Perioperative Opioid-Sparing Analgesia Strategies for Enhanced Recovery After Surgery

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Disclosures

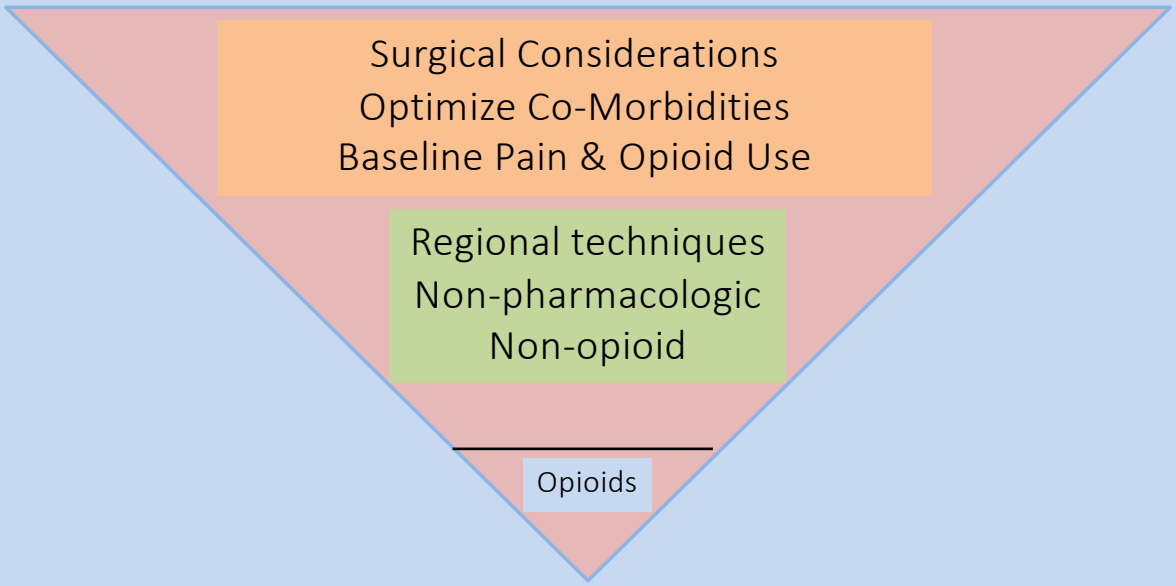
- I have no relevant relationships to disclose

Learning Objectives

After this lecture, the listener should be able to:

- Identify risks associated with the perioperative use of opioids
- Determine opioid-sparing systemic pharmacologic analgesics options
- Organize a perioperative analgesic plan to decrease postoperative pain, reduce opioid use, hasten recovery, and improve patient safety

Paradigm Shift



Reasons to Reduce Peri-operative Opioid Use

- Relapse risk in patients with a history of opioid use disorder
- Improved post-operative recovery
- Acute risks
- Chronic risks

Opioid Use Disorder Relapse

- In 2016, 1.8 million people had prescription pain medication use disorder, 5.5% of population
- High risk group
- Poor evidence for pain management options
- Perioperative exposure to relapse triggers:
  - Stress
  - Agent of abuse

Ward EN, Quaye AN, Wilens TE. Opioid Use Disorders: Perioperative Management of a Special Population. Anesth Analg. 2018 Aug;127(2):539-547.

ERAS Colorectal Surgery

- 13 major perioperative categories
- 3 rely heavily on opioid reduction
  - Multimodal, opioid-sparing pain management
  - PONV prevention
  - Ileus reduction
- ERAS protocols reduce
  - Length of hospital stay
  - Costs
  - Minor complications

Carmichael JC, Keller DS, Baldini G, Bordeianou L, Weiss E, Lee L, Boutros M, McClane J, Feldman LS, Steele SR. Clinical Practice Guidelines for Enhanced Recovery After Colon and Rectal Surgery From the American Society of Colon and Rectal Surgeons and Society of American Gastrointestinal and Endoscopic Surgeons. Dis Colon Rectum. 2017 Aug;60(8):761-784.

ORADES
(Opioid-Related Adverse Drug Events)

- *Respiratory depression*
- *Hyperalgesia*
- *Chronic pain*
- Nausea
- Vomiting
- Bradycardia
- Pruritus
- Cognitive impairment
- Withdrawal
- Urinary retention
- Tolerance
- Death
- Ileus
- 30-day readmission?

