Opioid-Free Anesthesia (OFA) for Thought

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NURSE ANESTHESIA PROGRAM

Introduction

- "The practice of anesthesia requires a full spectrum of drugs from which an anesthetic plan can be implemented to achieve a desired level of surgical anesthesia, analgesia, amnesia and muscle relaxation." ~ John J. Nagelhout
- Opioid Free Anesthesia (OFA) is a technique where no intra-operative systemic, neuraxial, or intracavitary opioid is administered during the anesthetic.
- Opioid-Free anesthesia is possible ~ Jan P. Mulier
  - An alternative to opioid Anesthesia
  - Provides benefits to selective group of patients
  - Facilitates postoperative analgesia with less opioids
  - Enhances recovery after surgery
- Optimal perioperative analgesia is the ability to reduce pain scores and enable earlier mobilization with enhanced rehabilitation, faster discharge and improved patient satisfaction. By reducing opioid-related adverse effects, OFA aims to enhance these goals. `

Unwanted clinical effects of Opioids

- Opioids have historically been a first-line therapy for surgical pain control.
- Opioid drugs produce pharmacologic activity by binding to opiate receptors, primarily located in the central nervous system, supraspinal and spinal, and peripheral sites.
- A prevalence of 30% of unwanted effects of opioids such as nausea, vomiting, dizziness and constipation
- Opioids can exacerbate obstructive sleep apnea and increase its severity
- Opioid tolerance to analgesia can occur after a single dose

Clinical Effects of Opioids produce desired as well as unwanted effects

TABLE 11-2

Actions Produced at Each Opioid Receptor Subtype

Effects	Mu (μ) Receptor	Kappa (κ) Receptor	Delta (δ) Receptor
IUPHAR name	MOP	KOP	DOP
Analgesia	Supraspinal Spinal	Supraspinal, spinal	Supraspinal, spinal; modulates mu-receptor activity
Cardiovascular	Bradycardia		
Respiratory	Depression	Possible depression	Depression
Central nervous system	Euphoria, sedation, prolactin release, mild hypothermia, catalepsy, indifference to environmental stimulus	Sedation, dysphoria, psychomimetic reactions (hallucinations, delirium)	
Pupil	Miosis	Miosis	
Gastrointestinal	Inhibition of peristalsis, nausea, vomiting		
Genitourinary	Urinary retention	Diuresis (inhibition of vasopressin release)	Urinary retention
Pruritus	Yes		Yes
Physical dependence	Yes	Low abuse potential	Yes
Antishivering		Yes	

BOX 11-2 Common Clinical Effects of Opioid Agonists

Acute	Chronic
Analgesia	Tolerance
Respiratory depression	Physical dependence
Sedation	Constipation
Euphoria	
Dysphoria	
Vasodilation	
Bradycardia	
Cough suppression	
Miosis	
Nausea and vomiting	
Skeletal muscle rigidity	
Smooth muscle spasm	
Constipation	
Urinary retention	
Biliary spasm	
Pruritus, rash	
Antishivering (meperidine only)	
Histamine release	
Hormonal effects	

Respiratory Depression

- All opiate agonists produce a depression of respirations via effects on mu and delta receptors in respiratory centers in the brainstem.
- Reduces responsiveness of the respiratory centers to increasing carbon dioxide and decreasing oxygen.
- Higher partial pressure of CO2 (pCO2) levels needed to maintain normal.respiration.
- Produces a shift to the right in the CO2 response curve for respiration.

Effects of Opioids on the Airway

The Laryngoscope

Systematic Review

The Effects of Anesthesia and Opioids on the Upper Airway: A Systematic Review

Zarmina Ehsan, MD; Mohamed Mahmoud, MD; Sally R. Shott, MD; Raouf S. Amin, MD; Stacey L. Ishman, MD, MPH

Objectives/Hypothesis: Drug-induced sleep endoscopy (DISE) is used to determine surgical therapy for obstructive sleep apnea (OSA); however, the effects of anesthesia on the upper airway are poorly understood. Our aim was to systematically review existing literature on the effects of anesthetic agents on the upper airway.

Data Sources: PubMed, CINAHL, EBM reviews and Scopus (all indexed years).

Review Methods: Inclusion criteria included English language articles containing original human data. Two investigators independently reviewed all articles for outcomes related to upper airway morphology, dynamics, neuromuscular response, and respiratory control.

