

The Use of Opioids in the Perioperative Setting for Laparoscopic Cholecystectomy: A Paradigm Shift

Michael W. Manning, MD, PhD

Assistant Professor

Division of Cardiothoracic Anesthesiology

Division of General, Vascular, and Transplant Anesthesiology

Duke University, Durham, NC

Twitter: @MikeManningMD



The Use of Opioids in the Perioperative Setting for Laparoscopic Cholecystectomy: A Paradigm Shift

Michael W. Manning, MD, PhD
Assistant Professor

Division of Cardiothoracic Anesthesiology
Division of General, Vascular, and Transplant Anesthesiology
Duke University, Durham, NC
Twitter: @MikeManningMD

Disclosures

None



Objectives

Understand Anesthesiologist's Approach for Care

Considerations when planning for an OF/OR technique.

The Perioperative management of the patient undergoing lap chole with OF/OR technique.

Potential impact of OF/OR techniques on post-anesthesia phase of care.

Current Evidence for OF/OR Anesthetic Techniques



The Problem...Over Prescribing

2013 National Survey

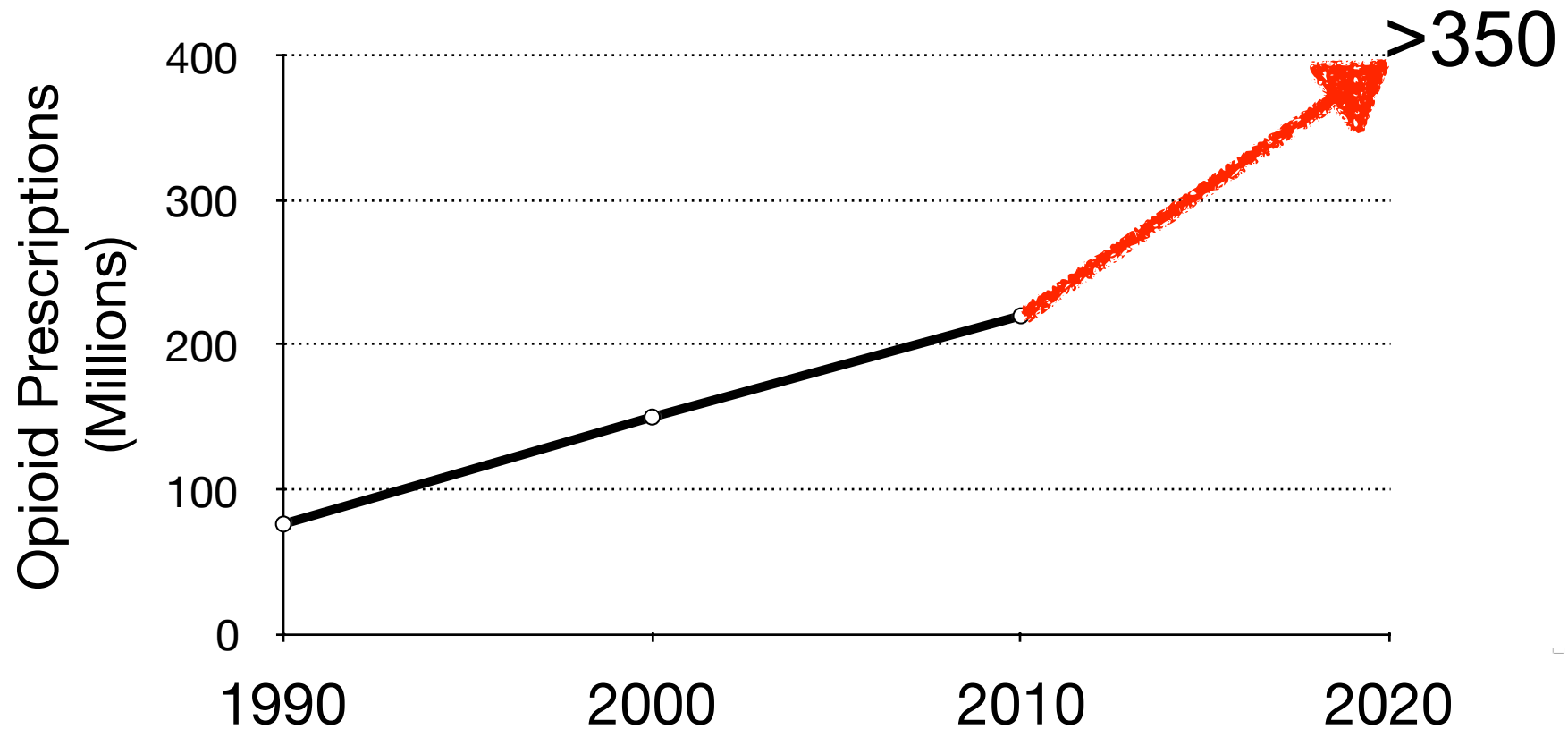
53% who abuse prescription opioids
obtained from friend/relative

84% of these prescriptions originated from
single physician (not doctor shopping)

Reuben DB, Alvanzo AAH, Ashikaga T, et al. *National Institutes of Health Pathways to Prevention Workshop: the role of opioids in the treatment of chronic pain*. Ann Intern Med. 2015;162(4):295-300. doi:10.7326/M14-2775.