Long DR, Lihn AL, Friedrich S, Scheffenbichler FT, Safavi KC, Burns SM, Schneider JC, Grabitz SD, Houle TT, Eikermann M. Association between intraoperative opioid administration and 30-day readmission: a pre-specified analysis of registry data from a healthcare network in New England. Br J Anaesth. 2018 May;120(5):1090-1102.

At Risk Patient Populations

- Increased risk of ORADES associated with:
  - Age 65 years or older
  - Male
  - Obese, OSA
  - Substance use disorder/preop opioid use
  - ↑ Charlson Comorbidity Index score

Weight	Clinical condition
1	Myocardial infarct Congestive cardiac insufficiency Peripheral vascular disease Dementia Cerebrovascular disease Chronic pulmonary disease Conjunctive tissue disease Slight diabetes, without complications Ulcers Chronic diseases of the liver or cirrhosis
2	Hemiplegia Moderate or severe kidney disease Diabetes with complications Tumors Leukemia Lymphoma
3	Moderate or severe liver disease
6	Malignant tumor, metastasis Aids

Figure 1 - Charlson comorbidity index – weighting of the clinical conditions present among secondary diagnoses.

Shafi S, Collinsworth AW, Copeland LA, Ogola GO, Qiu T, Kouznetsova M, Liao IC, Mears N, Pham AT, Wan GJ, Masica AL. Association of Opioid-Related Adverse Drug Events With Clinical and Cost Outcomes Among Surgical Patients in a Large Integrated Health Care Delivery System. JAMA Surg. 2018 Aug 01;153(8):757-763.
Kessler ER, Shah M, Gruschkus SK, Raju A. Cost and quality implications of opioid-based postsurgical pain control using administrative claims data from a large health system: opioid-related adverse events and their impact on clinical and economic outcomes. Pharmacotherapy. 2013 Apr;33(4):383-91.

ORADE: Respiratory Depression

- Incidence: 0.1 to <1%
- A significant cause of death and brain damage in the perioperative period
- CONCLUSIONS: "…opioid-related adverse events are …potentially preventable with improvements in assessment of sedation level, monitoring of oxygenation and ventilation, and early response and intervention…"

Weingarten TN, Herasevich V, McGlinch MC, Beatty NC, Christensen ED, Hannifan SK, Koenig AE, Klanke J, Zhu X, Gali B, Schroeder DR, Sprung J. Predictors of Delayed Postoperative Respiratory Depression Assessed from Naloxone Administration. Anesth Analg. 2015 Aug;121(2):422-9.
Cashman JN, Dolin SJ. Respiratory and haemodynamic effects of acute postoperative pain management: evidence from published data. Br J Anaesth. 2004;93:212–23.
Gordon DB, Pellino TA. Incidence and characteristics of naloxone use in postoperative pain management: a critical examination of naloxone use as a potential quality measure. Pain Manag Nurs. 2005;6:30–6.

ORADE: Hyperalgesia

- Controversial: Conflicting systematic review conclusions
- Higher intraop remifentanil infusion rates (>0.2 µg/kg/min) associated with
  - ↑ postoperative opioid consumption
  - ↓ mechanical pressure, cold, and pain thresholds
- Results suggest tolerance and hyperalgesia associated with intraoperative remifentanil use
- Impact of other opioids is less clear due to limited data

Yu EH, Tran DH, Lam SW, Irwin MG. Remifentanil tolerance and hyperalgesia: short-term gain, long-term pain? Anaesthesia. 2016 Nov;71(11):1347-1362.
Fletcher D, Martinez V. Opioid-induced hyperalgesia in patients after surgery: a systematic review and a meta-analysis. Br J Anaesth. 2014 Jun;112(6):991-1004.

