Perioperative Pregabalin & Ketamine as Multimodal Pain Management Strategies

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This presentation reviews off-label indications for pregabalin and ketamine.
Pharmacist & Nursing Learning Objectives

1. Review the evidence and guideline recommendations for the use of pregabalin and ketamine for perioperative pain management
2. Describe pregabalin and ketamine dosing and administration regimens
3. Discuss the major findings of a retrospective study utilizing pregabalin and ketamine as a multimodal pain management strategy within the bariatric surgery program at Parham Doctors’ Hospital
Pharmacy Technician Learning Objectives

1. Describe common dosage forms, dosages and adverse effects for pregabalin and ketamine
2. Describe the role of non-opioid adjuvant medications for pain management
3. List common complications of opioid use in obesity
### Definitions

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
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<tbody>
<tr>
<td>ADE</td>
<td>adverse drug effect</td>
</tr>
<tr>
<td>AAA</td>
<td>abdominal aortic aneurysm</td>
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<tr>
<td>BMI</td>
<td>body mass index</td>
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<tr>
<td>CNS</td>
<td>central nervous system</td>
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<tr>
<td>CrCl</td>
<td>creatinine clearance</td>
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<tr>
<td>GERD</td>
<td>gastroesophageal reflux</td>
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<tr>
<td>GFR</td>
<td>glomerular filtration rate</td>
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<tr>
<td>IBW</td>
<td>ideal body weight</td>
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<tr>
<td>LOS</td>
<td>length of stay</td>
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<tr>
<td>MED</td>
<td>morphine equivalent dose</td>
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<tr>
<td>MO</td>
<td>morbid obesity</td>
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<tr>
<td>NAFLD</td>
<td>nonalcoholic fatty liver disease</td>
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<tr>
<td>NASH</td>
<td>nonalcoholic steatohepatitis</td>
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<tr>
<td>NMDA</td>
<td>n-methyl-d-aspartate</td>
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<tr>
<td>NSAIDS</td>
<td>nonsteroidal anti-inflammatory drugs</td>
</tr>
<tr>
<td>OHS</td>
<td>obesity-hypoventilation syndrome</td>
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<tr>
<td>OSA</td>
<td>obstructive sleep apnea</td>
</tr>
<tr>
<td>PACU</td>
<td>post anesthesia care unit</td>
</tr>
<tr>
<td>PCA/PCEA</td>
<td>patient controlled (epidural) analgesia</td>
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<tr>
<td>PK</td>
<td>pharmacokinetic</td>
</tr>
<tr>
<td>POD</td>
<td>postoperative day</td>
</tr>
<tr>
<td>PONV</td>
<td>postoperative nausea vomiting</td>
</tr>
<tr>
<td>RYGB</td>
<td>roux-en-Y gastric bypass</td>
</tr>
<tr>
<td>TBW</td>
<td>total body weight</td>
</tr>
<tr>
<td>T ½</td>
<td>half life</td>
</tr>
<tr>
<td>V&lt;sub&gt;d&lt;/sub&gt;</td>
<td>volume of distribution</td>
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</tbody>
</table>
Pathophysiology of Pain

Multimodal Pain Management

- Two or more analgesics acting by different mechanisms to provide perioperative analgesia.
  - Non-opioid analgesics
  - Systemic adjuvants
  - Regional anesthesia and analgesia

- Multimodal analgesia is recommended for the treatment of postoperative pain (strong recommendation, high-quality evidence)
  - Scheduled non-opioid analgesics
  - Superior pain relief
  - Opioid-sparing

Pregabalin Mechanism of Action

**Pregabalin Pharmacokinetics**

- **A** Rapidly absorbed, bioavailability $\geq 90\%$, peak $\sim 1.5$ h
- **D** No plasma protein binding, wide distribution to spinal cord & brain
- **M** Negligible
- **E** $\geq 90\%$ renal, unchanged drug, $T\frac{1}{2} \sim 6$ h

Source: Lyrica ® (Pregabalin) [Package Insert]. Pfizer Pharmaceuticals LLC. Vega Baja, PR: 2011
Pregabalin Adverse Effects

