Managing Post-Operative Pain in the Severely Obese Patient: Treatment & Monitoring Challenges

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Conflict of Interest Disclosure

Maureen F. Cooney: Advisory Board Cadence Pharmaceuticals and Zogenix, Inc.
Denise Sullivan: No Conflict of Interest

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Obesity definitions

Classification of Overweight and Obesity by BME, Waist Circumference, and Associated Disease Risks

<table>
<thead>
<tr>
<th>BMI (kg/m²)</th>
<th>Obesity Class</th>
<th>Disease Risk* Relative to Normal Weight and Waist Circumference</th>
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<tbody>
<tr>
<td>≤ 18.5</td>
<td>Normal</td>
<td>Women &lt; 122 cm (48 in) or less</td>
</tr>
<tr>
<td>18.5-24.9</td>
<td>Overweight</td>
<td>Increased High</td>
</tr>
<tr>
<td>25.0-29.9</td>
<td>Obesity</td>
<td>High Very High</td>
</tr>
<tr>
<td>30.0-34.9</td>
<td>Extremely Obese</td>
<td>Extremely High Extra high</td>
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* Disease risk for type 2 diabetes, hypertension, and CVD.
+ Increased waist circumference also can be a marker for increased risk, even in persons of normal weight.

Prevalence* of Self-Reported Obesity Among U.S. Adults
BRFSS, 2012

Obesity
- A state of chronic low grade inflammation
- Adipose tissue secretes large amounts of cytokines (TNF, vascular endothelial growth factor, interleukin-6) causing disturbance of the immune and metabolic systems
- Inflammation may increase drug bioavailability

Pain Perception in the Obese vs. Non Obese
- Limited number of studies
- Contradictory results related to the impact of obesity on nociception.
  - Nociceptive flexion reflex
  - Mechanical pressure
  - Needle pressure
  - Transcutaneous electrical nerve stimulation
- Opioid requirement is variable

Obesity’s Influence on Pain

- BMI 35-39 = 1.9 times > chronic pain and > 40 = 2.3 times > than non-obese
- Osteoarthritis, DJD most common pain syndromes
- GERD (increased intra-abdominal pressure)
- Gout
- Fibromyalgia

Ms. K-33 y/o woman with 18 hr history of constant severe right pelvic pain, no radiation

- No aggravating/alleviating factors
- Some nausea, no vomiting
- PMH/PSH: Mild asthma; Para1/Grava1 c-sxn in 2010; appendectomy, age 17
- Soc: smokes 1 pk/wk; denies ETOH, other meds
- Meds: medroxyprogesterone

PE: 138/92, 96, 20 sat 95%, BMI: 35
- Awake, alert, grimacing
- Neck supple
- Lungs clear, BS diminishes at bases
- NSR, no m/r/g
- + BS, 4 quads; guarding R lower quad, + pain on palp, palpable mass RLQ, no rebound
- GYN: no chandelier sign, Bimanual deferred d/t pain
Labs: WBC: 9.2; HCG negative
Ultrasound abdomen/ pelvis: fluid collection and right ovarian enlargement
CT abd/pelvis: adnexal mass/enlargement and intraperitoneal fluid collection
A: Acute pelvic pain, ruptured ovarian cyst vs ovarian torsion
P: Emergent Exploratory Lap

Perioperative Course

Induction: fentanyl 100 mcg and midazolam 2mg; Intraop: rocuronium, sevoflurane, fentanyl 150mcg, ondansetron, hydromorphone 2mg
Postop Open Ex Lap
- extubated in OR;
- 1100: To PACU with non-rebreather; 138/90-94-15-99%
- arouseable with stimulation; Pain 4/10

11:30 Converted to nasal cannula O2 @ 2L/min
Pain 6/10: hydromorphone 0.5 mg q 15 min x 2 doses (last dose 11:45)
12noon: RR 9/min; O2 sat 95%; arouseable to strong tactile stimuli
12:05 Not arouseable; RR 8/min O2 sat 88%
Pathophysiological Mechanisms leading to Pulmonary Complications

Impact of Obesity on Respiratory Function

- Reduced lung function with increased atelectasis
- Derangements in respiratory system, lung, and chest wall compliance and increased resistance
- Moderate to severe hypoxemia