The Problem...Over Prescribing



The Problem...

All Clinicians have responsibility in the rising opioid use/abuse

Greatest number of opioid prescriptions are written by primary care physicians and advanced practice providers

The highest concentration of opioid prescribing is in:

Pain Management

Physical Medicine & Rehabilitation

Anesthesiology



The Problem...

All Clinicians have responsibility in the rising opioid use/abuse

Greatest number of opioid prescriptions are written by primary care physicians and advanced practice providers

The highest concentration of opioid prescribing is in:

Pain Management

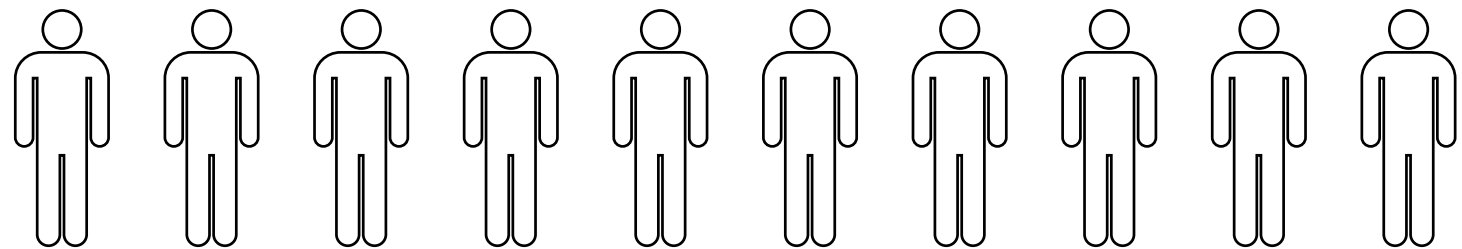
Physical Medicine & Rehabilitation

Anesthesiology

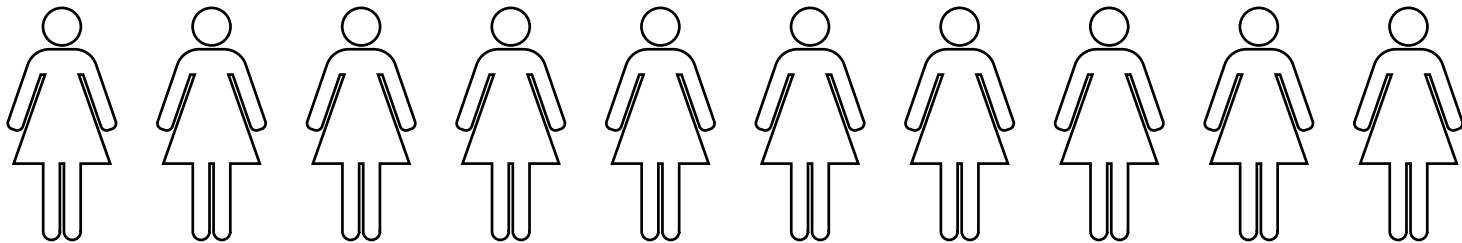


The Problem...Chronic Pain

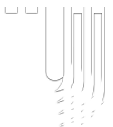
$\frac{1}{3}$



Population of the United States of America



Reuben DB, Alvanzo AAH, Ashikaga T, et al. *National Institutes of Health Pathways to Prevention Workshop: the role of opioids in the treatment of chronic pain.* Ann Intern Med. 2015;162(4):295-300. doi:10.7326/M14-2775.



The Problem...Chronic Pain Costs

Over \$600 Billion in costs annually

Lost work productivity

Increased medical expenses

Reuben DB, Alvanzo AAH, Ashikaga T, et al. *National Institutes of Health Pathways to Prevention Workshop: the role of opioids in the treatment of chronic pain*. Ann Intern Med. 2015;162(4):295-300. doi:10.7326/M14-2775.



Opioid Free / Opioid Reduced Anesthesia

UTILITY OF OPIOIDS IN ANESTHESIA ?



Why Use Opioids? - Beneficial Effects



Paul Janssen
(1926 - 2003)

Blunt the sympathetic and neuroendocrine response

Airway instrumentation

Surgical Incision (noxious stimulus)

No direct negative inotropic effects

Stable cardiovascular dynamics
(cardiac anesthesia)

Cytoprotective / Preconditioning

Potent acute analgesia

Reversal agents if needed



Opioids In the Peri-Operative Setting

High risk of respiratory depression in the surgical population

Alters immunologic function / produces differential effects

Cancer; angiogenesis; myocardial effects

Patients have differential tolerance

Produces hyperalgesia

Postoperative effects

nausea/vomiting; ileus; urinary retention, etc

negative effects on length and quality of recovery



Old Way...