Sources: Am J Health-Syst Pharm. 2007; 64: 1475-82
Lyrica®(Pregabalin) [Package Insert]. Pfizer Pharmaceuticals LLC. Vega Baja, PR: 2011
Pregabalin Evidence in Lap Cholecystectomy

**Agarwal A, et al. 2008**
- **Study Design:** Prospective, double-blind, randomized, placebo-controlled trial in patients undergoing laparoscopic cholecystectomy.
- **Objectives:** Determine effect of pregabalin on pain scores, fentanyl consumption and ADE at 0, 4, 8, 12 & 24 h postop.
- **Intervention:** Pregabalin 150 mg (N=27) vs. placebo (N=29) 1 h preop + postop fentanyl PCA.
- **Results:** Reduction in postop pain scores (p<0.05) & fentanyl consumption (p<0.05), no difference in ADE.
- **Limitations:** No multimodal analgesia described, non-U.S. (India), small sample size.

**Chang SH, et al. 2009**
- **Study Design:** Prospective, double-blind, randomized, placebo-controlled trial in patients undergoing laparoscopic cholecystectomy.
- **Objectives:** Determine effect of pregabalin on pain scores, ketorolac consumption & oversedation at 2, 4, 12, 24 & 48 h postop.
- **Intervention:** Pregabalin 300 mg (N=39) vs. placebo (N=38) 1 h preop and 12 h postop + rescue ketorolac 30 mg IV upon request.
- **Results:** No difference in pain scores or ketorolac consumption, pregabalin group with greater oversedation at 2 h (p<0.03).
- **Limitations:** No multimodal analgesia described, non-U.S. (South Korea), small sample size.

**Sarakatsianou C, et al. 2012**
- **Study Design:** Prospective, double-blind, randomized, placebo-controlled trial in patients undergoing laparoscopic cholecystectomy.
- **Objectives:** Determine effect of pregabalin on pain scores, morphine consumption & ADE at 0, 1, 8, 16 & 24 h postop.
- **Intervention:** Pregabalin 300 mg (N=20) vs. placebo (N=20) night before surgery and 1 h preop + postop paracetamol 1 gm IV q8h, morphine PCA.
- **Results:** Decreased pain scores (p<0.001) & morphine consumption (p<0.01-p<0.05) at all time points, increased dizziness (p<0.0001), no difference in PONV or sedation.
- **Limitations:** Non-U.S. (Greece), small sample size.

Sources:
Pregabalin Evidence in Hysterectomy

**Asgari Z, et al.** 2017
- **Study Design:** Prospective, double-blind, randomized, placebo-controlled trial in patients undergoing laparoscopic hysterectomy.
- **Objectives:** Determine effect of pregabalin on pain scores, meperidine use & sedation at 0, 2, 4, 6, 12 & 24 h postop.
- **Intervention:** Pregabalin 75 mg, 150 mg, 300 mg (N=20 each) vs. placebo (N=22) night before, 30 min preop & 6 h postop + diclofenac 100 mg IV and/or meperidine 50 mg IM upon request.
- **Results:** Reduced pain scores at all time points (p<0.001), less meperidine use (p<0.001), increased sedation (p<0.001)-300 mg driver for all.
- **Limitations:** No multimodal analgesia described, non-U.S. (Iran), small sample size, post-hoc between groups.

**Rajappa GC, et al.** 2016
- **Study Design:** Prospective, double-blind, randomized, placebo-controlled trial in patients undergoing vaginal hysterectomy.
- **Objectives:** Determine effect of pregabalin on pain scores, rescue analgesics & sedation at 30 min., 1, 2, 6, 12, 24 h postop.
- **Intervention:** Pregabalin 75 mg, 150 mg, 300 mg (N=20 each) vs. placebo (N=22) night before, 30 min preop & 6 h postop + diclofenac 100 mg IV and/or tramadol 50 mg IV.
- **Results:** Reduced pain scores at all time points (p<0.001), less meperidine use (p<0.001), increased sedation (p<0.001)-300 mg driver for all.
- **Limitations:** No multimodal analgesia described, non-U.S. (India), small sample size, post-hoc between groups.

