

1

**New Drugs, New Tricks,
Maximizing Outcomes**

Peter Strube

DNAP CRNA MSNA MBA APNP ARNP APRN LTC (Retired) FAANA
 Assistant Professor and Assistant Program Director Newman University
 Owner Troll Way Anesthesia and Strube Educational Services

2

Disclosure;

I tutor at-risk Nurse Anesthesia Residents for school, SEE, and NCE but have NO financial relationship with the big six review companies.

I am NOT an item writer!

pstrube3000@yahoo.com
 Cell is 608-469-1750

STORM ANESTHESIA
 recertCRNA

3

Important Notice

Every attempt has been made to us generic names when possible, at times brand names are used.

I do use the vernacular and most commonly used name

Mentioning a company does not imply endorsement

4

Disclaimer; Chronic Cough

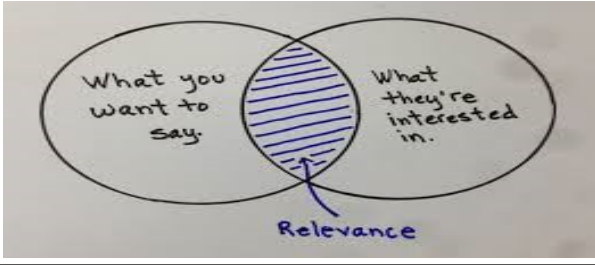
5

How Do You View Things?

The Same Problem, Different Path, but the Same Answers?

6

Clinically Relevant



7

14-17 Years



8



9



10

AFE – September 29, 2014 (presentation) Dr. B Leighton, Cooper, Otto (abstract fall 2013)

41 G8P3-39 weeks at 31 min ACLS: Given A-OK at 1mg/8mg/30mg

Survived and left hospital with small neuro deficits.

28 G2P1-39 weeks at ?? Min ACLS: Given A-OK at 0.8mg/4mg/30mg

Survived with no neuro issues

Thromboxane/serotonin

AMNIOTIC FLUID EMBOLISM

By T. Kyle Harrison, MD • Larry F. Chu, MD • Sara Goldhaber-Fabert, MD

Consider amniotic fluid embolism if there is the sudden onset of the following in a pregnant or postpartum patient:

1. Respiratory distress, decreased O₂ saturation
2. Cardiovascular collapse/hypotension, tachycardia, arrhythmias, cardiac arrest
3. Coagulopathy
4. Disseminated intravascular coagulation (DIC)
5. Seizures
6. Altered mental status

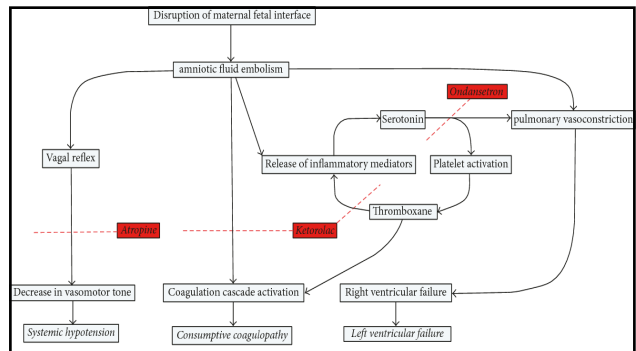
INFORM SURGEON CALL FOR HELP

1. Administer **100% O₂**.
2. **Consider/prepare for emergent intubation.**
3. Place patient in left uterine displacement (LUD).
4. Establish **IV access** (large volume lines).
5. Consider placing **invasive monitoring** (arterial line).
6. Anticipate possible **cardiopulmonary arrest and emergent C-section.**
7. Anticipate the **development of DIC.**
8. Support circulation with **IV fluid, vasopressors, and inotropes.**
9. Consider **circulatory support**: IABP/ECMO/CPB.