Results: The initial search yielded 180 abstracts; 56 articles were ultimately included (total population = 8,540). The anesthetic agents studied were: topical lidocaine, propofol, dexmedetomidine, midazolam, pentobarbital, sevoflurane, desflurane, ketamine, and opioids. Outcome measures were diverse and included imaging studies, genioglossus electromyography, endoscopic airway assessment, polysomnography, upper airway closing pressure, and clinical evidence of obstruction. All agents caused some degrees of airway collapse. Dexmedetomidine did not have dose-dependent effects when evaluated using cine magnetic resonance imaging, unlike sevoflurane, isoflurane, and propofol, and caused less dynamic collapse than propofol.

Conclusions: Studies assessing the effect of anesthesia on the upper airway in patients with and without OSA are limited, and few compare effects between agents. Medications with minimal effect on respiratory control (e.g., dexmedetomidine) may work best for DISE.

Key Words: Anesthesia, opioids, upper airway, obstructive sleep apnea, adult, children, systematic review, cine MRI, drug-induced sleep endoscopy, sedation.

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Effects of Opioids on the Airway

Opioid receptors are present in respiratory control centers of the central nervous system and in mechanosensory receptors in the airway. Opioids are known to depress both the ventilatory and pharyngeal neuromotor drive, therefore decreasing airway patency. Animal studies suggest that opioids activate laryngeal adductor motoneurons and depress laryngeal abductor and pharyngeal constrictor motoneurons, impairing upper airway caliber. In six of nine studies in this review, opioids resulted in clinical airway obstruction. Two studies demonstrated depression of upper airway reflexes, and another reported a decrease in respiratory compliance. All of these studies found that opioids increase upper airway obstruction.

Anesthesia Patient Safety Foundation

Section Editor: Sorin J. Brull

REVIEW ARTICLE

CME

Chronic Opioid Use and Central Sleep Apnea: A Review of the Prevalence, Mechanisms, and Perioperative Considerations

Denis Correa, MBBS, MD,* Robert J. Farney, MD,† Frances Chung, MBBS, FRCPC,* Arun Prasad, MBBS, FRCA, FRCPC,* David Lam, BMSc,* and Jean Wong, MD, FRCPC*

BACKGROUND: Chronic opioid use has been associated with the development of sleep-disordered breathing (SDB) such as central sleep apnea (CSA). Patients receiving chronic opioids may suffer from unrecognized sleep apnea that contributes to opioid-overdose death. Currently, information regarding the perioperative management of patients with chronic opioid-associated CSA is limited. The objectives of this review are to define the clinical manifestations of SDB associated with chronic opioid therapy, especially CSA, and to highlight their prevalence, mechanisms, risk factors, and perioperative management.

METHODS: We searched Medline (1983–2014), Medline In-Process and other nonindexed citations (July 2014), EMBASE (1983–2014), the Cochrane Database of Systematic Reviews (January 2005–2014), the Cochrane Central Registry of Controlled Trials (July 2014), and PubMed basic search for new materials (1983–2014). Anesthesia and Sleep Medicine meeting abstracts were also searched for relevant articles. We included all prospective, retrospective studies and case reports in which CSA and chronic opioid use was confirmed by polysomnography. CSA was defined as the absence of airflow for ≥10 seconds with the absence of breathing efforts. A Central Apnea Index ≥5 events/h was considered significant.

RESULTS: The search strategy yielded 8 studies which included 560 patients. The overall prevalence of CSA in patients taking chronic opioids was high (24%). The morphine equivalent daily dose (MEDD) was strongly associated with the severity of the SDB, predominantly CSA, with an MEDD of >200 mg being a threshold of particular concern. Concurrent use of benzodiazepines or hypnotics was associated with the severity of CSA in one study. Body mass index was inversely related to the severity of SDB. There were various recommendations regarding the best type of positive airway pressure therapy for the treatment of opioid-associated CSA. Continuous positive airway pressure may be ineffective in eliminating, or may even increase, CSA. Adaptive servoventilation and bilevel positive airway pressure ventilation were effective according to some reports.

CONCLUSIONS: The overall prevalence of CSA in patients taking chronic opioids was 24%. The most important risk factors for severity of CSA were an MEDD >200 mg, and low or normal body mass index. Continuous positive airway pressure is often ineffective for treating CSA. Limited data are available on the perioperative management of patients with CSA associated with chronic opioid use. Further prospective studies on the perioperative risks and management of these patients are needed. (Anesth Analg 2015;120:1273–85)

The Prevalence of Sleep disordered breathing in all populations receiving chronic opioids is high (42-85%).

The prevalence of central sleep apnea in all populations receiving chronic opioids is much higher than in the general population 24%.