Impact of Obesity on Respiratory Function

- Severe obesity: normal PaO2 while sitting up but reduced when supine
- V/Q mismatch: lung bases well perfused, but hypoventilated up to 5% due to airway closure and alveolar collapse
- Compliance is reduced due to effect of obesity on chest wall due to increase density and distribution of adipose tissue.
Most are eucapneic
- RR is 40% higher in eucapneic obese compared to normal
- Tidal volume reduced by 25% in OHS

Impact of Obesity on Respiratory Function
- Risk factor for obstructive sleep apnea syndrome (OSAS), obesity hypoventilation syndrome (OHS), acute hypercapnic respiratory failure and respiratory post-surgical complications.
- 10% OSAS pts have daytime hypercapnea, some with pulmonary hypertension

Obesity – Hypoventilation Syndrome
- Due to decreased lung volumes and reduced total lung compliance
- Hypercarbia and hypoxemia while awake
Obstructive Sleep Apnea and Obesity

- Obesity is a risk factor for OSA
- Incidence of OSA increases in proportion to level of obesity
- Prevalence of OSA in morbidly obese patient exceeds 77%
- OSA found in 40% of obese females and 50% of obese males


- Polysomnography (PSG) is the “gold standard” for diagnosis of OSA
- PSG may not be available to all and many go undiagnosed

OSA, Obesity, and Opioids: Deadly Trio!

- Sedatives, opioid analgesics and anesthetics alter airway tone
- Possible chronic hypoventilation with mild hypercarbia in the resting preoperative state
- Increased risk for aspiration and acute airway obstruction after extubation
- Airway obstruction and death reported in OSA patients with minimal doses of sedatives and anesthetics
Postop risks in the severely obese

- Greater risk of upper airway obstruction in sedated, obese patients from excess pharyngeal tissue.
- May have sudden drop in PaO2 during periods of obstruction or decreased ventilation
- Opioids and other meds associated with sedation and respiratory depression high risk in PACU.

Case Study Discussion: What happened to Ms. K?

- Patient concerns: Obese; asthmatic; active smoker; opioid naïve; abdominal pain
- Increased risk for OSAS, obesity hypoventilation syndrome
- Sedation, sudden decreases in oxygenation and respiratory depression may occur, particularly with the use of opioids
- Risk of re-sedation from redistribution of anesthetics and analgesics from the adipose tissue to the blood stream
Factors affecting pharmacokinetics

- Increased adipose tissue
- Increased blood volume
- Higher cardiac output
- Decreased total body water
- Altered protein binding
- Increased renal blood flow and glomerular filtration rate

Factors Affecting Tissue Distribution of Drugs

- Affinity of drug for plasma proteins
- Body composition
- Regional circulation

Normal Blood Flow

- 5% to Adipose tissue
- 73% to viscera
- 22% to lean tissue
Alterations in Obesity

- Only 2% to adipose
- Viscera well perfused
- Obesity increases both lean body mass and fat mass, but the percentage of fat increases more than the percentage of lean

- Increased circulating blood volume and higher than normal GFR which should increase the clearance of the drugs that are eliminated primarily by glomerular filtration.
- Pharmacologic studies of renal function in obese patients provided varying results

Implications:

- Muscle tissue holds more water than fat, so hydrophilic drugs should be dosed based on IBW.
- Lipophilic:
  - less predictable; if highly absorbed by adipose tissue, requires dosing based on TBW
  - Due to decreased circulation to adipose tissue, may have decreased clearance, elimination half life may increase.
  - If normal renal function, will have increased drug clearance due to increased cardiac output; common co-morbidities (DM, HTN) often decrease renal function
Re-sedation Risk!

- Re-distribution of lipophilic anesthetics or analgesics from adipose tissue to blood stream is possible!

