

Can we do an anesthetic without
narcotics?
Bold or Crazy Question?



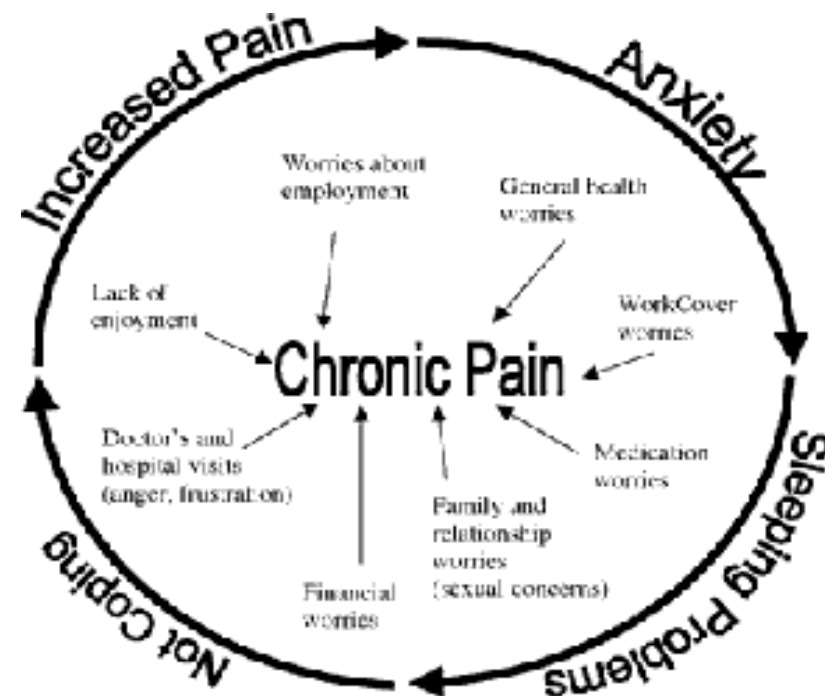
Master title style

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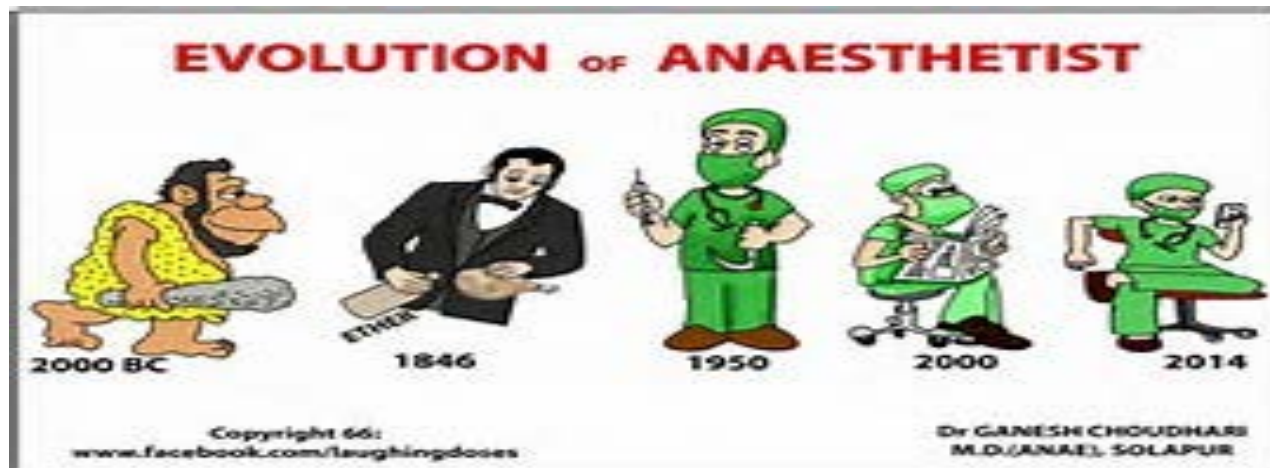


Financial Disclosure

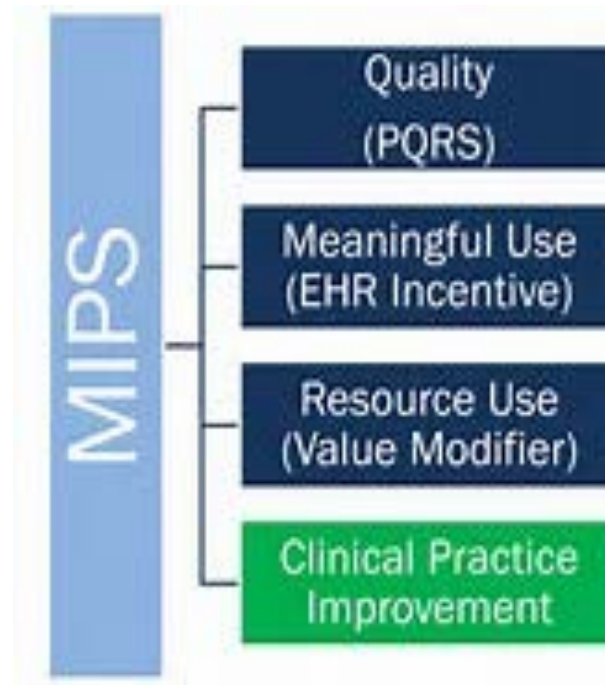
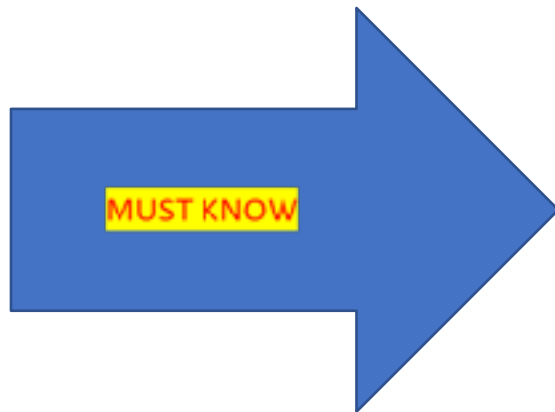
There is no financial conflicts with this presentation.

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.



Applying Continuous Quality Improvement in Clinical Practice



Surgery Before Anesthesia and Pharmacology



Mural of Dr. Villander, Hôtel de Dieu, Paris.

A



From *Behind the Doctor*, by Logan Clendinning, published by Alfred A. Knopf.

B

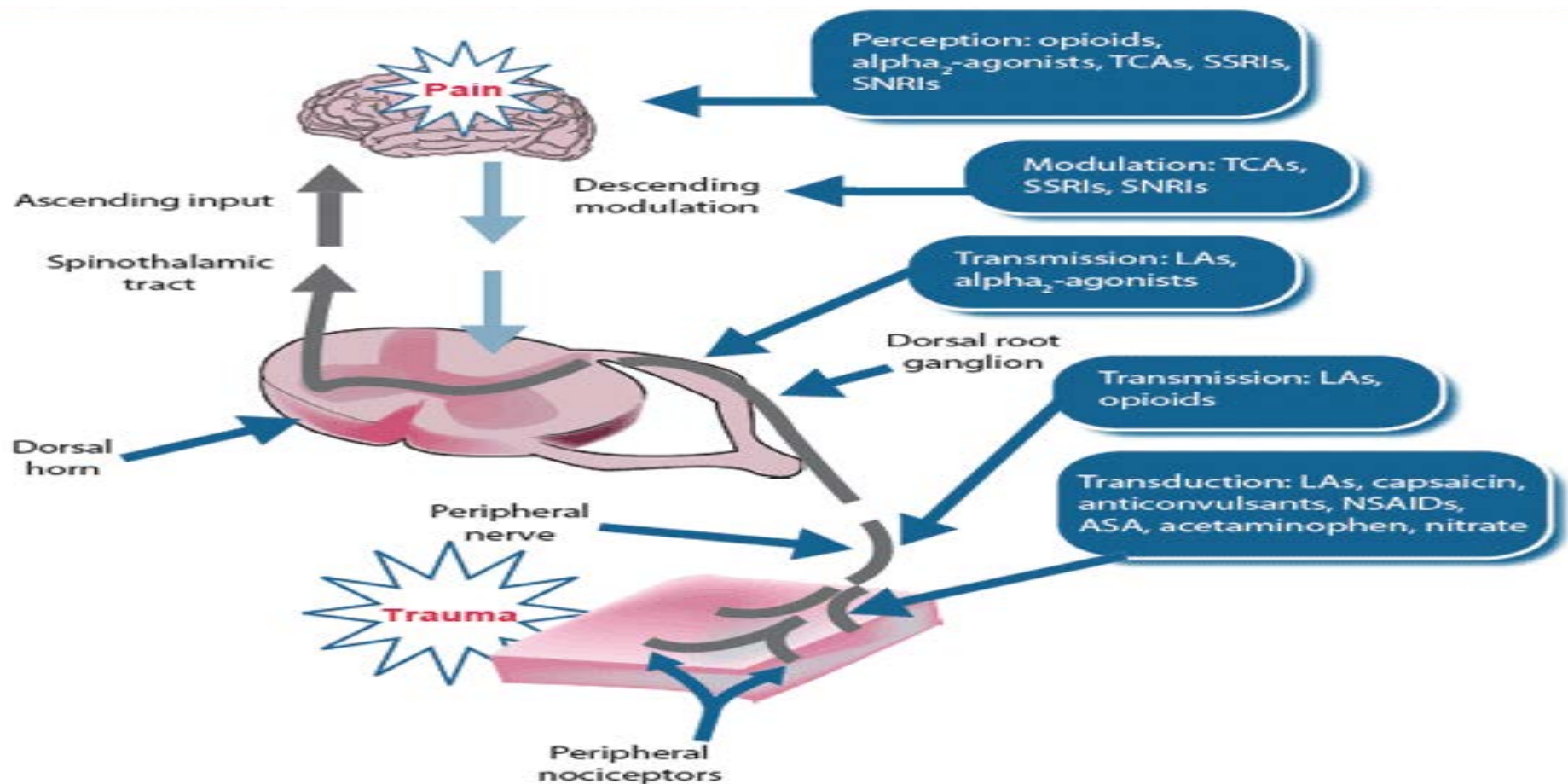


From *Devil's, Drugs and Doctors*, by Howard W. Haggard, M.D., published by Harper and Brothers.

C

PICTORIAL RECORDS OF THE AGONY ENDURED IN OPERATIONS BEFORE THE ADVENT OF ANESTHESIA

- A. A surgeon cutting with his big saw.
- B. A very painful operation of the seventeenth century.
- C. A surgeon torturing his patient.





Pain Targets



Godmother of Pain

Margo McCaffery RN 1968



Pain is a unpleasant sensory and emotional experience associated with actual or potential tissue damage.

Pain in whatever the experiencing person says it is

May not be directly proportional to amount of tissue injury

Highly subjective, leading to under treatment

Goal of Pain Management...



Reduction of pain and suffering with consequent improvement in function.

Seems like a very straight forward goal?

Can we do it without Narcotics?

Pain is all consuming

Pain drives everything.....





Multimodal

A combination regimen using two or more medications or interventions

Synergistic effects

Pre-emptive Anesthesia!

This action enhances the analgesic effects of each drug

Using different drugs decreases the dose of each and decreases potential side effects and limits the ceiling



The preparation for Post-Operative Analgesia should start in the Pre-Operative

Multimodal Treatment



**Certified
Registered
Nurse
Anesthetist**

The Joint Commission Sentinel Event Alert

Joint Commission Sentinel Event Alert Entitled “Safe use of opioids in hospitals” (08-Aug-12)

Recommendations include advising clinicians who prescribe pain medications to use both non-pharmacologic and pharmacologic alternatives

Non-pharmacologic therapies: physical therapy, acupuncture, manipulation or massage, ice, etc.

Pharmacologic treatment: non-opioid analgesics, such as acetaminophen, NSAIDs, antidepressants, anticonvulsants, and muscle relaxants, can be used before prescribing an opioid

When used in combination with opioids, these non-opioid pharmacologic treatments may reduce the dose of opioids required to effectively manage pain

The Joint Commission Sentinel Event Alert. Safe use of opioids in hospitals. Issue 49; August 8, 2012. Available at: <http://www.jointcommission.org>.

Music

Music interventions have been suggested as a nonpharmacological intervention to alleviate pain and anxiety during surgical treatment.

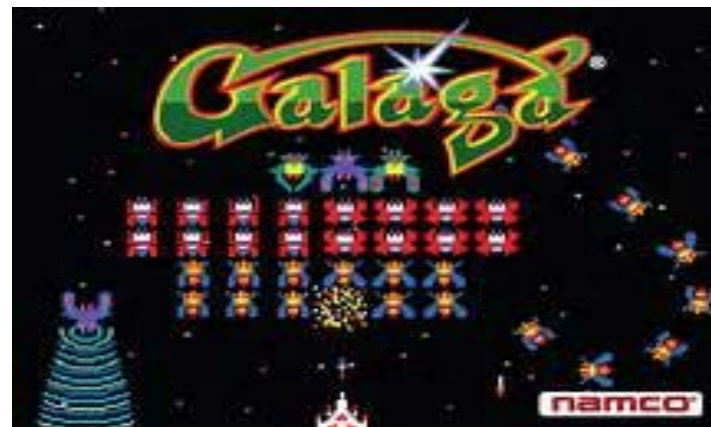
Most of the studies found in the literature involve passive music listening via headphones. The data suggest that researcher-selected music is most effective in reducing anxiety, primarily because it incorporates evidence-based parameters such as consistent tempo and dynamics, stable rhythms, and smooth melodic lines. Finally, the literature suggests that music therapists can serve as experts to help medical personnel identify effective implementation strategies.



