only if clearly needed.

Skeletal malformations (4.3%) was similar to the rate in a control study from the National Birth Defects Prevention Study which showed that 1.61% of children had skeletal malformations. In contrast, acetaminophen has been demonstrated to be dose proportional in adults and the maximum human daily dose (MHDD = 4 grams/day, based on a body surface area comparison).

The pharmacokinetic exposure of OFIRMEV was demonstrated to be dose proportional in adults and the maximum human daily dose (MHDD = 4 grams/day, based on a body surface area comparison).

There are no adequate and well-controlled studies in pregnant women. Therefore, the use of OFIRMEV in pregnant women has not been studied. OFIRMEV should be given to pregnant women only when clearly needed.

In a non-controlled dose-finding study conducted in 101 patients with postoperative pain, 48% of patients achieved 48 hours post-treatment. Treatment

OFIRMEV is supplied in a 100 mL glass vial containing 100 mg acetaminophen (100 mg/mL). Carton of 24 vials, NDC 43825-102-01

In studies conducted by the National Toxicology Program, carcinogenicity assessments have been completed in male and female rats and mice. In rats, acetaminophen has been reported to be carcinogenic in males, with a threshold of 3.6 times the MHDD (based on a body surface area comparison). In contrast, no carcinogenicity studies have been conducted in female rats.

In a study conducted by the National Toxicology Program, the maximum human daily dose (MHDD) of 4 grams/day, based on a body surface area comparison, is 1.2 times the maximum human daily dose (MHDD) of 3.6 grams/day, based on a body surface area comparison.

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