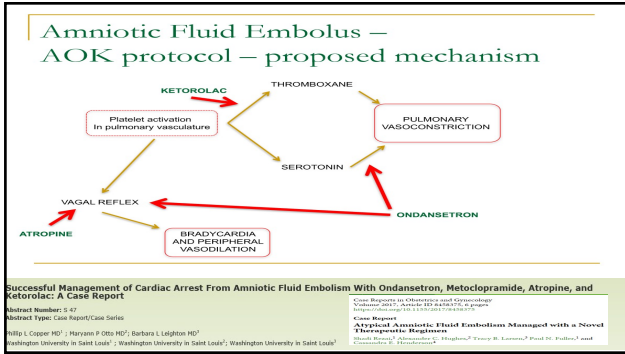
Rule out other causes that might present in a similar fashion:

1. Eclampsia
2. Hemorrhage
3. Air embolism
4. Anesthetics
5. Anaphylaxis
6. Pulmonary embolism
7. Anesthetic overdose
8. Sepsis
9. Cardiomyopathy/cardiac valvular abnormality/MI

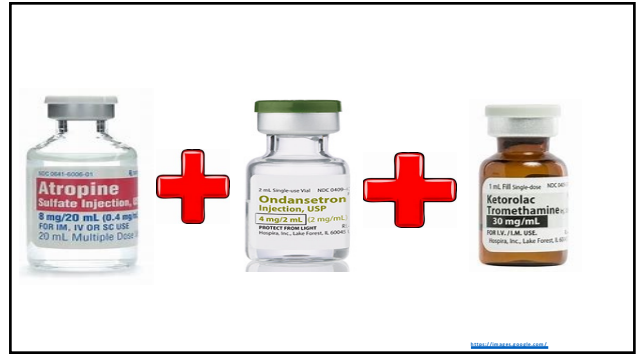
11



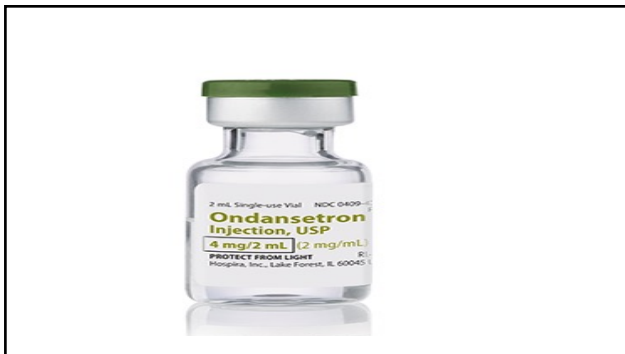
12



13



14



15

Postoperative Nausea and Vomiting: Prevention of Postoperative Nausea and Vomiting:

Adult Studies: Adult surgical patients who received ondansetron immediately before the induction of general balanced anesthesia (barbiturate, thiopental, methohexital, or thiamylal; opioid: alfentanil or fentanyl; nitrous oxide; neuromuscular blockade: succinylcholine/curare and/or vecuronium or atracurium; and supplemental isoflurane) were evaluated in two double-blind US studies involving

Zofran package insert!

16



17

Demerol is EVIL

18

Linezolid

19

α 2-Adrenergic Agonists

Shivering center is under inhibiting control of the preoptic anterior hypothalamic region α 2-Adrenergic Agonists probably strengthened it.

25-75mcg IV can be used to stop shivering, as clonidine inhibits central thermoregulatory control

Int J Med Sci. 2013; 10(10): 1327-1332. PMID: 23983593
Published online 2013 Aug 13. doi: 10.7155/ijms.6531
Optimal Dose of Prophylactic Dexmedetomidine for Preventing Postoperative Shivering
Yong-Shin Kim,¹ Yong-II Kim,² Kwun-Hui Seo,¹ and Hye-Rim Kang¹
Koranda L, Beckman J, & Kim A. (2005). Postoperative complications of hypothermia. Best Practice & Research Clinical Anesthesiology, 21 (4): 441-457.
Hagerty and L.2005. "New" knowledge of inducible hypothermia. Journal of Intensive Perioperative Care, 4(3): 13-42.