———— Dexmedetomidine
Lidocaine

———— Regional Anesthesia

———— Opioid PCA
Acetaminophen
Ketamine

———— Opioids



A New Way...

———— Opioids

———— Ketamine
Dexmedetomidine

———— Lidocaine
Magnesium

———— Regional Anesthesia
Acetaminophen
NSAIDS



Opioid Free / Opioid Reduced Anesthesia

GIMMICK OR REAL PRACTICE ?



Opioid Free Anesthesia



Jan Paul Mulier, MD, PhD
Bariatric Anesthesiologist
AZ Sint-Jan Brugge-Oostende AV
Bruges, Belgium



Opioid Free Anesthesia



Who Does Opioid Free Anesthesia??

Countries Performing OFA Routinely

Canada
United States
Mexico



Slide number # 19

Who Does Opioid Free Anesthesia??

Countries Performing OFA Routinely

Brazil

Argentina



Who Does Opioid Free Anesthesia??

Countries Performing OFA Routinely

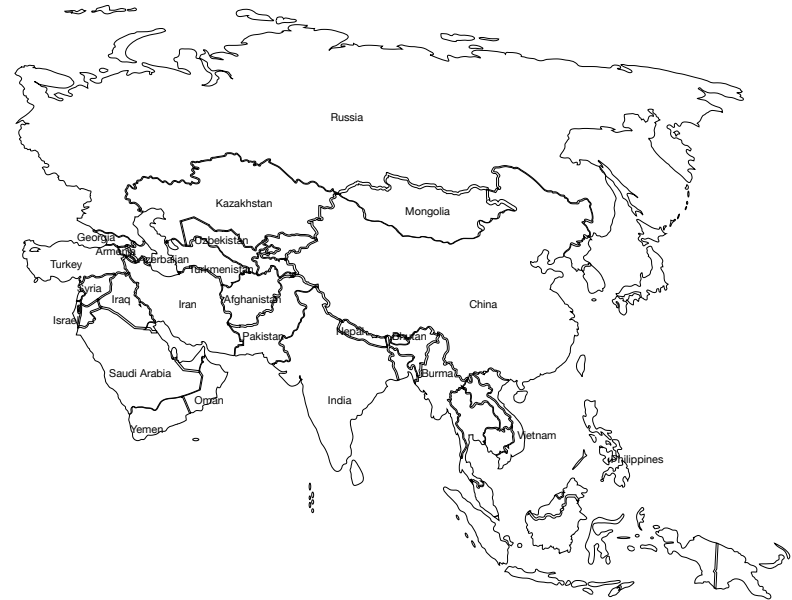
United Kingdom
France
Belgium
Netherlands
Poland
Denmark
Greece
Turkey
Switzerland
Russia



Who Does Opioid Free Anesthesia??

Countries Performing OFA Routinely

Russia
China
Malaysia
Saudi Arabia
New Zealand
Israel
Egypt
Algeria
Nigeria



Preoperative Phase

PLANNING FOR THE OPIOID FREE OR
OPIOID REDUCED ANESTHETIC



Selection of Appropriate Patients

Same day surgery (outpatient Lap Chole)

History of PONV

Desire to return to full function (Motivation)

Co-morbidities (obesity, OSA, etc)

Avoidance of opioid side effects



A Real Patient...

59 year female

5' 8"; 94.8 kg

PSurHx:

1970 - appendectomy

1992 - Dermoid ovarian cysts

2010 - mastectomy

11/16/2016 - robotic right partial nephrectomy

11/29/2016 - acute cholecystitis requiring cholecystotomy tube with
klebsiella infection

PMedHx:

GERD; anxiety; depression; anemia; osteoarthritis

Medications:

Ambien; Effexor; Synthroid; Prilosec; Vitamin D supplements



Realign Appropriate Expectations for Patients

Reinforce expectations and review education of the patient about expectations for pain and pain control.

Pain of 2-3/10 is expected and reasonable.

Pain of 5/10 would be the point to ask for additional medication (if patient were at home – they would self-treat at a 5/10)

May have 'bloated' sensation this is residual from insufflation – normal and resolves over 12-24 hours without treatment



Realign Appropriate Expectations for Patients

Pt may experience referred shoulder pain due to irritation of CO₂ bubbles under the diaphragm.

Walking or changing positions will relieve this “aching pain”.

Inform patient this will feel like an “over-use or strain” type of an ache.

Provide reassurance that this usually resolves over 12-24 hours.

Opioids will not treat this type of pain.



