Robotic sleeve gastrectomy

Anthony Gonzalez, MD, Chief of Surgery, Baptist Hospital, Miami, FL

CASE PRESENTATION
A 34-year-old female with history of morbid obesity (135 kg, 5’6”, BMI 48) who has failed multiple medical attempts for weight loss, presented for bariatric surgery evaluation. Her past medical history included obstructive sleep apnea and fibrocystic breast disease. Her social history included rare tobacco use and alcohol consumption of a few drinks a week.

DIAGNOSIS AND RECOMMENDED PROCEDURE

- Robotic sleeve gastrectomy, robotic hiatal hernia repair, intraoperative upper endoscopy
  - Via 4 laparoscopic incisions 5-12 mm in size, a robotic sleeve gastrectomy was created over a 36 Fr bougie. The staple line was oversewn. The hiatal hernia was repaired with non-absorbable sutures. An endoscopy was performed at the completion.
  - Duration of procedure was 1 hour and 23 minutes.

PATIENT'S PERIOPERATIVE ANALGESIC PROTOCOL

<table>
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</thead>
<tbody>
<tr>
<td>OFIRMEV® (acetaminophen) injection</td>
<td>1 g</td>
<td></td>
<td>1 g q6h</td>
<td>1 g q6h</td>
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<td></td>
<td></td>
<td></td>
<td>(One dose)</td>
<td>(Three doses)</td>
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<tr>
<td>IV fentanyl</td>
<td></td>
<td>100 μg</td>
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<tr>
<td>IV morphine</td>
<td></td>
<td>10 mg</td>
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<td></td>
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<tr>
<td>IV hydromorphone</td>
<td></td>
<td></td>
<td>1 mg q4h</td>
<td>1 mg q6h</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>(Two doses)</td>
<td>(Two doses)</td>
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<tr>
<td>IV ketorolac</td>
<td></td>
<td></td>
<td>30 mg</td>
<td>30 mg</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>(Two doses)</td>
<td>(One dose)</td>
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<tr>
<td>PO acetaminophen</td>
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<td></td>
<td></td>
<td></td>
<td>650 mg</td>
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<tr>
<td>PO oxycodone</td>
<td>prn</td>
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</table>

- 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

#### PAIN ASSESSMENT*

<table>
<thead>
<tr>
<th></th>
<th>OPIOID CONSUMPTION</th>
</tr>
</thead>
<tbody>
<tr>
<td>PACU: 7/10</td>
<td>• PostOp Day 0: 2 mg IV hydromorphone</td>
</tr>
<tr>
<td>PostOp Day 0: 4/10 (32 minutes after Dose 1 of OFIRMEV)</td>
<td>• PostOp Day 1: 2 mg IV hydromorphone</td>
</tr>
<tr>
<td>PostOp Day 1: 0/10 (30 minutes after Dose 1 of OFIRMEV)</td>
<td>• PostOp Day 2: none given</td>
</tr>
<tr>
<td>PostOp Day 1: -4/10 (30 minutes after Dose 2 of OFIRMEV)</td>
<td>Patient did not need PO oxycodone during her stay.</td>
</tr>
</tbody>
</table>

*Based on a 10-point visual analog scale (VAS).

#### PATIENT AMBULATION/DISCHARGE

- First ambulation of 50 yards on PostOp Day 0, and ambulation of more than 200 yards on PostOp Days 1 and 2.
- Patient was discharged from the PACU after 70 minutes.
- Total length of hospital stay was 2 days.

#### 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.
- **Serious adverse reactions** may include hepatic injury, serious skin reactions, hypersensitivity, and anaphylaxis. **Common adverse reactions** in adults include nausea, vomiting, headache, and insomnia. **Common adverse reactions** in pediatric patients include nausea, vomiting, constipation, pruritus, agitation, and atelectasis.

**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.
**CONTRAINDICATIONS**

Children: 

- Children under 12 years of age 
- Children weighing less than 25 kg

These contraindications apply to the use of acetaminophen at doses that exceed the recommended dosage limits, and often involve more than one acetaminophen-containing product.

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**INDICATIONS AND USAGE**

- OFIRMEV (acetaminophen) injection is indicated for:
  - Children: 2 to 12 years of age
  - Adults and adolescents weighing 50 kg and over:
  - Pregnancy: Category C

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**DOSE AND ADMINISTRATION**

- **Children**: 2 to 12 years of age: 15 mg/kg every 6 hours or 12.5 mg/kg every 4 hours to a maximum of 75 mg/kg per day.

- **Adults and Adolescents Weighing 50 kg and Over**: 500 mg intravenous injection every 4 hours to a maximum of 2000 mg per day.

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**ADVERSE REACTIONS**

- Injections for intravenous infusion.

- Hepatic injury:

  - Maximum total exposure was 7.7, 6.4, 6.8, and 7.1 days in neonates, 5 days in infants, 2 days in children, and 4 days in adults. The maximum single dose of acetaminophen of 75 mg/kg per day.

- **5.2 Serious Skin Reactions**

  - Acute hypersensitivity reactions associated with the use of acetaminophen, including angioedema, urticaria, and allergic-type reactions (see Warnings and Precautions).

- **5.3 Risk of Medication Errors**

  - Use caution when administering acetaminophen in patients with the following conditions: hepatic impairment or active liver disease, moderate to severe renal impairment, alcoholism, or congestive heart failure (see Warnings and Precautions).