20

Ondansetron Given Before Induction of Anesthesia Reduces Shivering After General Anesthesia

Powell, Robert M. FRCA, Buggy, Donal J. MD, MSc, MRCP, DME, FFARCSI

Anesthesia & Analgesia: June 2000 - Volume 90 - Issue 6 - p 1423-1427

4mg IV as single dose immediately before induction of anesthesia

21

Anesth Analg. 2005 Nov;101(5):1516-20.

Prophylactic intravenous ondansetron and dolasetron in intrathecal morphine-induced pruritus: a randomized, double-blinded, placebo-controlled study.

Anesthesiology, 2015; 15(18)

30 minutes before injecting narcotic spinal or epidural

22

Clinical Trial > Anesth Analg. 2005 Nov;101(5):1516-1520.
doi: 10.1213/01.ANE.0000181338.35454.6A.

Prophylactic intravenous ondansetron and dolasetron in intrathecal morphine-induced pruritus: a randomized, double-blinded, placebo-controlled study

Christos A Iatrou¹, Christos K Dragoumanis, Theodosia D Vogiatzaki, George I Vretzakis, Constantinos E Simopoulos, Vasilios K Dimitriou

Affiliations + expand
PMID: 16244023 DOI: 10.1213/01.ANE.0000181338.35454.6A

23

Koju et al. BMC Anesthesiology 2015, 15:18
http://www.biomedcentral.com/1471-2253/15/18

BMC Anesthesiology

RESEARCH ARTICLE **Open Access**

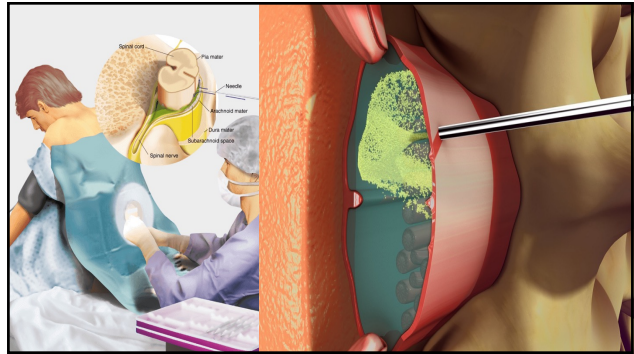
Prophylactic administration of ondansetron in prevention of intrathecal morphine-induced pruritus and post-operative nausea and vomiting in patients undergoing caesarean section

Ram Bhakta Koju^{1,2*}, Bandana Sharma Gurung³ and Yashad Dongol⁴

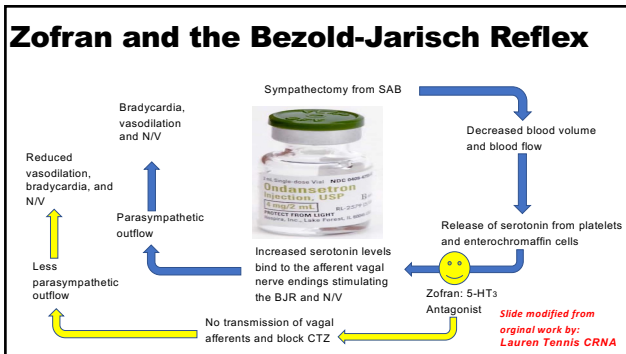
24



25



26



27

Bezold-Jarisch Reflex

During spinal anesthesia, neuraxial blockade reduces venous return. The reduction in preload triggers the BJR, which is mediated by the peripheral 5-HT3 type receptors.

The BJR is an inhibitory cardiovascular response to noxious chemical substances and ventricular stretch sensed by the chemoreceptors and mechanoreceptors, which are primarily located in the wall of the left ventricle.