**Yucel A, et al.** 2011
- **Study Design:** Prospective, double-blind, randomized, placebo-controlled trial in patients undergoing abdominal hysterectomy.
- **Objectives:** Determine effect of pregabalin on pain scores, morphine consumption & sedation at 0, 2, 4, 6, 24 h postop.
- **Intervention:** Pregabalin 150 mg, 300 mg vs. placebo (N=30 each) 4 h preop and 12 h postop + postop morphine PCA.
- **Results:** Reduced 0-12 h pain scores (p<0.001), 24 h morphine use (p<0.001), increased 0-6 h sedation (p<0.001-p<0.01)-300 mg driver for all.
- **Limitations:** No multimodal analgesia described, non-U.S. (Turkey), small sample size, post-hoc between groups.

Pregabalin Evidence in Bariatric Surgery

Cabrera MC, et al. 2010

- **Study Design**: Prospective, double-blind, randomized, placebo-controlled trial in laparoscopic sleeve gastrectomy
- **Objectives**: Determine effect of pregabalin on pain scores, morphine consumption, PONV & ADE 24 h postop
- **Intervention**: Pregabalin 150 mg (N=39) vs. placebo (N=41) 2 h preop + postop ketoprofen 300 mg/24 h infusion + morphine 2 mg IV rescue
- **Results**: Reduction in total morphine use (p<0.0001), reduction in pain scores (p<0.05) and PONV (p<0.05), no ADE noted in either group
- **Limitations**: Multimodal pain management not described, non-U.S. (Chile), small sample size


- **Study Design**: Non-randomized trial in laparoscopic gastric bypass
- **Objectives**: Determine effect of pregabalin on pain scores and PONV 24 h postop
- **Intervention**: Pregabalin 300 mg 1 h preop (N=30) vs. historic control (N=30) + postop morphine PCA
- **Results**: Reduction in pain scores (p<0.001) and PONV (p<0.001)
- **Limitations**: Multimodal analgesia, morphine use & sedation not described, non-randomized, small sample size, non-U.S. (Iran)

Pregabalin in the Guidelines

- Recommends that clinicians consider use of pregabalin as a component of multimodal analgesia (strong recommendation, moderate-quality evidence)

  - Associated with reduced opioid requirements and lower postoperative pain scores after major or minor surgical procedures

  - Typical doses: pregabalin 150-300 mg PO, 1-2 h preoperatively, although some trials also found regimens that included postoperative dosing to be effective (150-300 mg after 12 h)

  - Insufficient evidence to determine optimal dose; although higher doses might be more effective, they might also be associated with more sedation

# Ketamine Mechanism of Action

<table>
<thead>
<tr>
<th>Primarily a NMDA receptor antagonist</th>
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<tbody>
<tr>
<td><strong>Other Mechanisms</strong></td>
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<tr>
<td>Opioid receptors</td>
</tr>
<tr>
<td>Monoaminergic, muscarinic, nicotinic receptors</td>
</tr>
<tr>
<td>Voltage sensitive electrolyte channels</td>
</tr>
</tbody>
</table>

Sources: Tomek S. Pharmaceuticals. 2013; 6(2): 251-268
Ketamine Pharmacokinetics

- **A**: Rapidly absorbed, onset ~ 30 sec
- **D**: High lipid solubility and low plasma protein binding
- **M**: Hepatic metabolism via N-dealkylation to active metabolite norketamine
- **E**: Primarily renal, T½ 2-3 h

Sources:
- Ketalar © (Ketamine) [package insert] Rochester, MI: JHP Pharmaceuticals, LLC; Revised March 2012.
# Anesthesia vs. Analgesia