Definitions:

- TBW: Total Body Weight
- IBW: Ideal Body Weight
  - IBW = hgt (cm) - 105 (female) or 100 (male)
- LBM: Lean Body Mass

Recommendations:

- Loading doses should be based on IBW when drug distribution is restricted to lean tissues
- Loading doses based on IBW + % of TBW when distribution to lean tissue and partially to fat tissue
- Loading doses based on TBW when distributed to lean and fat tissues or markedly in fat tissue
- Maintenance doses depend on ability to clear medications. If CL is decreased, dose based on IBW
Morphine

- Hydrophilic
- Little or no change in volume of distribution with obesity; does not accumulate in adipose tissue
- Dose to IBW
- May be opioid of choice in obesity

Fentanyl

- Lipophilic
- Higher doses needed in obesity due to elevated volume of distribution compared with non-obese patients.
  - Lotia and Bellamy, 2008.
- Clearance higher and increases with TBW, but not a linear relationship
- Administer infusions using IBW or LBW

Remifentanil

- Ultra short acting, peak effect 1 minute
- Pharmacokinetics not appreciably different in obese compared to normal
- Distributed less in obese, with less clearance
- Dose based on IBW or LBM
- Risk of apnea, severe bradycardia or hypotension if dose to TBW
Sufentanil

- Distributed as extensively in excess body mass as lean tissue
- Loading dose should account for total body weight (TBW)
- Elimination is decreased in obese, so smaller maintenance doses

Methadone

- Lipophilic
- Very high distribution on adipose tissue resulting in long duration of action and half life of 12-150 hours

Midazolam

- Lipophilic: Prolonged sedative effects
- Inhibition of CYP450 3A4 by other drugs or obesity itself will reduce clearance
- Continuous infusion rate should be adjusted to IBW to avoid oversedation
- Daily discontinuation and re-titration to sedation scale target
Propofol

- Highly lipophilic, rapid distribution to peripheral tissues
- Short duration of action although longer than usual recovery times were reported after prolonged infusion
- Maintenance dosing to TBW may lead to deep anesthesia and deleterious cardiac effects
- Dose infusions to IBW or LBM

Ketamine

- Lipophilic
- Use has been proposed in obese patients but study is limited

Ibuprofen

- Pharmacologic data for ibuprofen suggest that doses may need to be increased without changing dosing intervals

Acetaminophen

- Administration of a normal dose of acetaminophen to an obese patient should yield plasma levels in the same range as persons of normal weight.
  

Challenges

- Individuals with same BMI may have different body compositions and fatness; ethnic groups
- Clinical situations may cause variation in hepatic metabolism of drugs

The bottom line....

- Hydrophilics are much more predictable.
- Difficult to predict impact of obesity on pharmacokinetics of lipophilic drugs.
- Monitor and titrate to effect!
“Each drug may behave differently, and our present knowledge of the influence of obesity on pharmacokinetics is limited.” (Cheymol, 2000)
Pain Management Recommendations

- Anesthesiologist with special interest in anesthetic care and pain management should be identified to serve as interdepartmental liaison
- Utilize opioid sparing multimodal strategies intraoperatively when possible
- Avoid sedatives in combination with opioids


Pre-Op Guidelines

- Anesthesiology consult at least one day prior to surgery if possible
- Assessment for sleep apnea-polysomnography for select patients
- Smoking cessation at least 6 weeks before surgery

(Schumann, R., Jones, S.B. et al. 2005)

STOP-Bang Scoring Tool

To Detect Suspected Obstructive Sleep Apnea (OSA)

1. Do you snore loudly?
2. Do you often feel tired, fatigued, or sleepy during daytime?
3. Has anyone observed you stop breathing during your sleep?
4. Do you have, or are you being treated for high blood pressure?
5. BMI more than 35?
6. Age – Over 50 yr old?
7. Neck circumference greater than (17”-male) or (16”-female)?
8. Gender – Male?

Acuity: Three “Yes” responses place the patient in the category of suspected high risk of having OSA.

STOP-Bang score of 4 has high sensitivity of 88%.

Intraoperative Anesthetic Management of the Patient with OSA

- Avoid sedating premedication
- Alpha-2 adrenergic agonist (clonidine, dexmedetomidine) may reduce intraoperative anesthetic requirements and have an opioid-sparing effect
- Minimize use of opioids for analgesia; Use of short-acting agents (remifentanil)
- Regional and multimodal analgesia (NSAIDs, acetaminophen, tramadol, ketamine, gabapentin, pregabalin, dexmedetomidine, dexamethasone)


Intraoperative Anesthetic Management of the Patient with OSA (cont.)