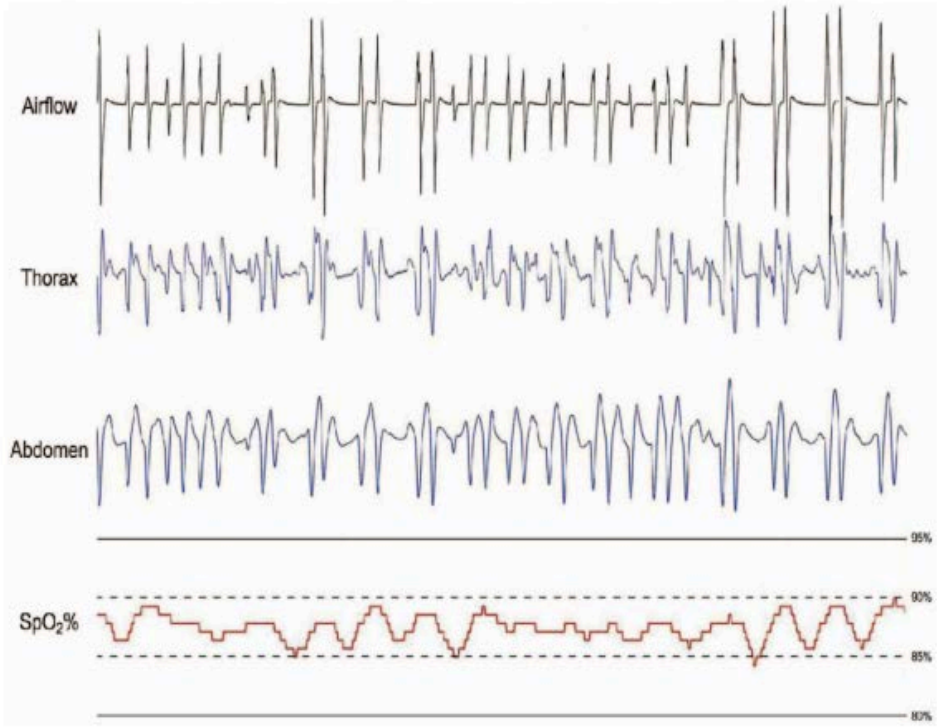

Figure 4. Opioid-induced ataxic and cluster breathing. The respiratory pattern is characterized by a highly irregular rhythm, varying in rate and amplitude as originally described by M.C. Biot. There are a few scattered central apneas with a "cluster" pattern. Spo_2 = oxygen saturation.

Functional consequences of acute and chronic opiate receptor activation-G

- Loss of effect with exposure to opiates occurs over short and long-term intervals

- Desensitization
  - Acute tolerance (desensitization) occurs in the face of transient (minutes to hours) activation of intracellular signaling when acute agonist occupies an opiate receptor.
  - Desensitization disappears at the same time as agonist clearance
  - Desensitization involves phosphorylation of receptors resulting in an uncoupling of receptor from its G-protein and/or internalization of the receptor.

- Tolerance
  - Sustained (days to weeks) administration of an opiate agonist leads to loss of drug effect.
  - Reduction in maximum achievable effect or a right shift in dose-effect curve
  - Changes in response is time-dependent with changes occurring over short term (minutes to hours as with desensitization)

- Dependence
  - State of adaptation manifested by receptor/drug class-specific withdrawal syndrome produced by cessation of drug exposure or administration of antagonist
  - Withdrawal is manifested by the exaggerated appearance of enhanced signs of cellular activation

Opioid-induced Hyperalgesia (OIH)

5.2 During Perioperative Exposure to Opioids

A small number of clinical studies have looked at OIH in the setting of acute perioperative period exposure. Two prospective controlled clinical studies have reported increased postoperative pain despite increased postoperative opioid use in patients who received high doses of intraoperative opioids (30,101). However, others have shown no significant difference in postoperative pain sensitivity based on intraoperative opioids (102-104).

Consequently, the observations provide mixed support for the hypothesis of development of OIH after acute perioperative opioid exposure.

5.3 In Healthy Volunteers

Several studies have examined the development of OIH in humans after acute short-term exposure to opioids. Multiple investigators, in combination, have provided direct evidence for development of OIH in humans using models of secondary hyperalgesia and cold pressor pain (51,105-108).

Compton et al (108,109) found increased sensitivity to cold pressor pain in a small cohort of healthy human volunteers following precipitated opioid withdrawal after injection of acute physical opioid dependence .