Preoperative Planning & Pre-medications

Acetaminophen - 975 mg PO

Gabapentin - 300 mg PO

Celecoxib - 400 mg PO (Omit if RENAL IMPAIRMENT)

Aprepitant - 40 mg PO for patients with proven history of PON/V & previously failed Scopolamine patch

Glycopyrrolate - 0.2 – 0.3 mg IV (↓ secretions w/ Ketamine use)

Omit midazolam unless h/o of anxiety or currently on benzodiazepines



Intra-Operative Phase

INDUCTION AND MAINTENANCE



Induction of Anesthesia

Lidocaine IV - 1.0-1.5 mg/kg

Propofol - 1.0-1.5 mg/kg

Ketamine IV Bolus - 0.25 mg/kg. Max 40mg
(i.e. – 80 kg pt would receive 20 mg)

Magnesium IV Bolus - 2 g
(If patient has ESRD, is dialysis dependent, or Cr > 2.0 consider 1g)

Paralytic of choice for situation

Rocuronium - 0.6 - 1.2 mg/kg

Esmolol - 0.5 mg/kg (Substitute for induction opioids)



A Real Patient...

Preoperatively:

Gabapentin 300 mg

Tylenol 975 mg

Midazolam 1 mg

Intraoperatively:

Dexamethasone 4 mg

Lidocaine 180 mg (80 mg & 100mg)

Propofol 130 mg

Ketamine 25 mg

Ketoralac 30 mg

Esmolol 100 mg bolus & Infusion @ 30-70 mcg/kg/min (500 mg total)

Magnesium 2 gm



Maintenance of Anesthesia

Desflurane Anesthesia using low flows to maintain temp.

Preventative Ventilation Strategies

Maintain TV 6-8 ml/kg (based on Pt's IDEAL body weight).

Minimize FiO₂ to 35%-40% to decrease absorptive atelectasis.

Maintain PEEP at 7-8 cm H₂O during insufflation.

Fluid Therapy follows ERAS protocols

PON/V Prophylaxis

Dexamethasone 4-8mg after induction prior to incision

Ondansetron 4 mg prior to emergence from anesthesia



Emergence from Anesthesia

Ketorolac 15 mg - 30 mg when “bag in the bag”

30° Trendelenberg during decannulation to vent CO₂

Request surgeons inject local in port sites prior to closure

Ketamine 10-20 mg (clinical judgement)

Lidocaine IV - 1-1.2 mg/kg 5 min prior to extubation



Post Operative Planning Phase

PACU COURSE AND BEYOND



Where in the PACU shall they go??

Phase I or Phase II ??

Clinical Judgment

Presenting Co-Morbidities

Intraoperative Course

Clinical Expectations for Recovery

Chronic Pain; History of PON/V; Delayed Surgical Issues

Planned Discharge Disposition



Arrival in the PACU

Pain Control PRN

Tylenol 975 mg once when taking PO

Fentanyl 25 mcg/dose; Q15 min x 4 doses

Dilaudid 0.2-0.4 mg/dose; Q20 min x 2 doses

Morphine 0.06-0.1 mg/kg IBW; Q20 min x 2 doses

PON/V PRN

Haldol 1 mg/dose; Q 20 min x 2 doses

Reglan 10 mg/dose; once (omit if > 60 yrs)

Benadryl 6.25 mg/dose; Q30 min x 2 doses

Phenergan 6.25 mg/dose

(last resort - can be very sedating)

Fluids

Ringer's Lactate - 125 mL/hr



A Real Patient...

Surgery began @ 0842
Pain Scores on Floor - 0/10 - 4/10
Surgery ended @ 1139
(% headaches - chronic)
Total Operative Time: 177 minutes

Denies any surgical site pain
Admitted to PACU @ 1150

Discharged to 23° Observation @ 1316
Given 5 mg oxycodone on discharge at 0722 the
Total PACU Time: 86 minutes
following morning < 24 hours postoperative

Pain Score During PACU - 0/10
(% Caffeine withdraw headache)



Opioids are Dangerous in Peri-Operative Settings

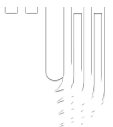


PAIN MEDICINE

Postoperative Opioid-induced Respiratory Depression

A Closed Claims Analysis

Lorri A. Lee, M.D., Robert A. Caplan, M.D., Linda S. Stephens, Ph.D., Karen L. Posner, Ph.D.,
Gregory W. Terman, M.D., Ph.D., Terri Voepel-Lewis, Ph.D., R.N., Karen B. Domino, M.D., M.P.H.