28

Ondansetron Given Intravenously Attenuates Arterial Blood Pressure Drop Due to Spinal Anesthesia: A Double-Blind, Placebo-Controlled Study

Radosław Owczuk, M.D., Ph.D., Wojciech Wenski, M.D., Agnieszka Polak-Krzeminska, M.D., Paweł Twardowski, M.D., Renata Arszulowicz, M.D., Anna Dylczyk-Sommer, M.D., Magdalena A. Wujtewicz, M.D., Ph.D., Wioletta Sawicka, M.D., Ewa Morzuch, M.Sc., Maciej Smetanski, M.D., Ph.D., and Maria Wujtewicz, M.D., Ph.D.

Reduction in spinal-induced hypotension with ondansetron in parturients undergoing caesarean section: A double-blind randomised, placebo-controlled study

T. Sahoo, C. SenDasgupta, A. Goswami, A. Hazra

Effects of intravenous ondansetron and granisetron on hemodynamic changes and motor and sensory blockade induced by spinal anesthesia in parturients undergoing cesarean section

Manal M. Rashad *, Manal S. Faramawy

Efficacy of prophylactic intravenous ondansetron on the prevention of hypotension during cesarean delivery: a dose-dependent study

Ming Wang¹, Lang Zhuo², Qun Wang³, Ming-Kun Shen⁴, Yan-Yun Yu⁵, Jun-Jing Yu⁶, Zhi-Ping Wang⁶

29

Somebody Will Say; "But I Have Never Heard of That?"

30

Pain on Injection

31

300 mg Magnesium and 40 mg of Lidocaine

Clinical Therapeutics/Vol 38, Number 1, 2016

Magnesium Sulfate Plus Lidocaine Reduces Propofol Pain: A Double-blind, Randomized Study

Jiahao Sun, MD, Riyong Zhou, MD, Wendong Lin, MD, Jiahao Zhou, MD, and Weijian Wang, MD
Department of Anesthesiology, 1st Affiliated Hospital, Wenzhou Medical University, Wenzhou, China

Ondansetron Pretreatment to Alleviate Pain on Propofol Injection: A Randomized, Controlled, Double-Blinded Study

Amresh, Sushil P. MD, Dubey, Prakash K. MD, Sinha, Prabhakar K. MD

Ondansetron Pretreatment Reduces Pain on Injection of Propofol

Enaid Zahedi, Anahid Maliki, and Chaharresa Rostami
Department of Anesthesiology, Farabi Eye Hospital, Tehran University of Medical Science, Tehran, Iran

Received: 7 Mar. 2012; Received in revised form: 2 Jul. 2012; Accepted: 30 Jul. 2012

32

Ondansetron

Ondansetron Pretreatment to Alleviate Pain on Propofol Injection: A Randomized, Controlled, Double-Blinded Study

Amresh, Sushil P. MD, Dubey, Prakash K. MD, Sinha, Prabhakar K. MD

Anesthesia & Analgesia July 1999 - Volume 89 - Issue 1 - p 197-199
doi: 10.1213/00000539-199907000-00035
General Articles

33

Postoperative Nausea and Vomiting

34

Pathophysiology of PONV (What about learned response?)

Cerebral cortex (sight, smell, taste)

Vestibular apparatus (motion)

Pharyngeal afferents (gagging)

Enterochromaffin cells in GI tract release serotonin, which binds to visceral 5-HT₃ receptors (mechanical or medication)

Vagal afferents in GI tract

CTZ = chemoreceptor trigger zone.

Adapted from: Agilducci et al. Anesthesiology. 1999; 91:693-700
Gao TT et al. Anesth Analg. 2007; 105:1615-1619

35

Oxygen

Hypoxia triggers cortical afferents which triggers the vomiting center which leads to the act of vomiting

Anesthesiology. 2013 Aug;119(2):303-316. doi: 10.1097/ALN.0b013e31829a0f4

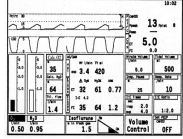
Effect of intraoperative high inspired oxygen fraction on surgical site infection, postoperative nausea and vomiting, and pulmonary function: systematic review and meta-analysis of randomized controlled trials.