Video Games?

Video games may help relieve pain?

Emory University—Nadine Kaslow



The next time you habitually search your bathroom cabinet for some pain medication, you may want to consider playing a video game first. Research has shown that psychology plays an important part in how we experience both acute and chronic pain -- and that painful sensations can be manipulated by what we think and feel.

Such approaches to pain relief are looking increasingly promising thanks to rapid advances in technology. Virtual reality games are already showing promise in tackling acute pain, seemingly by simply helping us focus on other things. Now a new study has shed some light on how this might work and how it could be improved in the future.

Oculus Rift and Google Glass Augment Surgery at Spanish Hospital

Doctors have found a novel use for the Oculus Rift virtual reality headset as a means of easing patient anxiety during surgery. 7/11/14

<http://www.mddionline.com/article/oculus-rift-and-google-glass-augment-surgery-spanish-hospital-140711>



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

CDC Statement – Worst EVER?

A 'civil war' over pain medication separates the medical community



September 26, 2016

The Issues With the CDC Guidelines on Opioids for Chronic Pain, According to AAPM's Director

Dr Twillman extensively emphasized the fact that these CDC guidelines are expert-based and not evidence-based. In addition, most of these experts are strongly biased, as indicated by their affiliations to, for example, anti-opioid advocacy groups.

"There's a civil war in the pain community," said Dr. Daniel B. Carr, president of the [American Academy of Pain Medicine](#). "One group believes the primary goal of pain treatment is curtailing opioid prescribing. The other group looks at the disability, the human suffering, the expense of chronic pain."

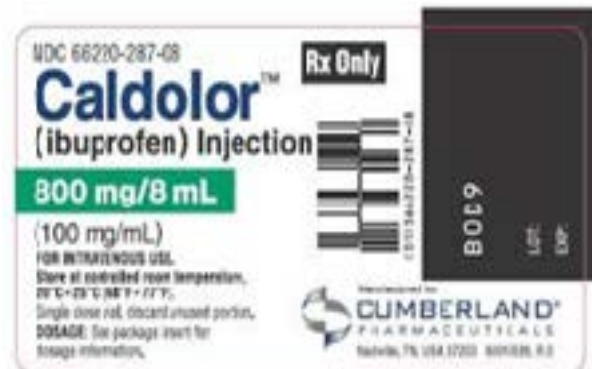


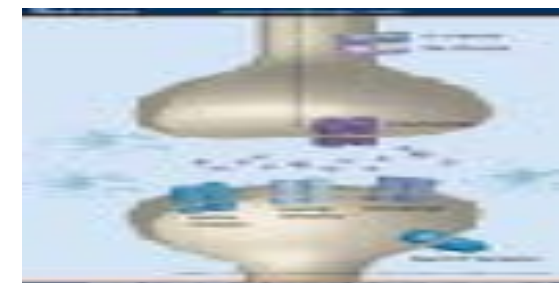
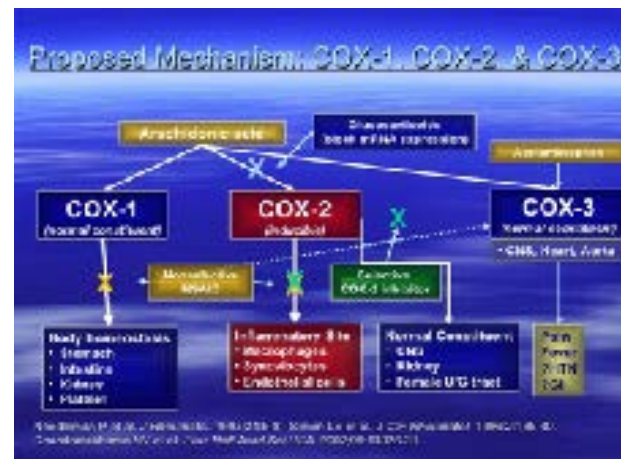
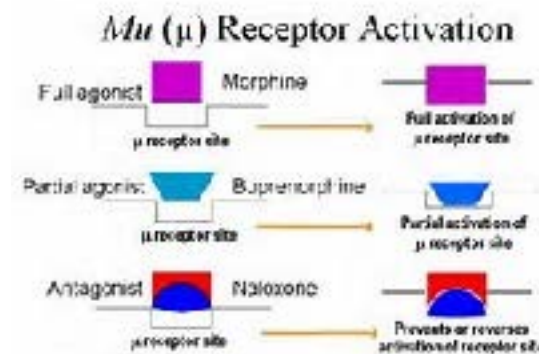
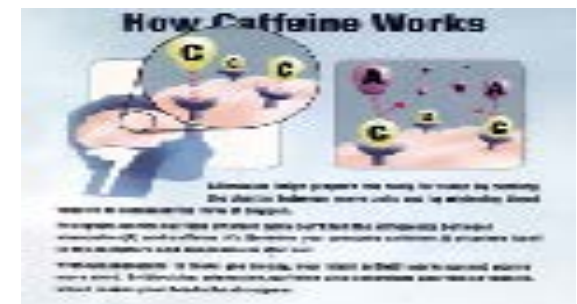
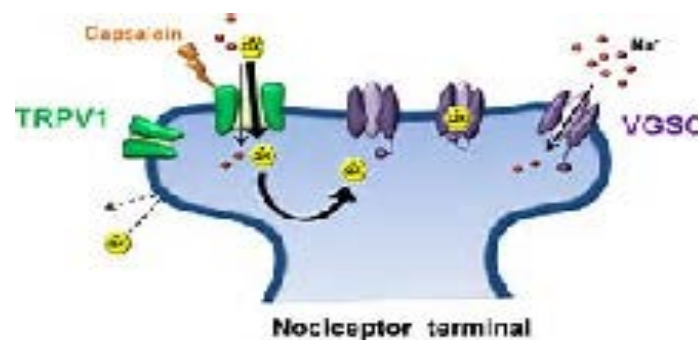
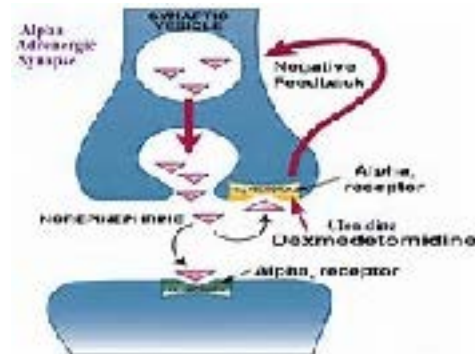
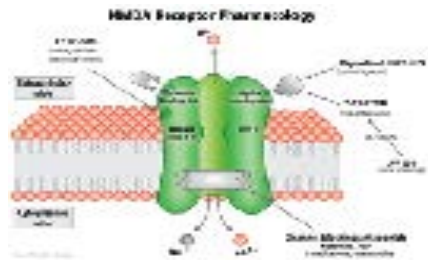
We Must Start to Think Differently!

Multi-Modal

Synergy

Pre-emptive



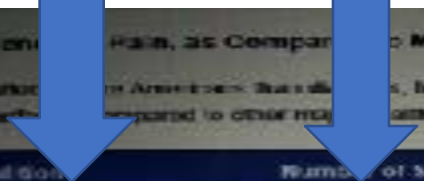


New Field of Study

Terms to know:

Multi-Modal, Pre-emptive, and Synergy

Sound familiar?



Incidence of Pain, as Compared to Major Conditions

Pain affects more Americans than diabetes, heart disease and cancer combined. The chart below depicts the magnitude of chronic pain as compared to other major health conditions.

Condition	Number of Americans	Source
Chronic Pain	100 million Americans	Institute of Medicine of The National Academies (2)
Diabetes	25.6 million Americans (16.9 million are undiagnosed)	American Diabetes Association (3)
Coronary Heart Disease (heart attack and heart pain) Stroke	16.3 million Americans 7.0 million Americans	American Heart Association (4)
Cancer	17.5 million Americans	American Cancer Society (5)

Pain is a new field and is subject to change

Dr Mackey 2017, 1 BILLION people world wide have chronic pain

What is the most Prescribed Med in America?

Think about it?

Pain and Pain management is critical and has great financial impacts.

**Americans Consume
Eighty Percent of the
World's Pain Pills as
Prescription Drug Abuse
Epidemic Explodes**

**"America consumes 80% of
the world's opioid pain
relievers and 99% of the
world's hydrocodone."**

Hydrocodone

(combined with acetaminophen)

131.2 million prescriptions

<http://www.webmd.com/news/20110420/the-10-most-prescribed-drugs>

FDA & Washington Alerts

+ SHARE

PRINT

FDA Issues Enhanced Warnings for Opioids

03/23/16

On March 22, 2016, the U.S. Food and Drug Administration (FDA) announced enhanced warnings for immediate release opioid pain medications. As part of a continuing effort to educate prescribers and patients about the potential risks related to opioid use, the FDA is requiring a new boxed warning about the serious risks of misuse, abuse, addiction, overdose and death. In addition to the boxed warning, FDA is also requiring several additional safety labeling changes across all prescription opioid products to include additional information on the risk of these medications. This is part of the agency's overall effort to help inform prescribers about the importance of balancing the serious risks of opioids with their role in managing pain.

Acute Perioperative Pain

Perioperative pain



Approximately 46 million inpatient procedures and 35 million outpatient surgeries were performed in the US in 2006

Despite new treatment standards, guidelines, and educational efforts, acute postoperative pain continues to be undertreated, with **up to 75% of patients in the US still failing to receive adequate postoperative pain relief**

11 % severe pain

DeFrances CJ, et al. Natl Health Stat Report. 2008 Jul 30;(5):1-20. Cullen KA, et al. Natl Health Stat Report. 2009 Jan 28;(11):1-25. Wu CL, et al. Lancet. 2011;377:2215-2225. Phillips DM. JAMA. 2000; 284(4):428-429

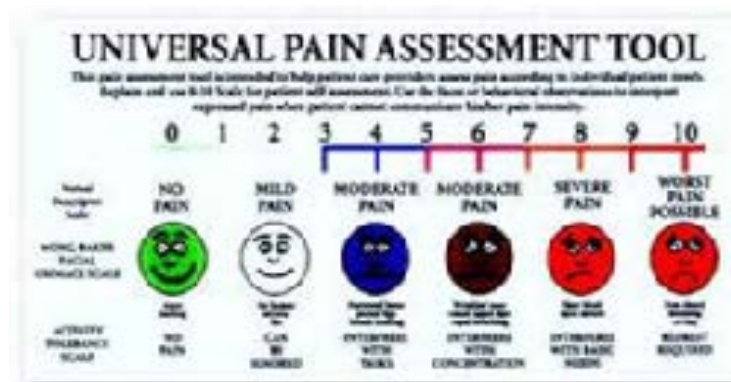
Pain assessment

Each person brings unique perspective of pain.

Listen to patient—most indicators very nonspecific

Many factors influence patient pain experience:

- ◆ Culture
- ◆ Previous pain experience(s)
- ◆ Religion/spirituality
- ◆ Current medications
- ◆ Coping skills
- ◆ Physical aspects
- ◆ Behavior



First Step.. Do we really do a good Pre-op related to pain

Discuss the history of acute and chronic pain

Identify the history of pain and their meds

Ask “what had worked”

How long have they been on meds?

People want to get rid of
pain, not the cause of the
pain itself.

- Ruben Papian

Allergies?

Discuss pain management –sound familiar??

Standard is a bad term....



ASK direct questions>>> talk about the pain.... Don't avoid the subject.

Talk about the post operative pain control plan

Pain management before OR

When we treat the pain the OR.... The receptors and the transmitters are already being fired..... Why not treat prior to that?

The study of Pain is a new issue... we have only really cared for the last few years... why should YOU care?

Cost.. Money and patient satisfaction...

“Patients who are pretreated with pain meds, anxiolytic or NSAIDS prior to surgery” –“have a greater decrease in postoperative pain” --- “decrease in postoperative anxiety”

Wow.....

“You shouldn’t have that much pain?”

“Pain doesn’t raise your blood pressure”

“You should feel this way”

“This won’t be that painful”

“Do you have any pain?

verse how do you feel?”





Oxytocin is also thought to modulate [inflammation](#) by decreasing certain [cytokines](#). Thus, the increased release in oxytocin following positive social interactions has the potential to improve wound healing.



Marazziti D, Dell'Osso B, Baroni S, Mungai F, Catena M, Rucci P, Albanese F, Giannaccini G, Betti L, Fabbrini L, Italiani P, Del Debbio A, Lucacchini A, Dell'Osso L (2006). ["A relationship between oxytocin and anxiety of romantic attachment"](#). Clinical Practice and Epidemiology in Mental Health **2** (1): 28. doi:[10.1186/1745-0179-2-28](#). PMC [1621060](#). PMID [17034623](#).