Opioids In the Peri-Operative Setting

357 acute pain claims reviewed between 1990-2009
92 attributed to respiratory depression events

88% occurred within 24 hours of surgery
(convergence of recovery from GA, optimization of opioid analgesics, sedating antiemetics, sleep deprivation)

77% resulted in ***severe brain damage or death***



Opioids In the Peri-Operative Setting

Table 1. Characteristics of Respiratory Depression Claims*

Characteristic	n (%)
Female (n = 91)	52 (57)
Obese (n = 71)	** 47 (66)
ASA physical status 1–2 (n = 87)	55 (63)
Age (mean ± SD), yr, (n = 85)	50 ± 17.7
Patient ≥50 yr old (n = 85)	37 (44)
History of chronic opioid use	7 (8)
OSA diagnosis	** 15 (16)
High risk of OSA†	** 8 (9)
Lower extremity surgery	38 (41)



Opioids In the Peri-Operative Setting

Table 2. Medication Factors Associated with Respiratory Depression

	n (%)
Routes of Opioid Therapy	
PCA only	17 (18)
Neuraxial only	16 (17)
Other only*	16 (17)
Multimodal†	43 (47)
Continuous infusion of opioids	42 (46)
Interaction of opioid and nonopioid sedative medications	31 (34)
More than one physician prescribing (n = 91)	30 (33)
Excessive opioid dose	15 (16)



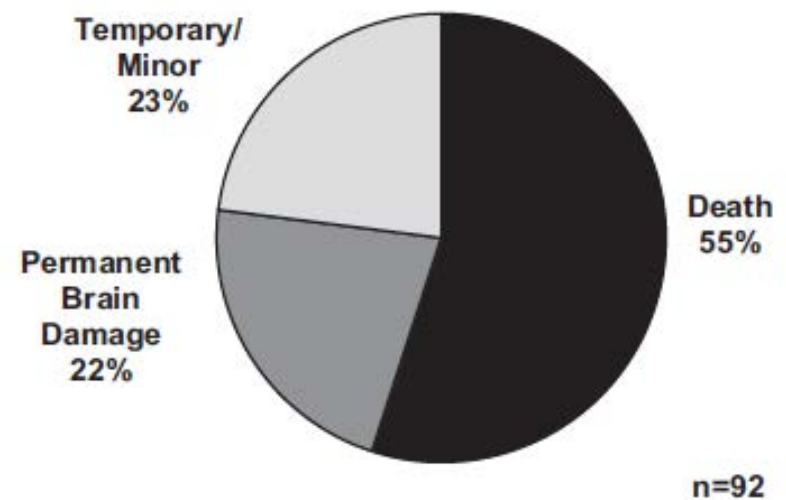
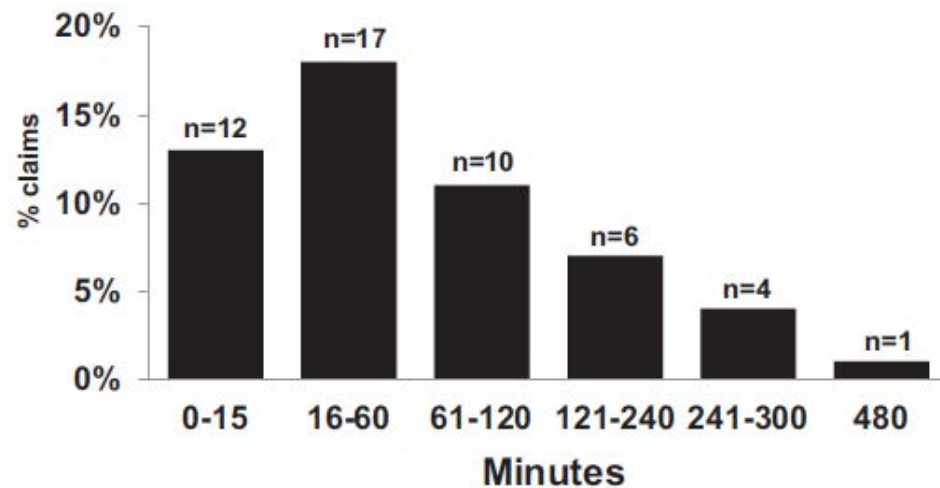
Opioids In the Peri-Operative Setting

Table 3. Postoperative Opioids by Routes of Administration*

	All Claims (n = 92)	Neuraxial† (n = 36)	PCA (n = 49)	IV bolus (n = 49)
	n (%)	n (%)	n (%)	n (%)
Opioid				
Morphine	59 (64)	17 (47)	33 (67)	29 (59)
Fentanyl	23 (25)	19 (53)	2 (4)	5 (10)
Meperidine	22 (24)	1 (3)	6 (12)	14 (29)
Hydromorphone	23 (25)	0 (0)	14 (29)	13 (27)
Other‡	11 (12)	4 (12)	1 (2)	1 (2)
Continuous infusion of opioids				
Yes §		27 (75)	16 (33)	
No		9 (25)	4 (8)	
Unknown		0 (0)	29 (59)	



Opioids In the Peri-Operative Setting



Opioids + Obstructive Sleep Apnea

Pharyngeal dilator muscles relax; Wakefulness drive

Subset rely heavily on wakefulness drive to restore airway patency
(HIGHEST RISK with opioids!)