<table>
<thead>
<tr>
<th>ANESTHESIA</th>
<th>ANALGESIA</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Anesthesia is obtained with dose of</strong></td>
<td><strong>“Low dose” ketamine considered &lt; 1 mg/kg</strong></td>
</tr>
<tr>
<td>2 mg/kg IV</td>
<td>Analgesia is obtained with doses of</td>
</tr>
<tr>
<td></td>
<td>0.2-0.75 mg/kg IV</td>
</tr>
<tr>
<td><strong>ADE</strong></td>
<td><strong>ADE</strong></td>
</tr>
<tr>
<td>Emergence reactions – dose related</td>
<td>Generally well tolerated at sub-anesthetic doses</td>
</tr>
<tr>
<td>Vivid hallucinations</td>
<td>Nausea/vomiting</td>
</tr>
<tr>
<td>CV system stimulation</td>
<td>Emergence reactions</td>
</tr>
<tr>
<td>Tachycardia</td>
<td>Sub-anesthetic doses 0.1-1 mg/kg IV</td>
</tr>
<tr>
<td>Hypertension</td>
<td></td>
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<tr>
<td>Increased cardiac output</td>
<td></td>
</tr>
<tr>
<td>Bronchodilation</td>
<td></td>
</tr>
<tr>
<td>Nausea/vomiting</td>
<td></td>
</tr>
</tbody>
</table>

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**Sources:**
- Ketalar © (Ketamine) [package insert] Rochester, MI: JHP Pharmaceuticals, LLC; Revised March 2012.
Ketamine Evidence in Abdominal Surgery

**Guillou N, et al. 2003**

- **Study Design:** Prospective, randomized, double-blinded, placebo-controlled trial in patients undergoing major abdominal surgery
- **Objectives:** Determine the effect of ketamine on pain scores, morphine consumption & ADE 48 h postop
- **Intervention:** Ketamine 0.5 mg/kg IV bolus with 2 mcg/kg/min x 24 h then 1 mcg/kg/min x 24 h (N=41) vs. saline placebo (N=52) + postop morphine PCA
- **Results:** Surgery type mainly hepatectomy (54% & 44%). No difference in pain scores, sedation or ADE. Morphine consumption lower at all time points up to 48 h postop (p<0.05).
- **Limitations:** Multimodal analgesia not described, small sample size, non-U.S. (France)

**Zakine J, et al. 2008**

- **Study Design:** Prospective, randomized, double-blinded, placebo-controlled trial in patients undergoing major abdominal surgery
- **Objectives:** Determine the effect of ketamine on pain scores, morphine consumption & ADE 48 h postop
- **Intervention:** Ketamine 0.5 mg/kg IV bolus & 2 mcg/kg/min x 48 h (N=23) vs. bolus + intraoperative infusion only (N=27) vs. saline placebo (N=27) + postop morphine PCA
- **Results:** Surgery types included nephrectomy, prostatectomy & AAA evenly distributed between groups (~30% each). Less morphine consumption in the 48 h group vs. other groups (p=0.008) & no difference between intraop vs. placebo. Pain scores lower in both treatment groups compared to placebo (p=0.001). No difference in sedation. No psychiatric ADE. Less PONV at 48 h vs. placebo (p=0.005).
- **Limitations:** No postop multimodal analgesia provided, small sample size, non-U.S. (France), post hoc between groups

**Sources:**
**Ketamine Evidence in Laparoscopic Surgery**

**Singh H, et al. 2003**
- **Study Design:** Prospective, randomized, double-blind, placebo-controlled trial in patients undergoing laparoscopic cholecystectomy.
- **Objectives:** Determine effect of ketamine on postop pain scores, opioid consumption & ADE.
- **Intervention:** Ketamine 1 mg/kg, 0.75 mg/kg and 0.5 mg/kg IV (N=20 each) vs. saline placebo (N=20) + post op IV fentanyl rescue.
- **Results:** Reduction in pain scores at 0, 0.5, 3-6 & 12 h all groups vs. placebo. Total opioid doses lower in treatment groups vs. placebo. No differences in pain scores/opioid doses between treatment groups. No differences in PONV. Hallucinations 10% with 1 mg/kg, 0% in other groups.
- **Limitations:** No reported p values, no multimodal analgesia described, small sample size, non-U.S. (India), post hoc between groups.