Acute

Immediate

Serves as a warning

Typically easier to treat

Typically has a end

Less 3-6 months and

subsides once the healing process is accomplished.

Acute pain serves the evolutionary function of warning for tissue damage, but chronic pain does little except to annoy and sometimes immobilize our ailing population.



Chronic Pain



Involves complex processes and pathology. Usually involves altered anatomy and neural pathways. It is constant and prolonged, lasting longer than 6 months and sometimes for life.

Last Longer than 3-6 months

Serves NO purpose

Typically can not identify a cause



Leads to pain behaviors: Negative emotions, anxiety, depression, sleep deprivation, May lead to the patient seeking active end of life.

Very difficult to treat

What if the chronic pain patient looked like this?



GET RID OF PERSONAL BIASES



Nonspecific Low Back Pain and Return to Work

PDF PRINT COMMENTS

SHARE

TRANG H. NGUYEN, MD, and DAVID C. RANDOLPH, MD, MPH, University of Cincinnati College of Medicine, Milford, Ohio

Am Fam Physician. 2007 Nov 15;76(10):1497-1502.

90 % of chronic pain patients choose to work

They feel psychologically better

Chronic pain is the number one cause of adult disability in the United States. Approximately 50 million Americans live with chronic pain today. • Chronic pain costs society more than \$100 billion each year.

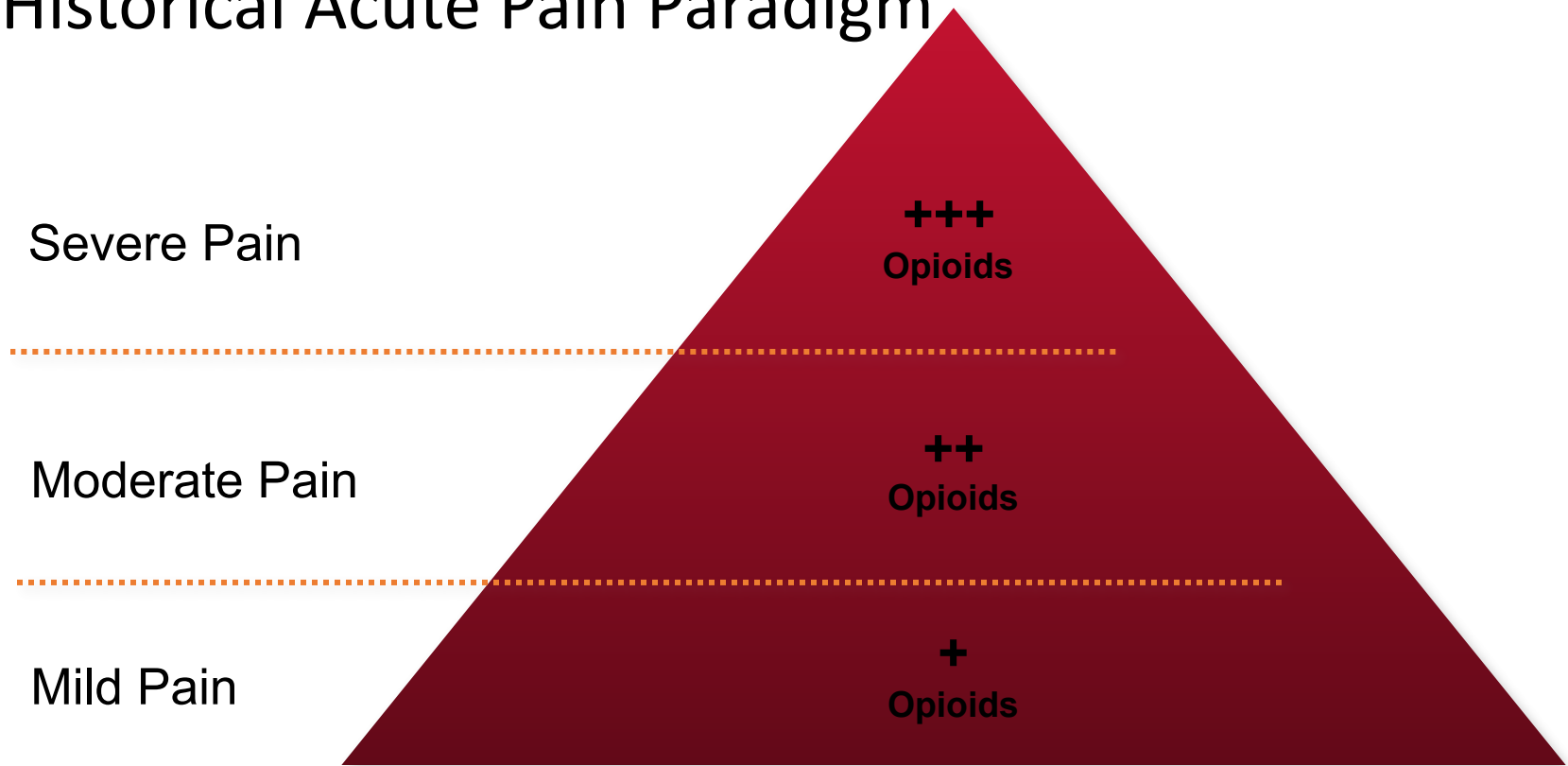
Nearly a third of Americans will experience chronic pain at some point in their lives

Seventy to 85 percent of adults in the United States have back pain at some point in their lives.

American Chronic Pain Association (ACPA) http://www.theacpa.org/pu_main_02.asp
<http://www.webmd.com/content/Article/57/66051.htm?pagenumber=2>
http://www.theacpa.org/documents/ToolKit_Older%20Adults.pdf
<http://wo-pub2.med.cornell.edu/cgi-bin/WebObjects/PublicA.woa/9/wa/viewHContent?website=nyp&contentID=1152&wosid=y5xn3abTI3vbrToTa2b5Gg>



The Historical Acute Pain Paradigm



Aubrun et al., 2003¹

Opioid analgesics rank among the drugs most frequently associated with adverse drug events

Aubrun F, et al. Anesthesiology. 2003;98(6):1415-1421. The Joint Commission Sentinel Event Alert. Safe use of opioids in hospitals. Issue 49; August 8, 2012. Available at: <http://www.jointcommission.org>

Yefei F, Tian H, Salim R, et al. Fixed time interval compared with on-demand oral analgesia protocols for post-caesarean pain: a randomised controlled trial [published online February 25, 2017]. *BJOG*. doi:10.1111/1471-0528.14540



Severe Pain

STEP 3
STEP 2
and
Higher doses of opioids

Moderate Pain

STEP 2
STEP 1
and
Low doses of opioids

Mild Pain

STEP 1
Acetaminophen, NSAIDs, or COXIBs
and
Local/regional anesthesia

Crews JC. *JAMA*. 2002;288:629-632. World Health Organization. Pain relief ladder. <http://www.who.int>. Accessed November 21, 2011. Ventafridda V, et al. *Cancer*. 1987;59:850-856. ASA Task Force. *Anesthesiology*. 2004;100:1573-1581.

So Why Should we Treat Pain?

Dozens of physiological needs to treat pain....

Increased hospital stay and cost

Decrease patient satisfaction

Increased Catecholamine; tachycardia, hypertension, increased cardiac workload, increased myocardial oxygen consumption.

Psychological: FEAR, ANXIETY, INSOMNIA<<<< fear of healthcare



AANA Journal June 2015



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

Yu, Sawo K. H. BHSoc; Tait, Gordon PhD; Karkout, Koryan MD, MSc, FRCP; Wijesundera, Duminda MD, FRCP; MacIntyre, Stuart MD, PhD, FRCP; Harkin, W. Scott MD, PhD, FRCP

Anesthesia & Analgesia 1 February 2011 - Volume 112 - Issue 2 - p 267-281
doi: 10.1213/ANE.0b013e3182025a17
Continuum of Anesthesiology Research & Reports

Year: 2012 | Volume: 12 | Issue: 1 | Page: 26-39

The Effect of preoperative esmolol on early postoperative pain: A systematic review and meta-analysis

Richard Webb¹, Visalakshy Thiruvallathar¹, Marii Carvill², Deema Khowaima³, Rudolf M van Nijl⁴

¹Department of Anaesthesia, The James Spence Institute, University of Leeds, Leeds LS2 9LN, UK; ²Department of Anaesthesia, The University of Leeds, Leeds LS2 9LN, UK; ³Department of Anaesthesia, The University of Leeds, Leeds LS2 9LN, UK; ⁴Department of Anaesthesia, The University of Leeds, Leeds LS2 9LN, UK

⁵Department of Anaesthesia, The University of Leeds, Leeds LS2 9LN, UK

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

Article (PDF Available) in: Anesthesia and Analgesia 112(2):267-01 February 2011 with 246 Reads

*** 10 YEARS BEHIND THE CURTAIN ***

See the article [Esmolol versus ketamine-remifentanyl combination for early postoperative analgesia after laparoscopic cholecystectomy: a randomized controlled trial](#)

Download PDF

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

Can you do an anesthetic without narcotics?

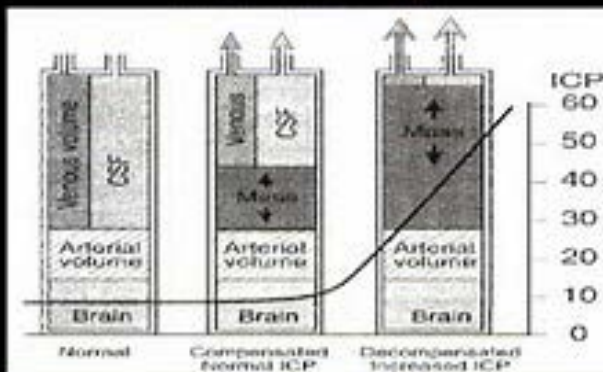


Number one consumed psychoactive drug

PDE inhibitor



Monroe-Kellie Principle



Copied from: Rogers (1996) Textbook of Pediatric Intensive Care p. 646

Anesth Pain Med. 2016 Mar 26;6(3):e33193. doi: 10.5812/aapm.33193. eCollection 2016.

The Role of Caffeine in Pain Management: A Brief Literature Review.

Barallob A¹, Rouhipour A², Forouzanfar MM¹, Safari S¹, Amini M³, Negida A⁴.

⊕ Author Information

Abstract

CONTEXT: Caffeine is the most commonly used psychoactive legal drug in the world. Caffeine's role in controlling pain has received less attention in the past, yet is being increasingly considered. This article briefly reviewed the literature to clarify the role of caffeine as a drug for pain control and attract investigators to this topic.

EVIDENCE ACQUISITION: The data on Caffeine as an adjuvant therapy or as a main component for pain modulation has been narratively reviewed.

RESULTS: Caffeine plays an important role in pain modulation through their action on adenosine receptors which are involved in nociception. The use of caffeine as adjuvant treatment was well-established in the literature and caffeine is currently available in some over the counter medications. Studies showed controversial results about the interaction between caffeine and morphine for pain relief in patients with terminal stage cancer. As a main component for pain modulation, Caffeine can be used for hypnic headache and postdural puncture headache.

CONCLUSION: Caffeine has a potential role for pain modulation. Current evidence on caffeine use for migraine and terminal stage cancer is not well-established. Future studies should address the use of caffeine alone for different types of pain with dose escalation and standardization of outcome measurement.

Pain Control with a Old Drug?

Phantom pain... Calcitonin



Calcitonin is a 32 amino acid peptide hormone which regulates calcium homeostasis in vertebrates. It also has analgesic properties, primarily through receptor mediated modulation of serotonergic pain pathways in the central nervous system

A meta-analysis concluded that calcitonin was effective in the treatment of complex regional pain syndrome and systematic reviews reported benefit in the treatment of acute vertebral fracture pain. A randomized controlled trial (RCT) showed calcitonin was effective in the treatment of acute phantom limb pain, however a Cochrane review did not support its use in the treatment of metastatic bone pain although individual RCTs suggested benefit.



Pain Res Manag. 2015 Sep-Oct;28(5):229-33. Epub 2015 Aug 20.

Use of calcitonin in recalcitrant phantom limb pain complicated by heterotopic ossification.

Viana R, Faine MW.

Abstract

BACKGROUND: Phantom limb pain (PLP) is a common complication after amputation, affecting up to 80% of the amputee population. However, only 5% to 10% of amputees have severe PLP impacting daily function. The present report details the management of severe, treatment-resistant PLP in a 72-year-old man with a traumatic left transradial amputation and a comorbid complication of heterotopic ossification (HO).

OBJECTIVE: To describe a case of PLP with HO and the possible role of calcitonin in the treatment of both conditions.

METHODS: A systematic review of the literature regarding the management of PLP.

RESULTS: Seventeen articles that directly addressed PLP were identified; 11 were randomized controlled trials. All involved small samples and follow-up ranged from 5 h to one year, with the majority limited to six weeks.

DISCUSSION: In the present case, medication management was limited by side effects, lack of response and the patient's desire to avoid long-term medication. Investigations revealed HO, which was suspected to envelop the median nerve in the proximal forearm. After several unsuccessful medication trials, the literature was reviewed in search of common variables between HO formation and persistent PLP. Ultimately, the biochemical effects associated with nerve injury were identified to be a possible factor in both HO and PLP development. Calcitonin's proposed mechanisms of action may help to manage HO and PLP at multiple stages of disease development and maintenance. In the present case, a four-week trial of intranasal calcitonin was successful, with pain control lasting at least 18 months.