Central respiratory drive decreases (\uparrow PaCO₂ \rightarrow \downarrow PaO₂)

OSA leading to hypoxia produces competing effects on pain

Hypoxemia \rightarrow \uparrow sensitivity to opioid analgesia

More effective at \downarrow doses

Increased reports of pain \rightarrow \uparrow pain perception
(chronic inflammatory state)



Opioids + Sleep

Sleep fragmentation

Decreased REM sleep

May promote hyperalgesia

Chronic opioids and high prevalence of central
sleep apnea

Increased Incidence of Delirium



What about Opioids & Pain in the Perioperative Setting?

Acute opioid administration can create analgesic tolerance and hyperalgesia

Leads to higher pain and increased opioid requirement

Remifentanyl - most extensive data

Fewer studies are available for fentanyl, sufentanyl

Tolerance vs Hyperalgesia

Difficult to differentiate in clinical setting

Both resulting in dose escalation of opioids



Is there a dose-relationship to opioids and increased postoperative pain?

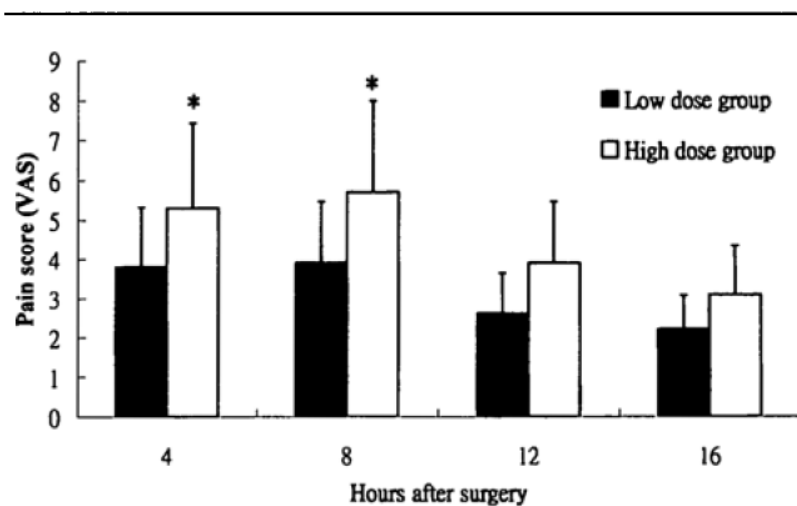


FIGURE 1 Postoperative visual analogue scores (VAS) (mean \pm SD) during the first postoperative 16 hr. *: $P < 0.05$.

Chia Yuan. *Can J Anesthesia* 1999

60 patients, double-blind RCT

ASA I - II

Total Abdominal Hysterectomy

General anesthesia (halothane)

Intra-operative Fentanyl:

High - 15 mcg/kg + 100 mcg/hr

Low - 1 mcg/kg + no more

Postop:

Fentanyl IV PCA



Higher Dose Fentanyl Increases Postoperative Opioid Requirements

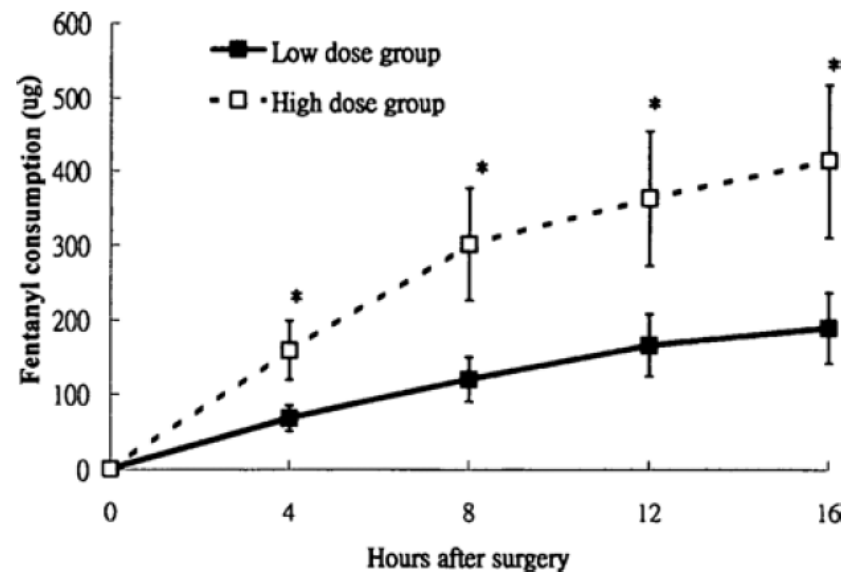


FIGURE 2 Postoperative accumulated fentanyl consumption (µg) (mean ± SD) during the first 16 hours after surgery. *: $P < 0.05$.