It also has been shown that there is a reduction in physical pain sensitivity in response to social exclusion and social encounters (110). Enhanced central thermal nociception has been reported in mildly depressed nonpatients and transiently sad healthy individuals.

- State of nociceptive sensitization caused by exposure to opioids.
- The condition is characterized by a paradoxical response whereby a patient receiving opioids for the treatment of pain might actually become more sensitive to certain painful stimuli.
- Chronic opioid consumption produces changes in CNS similar to central sensitization. They activate mu-receptors which increase effectiveness of glutaminergic synapses at NMDA receptors resulting in OIH.
- The type of pain experienced might be the same as the underlying pain or might be different from the original underlying pain.
- OIH appears to be a distinct, definable, and characteristic phenomenon that could explain the loss of opioid efficacy in some cases.

Does Fentanyl Lead to Opioid-induced Hyperalgesia in Healthy Volunteers?

A Double-blind, Randomized, Crossover Trial

Eckhard Mauermann, M.D., Joerg Filitz, M.D., Patrick Dolder, M.Sc., Katharina M. Rentsch, Ph.D., Oliver Bandschapp, M.D., Wilhelm Ruppen, M.D.

ABSTRACT

Background: Although opioids in general and remifentanil in particular have been shown to induce hyperalgesia, data regarding fentanyl are scarce. Thus, the authors investigated the effect of fentanyl dosing on pain perception and central sensitization in healthy volunteers using established pain models.

Methods: Twenty-one healthy, male volunteers were included in this randomized, double-blind, crossover study and received either intravenous low-dose (1 μg/kg) or high-dose (10 μg/kg) fentanyl. Pain intensities and hyperalgesia were assessed by intracutaneous electrical stimulation, and cold pressor pain was used as an additional measure of acute pain. The primary

What We Already Know about This Topic

- The intravenous administration of remifentanil is associated with enhanced hyperalgesia
- Relatively little information is available concerning the ability of fentanyl to enhance hyperalgesia after intravenous administration

What This Article Tells Us That Is New

- High-dose (10 μg/kg) fentanyl infusion can increase cold pressor test pain threshold and tolerance 4.5 to 6.5 h after infusion
- Simultaneously, high-dose fentanyl infusion can increase the area of hyperalgesia caused by electrical burn

Fig. 3.

Fentanyl concentrations and outcome variable of intradermal electrical stimulation. All values are represented as mean ± SE. Fentanyl concentrations were calculated by the iTIVA app (Shafer Model); *P* values from 4.5 to 6.5 h are based on the mixed-effects model; *P* values for 0 to 2 h are based on the area under the curve and a paired Wilcoxon Mann–Whitney *U* test. NRS = numeric rating scale.

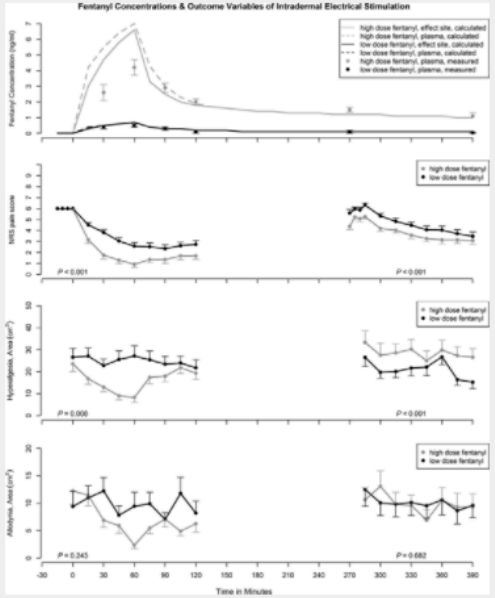

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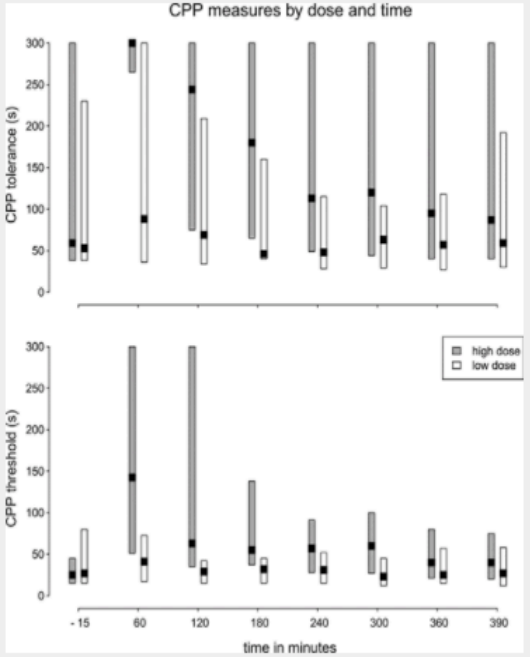
Fig. 4.