Chronic Postsurgical Pain

- Leading cause of chronic pain clinic visits
- Chronic postsurgical pain:
  - Amputation 50-85%
  - Cardiac surgery 30-55%
  - Thoracotomy 5-65%
  - Hip replacement 12%
  - Cesarean section 6%
  - Mastectomy 20-50%
  - Hernia repair 5-35%
  - Cholecystectomy 5-50%

Thomson S. Failed back surgery syndrome - definition, epidemiology and demographics. Br J Pain. 2013 Feb;7(1):56-9.
Bouman EA, Theunissen M, Bons SA, van Mook WN, Gramke HF, van Kleef M, Marcus MA. Reduced incidence of chronic postsurgical pain after epidural analgesia for abdominal surgery. Pain Pract. 2014 Feb;14(2):E76-84.
Reddi D, Curran N. Chronic pain after surgery: pathophysiology, risk factors and prevention. Postgrad Med J. 2014 Apr;90(1062):222-7; quiz 226.
Schug SA, Bruce J. Risk stratification for the development of chronic postsurgical pain. Pain Rep. 2017 Oct 31;2(6):e627.

ORADE: Chronic Pain

Intraop remifentanil vs intermittent fentanyl:

- Cardiac surgery, thermal detection & pain threshold @12 months (RCT)
  - No difference in warm/cold detection & pain
- Cardiac surgery, chronic pain @3 & 12 months (RCT)
  - No difference in chronic postoperative pain @12 months
  - Increased postop analgesic requirements and thoracic pain until 3 months after surgery in remifentanil group
    - Associate with younger pts & higher dose

de Hoogd S, Valkenburg AJ, van Dongen EPA, Daeter EJ, van Rosmalen J, Dahan A, Tibboel D, Knibbe CAJ. Short and long-term impact of remifentanil on thermal detection and pain thresholds after cardiac surgery: A randomised controlled trial. Eur J Anaesthesiol. 2018 Sep 11. de Hoogd S, Ahlers SJGM, van Dongen EPA, van de Garde EMW, Daeter EJ, Dahan A, Tibboel D, Knibbe CAJ. Randomized Controlled Trial on the Influence of Intraoperative Remifentanil versus Fentanyl on Acute and Chronic Pain after Cardiac Surgery. Pain Pract. 2018 Apr;18(4):443-451.

ORADE: Chronic Pain

- Thoracic surgery, neuropathic pain @9 months (RCT):
  - Patients who received high-dose remifentanil (55%) vs those who received low-dose remifentanil + epidural (11%)
- Cardiac surgery, pain @12 months (retrospective):
  - intraoperative remifentanil was predictive for chronic thoracic pain in a dose-dependent manner (OR 8.9)
- Cardiac surgery, pain @3 months (RCT):
  - Intraoperative remifentanil (51%) versus intermittent fentanyl (33%) increases analgesic requirements and thoracic pain

Salengros JC, Huybrechts I, Ducart A, Faraoni D, Marsala C, Barvais L, Cappello M, Engelman E. Different anesthetic techniques associated with different incidences of chronic post-thoracotomy pain: low-dose remifentanil plus presurgical epidural analgesia is preferable to high-dose remifentanil with postsurgical epidural analgesia. J Cardiothorac Vasc Anesth. 2010 Aug;24(4):608-16.

Modifiable Risk Factors for Chronic Pain After Surgery

- Preoperative pain, esp. moderate-severe
- Postoperative pain, moderate-severe > mild
- Morphine consumption >6 mg, 48h postop
- Neuropathic pain symptoms, 1 week postop

Artus M, Laviolle B, Maurice A, Malledant Y, Beloeil H. Risk factors for persistent pain after urological surgery. Ann Fr Anesth Reanim. 2014 May;33(5):e89-94.
Andersen KG, Duriaud HM, Jensen HE, Kroman N, Kehlet H. Predictive factors for the development of persistent pain after breast cancer surgery. Pain. 2015 Dec;156(12):2413-22.

Therapies to Decrease Chronic Postop Pain

- Mixed evidence
- Postoperative NSAID
- Perioperative gabapentin and pregabalin
- Intravenous ketamine
- Perioperative lidocaine infusion
- Regional anesthesia

Clarke H, Bonin RP, Orser BA, Englesakis M, Wijeysundera DN, Katz J. The prevention of chronic postsurgical pain using gabapentin and pregabalin: a combined systematic review and meta-analysis. Anesth Analg. 2012 Aug;115(2):428-42.
Bailey M, Corcoran T, Schug S, Toner A. Perioperative lidocaine infusions for the prevention of chronic postsurgical pain: a systematic review and meta-analysis of efficacy and safety. Pain. 2018 Sep;159(9):1696-1704.