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**FULL PRESCRIBING INFORMATION: CONTEXT**

- **WARNING**: Risk of Medication Errors and Hepatotoxicity

- **INDICATIONS AND USAGE**

- **DOSE AND ADMINISTRATION**

- **ADVERSE REACTIONS**

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- **DOSE AND ADMINISTRATION**

- **ADVERSE REACTIONS**

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**TREATMENT OF OVERDOSE**

- Discontinue acetaminophen therapy, and provide supportive care.

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**TREATMENT OF OVERDOSE**

- Discontinue acetaminophen therapy, and provide supportive care.
The pharmacokinetic exposure of OFIRMEV observed in infants is similar to that observed in children age 2 years and older. At therapeutic levels, binding of acetaminophen to plasma proteins is low (ranging from 10% to 25%). Acetaminophen appears to be widely distributed throughout most body tissues and fluids except for the central nervous system and GI tract. Acetaminophen is not bound to plasma proteins in humans.

Acetaminophen is metabolized in the liver by first-order kinetics and involves three principal pathways: conjugation with glucuronic acid, glutathione, and sulfate, and oxidation via the cytochrome P450 enzymes. Pathway I: glucuronidation results in a reactive intermediate metabolite (N-acetyl-p-benzoquinone imine or NAPQI). NAPQI is conjugated with glutathione and is then further metabolized to form cysteine and cysteine conjugates. Acetaminophen metabolites are mainly excreted in the urine. Less than 5% is excreted in the urine as unreacted free or conjugated acetaminophen. The maximum human daily dose (MHDD) of 4 grams/day, based on a body surface area comparison. In contrast, there was no evidence of carcinogenic activity in male rats (0.7 times the MHDD, based on a body surface area comparison).

OFIRMEV was studied in 355 pediatric patients in two active-controlled phase 3 clinical trials and pharmacoeconomic trials (see in Specific Populations (8.4)).

The efficacy of OFIRMEV 1000 mg in the treatment of adult fever was evaluated in an randomized, double-blind, placebo-controlled clinical trial. The study was a 6-hour, single-dose, endotracheal-injected study in healthy adult males. A statistically significant antipyretic effect of 1000 mg was demonstrated in both treatment groups in children age 4 years of age and older.

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16 HOW SUPPLIED/STORAGE AND HANDLING
NDC: 0281-102-01 - OFIRMEV (acetaminophen) Injection [USP] for the treatment of pain and fever in pediatric patients (100 mg in 24 mL of saline, 1000 mg in 100 mL of saline). Each mL of OFIRMEV is supplied in a 100 mL glass vial containing 1000 mg OFV1569MK of Mallinckrodt company.

15 NONCLINICAL TOXICOLOGY
15.1 Carcinogenesis, Mutagenesis, Impairment of Fertility
Carcinogenesis
Long-term studies in mice and rats have been completed by the National Toxicology Program to evaluate the carcinogenic potential of acetaminophen. In 2-year feeding studies, F344 rats and B6C3F1 mice were fed diets containing acetaminophen up to 6000 ppm. Female rats demonstrated equivocal evidence of carcinogenic activity based on increased incidences of mononuclear cell leukemia at 38 times the maximum human daily dose (MHDD) of 4 grams/day, based on a body surface area comparison. In contrast, there was no evidence of carcinogenic activity in male rats (0.7 times the MHDD, based on a body surface area comparison).

Mutagenicity
acetaminophen was not mutagenic in the bacterial reverse mutation assay (L5178Y). In contrast, acetaminophen tested positive in the mouse lymphoma tk+/- assay and in a chromosomal aberration assay using human lymphocytes. In Clinical Pharmacology (1.2): A reduced total daily dose of acetaminophen may be warranted.

8.4 Pediatric Use
OFIRMEV should be given to a pregnant woman only if clearly needed.

Caution should be exercised when OFIRMEV is administered to a nursing woman.

There is one well-documented report of a rash in a breast-fed infant that resolved when the mother stopped acetaminophen therapy. While studies with OFIRMEV have not been conducted, acetaminophen is secreted in human milk in small quantities. Clinically meaningful differences in responses between the elderly and younger subjects, and other reported clinical experience has not identified differences in responses between the elderly and younger patients, but greater caution is warranted because of age-related changes in hepatic metabolism and pharmacokinetics.

Pharmacokinetics (12.3)
Table 4: OFIRMEV Pharmacokinetic Parameters

The pharmacokinetic exposure of OFIRMEV observed in infants is similar to that observed in children age 2 years and older.

For additional information, call a poison control center at 1-800-222-1222.

Figure 1: Mean Temperature (°C) Over Time

Figure 2: Time Post Dose (h) Over Time

The safety and effectiveness of OFIRMEV for the treatment of acute pain and fever in pediatric patients 2 years of age and older is supported by evidence from adequate and well-controlled studies of OFIRMEV in adults. Studies in pregnant rats that administered to a pregnant woman. OFIRMEV should be given to a pregnant woman only if clearly needed.

studies have not been conducted with IV acetaminophen, and differences in responses between the elderly and younger subjects, and other reported clinical experience has not identified differences in responses between the elderly and younger patients, but greater caution is warranted because of age-related changes in hepatic metabolism and pharmacokinetics.

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