My Approach to Minimizing Pain in Ambulatory Shoulder Surgery

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Pain

- Pain is an “unpleasant sensory and emotional experience associated with actual tissue damage”

- Acute Pain: Commonly after surgery

- Chronic Pain: > 3 months
Pain begins with injury, but…

Minimize pain with pre-emptive, multimodal approach

Day of Surgery – Holding area

- Pregabalin 100 mg PO
- Celecoxib 400 mg PO
- Acetaminophen 1000 mg IV
- Scopolamine Patch
Interscalene Block

• Preemptive analgesia
• Avoid general anesthesia in many cases
• Active mobilization of a joint by the patient at the request of the surgeon
• Postoperative analgesia (hours to days)
• Reduced narcotic usage with lower incidence of side effects
• Reduced PO Nausea/Vomiting
• Early discharge

Ultrasound Guided Technique BETTER than Electrical Stimulation
Prevent Nausea

(*most common reason = Narcotic use*)

Ondansetron 4 mg
Ketorolac 30 mg
Dexamethasone 8 mg
Plenty of IV Fluids
  – Foley catheter
Postoperative

Oxycodone/Acetaminophen 5mg/325mg
1 tab PO q6h till block wears off

After block:
- Pain 1-5: 5mg PO q6h
- Pain 6-10: 10mg PO q6h

Celecoxib 200 mg qD
Pregabalin 50 mg BID
Zolpidem 10 mg qhs prn

Shoulder Replacement or Open Cuff:
- ASA 325mg bid start day of surgery
- Enoxaparin or Warfarin
Discharge Medications

Oxycodone/Acetaminophen 5/325
  – 1-2 tab PO q6h #60

Meloxicam 15mg
  – 1 tab PO qD #30

Pregabalin 50mg
  – 1 tab PO BID #28

Metoclopramide 10 mg
  – 1 tab PO q8h prn nausea

Docusate sodium/sennosides
  – 2 tabs BID till normal BM

Aspirin EC
  – 1 tab PO BID #42

NO Refills
Biochemical Response to Surgery

Early Events

- AMPA
- NMDA
- SP, CGRP, NKA
- Ca\(^{2+}\), NO, PKC, PG
- c-fos

Late Events

- VIP
- Growth factors
- Dynorphin
- Neuropeptide
- Galanin
- Cholecystokinin
- ? Cell Death?

Stimulus

Dorsal horn sprouting/remodeling 1 hr
Surgery

Primary Afferent Nerve Fiber

A-fiber Connections

Axon Sprout

Microglial Cells

Synaptic Removal

Interneuron Cell Death

PG, NO

NOS

NO

Arachidonic Acid

COX-2

PGE$_2$, PGI$_2$

NMDA

Mg$^{2+}$

Glu

Glu

sP

NO,
PG

PG

PG

PG

PG

Inflammation

Hyperexcitability

Toxicity?

Spinal Sensory Neuron

Genome Activation, RNA and Protein Synthesis, Hyperexcitability, Toxicity

2nd Messengers, (PKC, cGMP)

Nitric Oxide

PG, NO

NO

Hyperexcitability

Toxicity?
Multimodal Analgesia

- **Definition**: Combination of different analgesics that act by different mechanism, resulting in additive or synergistic analgesia with lowered adverse effects; compared to sole administration of an individual pharmacological agent

- **Goal**: Decrease use of Postoperative Opioids

Respiratory Depression (RD)

- Most feared opioid side effect (by anesthesiologist)
- Decreased sensitivity of chemo-receptors in medulla to CO₂
- RD is reduced by pain
- Decreased rate, tidal volume, or both
- High CO₂ levels produce narcosis!
- Closed head injuries, increased CSF pressure
- BEWARE of THE SEDATED/OBTUNDED PATIENT = impending respiratory arrest
Opioids and Respiratory Depression

- Opioids are known to inhibit the ventilatory response to both hypoxia and hypercapnia
  - Opioids can exacerbate OSA causing hypoxia
- Opioid induced apnea is observed with remifentanil infusion in volunteers with OSA but appears to be CSA!\(^1\)
- Up to 50% of long term opioid dependent patients will have CSA\(^2\)
  - Opioids suppress REM sleep

Obstructive Sleep Apnea

- Recurrent complete or subtotal airway obstruction during sleep despite intact respiratory effort\(^1\)
- 2 - 4\% incidence and rising\(^1\)
- OSA may coexist with central sleep apnea (CSA) – Complex Sleep Apnea (CompSA)\(^2\)
  - 6.5\% of OSA on CPAP had CSA
- Majority of OSA is undiagnosed 80-90\%\(^3\)
  - *Many at-risk patients are NOT* obese!