Box plots of cold pressor pain (CPP) tolerance (*top*) and threshold (*bottom*) in seconds for high and low doses during the course of the trial. *Black squares* indicate medians, and *boxes* indicate the interquartile range.



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Indications for Opioid—Free Anesthesia

- Narcotic abuse history
  - Acute and chronic opioid addiction
- Opioid intolerance
- Morbidly obese patients with obstructive sleep apnea
- Hyperalgesia
- History of chronic pain
  - Immune deficiency
  - Oncologic surgery
  - Inflammatory diseases
- Less analgesic requirement postoperatively
- Enhanced Recovery after surgery and anesthesia (ERAS)
- Decrease postoperative nausea and vomiting
- Decrease postoperative pulmonary morbidity – COPD, Asthma, and respiratory insufficiency
- Decrease histamine release – Allergy/anaphylaxis
- Patient Satisfaction

Contraindications

- **Absolute**
  - Allergy to any adjuvant drugs
- **Relative**
  - Disorders of autonomic failure
  - Cerebrovascular disease
  - Critical coronary stenosis acute coronary ischemia
  - Heart block / extreme bradycardia
  - Non-stabilized pypovolemic shock or polytrauma patients
  - Controlled hypotension for minimal blood loss
  - Elderly patients on beta-blockers

Opioid-Free Anesthesia Toolbox

- **Ketamine**
  - NMDA antagonist
  - Doses less than 0.5 mg/kg reduces postoperative analgesic needs and especially seen in opioid-tolerant patients
  - It has anti-hyperalgesic and anti-allydonic and anti-tolerance effects.
  - Reduction up to 20 -25% in pain intensity and 30 – 50% in analgesic consumption up to 48 hours after surgery
  - Associated decrease in PONV
  - Uncommon psychomimetic effects – hallucinations, nightmares

Opioid-Free Anesthesia Toolbox

- **Gabapentinoids**
  - Act on alpha-2-deta-1 subunit of presynaptic calcium channels and inhibit neuronal calcium channel influx. Results in reduction in release of excitatory neurotransmitters such as glutamate, substance P and calcitonin gene-related peptide from primary afferent nerve fibers, suppressing neuronal excitability after nerve or tissue injury
  - May prevent central sensitization and hyperalgesia and alllydonia
  - Better postoperative pain management, enhance opioid analgesia, prevent opioid tolerance and CPSP
  - Anxiolytic and sleep-modulating properties
  - Pregabalin – 225 – 300 mg lowest effective dose and 300 – 600 mg produced identical results
    - Decreased pain intensity and opioid consumption
  - Gabapentin – Analgesic ceiling effect at 600 mg
    - Decreased opioid consumption by 20 – 62% during first 24 hours
    - Decrease in opioid-related unwanted clinical effects: PONV, urinary retention and pruritus
    - Main Side effect – dizziness and sedation

Opioid-Free Anesthesia Toolbox

- **Intravenous lidocaine**
  - Local Anesthetic – Na-channel blocker
  - Bolus dose of 100 mg or 1.2 - 2mg/kg followed by infusion 1.33 – 3 mg/kg/h and can be continued postoperatively up to 24 hours. Plasma concentration of 2 – 5 mcg / ml
  - Analgesic – mediated by suppression of spontaneous impulses generated from injured nerve fibers and proximal dorsal root ganglion. Occurs by inhibition of NA-channels, NMDA and G-protein coupled receptors
  - Anti-inflammatory – attributed to blockade of neural transmission at site of injury. It inhibits migration of granulocytes and release of lysosomal enzymes leading to decreased release of pro and anti-inflammatory cytokines.
  - Anti-hyperalgesic properties – Mechanism described above results in suppression of peripheral and central sensitization.
  - Useful during abdominal surgeries → reduction in opioid consumption, opioid-related unwanted clinical effects and pain intensity and decreased incidence of postoperative ileus.
  - Preventative effect on postop pain for up to 72 hours after abdominal surgery