Curr Pharm Des. 2009;15(2):2659-76.

Calcitonin for osteoporosis and bone pain.

Nehra HM¹, Mukherjee A, Gilliam JP.

Author information

Abstract

Calcitonin has been approved for the treatment of osteoporosis and other diseases involving accelerated bone turnover for approximately 25 years. The most commonly studied and prescribed form is salmon calcitonin, which has a greater efficacy in clinical use. A wealth of well-controlled clinical studies have demonstrated that calcitonin preserves or increases bone mineral density (BMD) and reduces the risk of vertebral fractures in osteoporosis. Recent studies have indicated that while a low BMD is correlated with an increase in fracture risk, increases in BMD alone do not explain the antifracture efficacy of antiresorptive therapies such as calcitonin. Therapies that moderately increase BMD may reduce fracture risk by reducing the rate of bone turnover and maintaining the integrity of the trabecular architecture, resulting in the preservation of bone strength and quality in osteoporosis patients. An advantage of calcitonin that is not shared by other antiresorptive therapies is its direct analgesic effect on bone pain. Calcitonin has been demonstrated to be clinically useful in improving pain, not only from the acute vertebral fractures of osteoporosis, but also in Paget's disease, bone malignancies, and other sources of musculoskeletal pain. Drugs containing calcitonin may be approved for additional indications in the near future, and as more convenient routes of administration such as the oral route become available, the demand for the calcitonin peptide is expected to increase.

One or two doses of IV calcitonin 200 IU



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Back Pain

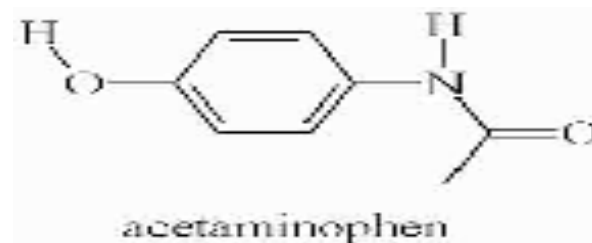
Valium for Spasm.... Preop for Anxiety and Pain

Muscle Relaxants

A combination of nonsteroidal anti-inflammatory drugs and muscle relaxants -- such as cyclobenzaprine (Flexeril), diazepam (Valium), carisoprodol (Soma), or methocarbamol (Robaxin) -- are sometimes used for patients with acute low back pain. Evidence has shown that they can help relieve non-specific low back pain, but some experts warn that these drugs should be used cautiously, since they target the brain, not the muscles. Patients who take muscle relaxants may experience a number of central nervous system side effects, such as drowsiness. The muscle relaxant Soma can be addictive and does little more than induce sleep.



Acetaminophen



Not considered a 'true' NSAID because it lacks significant anti-inflammatory effects

No gastric irritation, platelet problems

Hepatic necrosis and death may accompany a single dose of acetaminophen > 15 g. At doses > 4g, hepatotoxicity may occur (especially with ETOH use).

Remember that toxicity/necrosis occurs because of glutathione depletion.

Acetylcysteine increases glutathione stores and is most effective when given within 8 hours of ingestion

NOW AVAILABLE IN THE US>>> OFIRMEV-- Cadence

NO antiplatelet effects

NO effect on wound healing or bones

- ◆ does not affect major organs in small doses

NO real reason why it works?? Mechanism of action is poorly understood – It may be working on a COX—3 route

This is a safe weak to moderate analgesic



OFIRMEV 1000mg Bottle

IV acetaminophen injection: Cadence Pharm

◇ (Cadence was bought out) (price spike)

Minimum dosing interval is every 4 hours

No change when going from IV to Oral

Administer over 15 min.....well....?????

◇ www.ofirmev.com

Do not exceed max daily doses.. Adult is 4 grams per day

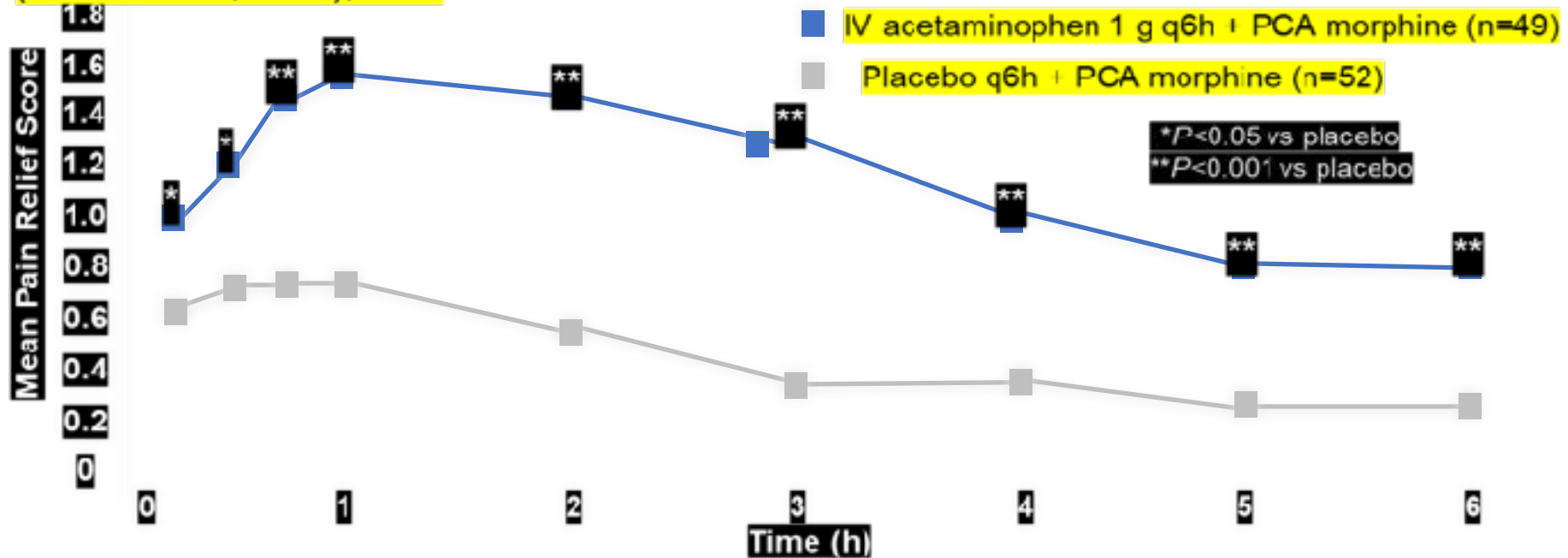
Pediatric is dosed at 15mg/kg with max of 75 mg/kg/day

CHEAPPPPPPPP ---- WELL NOT ANYMORE





Study in Major Orthopedic Surgery
(Sinatra et al., 2005), cont.



	IV Acetaminophen	Placebo	P value
Patient satisfaction: good to excellent at 24 h	40.8%	23.1%	0.004 ^{†2}
Median time to first use of rescue	3.0 h	0.8 h	0.0001
Morphine consumption over 24 h [†]	38.3 mg (33%↓)	57.4 mg	<0.01
Safety (adverse reactions)	IV acetaminophen is comparable to placebo		

[†] Based on Cochran-Mantel-Haenszel Test

[‡] The clinical benefit of reduced opioid consumption was not demonstrated

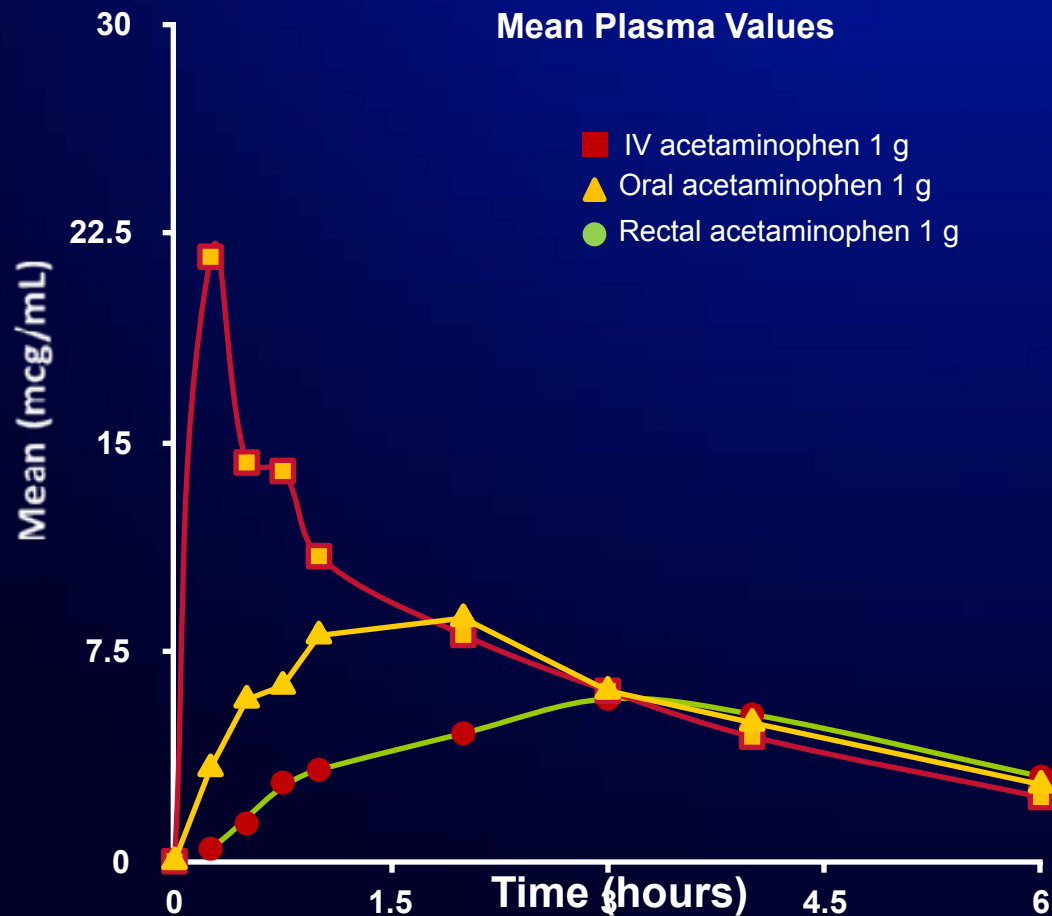
1. Sinatra RS, et al. *Anesthesiology*. 2005;102:822-831. 2. Data on file, Cadence Pharmaceuticals, Inc.



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Study of Acetaminophen Plasma Pharmacokinetics (IV, PO, PR) (Singla et al., 2012)

Randomized, 3-way, cross-over design in 6 healthy volunteers; efficacy was not assessed



- The IV route produced a 76% higher mean plasma C_{max} ($p = 0.0004$) than PO, and 256% higher ($p < 0.0001$) than PR
- The median plasma T_{max} for the IV route was earlier (0.25h) than PO (1.0h, $p = 0.0018$) or PR (2.5h, $p = 0.0025$)

Note: PR acetaminophen data reflects standardization of the 1300 mg dose to 1000 mg (linear kinetics)

Modified from Singla N et al. *Pain Pract.* 2012 12(7):523-532.

OFIRMEV

Liver issues is big



Contraindicated in patients with liver failure/hepatic injury or with known hypersensitivity to acetaminophen...