A Multimodal Approach to Better Address Complex Nature of Pain Transmission

Inhibition:
- Norepinephrine-serotonin
- Dopamine
- Opioids
- GABA
- Cannabinoids
- Adenosine

Ascending (facilitation)
- Substance P
- Glutamate
- Nerve Growth factor (NGF)
Multimodal Analgesics for Postoperative Pain

Ketamine, Dextromethorphan, Memantidine
Clonidine, Dexmedetomidine, Gabapentin, Pregabalin,
COX-1 & 2 inhibitors, Acetaminophen, Tapentadol

Ketamine, Dextromethorphan, Magnesium, Celecoxib, Clonidine,
Dexmedetomidine, Gabapentin, Pregabalin, Neostigmine, Local
anesthetics, COX-1 and COX-2 inhibitors, Tapentadol

Clonidine, Steroids, Neostigmine, local anesthetics

Local Anesthetics,
COX-1 &2 inhibitor

Tissue

NGF
Surgical Pain and Central Sensitization

- Incisional pain is associated with secondary punctate hyperalgesia that is ketamine sensitive with no spread in thermal sensitivity indicating induction of central sensitization.

- As such the postoperative analgesia needs to be continued until surgical healing is well established.

Woolf C: Pain 2011
Persistent Postsurgical Pain after TKR: 15% Incidence*

<table>
<thead>
<tr>
<th>Year</th>
<th># of TKR cases/year</th>
<th># of patients with PPP</th>
</tr>
</thead>
<tbody>
<tr>
<td>2008</td>
<td>0.5 Million</td>
<td>75,000</td>
</tr>
<tr>
<td>2030</td>
<td>3.48 Million</td>
<td>522,000</td>
</tr>
</tbody>
</table>

HUCPNet: National Statistics 2009 (web)
Local Anesthetic Infiltration for Orthopedic Surgery

- Local anesthetic continuous infusion has been shown to be beneficial in > 4000 patients.

- However, the question remains:
  - What is the optimal concentration?
  - Where should the catheter be placed – deep muscle layers?
  - Cartilage injury with local anesthetics?
14 clinical trials for TKA:
- Relative small sample size (n < 100), non-RCT
- ↓ pain scores in the immediate postop period
- No long term benefit
- The role of continuous catheters needs to be examined

6 clinical trials for THA:
- Not uniform to make conclusion
- When oral multimodal analgesia is used, probably local anesthetic infiltration does not add any benefit
- No difference in hospital discharge time

Acta Anaesthesiol Scand 2011
Facts: Regional Analgesia & Surgery

- Peripheral regional nerve blocks are superior to parental opioids for postoperative pain.
- Continuous catheters if indicated will facilitate long-term improvement.
- Neuroaxial analgesia is superior to GA for postoperative pain control with improved outcomes.
- Recent meta-analysis of patients undergoing TKA with femoral nerve block has been demonstrated to be superior to IV PCA in 23 RCT.

Paul JE et al: Anesthesiology, October 2010

Hanna MN et al: Curr Opin Anaesthesiol 2009
RCT: 2 groups, n=40

- Group 1: Interscalene block + 0.5% ropivacaine IA infusion 2ml/hr for 48 h
- Group 2: Interscalene block + saline IA infusion 2 ml/hr

Outcome: ↓ Pain scores in ropivacaine IA group

Conclusion: Simple to place- an epidural catheter with multi-orifice catheter and hooked to a disposable pump.
Efficacy of interscalene block combined with multimodal pain control for postoperative analgesia after rotator cuff repair

Cho CH, Song KS, Min BW, Jung GH, Lee YK, Shin HK

- Reduced pain
- Reduced Narcotic use
- Reduced adverse events
- No complications related to block
- Randomized study, 2 groups of 30 (with and without block)
Ultrasound advantages