**Saxena D, et al. 2017**
- **Study Design:** Prospective, observational study in patients undergoing laparoscopic gynecological surgery.
- **Objectives:** Evaluate the effect of ketamine on rescue analgesia requirements & ADE within 8 h postop.
- **Intervention:** Ketamine 0.5 mg/kg IV, repeated q0.5h with 0.25mg/kg until end of surgery (N=70) + postop fentanyl IV rescue.
- **Results:** No rescue analgesia required up to 8 h in 93% (<30 min), 70% (31-60 min), 57% (61-90 min), 67% (91-120 min), 62% (121-150 min), 60% (151-180 min). PONV occurred in 2.85% of patients, psychotomimetic reactions and sedation occurred in 4.28% of patients.
- **Limitations:** No control group, no multimodal analgesia described, small sample size, non-U.S. (India).

**Gadre VN, et al. 2017**
- **Study Design:** Prospective, randomized, double-blind, placebo-controlled trial in patients undergoing laparoscopic surgery.
- **Objectives:** Compare efficacy of three small doses of ketamine for improving 24 h postop pain scores, opioid use & ADE.
- **Intervention:** Ketamine 1 mg/kg (N=30), 0.75 mg/kg (N=30), 0.5 mg/kg (N=30) vs. saline IV control (N=30) + postop fentanyl IV rescue.
- **Results:** Reduction in pain scores in all groups at 24 h at rest vs placebo (p<0.001). Lower total fentanyl IV rescue doses in all groups vs. placebo (p<0.0001). No reported hallucinations or PONV in any group.
- **Limitations:** Type of surgery or postop multimodal analgesia not described, post hoc between group analyses, small sample size, non-U.S. (India).

Gadre VN, Dhokte NS. Postoperative analgesia in laparoscopic surgeries with small dose of preemptive ketamine: A comparative study of three small doses. Indian Anaesth Forum 2017; 18: 3-8
Ketamine Evidence in Bariatric Surgery

**Feld JM, et al. 2003**

- **Study Design:** Randomized, double-blind trial in patients undergoing gastric bypass by open laparotomy
- **Objectives:** Determine the effect of a non-opioid analgesic regimen including ketorolac, clonidine, lidocaine, ketamine, magnesium & methylprednisolone compared to fentanyl analgesia on 16 h postop morphine use and pain scores
- **Intervention:** Ketamine 0.17 mg/kg/h (max 1 mg/kg) IV during case (N=15) vs. fentanyl 50 mcg bolus (Max 6 mcg/kg IBW) (N=15)
- **Results:** Reduction in total PACU morphine use (p<0.05) and PACU sedation (p<0.01). No difference in 16 h total morphine use (p=0.71) or pain scores (p=0.97)
- **Limitations:** Gastric bypass by open laparotomy no longer commonly performed, non-U.S. (Canada), small sample size, concomitant clonidine & lidocaine, sedation only evaluated in PACU, no postop multimodal analgesia described

**Sollazzi L et al. 2009**

- **Study Design:** Randomized, open-label trial in patients undergoing biliopancreatic diversion
- **Objectives:** Determine the effect of preop ketamine-clonidine on pain scores use at 30 min., 1, 6 & 12 h and total IV tramadol use
- **Intervention:** Ketamine 0.5 mg/kg-clonidine 3 mcg/kg (IBW) IV over 20 min (N=23) vs. control group (N=27) prior to induction of anesthesia + postop ketorolac 90 mg + tramadol 200 mg 2 mL/h continuous infusion + rescue tramadol IV 100 mg
- **Results:** Reduction in total tramadol use (p<0.05) and pain scores during first 6 h post-op (p<0.05)
- **Limitations:** Open biliopancreatic diversion no longer commonly performed, non-U.S. (Italy), open label, small sample size, concomitant clonidine

Ketamine in the Guidelines

- Recommends that clinicians consider use of IV ketamine as a component of multimodal analgesia in adults (weak recommendation, moderate-quality evidence)