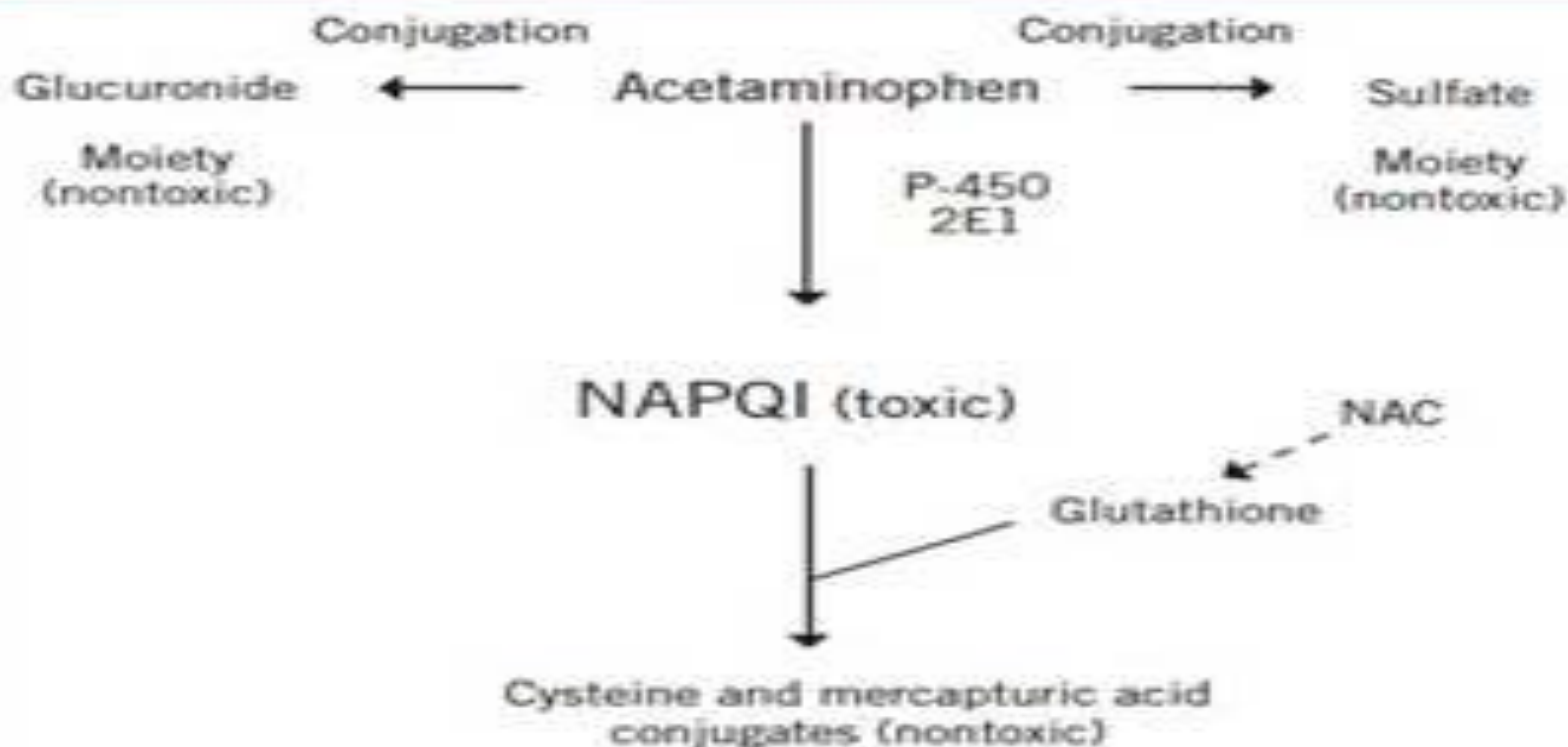
What about ETOH?

Common side effects are: N/V; HA: insomnia; constipation, pruritus and agitation and atelectasis

Using this drug may mask post surgical fever when used for post-operative pain.



Figure 1 – Acetaminophen metabolism



COX-3: the Acetaminophen Target Finally Revealed

It has been known for years that non-steroidal anti-inflammatory drugs (NSAIDs) such as aspirin, ibuprofen, and acetaminophen, provide relief from fever, pain, and inflammation through their actions on cyclooxygenase (COX) enzymes.¹ Two COX isozymes, COX-1 and -2, were first identified in the early 1990's as the catalysts for an important step in prostaglandin biosynthesis.² Although both enzymes have similar functions, their temporal and spatial expression patterns are very different.³ COX-1 is constitutively expressed in many somatic cell types and is considered a "housekeeping" enzyme with roles in such processes as vascular hemostasis and gastroprotection.⁴ In contrast, COX-2 expression is primarily induced by factors such as endotoxins, cytokines, and growth factors.² COX-2 is expressed at sites of inflammation and produces prostaglandins that mediate inflammatory and pain sensation responses.⁴ COX involvement in inflammation, pain, and a variety of diseases has inspired researchers to investigate the actions of NSAIDs on these enzymes. Although many advances have been made over the last 10 years in understanding the pain relief and anti-inflammatory mechanisms of aspirin, ibuprofen, and the new COX-2 inhibitors, the mechanism of acetaminophen action has remained elusive.^{7,8}

Finally, identification of a new isozyme, COX-3, suggests that it is the target for acetaminophen.⁹ COX-3 was discovered by Northern analysis of canine cerebral cortex RNA using a COX-1 cDNA probe. The COX-1 probe unexpectedly illuminated a band at 2.6 kb, labeling a transcript later confirmed to be COX-3, an alternate splice variant of COX-1 in which intron 1 is retained (Figure 1). Interestingly, intron 1 is not only present in canine, human, and murine versions of COX-3, but it is conserved in length and sequence in these species as well. While COX-3 retains all of the important catalytic and structural features of COX-1 and -2, it is likely that intron 1 is responsible for the deviant enzymatic properties of COX-3 perhaps via subtle alterations in structure, glycosylation state, and/or expression.⁹

COX 2 inhibitors



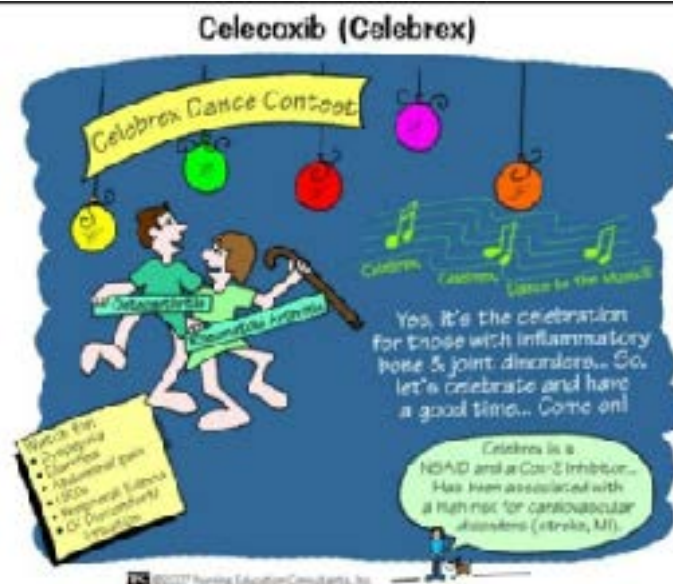
Lack of effects on platelet aggregation and bleeding is the primary advantage of COX 2 inhibitors vs nonselective NSAIDs

The first of the selective COX 2 inhibitors, celecoxib (Celebrex) is approved by the FDA for the treatment of osteoarthritis, rheumatoid arthritis, and psoriatic arthritis. Dose is 100-200 mg daily

A second COX 2 inhibitor, rofecoxib (Vioxx), was approved

Valdecoxib can be administered in a 40mg dose about 1 hour before surgery and another 40 mg can be given after surgery

Parecoxib is the only IV form of COX 2 inhibitor that is converted to Valdecoxib in vivo. Dosing is the same as Valdecoxib



Celebrex

Analgesic and anti-inflammatory agent.

Classified as a Cox-2

Action is in the periphery as well as the central nervous system

Stops pain at the site of transmission....noxious system.

200-400 mg

Contraindicated in renal insufficiency and a sulfa allergy



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 give anytime during the surgery... better now that we can give per--op



400mg/4ml or 800mg/8ml

Dilute and administer over 30 minutes

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



Ketorolac (toradol)



NO evidence of unwanted sedation, absence of tolerance, reduction in opioid related side effects.

Studies show use of Toradol with mild narcotics decreases hospital stay. Faster return to bowel function.

Perioperative Single Dose Ketorolac to Prevent Postoperative Pain: A Meta-Analysis of Randomized Trials

De Oliveira, Gildasio S. Jr. MD, MSCI; Agarwal, Deepti MD; Benzon, Honorio T. MD

Anesthesia & Analgesia: February 2012 Volume 114 Issue 2 p 424-433

doi: 10.1213/ANE.0b013e3182334d68

Analgesia: Research Reports

60 mg IM worked better than 30 mg

Ketorolac



NDC: 68387-440-30 Rx #
Generic: Toradol 10mg
Ketorolac tromethamine
Lot: X75785-1 Exp: 7/2018
NDC: 68387-440-30 Rx #
Generic: Toradol 10mg
Ketorolac tromethamine
Lot: X75785-1 Exp: 7/2018
NDC: 68387-440-30 Rx #
Generic: Toradol 10mg
Ketorolac tromethamine
Lot: X75785-1 Exp: 7/2018
NDC: 68387-440-30 Rx #
Generic: Toradol 10mg
Ketorolac tromethamine
Lot: X75785-1 Exp: 7/2018

Very effective analgesic, anti-inflammatory, and antipyretic actions

Available IM/IV doses are 15, 30 and 60 mg dose

30 mg of Ketorolac = 10 mg Morphine=100 mg Meperidine

After IM injection, peak plasma concentrations in 45-60 minutes

Half-life of about 6 hours

Contraindications: bronchospasm, angioedema, nasal polyps, concurrent use of other NSAIDs, known allergy or intolerance to aspirin, history of GI bleeding, renal dysfunction, volume-depleted patient

Accounted for the original Glassman Study flaws

Ketorolac and Spinal Fusion

Does the Perioperative Use of Ketorolac Really Inhibit Spinal Fusion?

Ben B. Pradhan, MD, MSc,* Robert L. Tatsami, MD,† Jason Gallina, MD,‡
Craig A. Kahns, MD,§ Jeffrey C. Wang, MD,¶ and Edgar G. Dawson, MD||

Study Design. Retrospective review.

Objective. To evaluate the effect of postoperative use of ketorolac (Toradol) on spinal fusion in humans.

Summary of Background Data. The value of parenteral ketorolac in postoperative analgesia has been well documented across surgical specialties. However, some studies have shown that ketorolac may adversely affect osteogenic activity and fracture healing.

Methods. A total of 405 consecutive patients who underwent primary lumbar posterolateral intertransverse process fusion with pedicle screw instrumentation were included in this retrospective study. A subset of 228 patients received Toradol after surgery for adjunctive analgesia. Each patient received a mandatory dose of 30 mg intravenously every 6 hours for 48 hours. The same surgeon performed the fusion procedure on all of these patients. Historical controls included 177 patients who did not receive Toradol after surgery. The minimum follow-up period was 24 months. Mismatches were diagnosed by analyzing sequential radiographs, flexion-extension radiographs, and compared tomography with multplanar reconstructions. The gold standard of surgical exploration was performed in symptomatic patients with diagnostic ambiguity or nonunions diagnosed by imaging.

Results. There were no smokers in the study population. Pseudarthrosis was identified in 12 of 228 patients (5.3%) who received Toradol after surgery, and in 11 of 177 patients (6.2%) who did not. There was no significant difference detected in the nonunion rates between the two groups ($P > 0.05$, χ^2 method).

benefits of NSAIDs include reduced pain, improved postoperative ambulation, shorter hospitalization and decreased nausea, emesis and sedation.²⁻⁴ NSAIDs have documented efficacy when administered as the sole analgesic after minor surgical procedures and adjuvants to other analgesics after major surgery.^{5,6} Ketorolac (Toradol, Roche Laboratories, Nutley, NJ), approved by the Food and Drug Administration in November 1989 for the control of postoperative pain, enhances the effect of narcotics, and decreases narcotic requirement.^{4,7-10} Especially the authors have observed a more comfortable postoperative hospital course in spinal fusion patients who received parenteral Ketorolac at our institution without any attendant increase in complications.

NSAIDs, however, have a myriad of undesirable side effects especially in the perioperative period and includes gastrointestinal bleeding or ulcers, wound healing problems or bleeding, and renal failure.^{7,16-22} NSAIDs may also adversely affect osteogenic activity and fracture healing.²³⁻²⁵ Regarding spinal surgery, a number of studies have shown adverse effects on fusion rates in animals.²²⁻²⁴ This may occur through any one or all of several mechanisms.^{22,23,26} Glassman *et al*²⁵ examined the influence of ketorolac on spinal fusion in humans and concluded that this drug significantly inhibited fusion at doses typically used for postoperative pain control and that NSAIDs should be avoided in the early postoperative

Sprix-Nasal Ketorolac

Short Term use... Up to five days.

Some risk as IV or IM Ketorolac

Dose: 31.5mg or 15.75 mg each spray per nostril

Max daily dose is 63 mg



Alkermes Pharm—Meloxicam IV

J Oral Maxillofac Surg. 2012 Jan;70(1):31-6. doi: 10.1016/j.joms.2011.03.039. Epub 2011 Jul 23.

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

Isiordia-Espinoza MA¹, Sánchez-Prieto M, Tobías-Azúa F, Reyes-García JG.

Am Fam Physician. 2000 Jun 15;61(12):3669-76.

Cyclooxygenase-2 enzyme inhibitors: place in therapy.

Noble SL¹, King DS, Ostade JJ.

Ⓜ Author information

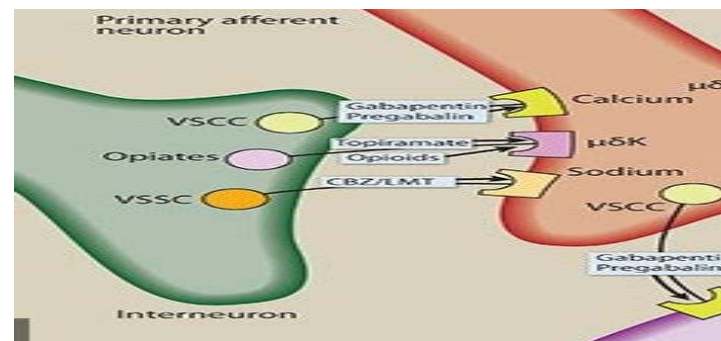
Abstract

Nonsteroidal anti-inflammatory drugs (NSAIDs) play a major role in the management of inflammation and pain caused by arthritis. A new class of NSAIDs that selectively inhibit the cyclooxygenase-2 (COX-2) enzyme has been developed. The first COX-2 inhibitors, celecoxib and rofecoxib, are said to provide therapeutic benefit with less toxicity than traditional NSAIDs. A third COX-2-selective inhibitor, meloxicam, has recently been introduced. COX-2 inhibitors and traditional NSAIDs do not appear to differ significantly in their effectiveness in alleviating pain or inflammation. They have similar gastrointestinal side effects, including abdominal pain, dyspepsia and diarrhea. However, short-term studies show fewer gastrointestinal ulcers in patients treated with COX-2 inhibitors compared with traditional NSAIDs.