Hovavagimian F, Lysakovskii C, Elia N, Tramer MR.

Frederique Hovavagimian, Christopher Lysakovskii, Nadia Elia, Martin R. Tramer: Effect of Intraoperative High Inspired Oxygen Fraction on Surgical Site Infection, Postoperative Nausea and Vomiting, and Pulmonary Function: Systematic Review and Meta-analysis of Randomized Controlled Trials. Anesthesiology 2013;119(2):303-316. doi: 10.1097/ALN.0b013e31829a0f4

36

Perioperative clinical factors & immune function



Supplemental perioperative oxygen improves postop outcomes

FiO₂ of 0.8 doubles subcut O₂ tension & halves postop wound infection rate

Supplemental O₂ ↓ PONV after laparoscopies & laparotomies

Curr Opin Anesthesiol 2006;19:11-18

Perioperative Medicine | August 2013

Effect of Intraoperative High Inspired Oxygen Fraction on Surgical Site Infection, Postoperative Nausea and Vomiting, and Pulmonary Function: Systematic Review and Meta-analysis of Randomized Controlled Trials

Frédérique Hovagimian, MD; Christopher Lyakowski, MD; Nadia Elia, M.D., M.Sc.; Martin R. Tramer, M.D., D.Phil.

Kabon B, Kurz A. Optimal perioperative oxygen administration. Current Opin in Anesthesiology. 2006;19(1):11-18. doi:10.1097/D1.aco.0000192775.24774.15. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1460001/>

37

Non-Pharmacologic Methods for PONV Alcohol Pad—Queese Ease!

September 2013; Anesthesia and Analgesia: Aromatherapy as Treatment for Postoperative Nausea: A Randomized Trial Hunt, Ronald MD; Dienemann, Jacqueline PhD, RN; Norton, H. James PhD; Hartley, Wendy MSN, RN; Hudgens, Amanda BSN, RN; Stern, Thomas MD; Divine, George PhD



38

39

Ginger

American Society of Clinical Oncology, May 2009
644 cancer patients



Patients received 0.5, 1, or 1.5 grams of ginger or placebo daily x 3 days prior to chemotherapy

Patients taking ginger experienced significantly reduced nausea

40

Ginger

Ernst et al,



Ginger administered prior to induction of anesthesia can be prophylactic for PONV (1 gram) TOXIC if greater than 2mg/kg/day

Ernst, E. and Pittler, M. (2000). Efficacy of ginger for nausea and vomiting: a systematic review of randomized clinical trials. *British Journal of Anaesthesia*, 84(3), pp.367-371.

Chaiyakunapruk N, Kilkanrakom N, Nathisuwan S, Leepakobboon K, Leesetsatagol C. The efficacy of ginger for the prevention of postoperative nausea and vomiting: A meta-analysis. *American Journal of Obstetrics and Gynecology*. 2006;194(1):95-99. doi:10.1016/j.ajog.2005.06.046.

41

42



43



44



45



46

20-30 mg Propofol

Propofol, in small doses (20 mg as needed), can be used for rescue therapy for patients in the direct care environment, for example, PACU, and has been found as effective as ondansetron.

Unkigerc H, Guler T, Guney Y, Isik G. Comparative study of the antiemetic efficacy of ondansetron, propofol and midazolam in the early postoperative period. Eur J Anaesthesiol 2004;21:40-5

47

Ketamine-like nasal spray for depression approved by the FDA

By Debra Goldschmidt, CNN 3/6/2019

Spravato (esketamine) nasal spray
Now Approved

SPRAVATO™ is a prescription medicine, used along with an antidepressant taken by mouth, for treatment resistant depression (TRD) in adults.

<https://www.spravato.com/>

Nasal Spray: 28 mg of esketamine per device. Each nasal spray device delivers two sprays containing a total of 28 mg of esketamine.

The boys trapped in a Thai cave were given ketamine to stop them from panicking during their terrifying rescue

Source: CNN.com - 3/6/2019

48

Fentanyl
INSYS
THERAPEUTICS, INC.