Analgesic Modalities

- Optimize co-morbid diseases
- Non-pharmacologic strategies
- Regional anesthesia
- Pharmacologic systemic agents

Barreveld A, Witte J, Chahal H, Durieux ME, Strichartz G. Preventive analgesia by local anesthetics: the reduction of postoperative pain by peripheral nerve blocks and intravenous drugs. Anesth Analg. 2013 May;116(5):1141-61. Gerbershagen HJ, Dagtekin O, Rothe T, Heidenreich A, Gerbershagen K, Sabatowski R, Petzke F, Ozgür E. Risk factors for acute and chronic postoperative pain in patients with benign and malignant renal disease after nephrectomy. Eur J Pain. 2009 Sep;13(8):853-60.

Optimize Co-Morbid Disease

- Risk factors for severe postoperative pain and chronic postoperative pain include:
  - Anxiety
  - Depression
  - Catastrophizing

Ip HY, Abrishami A, Peng PW, Wong J, Chung F. Predictors of postoperative pain and analgesic consumption: a qualitative systematic review. Anesthesiology. 2009 Sep;111(3):657-77.Radinovic K, Milan Z, Markovic-Denic L, Dubljanin-Raspopovic E, Jovanovic B, Bumbasirevic V. Predictors of severe pain in the immediate postoperative period in elderly patients following hip fracture surgery. Injury. 2014 Aug;45(8):1246-50. Correll D. Chronic postoperative pain: recent findings in understanding and management. F1000Res. 2017 Jul 4;6:1054.

Pharmacologic Systemic Opioid-Sparing Options

- NMDA receptor antagonists
  - Ketamine
  - Amantadine
  - Dextromethorphan
  - Magnesium
- Gabapentinoids
- Esmolol
- NSAIDS
- Alpha-2 Agonists
- Intravenous lidocaine
- Acetaminophen
- Caffeine
- Dexamethasone

Acetaminophen

- Decreased pain and opioid consumption after most types of surgery
- Even a single dose can:
  - ↓ Pain for 4 hours
  - ↓ Opioid use for 6 hours
  - ↓ PONV

De Oliveira GS Jr, Castro-Alves LJ, McCarthy RJ. Single-dose systemic acetaminophen to prevent postoperative pain: a meta-analysis of randomized controlled trials. Clin J Pain. 2015 Jan;31(1):86-93.
McNicol ED, Tzortzopoulou A, Cepeda MS, Francia MB, Farhat T, Schumann R. Single-dose intravenous paracetamol or propacetamol for prevention or treatment of postoperative pain: a systematic review and meta-analysis. Br J Anaesth. 2011 Jun;106(6):764-75.
Blank JJ, Berger NG, Dux JP, Ali F, Ludwig KA, Peterson CY. The impact of intravenous acetaminophen on pain after abdominal surgery: a meta-analysis. J Surg Res. 2018 Jul;227:234-245.
Guo H, Wang C, He Y. A meta-analysis evaluates the efficacy of intravenous acetaminophen for pain management in knee or hip arthroplasty. J Orthop Sci. 2018 Sep;23(5):793-800.

NSAIDS

- Single dose provides good acute postoperative pain relief for 4-6h
  - Dipyrone (500mg)
  - Celecoxib (400mg)
  - Ibuprofen (200-400mg)
  - Ketorolac (30-60mg)
  - Etoricoxib (120 mg)
  - Diclofenac (50 mg)

Hearn L, Derry S, Moore RA. Single dose dipyrone (metamizole) for acute postoperative pain in adults. Cochrane Database Syst Rev. 2016 Apr 20;4:CD011421.
Derry S, Moore RA. Single dose oral celecoxib for acute postoperative pain in adults. Cochrane Database Syst Rev. 2013 Oct 22;(10):CD004233.
Derry C, Derry S, Moore RA, McQuay HJ. Single dose oral ibuprofen for acute postoperative pain in adults. Cochrane Database Syst Rev. 2009 Jul 8;(3):CD001548.
De Oliveira GS Jr, Agarwal D, Benzon HT. Perioperative single dose ketorolac to prevent postoperative pain: a meta-analysis of randomized trials. Anesth Analg. 2012 Feb;114(2):424-33.