Lots of exciting information coming about related to Meloxicam! More COX 2 than previous thought



Anti-Convulsants



Gabapentin and Pregabalin

This class of medications manage the spontaneous firing of sensory neurons associated with neuropathic pain

Reduces pain with movement and can reduce chronic post surgical pain syndromes by neuronal plasticity.

Pregabalin-lyrica

Pregabalin is a new synthetic molecule and a structural derivative of the inhibitory neurotransmitter γ -aminobutyric acid.

It has analgesic, anticonvulsant, anxiolytic, and sleep-modulating activities. Pregabalin binds potently to the $\alpha 2$ - δ subunit of calcium channels, resulting in a reduction in the release of several neurotransmitters, including glutamate, noradrenaline, serotonin, dopamine, and substance P.

Anticonvulsants work to decrease the hyperalgesic response from the central nervous system.

50, 75, 150 mg

Dose dependent on procedure and weight



Mathieson S, Maher CG, McLachlan AJ, et al. **Trial of pregabalin for acute and chronic sciatica.** *N Engl J Med.* 2017;376:1111-20. doi:10.1056/NEJMoa1614292

Gabapentin

Sicras-mainar A, Rejas-gutiérrez J, Pérez-páramo M, Navarro-artieda R. Cost of treatment of peripheral neuropathic pain with pregabalin or gabapentin in routine clinical practice: impact of their loss of exclusivity. *J Eval Clin Pract*. 2016. doi: 10.1111/jep.12634.



Gabapentin is typically well tolerated in the correct doses:

Doses range 300-1200 mg single doses for anesthesia : max dose is 1200mg TID or max of 3600mg/day

Typically single small doses (300-600) little problems

Keep in mind Half life of 5-7 hrs





J Pain Res. 2016 Sep 12;9:631-40. doi: 10.2147/NPR.S112626. eCollection 2016.

Use of preoperative gabapentin significantly reduces postoperative opioid consumption: a meta-analysis.

Avanuganti S¹, Lau CS², Chamberlain RS³

⊕ Author information

Abstract

OBJECTIVES: Effective postoperative pain management is crucial in the care of surgical patients. Opioids, which are commonly used in managing postoperative pain, have a potential for tolerance and addiction, along with sedating side effects. Gabapentin's use as a multimodal analgesic regimen to treat neuropathic pain has been documented as having favorable side effects. This meta-analysis examined the use of preoperative gabapentin and its impact on postoperative opioid consumption.

MATERIALS AND METHODS: A comprehensive literature search was conducted to identify randomized control trials that evaluated preoperative gabapentin on postoperative opioid consumption. The outcomes of interest were cumulative opioid consumption following the surgery and the incidence of vomiting, somnolence, and nausea.

RESULTS: A total of 1,793 patients involved in 17 randomized control trials formed the final analysis for this study. Postoperative opioid consumption was reduced when using gabapentin within the initial 24 hours following surgery (standard mean difference -1.35, 95% confidence interval [CI]: -1.95 to -0.73; $P < 0.001$). There was a significant reduction in morphine, fentanyl, and tramadol consumption ($P < 0.05$). While a significant increase in postoperative somnolence incidence was observed (relative risk 1.30, 95% CI: 1.10-1.54, $P < 0.05$), there were no significant effects on postoperative vomiting and nausea.

CONCLUSION: The administration of preoperative gabapentin reduced the consumption of opioids during the initial 24 hours following surgery. The reduction in postoperative opioids with preoperative gabapentin increased postoperative somnolence, but no significant differences were observed in nausea and vomiting incidences. The results from this study demonstrate that gabapentin is more beneficial in mastectomy and spinal, abdominal, and thyroid surgeries. Gabapentin is an effective analgesic adjunct, and clinicians should consider its use in multimodal treatment plans among patients undergoing elective surgery.

Gabapentin not just for pain! Pretreatment for Anxiety

Am J Anesth Resum. 2012 Oct;31(10):e223-7. doi: 10.1016/j.amfar.2012.05.008. Epub 2012 Jul 6.

Effects of a single 1200-mg preoperative dose of gabapentin on anxiety and memory.

Adam F¹, Dordeneau L, Gessler DJ, Chauvin M.

Author information

Abstract

BACKGROUND: Gabapentin has antihyperalgesic and potential anxiolytic effects. We therefore evaluated the effects of gabapentin premedication on anxiety, amnesia, and sedation. We tested the primary hypothesis that 1200mg of oral gabapentin 2 to 3h before surgery reduces preoperative anxiety. Our secondary hypothesis was that gabapentin administration is sedative without causing preoperative amnesia.

STUDY DESIGN: Prospective, randomized and placebo controlled study.

METHODS: Surgical patients having general anaesthesia were randomly assigned to either 1200mg oral gabapentin (n=32) or an identical-looking placebo (n=32) 2 to 3h before anaesthesia. Anxiety, sedation, and amnesia were quantified before premedication, 2h thereafter, and preoperatively. Preoperative anxiety was measured using the Spielberger state trait anxiety inventory (STAI state) and the visual analogue scale anxiety (VAS). Memory was assessed with the picture recall test of Snodgrass and Vanderwart. Results were compared with L Mann-Whitney U, or Chi(2) tests as appropriate, P<0.05 was considered statistically significant.

RESULTS: STAI state, our primary outcome, decreased significantly in the gabapentin group, from 37.2 to 30.8, and remained unchanged in the placebo group, from 39.3 to 37.9 (P=0.003). The VAS score for anxiety also decreased, but not significantly, from 28.2 to 19.2 in the gabapentin group and from 28.7 to 24.7 in the placebo group (P=0.065). No difference was observed in the amnesic effect, nor did the groups differ in terms of recovery times or sedation scores.

CONCLUSION: Gabapentin premedication, 1200mg, provided preoperative anxiolysis without causing sedation or impairing preoperative memory.

Gabapentin for PONV

Arch Gynecol Obstet. 2012 Mar;285(3):677-82. doi: 10.1007/s00404-011-2023-6. Epub 2011 Aug 5.

Effects of gabapentin on postoperative pain, nausea and vomiting after abdominal hysterectomy: a double blind randomized clinical trial.

Agar L¹, Nasari L, Meckoufard MM, Amiri Z.

Ⓒ Author Information

Abstract

PURPOSE: Gabapentin has demonstrated analgesic effects in some studies. This double blind randomized clinical trial (RCT) was conducted to evaluate whether the pre-emptive use of gabapentin 600 mg could reduce postoperative pain, nausea and vomiting, and meperidine consumption in patients after hysterectomy.

METHODS: Between 2009 and 2010, a total of 170 patients who were candidates for abdominal hysterectomy were assessed for eligibility to enter the study. Thirty patients were excluded for different reasons; and 140 included patients were randomly assigned to one of two groups according to the method of treatment, gabapentin or placebo, in a double-blind manner before hysterectomy. Postoperatively, the pain was assessed on a visual analogue scale (VAS) at 1, 4, 8, 12 and 24 h at rest. Meperidine intramuscularly was used to treat postoperative pain on VAS score and patients demand. Total meperidine and antiemetic drug consumption in the first 24 h after surgery was also recorded. The trial is registered at clinicaltrials.gov number: NCT01106165/29N1.

RESULTS: Patients in the gabapentin group had significantly lower VAS scores at all time intervals, than those in the placebo group. The total meperidine consumed in the gabapentin group was significantly less than in the placebo group. Postoperative nausea and vomiting (PONV) and antiemetic drug consumption were significantly decreased in gabapentin group.

CONCLUSION: Pre-emptive use of gabapentin 600 mg orally significantly decreases postoperative pain and PONV, and also reduces analgesic and antiemetic drug requirements in patients who undergo abdominal hysterectomy.

Dyloject

LAKE FOREST, Ill., Dec. 30, 2014 /PRNewswire/ -- [Hospira, Inc.](#) (NYSE: [HSP](#)), the world's leading provider of injectable drugs and infusion technologies, and a global leader in biosimilars, has received approval from the U.S. Food and Drug Administration (FDA) for Dyloject™ (diclofenac sodium) Injection, a proprietary nonsteroidal anti-inflammatory drug (NSAID) analgesic. Dyloject is indicated for use in adults for the management of mild to moderate pain and for the management of moderate to severe pain alone or in combination with opioid analgesics.

“While not a replacement for opioids, Dyloject is [an] injectable therapy option that can be administered more conveniently in a small-volume, intravenous bolus over 15 seconds as opposed to other injectable non-opioid analgesics that are formulated in large volumes or require dilution prior to administration and typically require an infusion of 15 to 30 minutes to administer the full dose.”



DYLOJECT

Tramadol (1-3 mg/kg) Single Pre-Operative Dose

NCBI will be taking some public web servers from 8:00 AM to 12:00 PM EDT (12:00-15:00 UTC) on Monday, September 26. You may experience problems with NCBI web sites during that time. Please plan accordingly. [Read more.](#)

Format: Abstract + Send to +

Full Text Provided by NCBI

Comparison of analgesic effect of tramadol alone and a combination of tramadol and paracetamol in day-care laparoscopic surgery.

[Abstract](#) [Full Text](#) [PDF](#)

Abstract

BACKGROUND: To compare the analgesic efficacy of tramadol alone (1.5 mg/kg, I.V.) with a tramadol (1 mg/kg, I.V.) and paracetamol combination in day-care laparoscopic patients.

METHODS: The analgesic efficacy of intravenous tramadol alone (1.5 mg/kg, I.V.) [group T] was compared with a combination of intravenous tramadol (1 mg/kg, I.V.) and oral paracetamol (1 g) [group TP] in 60 day-care laparoscopic patients in a prospective randomized double-blind clinical trial in a tertiary care hospital. Intraoperative haemodynamic responses and postoperative visual analogue scores were recorded to assess the analgesic efficacy.

RESULTS: Only one patient in group T received a single dose of rescue analgesia intraoperatively. The highest pain scores were recorded at 120 min postoperatively in both groups, and rescue analgesia was needed in eight patients in group T and in 12 patients in group TP ($P = 0.35$). The occurrence of vomiting, nausea and drowsiness was higher in group T ($P < 0.001$).

CONCLUSION: We conclude that utilizing the dose of tramadol 1.5 mg/kg, I.V. and combining it with paracetamol 1 g orally decreased the incidence of side effects without reducing analgesic efficacy.

DOI: [10.1186/s13047-016-0020-1](#)
(previously published in [BMC Anesthesiology](#))

Publication Types: [Mesh Terms](#) [Substances](#)

Similar articles

[\[Multimodal analgesia in elective laparoscopic cholecystectomy: a 400 \(C\) article \(Epub\) 2005\]](#)
The analgesic efficacy of subcutaneous morphine in comparison with ultrasound [Anesth Analg 2010]
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Epidural tramadol and morphine for postoperative analgesia in patients undergoing laparoscopic cholecystectomy: a randomized controlled trial [JAMA 2010]

Cited by 2 PubMed Central articles

[Comparison of the analgesic effect of intravenous paracetamol \(Compain\) alone with 1.5 mg/kg of tramadol \(Kronan\) alone in day-care laparoscopic surgery](#)

IV Tramadol



Tramadol Infusion for Postthoracotomy Pain Relief: A Placebo-Controlled Comparison with Epidural Morphine

Bloch, Mark B. FCA (SA)*, Dyer, Robert A. FCA (SA)*, Huijke, Sylvia A. FCA (SA)*, James, Michael F. PhD††

Anesthesiology & Analgesia
March 2007 - Volume 84 - Issue 3 - pp 503-508
doi: 10.1087/00000538-200303000-00009
Cardiovascular Anesthesia: Research Report

J Neurol Rural Pract. 2017 Jan Mar;8(1):55-59. doi: 10.1103/0976-3147.193535.

Epidural tramadol via intraoperatively placed catheter as a standalone analgesic after spinal fusion procedure: An analysis of efficacy and cost.

Ilangoan V¹, Vivakaran TT¹, Gunasekaran P², Devikala P²

Anesth Pain Med. 2016 Jul 26;6(5):e37778. eCollection 2016.

Combined Ketamine-Tramadol Subcutaneous Wound Infiltration for Multimodal Postoperative Analgesia: A Double-Blinded, Randomized Controlled Trial after Renal Surgery.

Khajavi MR¹, Navardi M¹, Shariat Moharari R¹, Pourfakhr P¹, Khalili N², Etezadi F¹, Imani F¹

Not Everything is it appears? Labor Epidurals going away?

Blair et al Patient-controlled analgesia for labor using remifentanil: a feasibility study?

Remifentanil PCA with a bolus dose in the range 0.25–0.5 $\mu\text{g kg}$ and a lockout time of 2 min appears a safe and effective drug for use in labor in patient-controlled analgesia systems



Is Nitrous Back? 2009

The position of the American College of Nurse-Midwives that women should have access to a variety of measures to assist them in coping with the challenges of labor. Among these should be nitrous oxide, which is commonly used in many other countries.