  - Associated with reduced opioid requirements and lower postoperative pain scores after major or minor surgical procedures

  - Ketamine has been administered preoperatively, intraoperatively, and/or postoperatively, at widely varying doses (ranging from boluses of 0.15-2 mg/kg before incision and at closure, with or without infusions ranging from 0.12 mg/kg/h to 2 mg/kg/h)

    - Insufficient evidence to determine optimal method for dosing ketamine, but suggests using a preoperative bolus of 0.5 mg/kg followed by an infusion at 10 mcg/kg/min intraoperatively, with or without a postoperative infusion at lower dosage

Efficacy of Preoperative Pregabalin & Ketamine as a Bariatric Surgery Pain Management Strategy
Bariatric Surgery Indications

- BMI $\geq 40 \text{ kg/m}^2$ without coexisting medical problems
- BMI $\geq 35 \text{ kg/m}^2$ and one or more severe obesity-related co-morbidities
  - Type 2 diabetes
  - Hypertension
  - Hyperlipidemia
  - OSA
  - OHS
  - Pickwickian syndrome (combination of OSA & OHS)
  - NAFLD or NASH
  - GERD
  - Pseudotumor cerebri
  - Asthma
  - Venous stasis disease
  - Severe urinary incontinence
  - Debilitating arthritis

Bariatric Surgical Procedures

**INTRAGASTRIC BALLOON**

**LAPAROSCOPIC ADJUSTABLE GASTRIC BAND**

Am J Health-Syst Pharm. 2014; 71: 1253-64
Bariatric Surgical Procedures

LAPAROSCOPIC SLEEVE GASTRECTOMY

LAPAROSCOPIC RYGB

Source: Am J Health-Syst Pharm. 2014; 71: 1253-64
## Limitations of Opioids in Obesity

### Predisposed to Opioid induced Airway Obstruction

- Approximately 70% of morbidly obese patients are afflicted with OSA
- Increased overall oxygen consumption
- Reduced functional residual capacity
- Anatomic changes including large necks, excess adipose tissue obstructing the airways

### Hormonal Dysregulation

- Excess endogenous opioids
- Decreased opioid receptors in the brain
- Postulated to regulate eating habits may also support need for reduction in opioid dose

### Physiologic Changes

- Increased adipose tissue
- Higher cardiac output
- Increased blood volume
- Decreased total body water
- Increased GFR
- Altered protein binding

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**Sources:**
Investigation of appropriate dosing strategies for opioids in obese patients should continue. Even when PK modeling is available, predicting the differences in analgesic requirements between lean and obese patients is difficult. The risk of adverse effects with the use of these agents in obese patients is high.

Bariatric Center of Excellence

- Parham Doctors’ Hospital (PDH) in Richmond, VA received accreditation by the Metabolic and Bariatric Surgery Accreditation and Quality Improvement Program (MBSAQIP) in February 2015.
- Earned designation as a Blue Distinction® Center+ for Bariatric Surgery in 2017.
- PDH performs > 350 bariatric surgeries annually:
  - Intragastric balloon
  - Laparoscopic adjustable gastric banding
  - Laparoscopic sleeve gastrectomy
  - Laparoscopic RYGB
- PDH has a multidisciplinary Metabolic and Bariatric Surgery Collaborative Practice Group (MBSCPG) which meets monthly to discuss all aspects of current practice, including multimodal pain management strategies.
Multimodal Pain Management Protocol

- Acetaminophen 1000 mg IV preoperative
- Ketorolac 15-30 mg IV preoperative
- Local bupivacaine 0.5% with epinephrine injection around laparoscopic sites
- Ketorolac 15-30 mg IV q6h x 6 doses postoperative
- Acetaminophen 1000 mg IV q6h x 3 doses postoperative
- Hydromorphone 0.5 mg IV q3h PRN pain scale 1-3
- Hydromorphone 1 mg IV q3h PRN pain scale 4-6
- Hydromorphone 2 mg IV q3h PRN pain scale 7-10
- Hydromorphone 2 mg PO q4h PRN pain scale 1-10 when tolerating PO
Change to the Multimodal Pain Management Protocol