SUBSYS[®]
(fentanyl sublingual spray)
100,200,400,600,800,1200,1600 mcg
www.subsysnspray.com

Actiq[®]
(fentanyl citrate) oral transmucosal lozenge

Lazanda[®]
Fentanyl Nasal Spray

Figure 2.

Product: ACTIQ[®] (fentanyl)
Handle: ACTIQ[®] (fentanyl)

49

Fentanyl Patch

• On Demand? Fentanyl iontophoretic transdermal system provides a 40-mcg dose of fentanyl per activation on-demand

Figure 8 : IONSYS[®] (fentanyl iontophoretic transdermal system)

**Light*
Dosing
Button**

**Digital
Display**

50

Sufentanil 30 mcg tablet

DSUVIA: Single-Dose Applicator (SDA)

Designed in Collaboration with the DoD
(Light-Weight, Extreme-Environment Tested, Easily Handled with Gloves)¹

Removable safety lock to avoid premature activation (not shown)

Clear plastic to allow tablet visibility

Non-retractable plunger

Pre-filled tablet

ACEIRX
Pharmaceuticals, Inc.

DSUVIA (package insert), Redwood City, CA: Aceirx Pharmaceuticals, Inc., 2018.

Minkwitz HS, Lerman D, Milson T, Singla N, DiDonato KP, Palmer PP. Sufentanil sublingual tablet 30 mcg for the management of pain following abdominal surgery: a randomized, placebo-controlled, phase-3 study. *Pain Pract*. 2017;17(7):848-858.

51

Role of Esmolol in Perioperative Analgesia and Anesthesia: A Literature Review

Esmolol versus ketamine-remifentanyl combination for early postoperative analgesia after laparoscopic cholecystectomy: a randomized controlled trial

The effect of perioperative esmolol on early postoperative pain: A systematic review and meta-analysis

The Safety of Perioperative Esmolol: A Systematic Review and Meta-Analysis of Randomized Controlled Trials

Year : 2017 | Volume : 33 | Issue : 1 | Page : 28-39

Richard Watts¹, Venkateshan Thiruvankatarajan¹, Miami Calvert², Graeme Newcombe¹, Roelof M van Wijk¹

¹ Department of Anaesthesia, The Queen Elizabeth Hospital, Woodville, Adelaide 5011; Discipline of Acute Care Medicine, The University of Adelaide, Adelaide 5000, South Australia

² Department of Anaesthesia, Royal Adelaide Hospital, North Terrace, Adelaide 5000, South Australia

Yu, Silvio K. H. BHSoc, Tall, Gordon PhD, Karkouti, Keyvan MD, MSc, FRCPCC, Wijeyesundera, Duminda MD, FRCPCC, McCusker, Stuart MD, PhD, FRCPCC, Beattie, W. Scott MD, PhD, FRCPCC

Anesthesia & Analgesia: February 2011 - Volume 112 - Issue 2 - p 267-281
doi: 10.1213/ANE.0b013e3181922026a17
Cardiovascular Anesthesiology: Research Reports

52

The Safety of Perioperative Esmolol: A Systematic Review and Meta-Analysis of Randomized Controlled Trials

Esmolol

Article (PDF Available) in *Anesthesia and analgesia* 112(2):267-1; February 2011; vol. 267; issue 2; pp 267-281

Anesthetic Sparing Effects

- Decreased propofol requirements when given in large quantities
- Decreased volatile anesthetic requirements when given with opiates
- Decreased use of perioperative and postoperative opioids

Mechanism of Pain Modulation: Unknown

- Decrease opioid metabolism, thus increasing opioid duration of action?
- Central actions: increase fentanyl penetration into central nervous system (CNS)?
- Modulation of neurotransmitter release in substantia gelatinosa?