NMDA Receptor Antagonists: Ketamine

- Subanaesthetic dose is effective in ↓ opioid requirements for 24h postop
  - May be no increased opioid-sparing effect above 30 mg/24 h
- ↓ PONV

Bell RF, Dahl JB, Moore RA, Kalso E. Perioperative ketamine for acute postoperative pain. Cochrane Database Syst Rev. 2006 Jan 25;(1):CD004603.
Ye F, Wu Y, Zhou C. Effect of intravenous ketamine for postoperative analgesia in patients undergoing laparoscopic cholecystectomy: A meta-analysis. Medicine (Baltimore). 2017 Dec;96(51):e9147.

Dexamethasone

- Effective (>0.1 mg/kg) in a wide variety of surgeries at ↓
  - Pain for 48 hours postop
  - Opioid consumption
  - LOS
  - PON
  - Pain at rest & with movement

Fan ZR, Ma J, Ma XL, Wang Y, Sun L, Wang Y, Dong BC. The efficacy of dexamethasone on pain and recovery after total hip arthroplasty: A systematic review and meta-analysis of randomized controlled trials. Medicine (Baltimore). 2018 Mar;97(13):e0100.
De Oliveira GS Jr, Almeida MD, Benzon HT, McCarthy RJ. Perioperative single dose systemic dexamethasone for postoperative pain: a meta-analysis of randomized controlled trials. Anesthesiology. 2011 Sep;115(3):575-88.

Alpha-2 Agonists

- Perioperative systemic α2 agonists ↓
  - Postop opioid consumption
  - Pain intensity at rest & with movement
  - PON
- Dexmedetomidine > clonidine (opioid sparing & duration)

Blaudszun G, Lysakowski C, Elia N, Tramèr MR. Effect of perioperative systemic α2 agonists on postoperative morphine consumption and pain intensity: systematic review and meta-analysis of randomized controlled trials. Anesthesiology. 2012 Jun;116(6):1312-22.

Gabapentinoids

- Mixed conclusions, but…
- Gabapentinoids appear to be effective for a wide variety of surgeries at ↓
  - Postoperative pain
  - Opioid consumption
  - PONV
- Pregabalin (150-300mg/d)
- Gabapentin (300-900mg/d)

Wang L, Dong Y, Zhang J, Tan H. The efficacy of gabapentin in reducing pain intensity and postoperative nausea and vomiting following laparoscopic cholecystectomy: A meta-analysis. Medicine (Baltimore). 2017 Sep;96(37):e8007.
Liu B, Liu R, Wang L. A meta-analysis of the preoperative use of gabapentinoids for the treatment of acute postoperative pain following spinal surgery. Medicine (Baltimore). 2017 Sep;96(37):e8031.
Lam DM, Choi SW, Wong SS, Irwin MG, Cheung CW. Efficacy of Pregabalin in Acute Postoperative Pain Under Different Surgical Categories: A Meta-Analysis. Medicine (Baltimore). 2015 Nov;94(46):e1944.

Intravenous Lidocaine

- Significant study heterogeneity
- May be beneficial for
  - laparoscopic > open abdominal surgery
- But overall, there is limited evidence of benefit on early pain scores, GI recovery, PONV, opioid consumption, and LOS

Weibel S, Jelting Y, Pace NL, Helf A, Eberhart LH, Hahnenkamp K, Hollmann MW, Poepping DM, Schnabel A, Kranke P. Continuous intravenous perioperative lidocaine infusion for postoperative pain and recovery in adults. Cochrane Database Syst Rev. 2018 Jun 4;6:CD009642.
Weibel S, Jokinen J, Pace NL, Schnabel A, Hollmann MW, Hahnenkamp K, Eberhart LH, Poepping DM, Afshari A, Kranke P. Efficacy and safety of intravenous lidocaine for postoperative analgesia and recovery after surgery: a systematic review with trial sequential analysis. Br J Anaesth. 2016 Jun;116(6):770-83.
Zhao JB, Li YL, Wang YM, Teng JL, Xia DY, Zhao JS, Li FL. Intravenous lidocaine infusion for pain control after laparoscopic cholecystectomy: A meta-analysis of randomized controlled trials. Medicine (Baltimore). 2018 Feb;97(5):e9771.

Magnesium

- Intravenous magnesium ↓
  - Cumulative morphine consumption
  - Rest & movement pain for up to 24h
- A single bolus 40-50 mg/kg as effective as bolus + infusion

Albrecht E, Kirkham KR, Liu SS, Brull R. Peri-operative intravenous administration of magnesium sulphate and postoperative pain: a meta-analysis. Anaesthesia. 2013 Jan;68(1):79-90.
De Oliveira GS Jr, Castro-Alves LJ, Khan JH, McCarthy RJ. Perioperative systemic magnesium to minimize postoperative pain: a meta-analysis of randomized controlled trials. Anesthesiology. 2013 Jul;119(1):178-90.