- Lack of studies utilizing pregabalin and ketamine in bariatric surgical patients
  - Pain management guidelines do not specifically address bariatric surgical patients

- The MBSCPG discussed the addition of pregabalin and ketamine as non-opioid adjunctive therapies in an attempt to improve patient satisfaction by reducing opioid use and pain scores

- Beginning April 3, 2017, bariatric surgery patients at PDH began receiving
  - Pregabalin 150 mg PO 1 h preoperatively
  - Ketamine 40 mg IV at the induction of anesthesia
### Study Overview

#### PURPOSE

- Determine if the addition of pregabalin and ketamine improved postsurgical pain control in patients undergoing primary bariatric surgery

#### OBJECTIVES

- **Primary objective**
  - Reduction in opioid consumption
- **Secondary objectives**
  - Reduction in pain scores
  - Safety of pregabalin and ketamine
Methods

- **Study Design**
  - Retrospective, observational chart review

- **Inclusion criteria**
  - 50 patients who underwent primary bariatric surgery prior to April 3, 2017
  - 50 patients who underwent primary bariatric surgery on or after April 3, 2017

- **Exclusion criteria**
  - Chronic pain
  - Secondary revision surgeries
  - Prior pregabalin or gabapentin use
  - CrCl < 15 ml/min or hemodialysis

- **Data collection**
  - Surgery type
  - Age
  - Weight, BMI
  - LOS
  - Pregabalin and ketamine doses
  - Pain scores
  - Antiemetic usage

- **Statistical Analysis**
  - A two tailed, student t-test for unpaired continuous data using Excel©
  - $\alpha < 0.05$
<table>
<thead>
<tr>
<th>Demographics</th>
<th>Pre-Intervention (N=50)</th>
<th>Post-Intervention (N=50)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Surgery Type N (%)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Band</td>
<td>0 (0%)</td>
<td>1 (2%)</td>
</tr>
<tr>
<td>Sleeve</td>
<td>43 (86%)</td>
<td>34 (68%)</td>
</tr>
<tr>
<td>RYGB</td>
<td>7 (14%)</td>
<td>15 (30%)</td>
</tr>
<tr>
<td><strong>Age (yr)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>49 (23-69)</td>
<td>47 (22-62)</td>
</tr>
<tr>
<td><strong>Weight (kg)</strong></td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>133 (83-244)</td>
<td>130 (83-211)</td>
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<tr>
<td><strong>BMI (kg/m²)</strong></td>
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</tr>
<tr>
<td></td>
<td>47 (31-82)</td>
<td>44 (31-62)</td>
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<tr>
<td><strong>LOS (days)</strong></td>
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<td></td>
</tr>
<tr>
<td></td>
<td>1 (0-2)</td>
<td>1 (0-2)</td>
</tr>
<tr>
<td><strong>Antiemetics (# doses)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>2 (0-9)</td>
<td>1 (0-6)</td>
</tr>
<tr>
<td><strong>Ketamine Dose N (%)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>40 mg</td>
<td>N/A</td>
<td>28 (56%)</td>
</tr>
<tr>
<td>50 mg</td>
<td>N/A</td>
<td>22 (44%)</td>
</tr>
<tr>
<td><strong>Pregabalin Dose N (%)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>150 mg</td>
<td>N/A</td>
<td>50 (100%)</td>
</tr>
</tbody>
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Morphine Equivalent Dose (MED) Utilization

- **Total IV M.E. (mg)**: 153
- **Total PO M.E. (mg)**: 8
- **Total M.E. (mg)**: 162.5

**Pre-Intervention**: 101
**Post-Intervention**: 104

- \( p < 0.012 \)
- \( p < 0.912 \)
- \( p < 0.018 \)
Limitations

- Retrospective, observational design
- Small sample size
- Varying mg/kg ketamine dose
- Initiated two interventions simultaneously
Conclusions

- Addition of preoperative pregabalin and ketamine in bariatric surgery
  - Reduced opioid use
  - Reduced pain scores
  - Well tolerated