- Use of regional blocks as a sole anesthetic technique
- Use of intraoperative capnography for monitoring of respiration
- Non-supine posture for extubation and recovery
- Resume use of positive airway pressure device

Multimodal OR management produced less postop sedation in PACU, decrease in PCA morphine use

- 60 mg methylprednisolone preop
- 30 mg ketorolac before and at end of case
- 300-500 mcg clonidine during 1st hr of anesthesia
- 100 mg lidocaine, then 4 mg/min for 1 hr, then 3 mg/min for second hr, then 2 mg/min for remainder of case
- 0.17 mg/kg/h ketamine infusion (max dose 1mg/kg)
- 80mg/kg magnesium sulfate


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Multimodal Anticonvulsants

- Pregabalin 150mg prior to lap sleeve gastrectomy resulted in improved analgesia, opioid sparing and reduced adverse effects such as nausea and vomiting.


Multimodal Acetaminophen and NSAIDS

- NSAIDS have a 30-50% opioid sparing effect. Balestrieri, Simmons, et al. (1997); Ready, Brown, et al. (1994).


- Multimodal approach with intravenous ketorolac and acetaminophen every 6 hours x 24 hours in bariatric surgery reduced opioid consumption by 41%. Time with an oxygen saturation below 90% reduced by 33.2%. (Zimmer-Gniral, ASMBS 2012 poster)

Multimodal Alpha 2 agonists


- Postop clonidine bolus of 3 mcg/kg with continuous infusion of 0.3 mcg/kg/h with PCA morphine with significant analgesia, reduced morphine consumption, reduced n/v. Jeffes, Hall, Morris (2002).
Multimodal Alpha 2 agonists

- Intraop dexmedetomidine in open WLS has similar anesthetic and opioid sparing effect as clonidine. Feld et al. (2006)

Postoperative Interventions

- Goals
  - Comply with respiratory physiotherapy
  - Early mobilization
- Interventions
  - Beach chair position (avoid supine)
  - Aggressive PT
  - Noninvasive respiratory support
  - Closely monitored fluid management and pain management

PCA Dosing

- Modify for age & co-morbidities especially sleep apnea
- Avoid basal infusions
- Weight: Consider lean body mass in dose calculation as adipose tissue serves as medication depot
- Prior opioid use: Larger doses, longer lockout interval
Post-op Pain Control in Obese Patients

- Premedicate with pregabalin (150mg 1hr pre-op, then q12)
- Acetaminophen 1gm IV q6h or celecoxib 200mg po q12h
- IV PCA opioids-fentanyl 10mcg q 5 min lockout
- Add ketamine infusion @8-10mg/hr if pain not controlled


RYGB Patient and Opioid Absorption

- Liquid preparations are preferred
- Avoid use of most long acting agents (may be possible if banding or sleeve with chronic pain)

Regional: Thoracic Epidural

- In comparison to opioids, better spirometric values and faster recovery
- Improved analgesia and respiratory parameters after cardiac surgery compared to conventional opioid based analgesia Sharma, Mehta, et al. (2010)
Regional: Thoracic Epidural

- Thoracic epidural analgesia provided best analgesia in open GBP.

- Epidural solutions for postop OSA should be opioid free. ASA practice guidelines (2006)

Regional Anesthesia

- 6920 overweight or obese patients with a variety of blocks overall success rate 89% but if BMI > 30, 1.62 times more likely to have a failed block. Nielsen, Guler, Steen, et al. (2005)

- Local anesthetic infiltration of wound is part of multimodal approach. Madan, Ternovits, Speck, Tichansky (2005)

- RYGB patients with LA infusion sat up ½ day earlier and ambulated one full day earlier. Lyer, Robertson, Lenkovsky et al. (2010)

- Bilateral TAP block-No difference in opioid consumption or pain scores between TAP group and control group. Albrecht, Krikham, Endersby, et al. (2013)
Complementary Medicine

- Lavender aroma therapy in morbidly obese patients in PACU in lap gastric banding
  - Opioid sparing effect
  - Required less morphine in the immediate postop period (Schug, Raymann, 2011)