Esmolol

- Intraoperative esmolol ↓
  - Intraoperative opioid use
  - PACU opioid consumption
- Bolus (0.5-1 mg/kg) + infusion (5-15 mcg/kg/min)

Gelineau AM, King MR, Ladha KS, Burns SM, Houle T, Anderson TA. Intraoperative Esmolol as an Adjunct for Perioperative Opioid and Postoperative Pain Reduction: A Systematic Review, Meta-analysis, and Meta-regression. Anesth Analg. 2018 Mar;126(3):1035-1049.

Dextromethorphan

- Perioperative dextromethorphan ↓
  - Postoperative opioid consumption up to 48h
  - Pain scores up to 24h
- PO/IM (30-90mg, 1-4 doses)

King MR, Ladha KS, Gelineau AM, Anderson TA. Perioperative Dextromethorphan as an Adjunct for Postoperative Pain: A Meta-analysis of Randomized Controlled Trials. Anesthesiology. 2016 Mar;124(3):696-705.

Multiple Opioid-Sparing Agents

- Ibuprofen (200mg) + acetaminophen (500mg)
  - ↑ Analgesia
  - ↓ Need for additional analgesia over 8h
  - ↓ Adverse event rate
- Ibuprofen (100-200mg) + caffeine (100mg)
  - NNT = 2, to achieve 50% maximum pain relief over 6h
  - Significantly reduces remedication rates

Derry CJ, Derry S, Moore RA. Single dose oral ibuprofen plus paracetamol (acetaminophen) for acute postoperative pain. Cochrane Database Syst Rev. 2013 Jun 24;(6):CD010210.
Derry S, Wiffen PJ, Moore RA. Single dose oral ibuprofen plus caffeine for acute postoperative pain in adults. Cochrane Database Syst Rev. 2015 Jul 14;(7):CD011509.

Multiple Opioid-Sparing Agents

- Pregabalin (150mg q12h) + dexamethasone (16mg)
  - ↑ Analgesia
  - ↓ Frequency of rescue analgesic
- Ketamine + dexmedetomidine
  - No difference in postoperative opioid consumption
  - ↓ PONV

Choi YS, Shim JK, Song JW, Kim JC, Yoo YC, Kwak YL. Combination of pregabalin and dexamethasone for postoperative pain and functional outcome in patients undergoing lumbar spinal surgery: a randomized placebo-controlled trial. Clin J Pain. 2013 Jan;29(1):9-14.
Ziemann-Gimmel P, Goldfarb AA, Koppman J, Marema RT. Opioid-free total intravenous anaesthesia reduces postoperative nausea and vomiting in bariatric surgery beyond triple prophylaxis. Br J Anaesth. 2014 May;112(5):906-11.

Multiple Opioid-Sparing Agents

- Mixed results but for some surgeries,…
- Intraop dexmedetomidine + lidocaine infusions may ↓ early
  - Pain scores
  - Opioid consumption

Xu SQ, Li YH, Wang SB, Hu SH, Ju X, Xiao JB. Effects of intravenous lidocaine, dexmedetomidine and their combination on postoperative pain and bowel function recovery after abdominal hysterectomy. Minerva Anestesiol. 2017 Jul;83(7):685-694.

Opioid-Free Anesthesia: Case Reports

- **Opioid-free** Analgesia for Posterior Spinal Fusion Surgery Using Erector Spinae Plane (Esp) Blocks in a Multimodal Anesthetic Regimen.
- Chin KJ, Lewis S.
- Spine (Phila Pa 1976). 2018 Aug 31.

- **Opioid-free** total intravenous **anesthesia** with ketamine as part of an enhanced recovery protocol for bariatric surgery patients with sleep disordered breathing.
- Aronsohn J, Orner G, Palleschi G, Gerasimov M.
- J Clin Anesth. 2018 Sep 11;52:65-66.

- An Evidence-Based **Opioid-Free** Anesthetic Technique to Manage Perioperative and Periprocedural Pain.
- Boysen PG 2nd, Pappas MM, Evans B.
- Ochsner J. 2018 Summer;18(2):121-125.