Opioid-Free Anesthesia Toolbox

- **Magnesium Sulfate**
  - Acts as non-competitive antagonist of NMDA glutamate receptors leading to decrease in entry of calcium and sodium ions into cell and prevents efflux of potassium.
  - Prevents depolarization and transmission of pain signals
  - Magnesium sulfate has been reported to be effective in perioperative pain treatment and in blunting somatic, autonomic and endocrine reflexes provoked by noxious stimuli
  - Usual regimens of magnesium sulfate administration were a loading dose of 30-50 mg/kg followed by a maintenance dose of 6-20 mg/kg/h (continuous infusion) until the end of surgery.
  - Many researchers reported that it reduced the requirement for anesthetics and/or muscle relaxants.
  - Intraoperative magnesium during surgery can reduce opioid consumption in the first 24 h postoperatively

Opioid-Free Anesthesia Toolbox

- **Alpha-2 adrenoreceptor agonists**
  - Present in both presynaptic (negative feedback loop inhibiting norepinephrine) and postsynaptic (inhibits sympathetic activity) neurons in central and peripheral nervous system.
  - At supraspinal level, alpha-2 receptors are present in high concentrations at the locus coeruleus in the brainstem. The origin of the medullospinal noradrenergic pathway known to be an important modulator of nociceptive neurotransmission.
  - At spinal level, stimulation of alpha-2 receptors in substantia gelatinosa in the dorsal horn results in inhibition of nociceptive neurons and in the release of substance P.
  - Activates G1-protein-gated K channels in neurons resulting in hyperpolarization
  - Reduce calcium conductance into cells via G-protein-coupled N-type voltage gated calcium channels. Prevents neuron firing and signal propagation.
  - Dexmedetomidine – 0.5mcg/kg loading dose over 10 minutes followed by infusion 0.1 – 0.3 mcg/kg/h
    - 8 X more specific at the receptor than clonidine.

Opioid-Free Anesthesia Toolbox

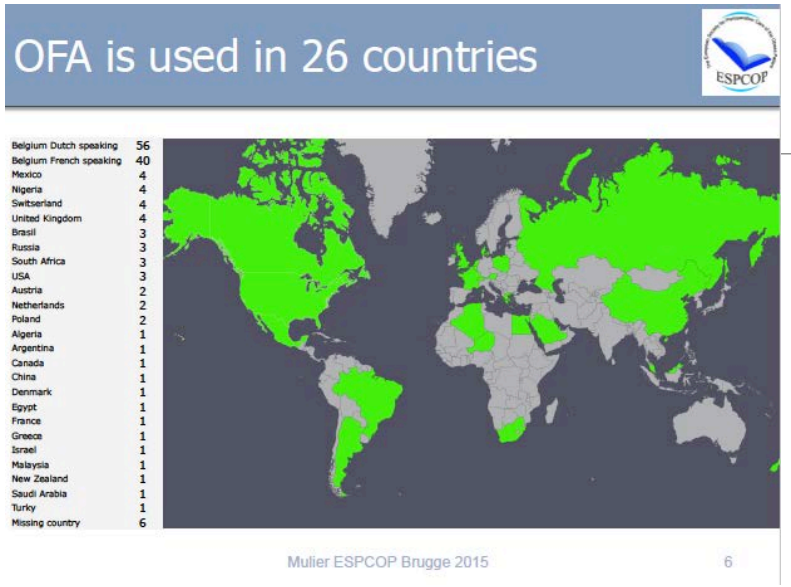
- **Beta-Blocker**
- Esmolol - selective β1-adrenoreceptor antagonist involved in the control of heart rate, contractility, and atrioventricular conduction
  - Literature supports its use perioperatively as an opioid-sparing adjunct, and it may have other anesthetic-sparing qualities as well.
  - Reasons for the opioids paring properties of esmolol are unclear.
  - One study suggests that decrease in opioid consumption was related to the decrease in hepatic metabolism of opioids by β-blockers, which prolong the action of the opioid and thereby reduce opioid requirements.
  - Esmolol does slow heart rate; thereby it decreases cardiac output, which decreases hepatic blood flow, so this may slow metabolism of other drugs that are hepatically metabolized, such as fentanyl.
  - Another study theorized that G proteins, which are involved in nociception, are activated through β-antagonism, which resembles the mechanism of central analgesia.
  - Central action theory