ESMOLOL HYDROCHLORIDE INJECTION

Article 1, Digi I, Oikar J, Alkivi M, Goren M, Gurnea M. A comparison of the effects of intravenous esmolol and fentanyl infusions on postoperative analgesia. *Journal of Anesthesia* - 1995; 20(4):211-213.

Chen Y, Chen X, Lu X. Role of Esmolol in anesthesia and postoperative pain management after hysterectomy. *British Journal of Anaesthesia*. 2004;92(7):948-951. doi: 10.1093/bja/92.7.948.

Hopwood R, Raman S. Esmolol and other removal of propofol and fentanyl. *U.K. Anaesthetist*. 2004; 52(1):10-11.

Johnson W, Schneider C, Winkler AM, Sahel P. Esmolol Potentiates Reduction of Minimum Alveolar Concentration by Alkylated Anesthetics. *Anesthesia & Analgesia*. 1998;87(5):1075-1078. doi: 10.1097/00000539-199805000-00004.

53

Intraoperative Esmolol Infusion in the Absence of Opioids Spares Postoperative Fentanyl in Patients Undergoing Ambulatory Laparoscopic Cholecystectomy

Vincent Collard, MD*
Giovanni Mistrarelli, MD*
Ali Taqi, MD†
Juan Francisco Asenjo, MD*
Liane S. Feldman, MD†
Gerald M. Fried, MD†
Franco Carli, MD, MPhil*

BACKGROUND: The use of opioids during ambulatory surgery can delay hospital discharge or cause unexpected hospital admission. Preliminary studies using an intraoperative continuous infusion of esmolol in place of an opioid have inconsistently reported a postoperative opioid-sparing effect. In this study, we compared esmolol versus either intermittent fentanyl or continuous remifentanyl on postoperative opioid-sparing, side effects, and time of discharge.

METHODS: Ninety patients (consisting of three groups) were enrolled in this prospective, randomized, and observer-blinded study. The control group (n = 30) received intermittent doses of fentanyl, the esmolol group (n = 30) received a continuous infusion of esmolol (5–15 µg · kg⁻¹ · min⁻¹) and no supplemental opioids during surgery, and the remifentanyl group (n = 30) received a continuous infusion of remifentanyl (0.1–0.5 µg · kg⁻¹ · min⁻¹). General anesthesia was standardized, and adjuvant medications included acetaminophen, ketorolac, local anesthetics in the skin incisions, dexmedetomidine, and droperidol. Postoperative analgesia included fentanyl.

Collard V, Mistrarelli G, Taqi A, Asejo J, S, Feldman L, S, Fried G, M, & Carli F. (2007). Intraoperative esmolol infusion in the absence of opioids spares postoperative fentanyl in patients undergoing ambulatory laparoscopic cholecystectomy. *Anesthesia & Analgesia*, 105(5), 1255-1262.

54

Ibuprofen-Caldolor \$10

Shares the name.....

Big differences... Less action on Cox 1 and more Cox 2 action..

What does this mean? Less bleeding. More pain control can be given at any time during the surgery. It is better now that we can provide per—op.

400mg/4ml or 800mg/8ml

Dilute and administer over 30 minutes

400mg-800mg Over 30 min repeat every 6 hours PRN*



55

Alkermes Pharm—Meloxicam IV

J Oral Maxillofac Surg. 2012 Jun;70(1):31-6. doi: 10.1016/j.joms.2011.03.038. Epub 2011 Jul 23.

Pre-emptive analgesic effectiveness of meloxicam versus tramadol after mandibular third molar surgery: a pilot study.

Isordia-Espinosa MA¹, Sánchez-Piñero M, Tobías-Azúa F, Reyes-García JS.

Anjeso is approved for the management of moderate to severe pain and will be administered as a once-a-day intravenous (IV) bolus push



56

Capsaicin (Zostrix) – First Agent Capsazepine

- Is a new Receptor Born? TRPV 1
- Selectively stimulates unmyelinated C fibers afferent neurons and cause release of substance P
- This continued release leads to depletion of substance P and decrease in pain

Atherosclerosis. 2017 Mar 10;260:13-19. doi: 10.1016/j.atherosclerosis.2017.03.016. [Epub ahead of print]

TRPV1 agonism inhibits endothelial cell inflammation via activation of eNOS/NO pathway.