- **Opioid-free anesthesia** using continuous dexmedetomidine and lidocaine infusions in spine surgery.
- Kim DJ, Bengali R, Anderson TA.
- Korean J Anesthesiol. 2017 Dec;70(6):652-653.

- **Opioid free anesthesia** with BIS/EMG monitored propofol-ketamine.
- Friedberg BL.
- Rev Esp Anestesiol Reanim. 2018 May;65(5):243-245.

Opioid-Free Anesthesia: RCT

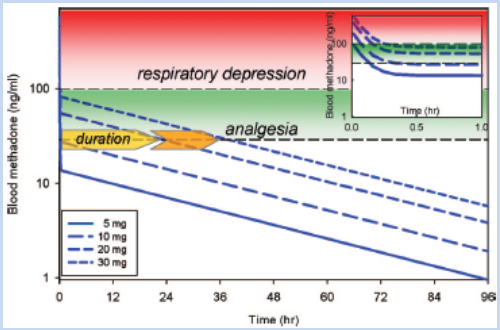
- POFA trial study protocol: a multicentre, double-blind, randomised, controlled clinical trial comparing opioid-free versus opioid anaesthesia on postoperative opioid-related adverse events after major or intermediate non-cardiac surgery.

- Beloeil H, Laviolle B, Menard C, Paugam-Burtz C, Garot M, Asehnoune K, Minville V, Cuvillon P, Oger S, Nadaud J, Lecoeur S, Chanques G, Futier E; SFAR research network.
- TRIAL REGISTRATION NUMBER: NCT03316339; Pre-results.
- BMJ Open. 2018 Jun 30;8(6):e020873.

- Opioid-free anaesthesia (OFA) is a multimodal anaesthesia associating hypnotics, NMDA antagonists, local anaesthetics, anti-inflammatory drugs and α-2 agonists.

Perioperative Methadone

- Methadone is fast acting
  - Time from IV injection to analgesic effect <10 minutes
- Methadone is effective
  - A single intraoperative bolus can improve pain for up to 72 hours postoperatively
- Methadone is safe
  - Peak respiratory depression with a single IV bolus is <60 minutes



Kharasch ED. Intraoperative methadone: rediscovery, reappraisal, and reinvigoration? Anesth Analg. 2011 Jan;112(1):13-6.

Intraop Analgesia

Mild
- Acetaminophen (PO/IV 10 – 15 mg/kg; PR 30 – 40 mg/kg)
- NSAIDS (IV ketorolac 0.5 mg/kg; max dose 30 mg)
- Dexamethasone IV (0.1 – 0.2 mg/kg)
- Dexmedetomidine IV (Bolus: 0.5 – 1.0 ug/kg; Infusion: 0.2 – 1.0 ug/kg/hr)
- Esmolol IV (Bolus: 0.5 – 1.0 mg/kg; Infusion: 5 – 15 ug/kg/min)

Moderate
- Ketamine IV (Bolus: 0.5 mg/kg IV bolus; Infusion: 1 – 10 ug/kg/min)
- Lidocaine IV (Bolus: 1.5 mg/kg; Infusion: 2 mg/kg/hr)
- Magnesium IV (40 – 50 mg/kg)

Severe
- Gabapentin PO (300 mg)
- Pregabaline PO (150 – 300 mg)
- Methadone IV (0.05 – 0.2 mg/kg)

Postoperative Analgesia

Mild

- Acetaminophen
- NSAIDS (choose 1): IV ketorolac, PO ibuprofen, PO naproxen

Moderate

- Caffeine PO (100 mg TID)
- Gabapentin PO: 100-600mg TID (or Pregabalin)
- Choose 1:
  - Ketamine IV 1 – 2 ug/kg/min
  - Lidocaine IV 1 mg/kg/hr
  - Dexmedetomidine IV 0.1 – 0.2 ug/kg/hr

Severe

- Choose 2:
  - Ketamine IV 1 – 2 ug/kg/min
  - Lidocaine IV 1 mg/kg/hr\Dexmedetomidine IV 0.1 – 0.2 ug/kg/hr
- Choose 1
  - Ketamine IV 3 – 5 ug/kg/min
  - Dexmedetomidine IV 0.3 – 0.5 ug/kg/hr