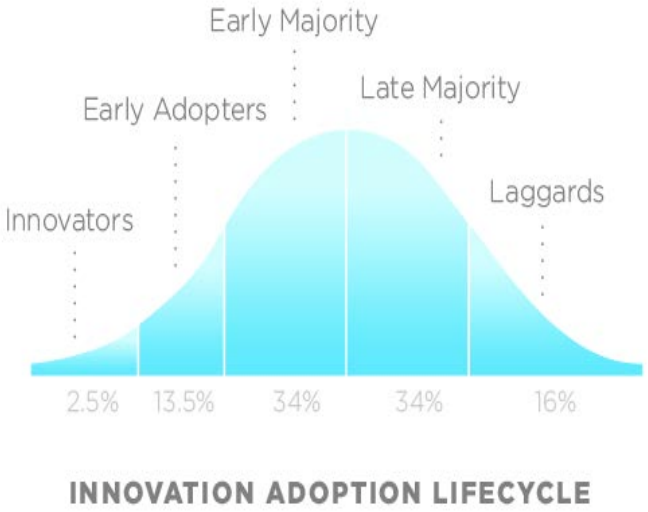
OFA Induction from Mulier

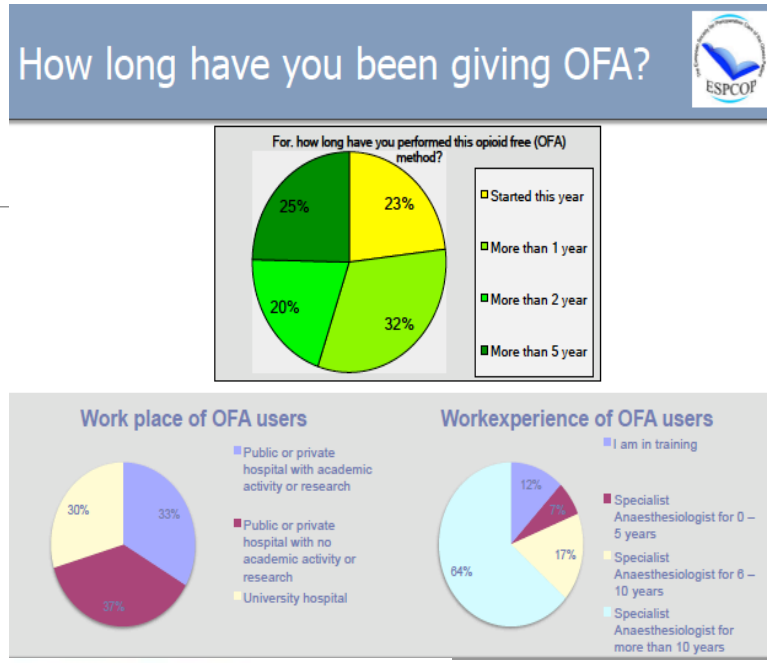
- 10 minutes prior to induction
  - Sympathetic Block – Dexmedetomindine 0.3 mcg/kg IBW (20-30 mcg)
- 1 minute prior to induction
  - Hypnotic and rapid stress block – Lidocaine 1.5 mg /kg (100 mg)
- Induction
  - Hypnotic and stress block – Propofol 2.5 mg/kg IBM (200mg)
- Hemodynamic Stabilization
  - Rapid preload reduction – Magnesium Sulfate 40 mg / kg IBW (2.5 g)
  - Neuromuscular Blocker if needed for anesthesia or surgery
- Anti-inflammatory agents before surgery – Dexamethasone 10 mg/ Diclofenac 75 – 150 mg
- NMDA antagonist – Ketamine 10 – 25 mg (bolus / slow infusion / end of surgery)
- On standby
  - Beta-Blocker – metoprolol 1 – 5 mg
  - Calcium channel blocker – nicardipine 1 – 5 mg
  - Ephedrine 3 – 9 mg
  - Phenylephrine 10 – 30 mcg

OFA Maintenance from Mulier

- Sympathetic Block
  - Dexmedetomidine 0.5 – 1 mcg/kg/h
  - Clonidine 150 mcg
- Local Anesthetics
  - Lidocaine 1% 1 – 3 mcg / kg /h
  - Procaine 0.1% – 6 mg/kg / h
  - Toxic doses > 10 mg / kg
- Magnesium Sulfate : 2.5 – 10 mg / kg IBW/ h
- Inhalation Agent
  - Sevoflurane / Desflurane 0.6 – 0.8 MAC with BIS around 40%
- Propofol infusion (higher dose than TIVA required)
- NMDA block (if opioids may be used postop)
  - Ketamine 50 mg over 12 hours
- IV tylenol: 1000 mg







SOFA
The Society for Opioid Free Anesthesia

Opioid-Free Anesthesia Trend

ELSEVIER

REVISTA BRASILEIRA DE ANESTESIOLOGIA

Official Publication of the Brazilian Society of Anesthesiology
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SCIENTIFIC ARTICLE

Opioid-free total intravenous anesthesia with propofol, dexmedetomidine and lidocaine infusions for laparoscopic cholecystectomy: a prospective, randomized, double-blinded study☆

Mefkur Bakan[a,*], Tarik Umutoglu[a], Ufuk Topuz[a], Harun Uysal[a], Mehmet Bayram[b], Huseyin Kadioglu[c], Ziya Salihoglu[a]

NEWSROOM

Breast Surgery without Opioids

Mastectomy Patient Embraces ComfortSafe Anesthesia, Recovers with No Nausea

September 20, 2016

"I absolutely cannot handle narcotics," said Cathy Kalimon, after learning that treating her breast cancer would mean surgery and anesthesia.