- Findings consistent with general surgical population

- The bariatric surgery program at PDH continues to utilize pregabalin and ketamine as part of a multimodal pain management strategy
Despite numerous limitations of available studies, pregabalin and ketamine have consistently demonstrated the ability to reduce postoperative opioid consumption and pain scores in a variety of surgeries:
- Pregabalin 150 mg PO 1 h prior to surgery most commonly balanced efficacy with risk of ADE
- Ketamine doses < 1 mg/kg IV bolus at the induction of anesthesia likely safe and effective

Obese patients are highly susceptible to ADE of opioids such as respiratory depression and investigation of non-opioid adjuvants are of particular importance in this patient population.

There is a lack of evidence for use of pregabalin and ketamine in bariatric surgery:
- Findings in a study by PDH are consistent with current literature in the general surgical population.
Assessment Question 1

Which of the following adverse drug effects is not associated with pregabalin?

A. Dizziness
B. Sedation
C. Emergence reactions
D. Ataxia
Response Question 1

Which of the following adverse drug effects is not associated with pregabalin?

A. Dizziness
B. Sedation
C. Emergence reactions
D. Ataxia
True or False:

Pregabalin and ketamine have demonstrated an ability to reduce pain scores but not opioid consumption in various types of surgeries.
True or False:

Pregabalin and ketamine have demonstrated an ability to reduce pain scores but not opioid consumption in various types of surgeries.
Assessment Question 3

Which of the following preoperative pregabalin and ketamine dosing regimens most likely balances safety with efficacy?

A. Pregabalin 300 mg 1 h preop and Ketamine 1 mg/kg IV at the induction of anesthesia
B. Pregabalin 150 mg 1 h preop and Ketamine 0.5 mg/kg IV at the induction of anesthesia
C. Pregabalin 150 mg 1 h preop and Ketamine 2 mg/kg IV at the induction of anesthesia
D. Pregabalin 300 mg 1 h preop and Ketamine 0.5 mg/kg IV at the induction of anesthesia
Response Question 3

Which of the following preoperative pregabalin and ketamine dosing regimens most likely balances safety with efficacy?

A. Pregabalin 300 mg 1 h preop and Ketamine 1 mg/kg IV at the induction of anesthesia
B. **Pregabalin 150 mg 1 h preop and Ketamine 0.5 mg/kg IV at the induction of anesthesia**
C. Pregabalin 150 mg 1 h preop and Ketamine 2 mg/kg IV at the induction of anesthesia
D. Pregabalin 300 mg 1 h preop and Ketamine 0.5 mg/kg IV at the induction of anesthesia
Use of opioids in obese patients are limited by which of the following?

A. Predisposition to airway obstruction due to anatomic changes and high incidence of obstructive sleep apnea

B. Hormonal dysregulation including excess endogenous opioids and decreased opioid receptors

C. Physiologic changes including higher cardiac output and GFR

D. All of the above
Use of opioids in obese patients are limited by which of the following?

A. Predisposition to airway obstruction due to anatomic changes and high incidence of obstructive sleep apnea

B. Hormonal dysregulation including excess endogenous opioids and decreased opioid receptors

C. Physiologic changes including higher cardiac output and GFR

D. All of the above
Assessment Question for Pharmacy Techs

Which of the following statements are true?

A. The benefit of adding non-opioid adjuvant medications to a multimodal pain management protocol is the potential reduction of postoperative opioid consumption and superior pain relief.

B. Pregabalin is only available as an oral dosage form, while ketamine is available in both oral and IV dosage forms.

C. A common complication of opioid use, particularly in obese patients, is respiratory depression.

D. A & C
Response Question for Pharmacy Techs

Which of the following statements are true?

A. The benefit of adding non-opioid adjuvant medications to a multimodal pain management protocol is the potential reduction of postoperative opioid consumption and superior pain relief

B. Pregabalin is only available as an oral dosage form, while ketamine is available in both oral and IV dosage forms

C. A common complication of opioid use, particularly in obese patients, is respiratory depression

D. A & C
Questions?

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