Sentinel Alert Joint Commission
Safe Use of Opioids in Hospitals 8/2/12

- Hospital opioid-related adverse drug events reported to The Joint Commission’s Sentinel Event database (2004-2011)
  - 47% wrong dose
  - 29% improper monitoring
  - 11% other factors (excessive dosing, medication interactions, adverse drug reactions)
- "Various patients are at higher risk including patients with sleep apnea, patients who are morbidly obese, who are very young, who are elderly, who are very ill, and who concurrently receive other drugs that are central nervous system and respiratory depressants (e.g., anxiolytics, sedatives)."

http://www.jointcommission.org/assets/1/18/SEA_49_opioids_8_2_12_FINAL.pdf

Monitoring

- Intermittent “spot checks” of oxygenation (pulse oximetry) and ventilation (nursing assessment) are not adequate for reliably recognizing clinically significant evolving drug-induced respiratory depression in the postoperative period.
- Continuous monitoring of oxygenation and/or ventilation of patients receiving opioids postoperatively.
- Utilize capnography in patients requiring supplemental oxygen.
ASPMN Nursing Guidelines on Monitoring for Opioid-Induced Sedation and Respiratory Depression (2011)

- Serial sedation and respiratory assessments are recommended to evaluate patient response during opioid therapy by any route of administration.
- Technology-supported monitoring (e.g., continuous pulse oximetry and capnography) can be effective for the patient at high risk for unintended advancing sedation and respiratory depression.
- More vigilant monitoring of sedation and respiratory status should be performed when patients may be at greater risk for adverse events.

Monitoring

- Pulse oximetry for every patient with clinically significant obesity, suspicion of OSA using opioid analgesics and PCA
- Alarms set for less than 90% saturation for 10 seconds


Monitoring

- Postop hypoxemia should be treated with early NIPPV Pelosi, Gregoretti (2010)
- Utilize supplemental postoperative O2 despite acknowledged risk of prolonged apneic episodes and reduced detection of complications; this also results in increased SQ and wound-tissue oxygen tension in morbidly obese patients - ASA Taskforce Guidelines on OSA patients
Ms. K-33 y/o female s/p exp lap
Management

- Patient stimulated; BVM with O2;
  Anesthesiology called and patient placed on BiPap
- Naloxone 0.4mg in 9ml NS (40mcg/ml); 2ml administered every 2 minutes x 2 doses
- Patient placed in high fowler’s position;
  frequent sedation and respiratory assessments
- 12:15 Arousable to verbal stimulation (Aldrete 1); RR 16/min; O2 sat 99%

Ms. K-33 y/o female s/p exp lap
Management

- Initiate opioid sparing strategies
  - Acetaminophen 1gm IVPB q 6h
  - Intravenous ketorolac 30mg IV q 6h
- Opioid changed to morphine IV PCA 0 basal rate, 1mg PCA dose, 10 minute lockout
- 3:30pm: Alert (Aldrete 2); RR 18/min; O2 sat 100%; Pain 4/10
- 4p: Converted to nasal O2 @2L; capnography monitoring; continuous pulse oximetry
Ms. K-33 y/o female s/p exp lap Monitoring

- Frequent sedation and respiratory assessments by nurse
- Continuous pulse oximetry and capnography
- Patient had two episodes of oxygen desaturation below 90%; O2 sat increased after stimulation; no further intervention was required
- Patient transferred to Step Down Unit with continuous pulse oximetry and capnography

Monitoring

- Oxygen discontinued 12 hours post op
- No further evidence of oxygen desaturation on room air over the next 8 hours
- Pain 4/10 with movement
- Transferred to general surgical floor POD # 1
- Converted to standing oral ibuprofen and prn oxycodone with acetaminophen

Take Home Points

- Morbidly obese patients are at increased risk for OSAS and hypoventilation syndrome
- Sedatives, anesthetics and opioids alter airway tone
- Re-distribution of lipophilic anesthetics or analgesics from adipose tissue into circulation and the CNS may cause re-sedation
- Dose opioids according to IBW or LBW
• Utilize opioid sparing strategies whenever possible
• More vigilant nurse assessment of sedation level and respiratory status over the first 24 hours
• Early intervention with NIPPV

Thank You!

References