Chia Yuan. *Can J Anesthesia* 1999



Opioid Free Anesthesia Improves Outcomes

Masour, M., et al. Saudi J Anaesth. 2013

Prospective Randomized, Double-Blind Study

28 Patients, BMI >50

Undergoing Lap Sleeve Gastrectomy via GETA

Treatment:

opioid free: ketamine bolus (0.5 mg/kg) & infusion (0.5 mg/kg/hr)

fentanyl bolus pre-induction and intermittent bolus

Results:

Less postoperative pain, higher nurse satisfaction in opioid free group (ketamine bolus and infusion)



Opioid Free Anesthesia Improves Outcomes

Bakan, M., et al. Brazilian Journal of Anesthesiology. 2015

80 Patients undergoing Lap Cholecystectomy

ASA I-II

Treatment:

Dexmedetomidine, lidocaine, propofol

Prop / Fentanyl + Remifentanyl

Results:

Lower max pain score, less pain with cough, less rescue analgesic, less zofran needed in opioid free group



Opioid Free Anesthesia Improves Outcomes

Ziemann-Gimmel, P., et al BJA 2014

Randomized Control Trial

119 Patients undergoing bariatric surgery via GETA

Treatment:

Opioid free: TIVA (ketamine, dex, prop)

Classic: opioid + volatile anesthetic

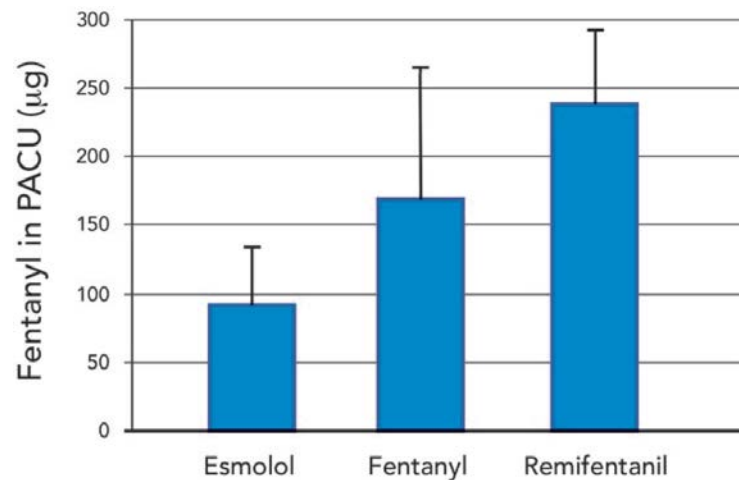
Results:

Opioid free reduced PONV beyond triple prophylaxis- 20% vs 37.3%
($p=0.04$), less rescue antiemetics

Similar pain scores, less opioid requirement in TIVA but not statistically significant



Effects of Avoiding Intraoperative Opioids on Postoperative Opioid Requirements



90 patients ambulatory Lap Chole
Randomized observer - blinded; n=30 each group

- 1) Intermittent fentanyl (mean 200 mcg intraop)
- 2) Esmolol - 5-15 mcg/kg/min
- 3) Remifentanyl - 0.1-0.5 mcg/kg/min

Statistically significant less fentanyl used in PACU with esmolol vs fentanyl or Remifentanyl

Statistically significant less PONV with esmolol

Discharged 40-60 min earlier in esmolol

*no difference in patient reported pain scale (1 min - 2 hr)



Reduced Postoperative Opioid Requirements after Opioid-Free Anesthesia (OFA)

Table 1. Opiate use in opiate anesthesia, opiate-sparing anesthesia, and opiate-free anesthesia patients. Opiate dosage in milligram of morphine equivalent \pm 1 standard deviation. Patients receiving OFA had the least requirement of opiate in PACU and in SPU. (Note: * denotes statistical significance)

Anesthesia Regimen	# Patients	Avg. Age	Duration of Surgery	Avg. BMI	Avg. PACU	Opiate Usage Intraoperatively * between all 3 groups	Opiate Usage in PACU * for OFA vs OS and OA	Opiate Usage in SPU * for OFA vs OS and OA	Zofran in PACU	Zofran in SPU
Opiate Anesthesia (OA) - Control	36	54.03	1:21	29.7	3:24	17.4 \pm 14.6	4.5 \pm 6.1	0.19 \pm 0.4	0.78 \pm 1.7	0
Opiate-Sparing Anesthesia (OSA)	143	54.4	1:39	28.5	1:52	1.8 \pm 2.6	5.03 \pm 6.5	0.25 \pm 0.4	0.73 \pm 1.6	0.11 \pm 0.7
Opiate-Free Anesthesia (OFA)	177	54.6	1:38	29.2	1:51	0	2.05 \pm 4.2	0.062 \pm 0.2	0.59 \pm 1.5	0.11 \pm 0.7

ASA 2016: David J. Samuels, M.D., Prachiti Dalvi, M.S., Abdullah AbouSamra, B.S., Devan and Mangar, M.D., Enrico M. Camporesi, M.D.. TeamHealth Anesthesia, Tampa, FL, USA.