- Better results
- Less time to perform
- Ability to place catheter effectively and efficiently
- Better visualization of nerves, arteries, veins
- Allows multiple injections
- Reduces volume needed
- Visualize spread
- Less risk to patients
General Contraindications to Peripheral Nerve Blocks

**Absolute contraindications:**
- Patient refusal
- Infection at the injection site
- A true allergy to local anesthetics
- Inability to guarantee sterile equipment
- High risk of local anesthetic toxicity (bilateral axillary block; or repeat one)

**Relative contraindications:**
- Combative, and/or demented patients.
- Pediatric patients (most blocks are placed after general anesthesia)
- Bleeding disorder/Coagulation disorder
- Pre-existing peripheral nerve neuropathies may increase the risk for permanent nerve damage (Careful documentation of sensory and motor deficits should occur prior to the initiation of a peripheral nerve block)
Mechanism of Peripheral Nerve Blocks

- Local anesthetics
  - block the generation and conduction of nerve impulses at the level of the cell membrane
  - bind directly within the intracellular portion of the voltage gated sodium channels in their ionized form when the channels are open
Potential Risks of All Peripheral Nerve Blocks

- Local Anesthetic Toxicity
  - Cardiac
  - Neurologic
  - Allergy
- Pain and Hematoma at puncture site
- Discomfort
- Risk of block failure or incomplete block
- Misevaluation of or changes in the surgical requirement
- Potential increased risk of permanent or transient nerve damage
Indications for Upper Extremity Blocks

- Shoulder Surgery
- Surgery above the elbow
- Elbow and forearm surgery
- Hand and wrist surgery
Interscalene Nerve Block
Interscalene U/S Anatomy
Ultrasound-guided Interscalene Technique
Benefits to the Patient

- Peripheral block lasts 12-36 hours as a single shot
- Reduced risk of nausea and vomiting and sedation
- Earlier ability to leave surgery center
- Early intake of food and drink
- Excellent pain control
- Lighter general anesthetic with speedier recovery from the anesthetic
- Less chance of an overnight stay at the hospital
Patient Instructions

• After leaving surgery center, extremely important that patients take regular painkillers at prescribed times from the moment the block begins to wear off.

• Necessary to avoid unpleasant pain when nerve block wears off (which can be in the middle of the night, may want to take prescribed pain meds before going to bed).

• Should carry “numb” arm in arm sling until normal sensation and motor function return and/or until physician instructs to stop wearing the immobilizer.

• Should take caution to not come in contact with extremely hot or cold items because lack of sensation will result in inability to protect oneself from injuries of extreme temperature.
Multimodal Analgesics for Postoperative Pain

- Ketamine, Dextromethorphan, Memantine, Gabapentin, Pregabalin, **COX-1 & 2 inhibitors**, Acetaminophen

- Ketamine, Dextromethorphan, Magnesium, Clonidine, Dexmedetomidine, Gabapentin, Pregabalin, Neostigmine, Local anesthetics, **COX-1 and COX-2 inhibitors**, Tapentadol

- Clonidine, Steroids, Neostigmine, local anesthetics

- Clonidine, Local Anesthetics, **COX-1 & 2 inhibitors**
Nonsteroidal Anti-Inflammatory (NSAID), COX-2 Inhibitors & Acetaminophen
Meta-analyses of NSAIDs, COX-2 inhibitors and Acetaminophen

52 RCT were included:

Results:

- 24 h morphine consumption: ↓ 20 - 40 %
- Postoperative VAS: ↓ 10-15 %
- Opioid related AE: ↓ 15 – 25 %

Adverse events:

- Severe bleeding: 0 to 1.7%
- Renal insufficiency in cardiac patients: 0 % to 1.4%

Paracetamol and selective and non-selective non-steroidal anti-inflammatory drugs for the reduction in morphine-related side-effects after major surgery: a systematic review

E. Maund*, C. McDaid, S. Rice, K. Wright, B. Jenkins and N. Woolacott

- 60 trials were included
- All patients received PCA morphine
- All surgical procedures were considered
- Primary outcome:
  - 24 hour morphine consumption
- Adverse effects:
  - 2.4% of NSAID surgical bleeding vs 0.4% for placebo