Cathy received her diagnosis in December 2015 shortly after she and her husband John returned from a getaway in the Shenandoah Mountains. Days later, Cathy met with breast surgeon Eleni Tousimis, MD and breast reconstruction surgeon Troy Pittman, MD. Cathy was scheduled for two surgeries. One surgery included two procedures in the same operation: a bilateral mastectomy with breast reconstruction.

Cathy's previous surgeries with standard anesthesia left her with unbearable nausea and vomiting. Dr. Tousimis comforted Cathy to let her know she had not forgotten her concern and introduced Cathy to her anesthesiologist.

Opioid-free total intravenous anaesthesia reduces postoperative nausea and vomiting in bariatric surgery beyond triple prophylaxis

P. Ziemann-Gimmel*, A. A. Goldfarb, J. Koppman and R. T. Marema

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Editor's key points

- Bariatric surgery is commonly associated with postoperative nausea and vomiting (PONV).
- The authors compared PONV among bariatric surgery patients randomized to opioid-free total i.v. anaesthesia (TIVA) or volatile-opioid anaesthesia.
- The incidence and severity of PONV were significantly lower in the opioid-free TIVA group.

Background. Patients undergoing bariatric surgery are at high risk of postoperative nausea and vomiting (PONV). Despite triple PONV prophylaxis, up to 42.7% of patients require antiemetic rescue medication (AERM).

Methods. This prospective, randomized study was conducted from November 2011 to October 2012. In the Classic group (n=59), patients underwent general anaesthesia with volatile anaesthetics and opioids. In the Total i.v. anaesthesia (TIVA) group (n=60), patients underwent opioid-free TIVA with propofol, ketamine, and dexmedetomidine. The severity of PONV was assessed using a Likert scale (none, mild, moderate, and severe).

Results. Patients in both groups had similar clinical characteristics, surgical procedure, and PONV risk scores and required similar amounts of postoperative opioid. In the Classic group, 22 patients (37.3%) reported PONV compared with 12 patients (20.0%) in the TIVA group [P=0.04; risk 1.27 (1.01–1.61)]. The absolute risk reduction was 17.3% (number-needed-to-treat=6). The severity of nausea was statistically different in both groups (P=0.02). The severity of PONV was significantly worse in the Classic group. There was no difference either in the number of patients requiring AERM in the postoperative period or in the number of AERM doses required.

Conclusions. This prospective randomized study demonstrates that opioid-free TIVA is associated with a large reduction in relative risk of PONV compared with balanced anaesthesia.

Postoperative Analgesia Impact of Narcotic Free Anesthesia (PAINFree)

This study is ongoing, but not recruiting participants.

Sponsor:
Université de Sherbrooke

Information provided by (Responsible Party):
Etienne de Medicis, Université de Sherbrooke

ClinicalTrials.gov Identifier:
NCT01544959

First received: September 9, 2010
Last updated: October 25, 2016
Last verified: October 2016
History of Changes

- Hypothesis of the study
  - substituting fentanyl by esmolol and metoprolol during general anesthesia for patients undergoing mastectomy will result in less pain and less narcotic consumption in the recovery room.
  - Verify the impact of that substitution on nausea and vomiting, on the time spent in the recovery room and on chronic postsurgical pain (3 and 6 months).
- Review the impact on breast cancer recurrence 5 years after the surgery.

Estimated Enrollment:	84
Study Start Date:	January 2010
Estimated Study Completion Date:	January 2018
Primary Completion Date:	January 2013 (Final data collection date for primary outcome measure)

Current Barriers to OFA practice

- Resistance to change
  - Increase in provider work and labor
- Cost of opioid-free therapy
- Need for more research and evidence-based practice
- Lack of training
- Insufficient guidelines
- Limited data

Conclusion

- OFA has the potential to offer select population an alternative to unwanted effects from opioids
- Keep an open mind. OFA can be an exciting field for growth in research and the anesthesia community!

Thank you!

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