Anesthesia Technique and Cancer Recurrence

Type of study	Reference	Surgery	Technique	Outcome
Retrospective	Gupta <i>et al.</i> 2011 ⁹¹	Open colectomy	GA+epidural (n=562) GA+PCA opioid analgesia (n=93)	GA+opioid group had higher mortality rate in <i>rectal</i> cancer (P=0.049) No difference with <i>colon</i> cancer (P=0.23)
Retrospective	Lin <i>et al.</i> 2011 ⁹²	Laparotomy for ovarian carcinoma	Epidural anaesthesia+analgesia (n=106) GA+opioid analgesia (n=37)	Epidural group had improved 3 yr and 5 yr survival rates (P=0.043)
Retrospective	De Oliveira <i>et al.</i> 2011 ⁹³	'Debulking' surgery for ovarian cancer carcinoma	Epidural (n=55) Opioid analgesia (n=127) (n=158)	Intraoperative epidural analgesia associated with reduced risk of cancer recurrence No difference in biochemical recurrence-free survival (P=0.42), cancer-specific survival (P=0.9), or overall survival (P=0.9)

Heaney, A., Buggy, D.J.
University College Dublin Ireland, Cleveland Clinic
Review in BJA 2012



Summary

Opioids can be harmful / dangerous in the perioperative setting

Opioid Free/Opioid Reduced anesthesia can improve patient outcomes and reduce risks

Opioid Free/Opioid Reduced anesthesia can provide the same level of analgesia or better



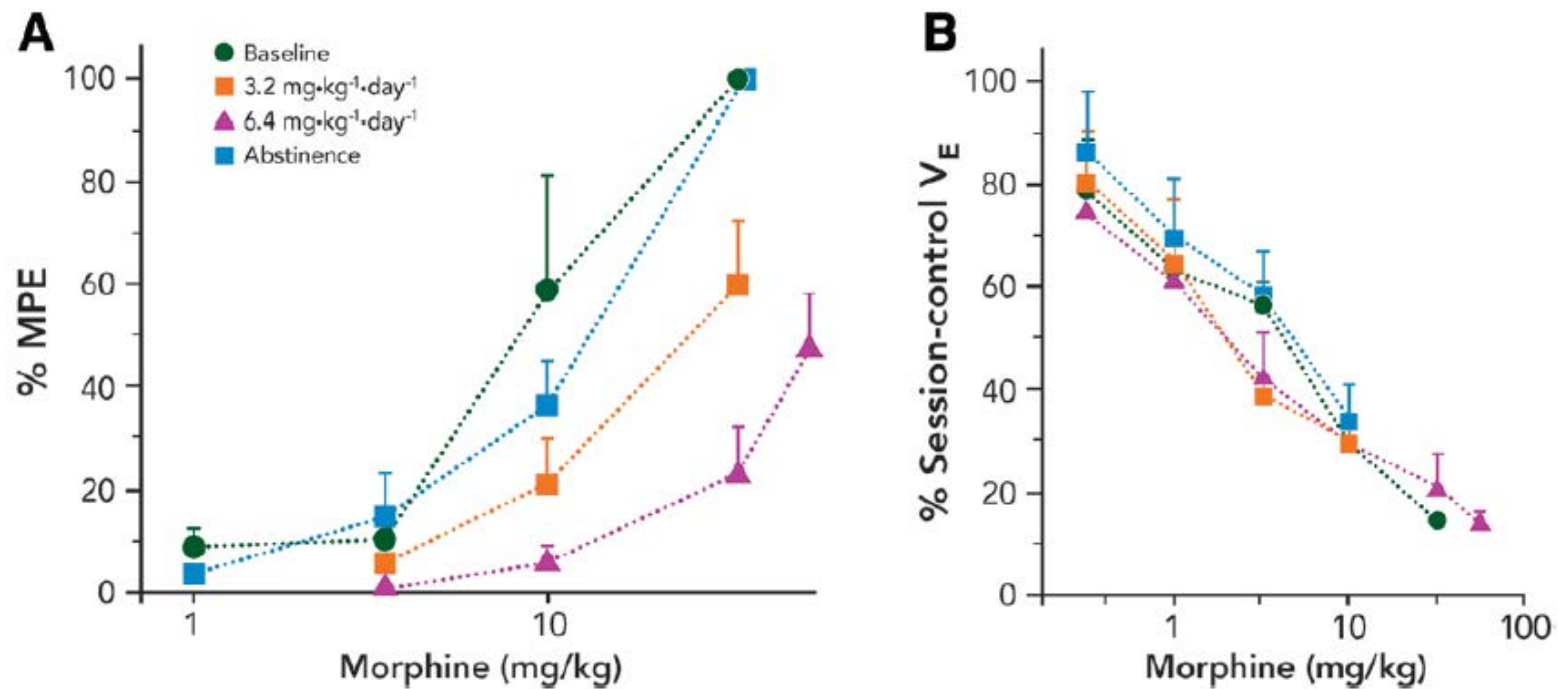


Duke Anesthesiology

DUKE UNIVERSITY

Extraordinary Care – Through a Culture of Innovation

Opioids & Differential Tolerance



What about Opioids & Pain in the Perioperative Setting?