NOTE: Paracetamol = Acetaminophen
### NSAIDs, COX-2 inhibitor & Acetaminophen

<table>
<thead>
<tr>
<th></th>
<th>Morphine consumption</th>
<th>PONV (odds ratio)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acetaminophen vs Placebo</td>
<td>- 8.68 mg</td>
<td>1.0</td>
</tr>
<tr>
<td>NSAIDs vs Placebo</td>
<td>- 9.45 mg</td>
<td>0.7</td>
</tr>
<tr>
<td>COX-2 vs Placebo</td>
<td>- 10.67 mg</td>
<td>0.8</td>
</tr>
<tr>
<td>NSAIDs vs Acetaminophen</td>
<td>- 0.77 mg</td>
<td>0.7</td>
</tr>
<tr>
<td>COX-2 vs Acetaminophen</td>
<td>- 1.99 mg</td>
<td>0.9</td>
</tr>
<tr>
<td>COX-2 vs NSAIDs</td>
<td>- 1.22 mg</td>
<td>1.2</td>
</tr>
</tbody>
</table>

Negative for morphine consumption means study drug better than control
Odds ratio < 1 intervention better than control
NSAIDs and Spinal Fusion

- Prostaglandins play an integral role in bone healing

- Limited use of NSAIDs for 48 hrs (n=228) demonstrated no difference in non-union
  Pradhan BB et al: Spine 2008; 33: 2079-2082

- 5 retrospective studies n=1403 (Meta-Analysis)
  - Non-union rate:
    - NSAID group: 12.9% (P=0.0008)
    - Non-NSAID: 5.2%

  Li Q et al: Spine 2011; 36: E461-468
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Ketamine, Dextromethorphan, Memantidine, Clonidine, Dexmedetomidine, Gabapentin, Pregabalin, COX-1 & 2 inhibitors, Acetaminophen

Ketamine, Dextromethorphan, Magnesium, Celecoxib, Clonidine, Dexmedetomidine, Gabapentin, Pregabalin, Neostigmine, Local anesthetics, COX-1 and COX-2 inhibitors, Tapentadol

Clonidine, Steroids, Neostigmine, local anesthetics
# Gabapentoids for Perioperative Pain

<table>
<thead>
<tr>
<th>Drug</th>
<th>Route of Administration</th>
<th>Efficacy</th>
<th>Side effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gabapentin</td>
<td>Oral</td>
<td>++</td>
<td>sedation</td>
</tr>
<tr>
<td>Pregabalin</td>
<td>Oral</td>
<td>++</td>
<td>sedation</td>
</tr>
</tbody>
</table>
12 RCT of 896 patients

Dose of gabapentin: 300 – 1200 mg

Outcome:
- ↓ Pain scores at 24 hours
- ↓ Opioid use in the postoperative period
- ↑ Sedation in the postoperative period
- No difference in serous adverse events

Similar results in a review of gabapentinoids in 2007 by Elina Tiippana et al from Finland published in Anesth & Analg
Mechanism of Analgesia

- Gabapentin and Pregabalin bind to the alpha-2-delta sub-unit of the N-type voltage gated calcium channel
  - Same mechanism of action whether it is neuropathic pain or inflammatory pain (post-surgical)

- This binding results in ↓ release of
  - Substance P, Calcitonin Gene-related peptide
  - Glutamate

- Little effect on normal neuronal tissue, but only effective in sensitized neuronal tissue
TKA and Chronic Persistent Pain of the Knee

- A survey of 7,230 patients in the UK
- 81.8% satisfied with TKA
- The common complaints:
  - Difficulty with kneeling: 57%
  - Persistent pain: 19.8% (2\textsuperscript{nd} most)
  - Pain on walking: 16.6%

Baker PN et al: JBJS 2007; 89: 893
Current Multi-Center Trial: Chronic Pain after Orthopedic Surgery

- 3 Centers with large volume
  - Rush University at Chicago
  - Hospital for Special Surgery (HSS) at New York
  - Mass General Hospital (MGH) at Boston

- TKA and THA and one Year Follow-up
- N= 665 for TKA

- Chronic pain at one year: 17.8%

- Predictor: Acute postoperative pain
  - NRS= 7.1 for patients that developed chronic pain
  - NRS= <4 for patients that did not develop chronic pain
Why do patients develop Chronic Pain after Surgery? And Prevention Strategy

1. On going inflammatory process from surgery
   - **Strategy to Prevent:** Aggressive Multimodal Analgesia

2. Surgical injury or irritation to peripheral nerves: Leads to chronic neuropathic pain
   - **Strategy to Prevent:** Education of our surgical colleagues of the incidence so that less invasive or meticulous surgical techniques
Why do patients develop Chronic Pain after Surgery?