Lowe, NK. The nature of labor pain. Am J Obstet Gynecol 2002;186(5):S16–24.

Marmor TR, Krol DM. Labor pain management in the United States: Understanding patterns and the issue of choice. Am J Obstet Gynecol 2002;186:S173–80.

Rooks JP. Nitrous oxide for pain in labor – why not in the United States? Birth 2007;34:3–.

Rosen MA. Nitrous oxide for relief of labor pain: A systematic review. Am J Obstet Gynecol 2002;186:S110–26

Declercq ER, Sakala C, Corry MP, Applebaum S. Listening to Mothers II: Report of the Second National U.S. Survey of Women's Childbearing Experiences. New York: Childbirth Connection, October 2006, p. 31.

Nitrous Oxide During Labor: Less Pain Relief, High Patient Satisfaction

Share this content:



Despite lower reported effectiveness for labor pain, the degree of patient satisfaction in women who received nitrous oxide is similar to that of women who received neuraxial modalities, according to a study described in *Anesthesia & Analgesia*.¹

Although physicians in other countries have used nitrous oxide for decades to alleviate labor pain, this option has only recently been adopted in the United States. Previous research regarding its analgesic effectiveness has been largely inconclusive, and few studies have explored patient satisfaction associated with this modality.^{2,3} In the current investigation, researchers at Vanderbilt University Medical Center in Nashville, Tennessee, retrospectively examined data collected since their facility began offering self-administered nitrous oxide as an analgesic option in 2011.



Nitrous oxide has only recently been adopted in the United States for alleviate labor pain.

References

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2. Rosen MV. Nitrous oxide for relief of labor pain: a systematic review. *Am J Obstet Gynecol*. 2002; 186(5 Suppl Nature): S110-23.
3. Likis FE, Andrews JC, Collins MR, et al. Nitrous oxide for the management of labor pain: a systematic review. *Anesth Analg*. 2014; 118(1):103-67. doi: 10.1213/ANE.0b013e3182a7f73c
4. Hodnett ED. Pain and women's satisfaction with the experience of childbirth: a systematic review. *Am J Obstet Gynecol*. 2002; 186(5 Suppl Nature): S160-72.

Cannabinoids

Salivex

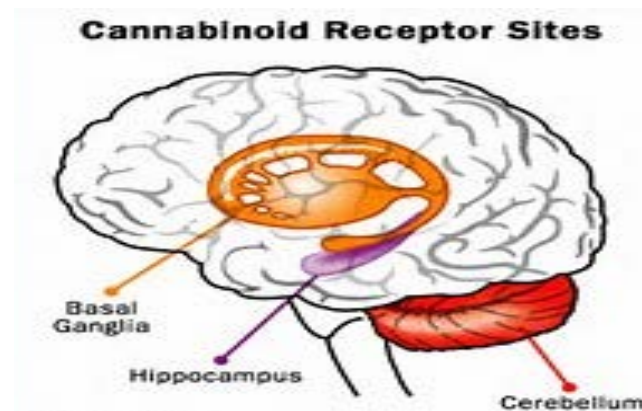
Ajulemic acid

Nabilone

Marinol

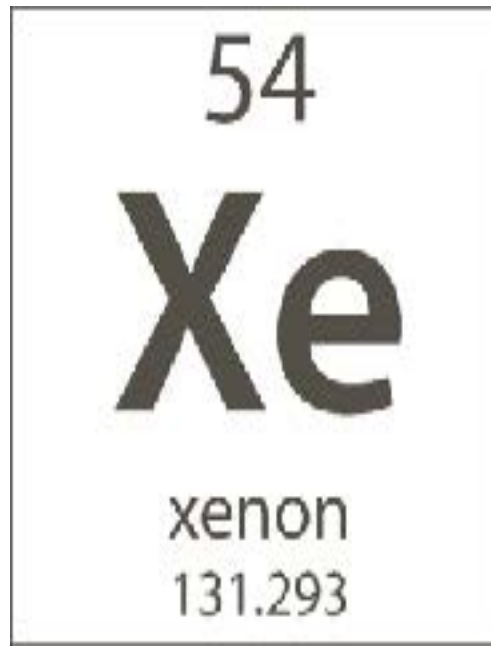
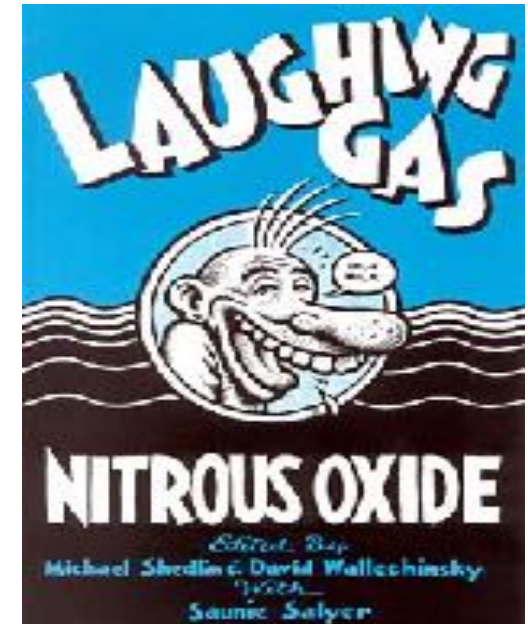
Cannadur

Cannabis



As of 2013; 23 controlled studies looking at Cannabinoids for pain management

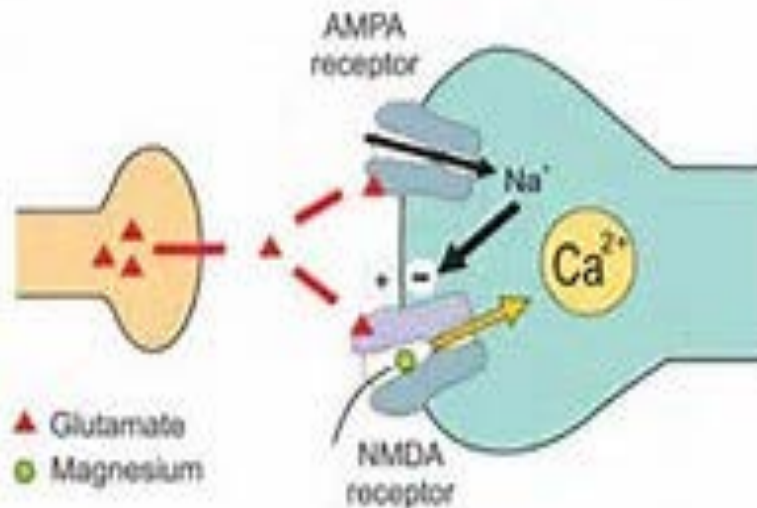
What about? What in Common?



What about the NMDA Receptor?

- ▶ Ketamine
- ▶ Magnesium
- ▶ Nitrous
- ▶ Xenon
- ▶ Methadone

NMDA Receptor Activation



Menantine, Amantadine,
Dextromethorphan



Ketamine

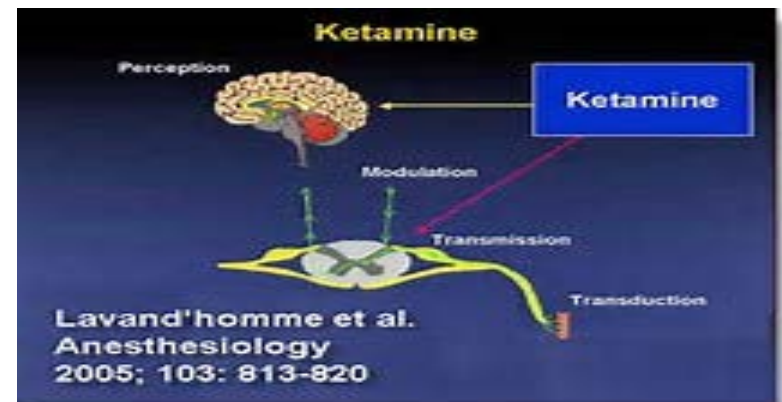
NMDA non-specific receptor antagonist

The only true single anesthetic drug

Causes dissociative anesthesia

NMDA plays a important role in processing pain via glutamate

20-30mg bolus with additional 8-16 mg/hr infusion. First line for chronic narcotic users... keep dose less than 0.75mg/kg (90kg pt -67.5 mg)



Ketamine

Analgesia; 0.1-0.2 mg/kg IV



At these low levels ; little if any side effects; (cardiovascular and psychological side effects)

At amnesia and analgesia doses; proper pretreatment with a benzo will help eliminate the psychological effects if any....

Keeping doses less than 1 mg/kg with a benzo is the max benefit of both drugs

10mg/ml



Ketamine

Onset of action:

IV <30 seconds

IM-- 3 – 4 minutes

Peak effects:

IV 1 minute.

IM-- 5 – 20 minutes

PO 30 minutes

Duration of action:

IV 5 - 15minute

IM--12 – 25 minutes

Epidural 4 hours



Alpha and Beta Phase---- Alpha 15-45; Beta 2.5 hours

REMIPHOL.....

Ketamine PCA

Acute Pain

Continuous intravenous or subcutaneous infusions at doses of 0.1-0.2 mg/kg/hr are commonly used in combination with an opioid Patient Controlled Analgesia (PCA) or opioid Infusion for the management of post-operative and post injury pain.

Commence ketamine infusion at (2- 4 mg / hr), (2mg/hr for elderly), and then titrate up according.

The recommended infusion rate is usually 2– 8 mg /hr and should only be prescribed by an anesthesia provider is available.

Chronic Pain

Patients with intractable chronic pain may be admitted for administration of ketamine infusion with escalation of dose as prescribed. This may be given by subcutaneous or infrequently by intravenous infusion.

The dose of ketamine may be increased and titrated by the pain medical officer as prescribed, according to analgesic response and/or side effects.





Magnesium

NMDA antagonist

Dose 1-2 grams in a normally healthy patient diluted in 50-100 ccs given over 30 minutes

Or: 30mg/kg bolus with 500mg/hr infusion for the duration of the case...

Blocks bradykinin release in the local vasculature; works great as a pre dosing agent in small doses for propofol -- dose this in mmols

Pain Medicine | July 2013

Perioperative Systemic Magnesium to Minimize Postoperative Pain: A Meta-analysis of Randomized Controlled Trials

Gildasio S. De Oliveira, Jr, M.D., M.S.C.I.; Lucas J. Castro-Alves, M.D.; Jamil H. Khan, B.S.; Robert J. McCarthy, Pharm.D.

[+ Author Affiliations & Notes](#)

Anesthesiology 0/ 2013, Vol.119, 1/8-190.
doi:10.1097/ALN.0b013e318297630d





December 14, 2016

Intra-Articular Magnesium for Arthroscopic Surgery-Related Pain

Review article

Peri-operative intravenous administration of magnesium sulphate and postoperative pain: a meta-analysis

E. Albrecht, K. R. Kirkham, S. S. Liu, R. Brull

First published: 1 November 2012 [Full publication history](#)

DOI: [10.1111/j.1365-2044.2012.07335.x](https://doi.org/10.1111/j.1365-2044.2012.07335.x) [View/save citation](#)

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3. Young A, Euvranch A. Multimodal systemic and intra articular analgesics. *Int Anesthesiol Clin.* 2011;49(4):117-133.



Certified
Registered
Nurse
Anesthetist



300 mg Magnesium and 40 mg of Lidocaine

Clinical Therapeutics/Volume 38, Number 1, 2016

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

Jiehao Sun, MD; Riyong Zhou, MD; Wendong Lin, MD; Jiahao Zhou, MD; and
Weijian Wang, MD

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Wolters



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Nitrous Oxide

Very useful has NMDA receptor activity.

Rapid onset of analgesia and rapid recovery

In concentrations of 50% is as potent as 10mg of IM morphine.



Methadone

Synthetic Opioid developed in Germany in 1937

Cheap and long acting

Half life 24-36 hours -- fat soluble

Mu-receptor with limited action on NMDA

5 -10 mg single dose decreases the intra and post operative opioid requirements

Additionally this drug does not have the euphoric effects that other narcotics have and this may be of great benefit in those with addictive personalities.



Pain

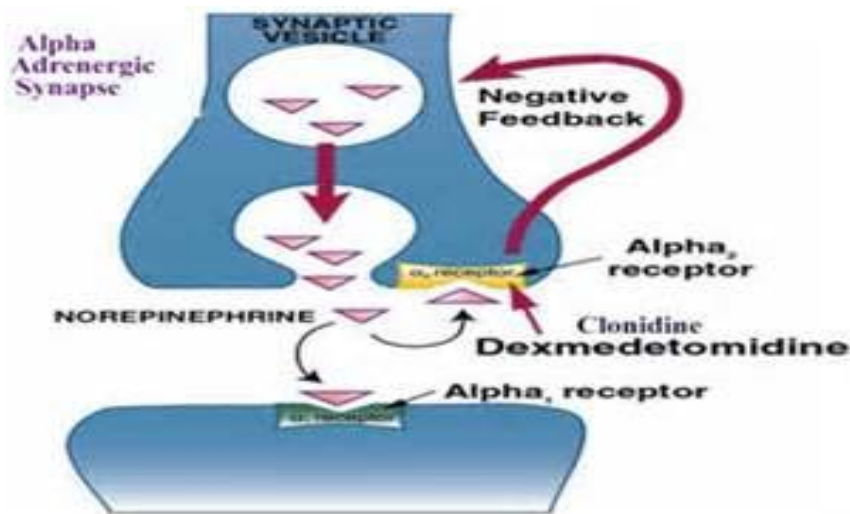
Clonidine works on what receptor?