Wang Y¹, Cai L², Xu H³, Liu SF⁴, Zhu EF⁵, Yan EF⁶, Shen SF⁷, Zhu M⁸.



Diab. Res. Treat. 2017;2017:7425907. doi: 10.1155/2017/7425907. Epub 2017 Feb 21.

Quantitative Thermal Testing Profiles as a Predictor of Treatment Response to Topical Capsaicin in Patients with Localized Neuropathic Pain.

Bernardo A¹, Torres D², Veciana M³, Caro C⁴, Montoro J⁵, Moxeral K⁶.

Diab. Metab. Res. 2017 Mar 15. doi: 10.2174/1567202614068170513105337. [Epub ahead of print]

Warming up to New Possibilities with the Capsaicin Receptor TRPV1: mTOR, AMPK, and Erythropoietin.

Mateos JC¹.

57

Qutenza 8%



Qutenza[®]
(capsaicin) 8% patch



58



59

PF-72 Hydrogel Formulation

2019 Mar 10;558:225-230.
j.ijpharm.2019.01.011. Epub 2019 Jan 14.

Preclinical studies of ropivacaine extended-release from a temperature responsive hydrogel for prolonged relief of pain at the surgical wound



60

Benzo's –PTSD?

Benzo's DO NOT WORK

Warning: Benzodiazepines (e.g., Xanax, Valium, Klonopin)

- Limited efficacy
- Increased safety concerns
- Even more risk for older people
 - Confusion, awkwardness, falls
- Not recommended for PTSD

Avoid Benzo's with patients with PTSD if possible

67

Selective Alpha 1 Antagonists –PTSD?

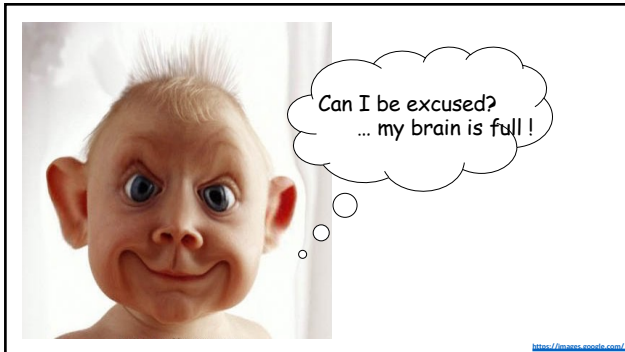
"-SIN's"

- Prazosin (minipress): Half life ~2-3 hours
- Dilates both arterioles and veins
- Used in the management of essential hypertension, Raynaud's, pheochromocytoma
- Receptor selectivity produces less chance of reflex tachycardia

HELPS WITH NIGHTMARES

Side effects: orthostatic hypotension, syncope, nasal congestion

68



69

Financial Disclosure

There is no financial conflicts with this presentation.

Lecturing about a topic does not constitute endorsement of any product. Please take the time to research each topic for more information.

Mentioning a product or company does NOT represent endorsement.

Every attempt has been made to use generic names when possible, at times brand names are used.

70

Copyright Disclaimer: Under Section 107 of the Copyright Act 1976, allowance is made for "fair use" for purposes such as criticism, comment, news reporting, teaching, scholarship and research. Fair use is a use permitted by copyright statute that might otherwise be infringing. Non-profit, educational or personal use tips the balance in favor of fair use.

71

Disclaimer and Notification Information

I owe the copyright to a lot of the photos used in this presentation.

Unless otherwise stated additional photos and graphics are used via public domain search and referenced to <https://images.google.com/> With the educational acceptations rule.

Every attempt has been made to use generic names when possible, at times brand names are used.

I do not do sale presentation or work for any drug company. I used the name of the pharmaceutical agent that is commonly accepted.

72