- Patient genetic make up or pre-operative factors such as preoperative chronic pain and opioid use:

- **Prevention**: With greater understanding of genetics and pain, may be in the future, we will be able to predict the patients who will develop chronic pain from gene isolation preop
Recently Approved drugs: Multimodal Analgesia
Injectable Acetaminophen

- Until recently, there has not been an IV acetaminophen b/c of it is poor solubility in water and not stable in solution.

- The IV form is *Superior* in opioid sparing compared to the oral.

- Approved for use in the US 2010, widely used in Europe for 20 years
Acetaminophen: Mechanisms of Action

- Exact mechanism of action still unclear\(^1\)
- Analgesic effect
  - Inhibits the synthesis of prostaglandins in the CNS (central acting) and peripherally blocks pain impulse generation\(^2\)
  - Unlike NSAIDs, not a strong peripheral COX inhibitor\(^1\)
  - Proposed serotonergic (5-HT) mechanism\(^3\)
- Antipyretic effect\(^2\)
  - Inhibition of hypothalmic heat-regulating center
  - No anti-inflammatory effects

Multimodal Therapy for Patient undergoing surgery

- COX-2 Inhibitor/NSAIDs
- Opioids
- Steroids
- Anti-convulsants
- Regional Analgesia
- NMDA Blocker
- Acetaminophen
- Alpha-2 agonist
Emerging Drugs that can be Used for Multimodal Analgesia
Depo-Bupivacaine

- Microscopic spherical particles composed of internal aqueous chambers containing an active drug ingredient
- Each chamber is separated from adjacent chambers by lipid membranes
- DepoFoam particles release drug over an extended period by erosion and/or reorganization of the particles’ lipid membranes
- Release rates determined by relative amounts of lipids
Procedure specific Consensus for TKA

- PROSPECT working study group on various surgeries
- 112 RCT trials examined for postop analgesic
- Evidence was graded depending on study
- **Grade A:**
  - Use of NSAIDs and COX-2 inhibitors
  - Femoral Nerve block, Spinal anesthetic
  - Strong opioids
- **Grade B:**
  - IV acetaminophen
  - Compression and cooling devices
- Others:
  - IA injections with local anesthetics

Practical Clinical Protocols that can be implemented for Orthopedic surgery

Preop:

- D/C NSAIDs 3-7 days preop
- Celecoxib 400 mg, acetaminophen 1-2 grams: 1-2 hours before surgery
- Pregabalin 75-100 mg
- Anti-emetic: scopolamine patch
- Preop hydration with IVF
Practical Clinical Protocols that can be implemented for Orthopedic surgery

- **Intraop:**
  - Regional anesthesia with clonidine and avoid narcotics (none)
  - IV ketamine with propofol mixed
  - Keep patient warm – normothermia: Bier huger, fluid warmer
  - Anti-emetic: Dexamethasone, Ondansetron (at the end)
Practical Clinical Protocols that can be implemented for Orthopedic surgery

Postop: day 1:
- Continue the regional analgesia
- Celecoxib 200 mg q 12h
- Pregabalin 50-75 mg q 12 h
- Cryotherapy
- Acetaminophen 1 gram

Postop: day 2:
- Stop the regional analgesia and start oral oxycodone or hydrocodone. If oxycodone continue with acetaminophen
- Celecoxib 200 mg q 12h, Pregabalin 50 mg q 12 h
- Cryotherapy
Practical Clinical Protocols for Orthopedic surgery

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- Cryotherapy
Practical Clinical Protocols for MIS Spine

- Starts in surgeon’s office at the time of scheduling surgery

- Multidisciplinary approach
  - All medical disciplines involved will be introduced to the patient