A. Alpha-2

B. Mu-2

C. NK-1

D. TRVP-1



Clonidine

REVIEW ARTICLE

Year : 2014 | Volume : 6 | Issue : 1 | Page : 92-96

Clonidine for management of chronic pain: A brief review of the current evidences

Anil Kumar, Souvik Mallik, Pooja Khanna, Dalini Kumar Baidya

Department of Anesthesia and Intensive Care, All India Institute of Medical Sciences, New Delhi, India

Alpha 2 agonist that works presynaptic centrally by inhibiting negative feedback and blocking neurotransmitter communication

When administered orally can augment spinally mediated opioid analgesia.

Can be administered anytime

Inhibits the release of substance P blocking pain reception

Half life 9-12 hours

Works great as a anxiolytic with minimal respiratory depression

α^2 -Adrenergic Agonists for Regional Anesthesia: A Clinical Review of Clonidine (1984 – 1995)

James C. Eisenach, MD; Marc De Kock, MD; Walter Klimscha, MD

[+ Author Notes](#)

Anesthesiology 9 1996, Vol.85, 655-674.. doi:

Precedex



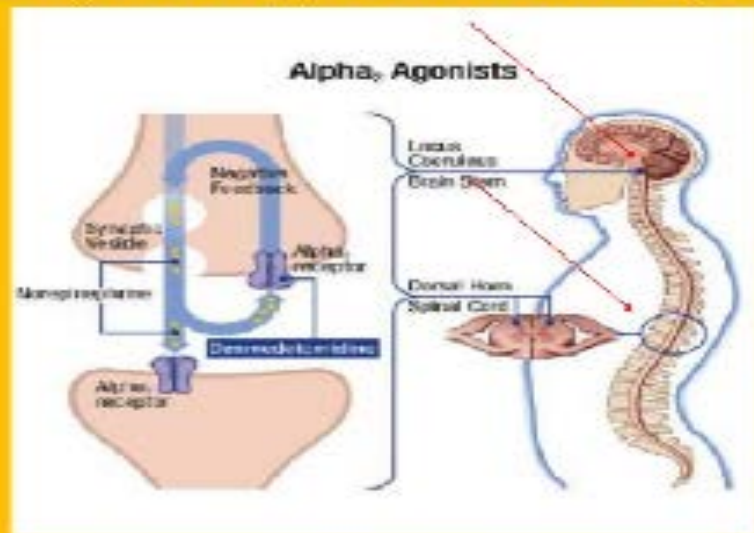
Zhonghua Yi Xue Za Zhi. 2017 Jan 24;97(4):295-299. doi: 10.3760/cma.j.issn.0378-2491.2017.04.012.

[Effect of dexmedetomidine alone for postoperative analgesia after laparoscopic cholecystectomy].

[Article in Chinese; Abstract available in Chinese from the publisher]

Chen XH¹, Wang ZJ, Xiang QM, Zheng JW.

Alpha 2 Agonists Pathways



Lidocaine Infusions

Half-life 8 minutes

90% hepatic metabolism P450-1A2—renal 10%

Bolus 1-2.5 mg/kg Load

Infusion 1-3 mg/min

Stop infusion 60 minutes post skin closure

Opioid Sparing effect

Improved pain scores—some studies showed this effect for 48-72 hrs.

Return to faster bowel function

Decreased length of stay



Anesthesiology. 2011;115:575-88
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

Doses of 0.1 mg/kg or less are great for PONV but don't help with pain relief.

Doses of about 0.15 mg/kg cover PONV and reduce postoperative pain and opioid demand. 100kg patient should be getting 15 mg

Doses above 0.2 mg/kg don't get you any more pain relief. An exception may be greater pain relief with movement (e.g. early ambulation in total joint patients?).

Giving dexamethasone *preoperatively* improves pain relief considerably more than giving it after induction. (Optimally 1-2 hours before incision.)

In general, we need not worry about side effects with 0.15 mg/kg any more than we do with current PONV doses.

It is OK.....

The Effect of Single Low-Dose Dexamethasone on Blood Glucose Concentrations in the Perioperative Period: A Randomized, Placebo-Controlled Investigation in Gynecologic Surgical Patients

Murphy, Glenn S. MD^{*}; Szokol, Joseph W. MD^{*}; Avram, Michael J. PhD[†]; Greenberg, Steven B. MD^{*}; Shear, Torin MD^{*}; Vender, Jeffery S. MD^{*}; Gray, Jayla BA^{*}; Landry, Elizabeth BA^{*}

Anesthesia & Analgesia:

June 2014 - Volume 118 - Issue 6 - p 1204-1212

doi: 10.1213/ANE.0b013e3182a53981

Ambulatory Anesthesiology: Research Report

Regional Anesthesia

Blocks... Do we not use them enough?

Prime example...

DPM comes in for a “simple” procedure... why are we not doing Blocks for this?

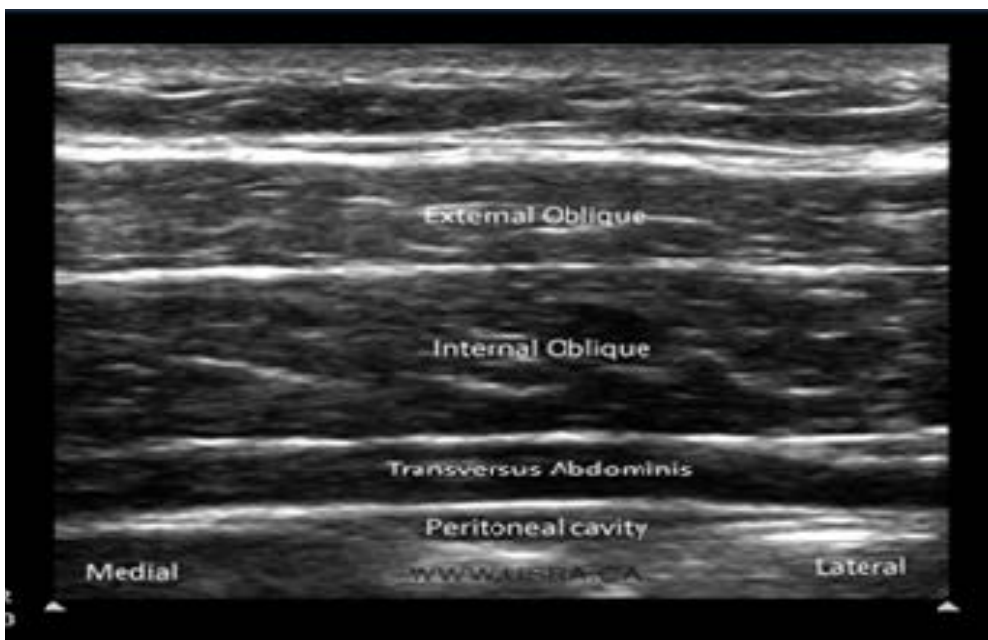
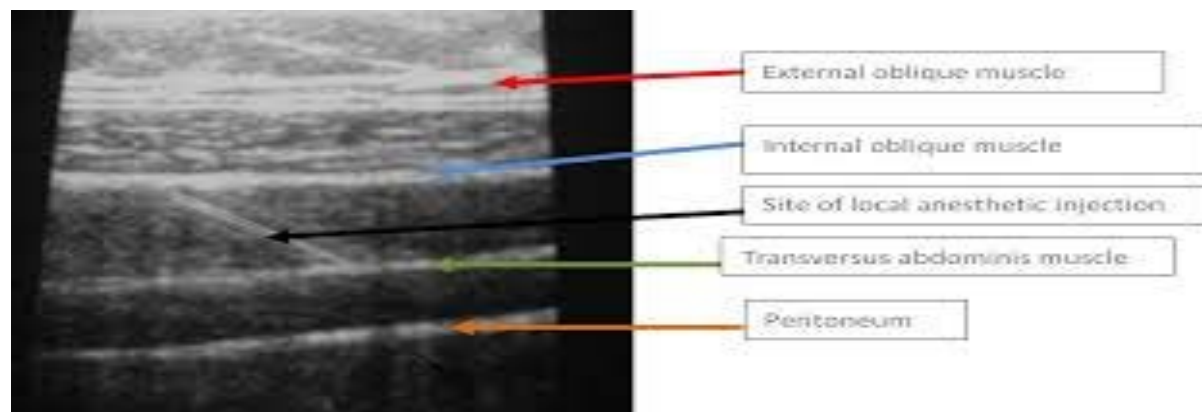
Thoughts?

Regional Question?

Have we skipped intrathecal narcotics?

Have we forgot about locals and instilling
locals into wounds...

TAP Block



Exparel

EXPAREL is a local analgesic that utilizes bupivacaine in combination with the proven product delivery platform, DepoFoam®. A single intraoperative injection given at the close of surgery delivers postsurgical pain control with reduced opioid requirements for up to 72 hours



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Silver Spring, MD 20933**TRANSMITTED BY FACSIMILE**

Dave Stack
President and CEO
Pacira Pharmaceuticals, Inc.
5 Sylvan Way
Parsippany NJ 07054

RE: NDA # 022496
EXPAREL® (bupivacaine liposome injectable suspension)
MAA 68

WARNING LETTER

Dear Mr. Stack:

As part of its routine monitoring and surveillance program, the Office of Prescription Drug Promotion (OPDP) of the U.S. Food and Drug Administration (FDA) has reviewed educational technique flashcards (EXP-AP-0124-201208 & EXP-AP-0134-201210) (administration guides) and a journal ad (EXP-AP-0039-201302) for EXPAREL® (bupivacaine liposome injectable suspension) (Exparel) submitted by Pacira Pharmaceuticals, Inc. (Pacira) under cover of Form FDA-2253. The journal ad was also submitted as a complaint to the OPDP Bad Ad Program. The administration guides provide evidence that Exparel is intended for new uses for which it lacks approval, and for which its labeling does not provide adequate directions for use, which renders Exparel misbranded within the meaning of the Federal Food, Drug, and Cosmetic Act (FD&C Act), and make its distribution violative. See 21 U.S.C. 355(a), 352(f); 331(a), (c), 21 CFR 201.5; 201.100; 201.115; 201.128. In addition, the journal

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Potential for Wrong Route Errors with Exparel

There is a dangerous potential for errors in the administration of two "look-alike" medications that are or will be common in anesthesia practice in this country: propofol and the new liposomal bupivacaine suspension Exparel, *not meant for IV administration*. Both are milky white suspensions, and because propofol has been the only such medication for many years, a real potential for error exists.

Exparel is a local anesthetic that is infiltrated into a surgical wound during a surgical procedure to produce postsurgical analgesia. It is not intended for systemic use. When prepared in syringes, these products essentially look identical. If Exparel is accidentally administered intravenously instead of propofol, *toxic blood concentrations might result, and cardiac conductivity and excitability may be depressed, which may lead to atrioventricular block, ventricular arrhythmias, and cardiac arrest.*

Propofol is used as an anesthetic during surgical procedures and as a sedative during procedures or for patients undergoing mechanical ventilation. Thus, Exparel and propofol may be used in similar healthcare settings.



Exparel



Conclusions:

Sources of Postoperative Pain

Acute nociceptive pain from incision

Musculoskeletal pain from abnormal body positioning and immobility during and after surgery

Neuropathic pain from excessive stretching or direct trauma to peripheral nerves.

Conclusions:

Not all patients are the same

Not all patients process and perceive pain the same way

Pain is unique

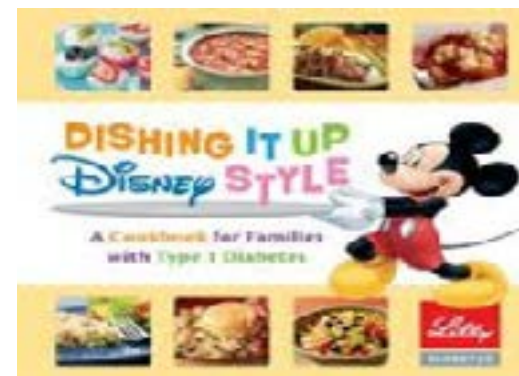
Opioids are not always the best choice

Not all patient react the same way

Don't be a cook book provider....

Opioids are the only group with no ceiling

All others have ceilings for use



Additional Thoughts?

Anti-depressants



Selective Serotonin reuptake inhibitors

◇ (Celexa, Luvox, Prozac, Paxil)

Serotonin norepinephrine reuptake inhibitors

◇ (Cymbalta, Effexor)

**The important part of this is continuing
therapy through perioperative period!**

Pain and Pain Management

This is a evolving field, this is only the tip of the iceberg. Keep learning.





Can I be excused?
... my brain is full !

Questions

Thank you!

Email me for the articles:
pstrube3000@yahoo.com