- Multimodal Approach
  - NSAID/ COX-2 Inhibitor + Sustained Release Opioid
    - Celecoxib prior to surgery: (Short-term study (n=1403) revealed normal-dose was safe, but high dose had increased risk of nonunion. Therefore NSAIDs/ COX-2 inhibitors are not recommended for Fusion patients)
    - Sustained Release Oxycodone 10-20mg bid

Surgeon’s Role

- Liberal use of Local Anesthetic
  - 1% lidocaine + Epinephrine prior to incision
  - Deeper Tissues
    - 0.25% Bupivacaine or 0.2% Ropivacaine
    - Care must be taken not to spread to nerve roots at the end of procedure

- At Closure
  - Ropivacaine infiltration and catheter placement for 24-48 hours
    - Ropivacaine 0.5% 30-40 mL in muscle and SQ tissues
    - RCT shown decreased post-op opioid consumption
    - May be good for MIS Fusion patients
Implementation of Protocols

- Is complex, messy and demanding
- Multidisciplinary collaboration and discussion:
  - Understanding the culture of the environment
  - All involved: Physicians, nurses, all health care providers involved with the patient such as PT, blood draws, environmental services etc.

- Motivating factors for change:
  - Monitoring your hospital against national standards
Effectiveness of multimodal Pain Management Protocol in TKA

- 2009 (control) with no multimodal (n=45) compared to 2010 with multimodal (n-66)
- Full team approach care to TKA
- Results:
  - ↓ length of stay in hospital by: 0.5 days
  - ↓ length of stay in PACU

Frame work for Implementation of Protocols

Practice Development (professional consensus)

Research (robust evidence)

Quality improvement work (Strong leadership to facilitate change)

Successful Implementation
Implementation tools

- **Culture** defined as: “How things are done around here”
  - These are from values embedded within the organization

- **Leadership:**
  - More of transformational or facilitative style
  - Inspire and challenge staff to achieve shared value

- **Facilitation:** ‘a technique by which one person makes things easier for others”
37 matched case records for MIS + multimodal analgesia

Multimodal Group: Preop: oxycodone + COX-2 inhibitor and then postop acetaminophen, oxycodone, regional analgesia, NSAIDs - vs prior to instituting protocol (control group)

<table>
<thead>
<tr>
<th></th>
<th>Multimodal</th>
<th>Control</th>
<th>Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medicare A (total)</td>
<td>$9,763</td>
<td>$13,895</td>
<td>$4,132 *</td>
</tr>
<tr>
<td>Room &amp; board</td>
<td>$2,679</td>
<td>$4,317</td>
<td>$1,638 *</td>
</tr>
<tr>
<td>Medicare B (total)</td>
<td>$2,053</td>
<td>$2,502</td>
<td>$449</td>
</tr>
<tr>
<td>Overall total</td>
<td>$11,816</td>
<td>$16,398</td>
<td>$4,582 *</td>
</tr>
</tbody>
</table>

With 500,000 case/year = cost savings will be in millions

10 year experience with an Multimodal Implemented Pathway in a University Hospital

- Form a pathway committee with regular monthly meetings with 2-3 goals for each session
- Members for committee from ALL specialties
- Everyone has an EQUAL voice to express their opinion
- Implement one strategy over the next 3 months and re-assess.
- Examine the outcomes every 3-6 months and patients
Hospital Care Quality Information from the Consumer Perspective (HCAHPS) for Rush University, Chicago, IL—Orthopedics

<table>
<thead>
<tr>
<th></th>
<th>FY 2010</th>
<th>FY 2011</th>
<th>FY 2012</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Joints</td>
<td>74%</td>
<td>77%</td>
<td>81%</td>
</tr>
<tr>
<td>Spine</td>
<td>64%</td>
<td>68%</td>
<td>71%</td>
</tr>
</tbody>
</table>

As of Jan 2012: 76% = 90% percentile
Thank you for giving us the opportunity to care for you.

The Pain Service cares about your comfort and well being. We want your pain to be as well controlled as possible.

We will continue to work with you and your care team to manage your pain. If you are experiencing pain, please tell your nurse, who is in contact with the Pain Service, so that we can look at other alternatives to manage your pain and maintain your comfort.

Sincerely,
Pain Service Team*
Conclusion

- Adequate preparation should be carried out to treat postoperative pain
- Multimodel approach to postoperative pain should be undertaken
Thank you!