Implementing the Use of Non-Opioid Medications for Treating Pain in the Hospital Setting

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Conflict of Interest Disclosure

• Author’s conflicts of interest:
  • Sharon Wrona, no conflict of interest
  • Lauren Renner, no conflict of interest

Educational Objectives

At the conclusion of this activity participants should be able to:
• Identify the role of gabapentin, lidocaine and ketamine for managing acute pain.
• Identify how the implementation was made possible
• Identify examples of how these non-opioid analgesics have been utilized in certain pediatric patient populations, procedures, and medical conditions will be described.
Gabapentin

• Gabapentin is an anticonvulsant
  • Used to treat seizures and as an adjunct in the treatment of neuropathic pain
  • In 2017 it was the 11th most commonly prescribed medication in the US

Gabapentin Mechanism of Action

Gabapentinoids inhibit neurotransmission of gamma-aminobutyric acid (GABA) and acts as a Ca channel blocker

Gabapentin

• Gabapentin dosing
  • 2-5 mg/kg/dose up to TID dosing
  • Comes in liquid, capsules and tablets at higher strengths
  • Consider renal impaired dosing and concurrent use with other sedating medications
  • Common S.E. sleepiness, memory/concentration issues, and dizziness
  • Can cause increased risk for SI, aggressive behavior
  • Risk for misuse and abuse
  • Especially in individuals with hx psychiatric disorders or substance use disorders

http://online.Lexi.com
Gabapentin

Implementation of pre-operative gabapentin for limb salvage and amputation patients:

• AIM of this project was to improve the level of functioning for patients undergoing limb salvage procedures by 6 months post-operative
• Other goals were to decrease post operative pain and opioid use in these patients

Multidisciplinary Team Approach

• Medical
• Oncology
• Pain Team
• Nursing
• Psychology
• Physical Therapy
• Massage
• Child Life
Limb Salvage QI – Aim & Key Drivers

**Specific Aim**

Improve the recovery of function of the affected limb back from 0% to 100% of baseline prior to disease at 6 months after the end of chemotherapy treatment in cancer patients undergoing limb salvage procedure.

**Key Drivers (WHAT)**

- Improve pain management
- Reduce opioid use
- Improve recovery of function of affected limb

**Overall Strategic Goal**

Multidisciplinary, individualized, coordinated care

**Multidisciplinary**

- Oncology
- Pain Team
- Orthopedics
- PT
- Massage
- Psychology

**Gabapentin Protocol**

- Gabapentin was started 10 days prior to surgery and then titrated up until the day of surgery

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<thead>
<tr>
<th>Dosage</th>
<th>Start</th>
<th>Titrate</th>
<th>End</th>
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<tbody>
<tr>
<td>900 mg/d</td>
<td>10 days</td>
<td>Day of surgery</td>
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Gabapentin Protocol

• All patients get a pain team consult, PT, massage and psychology consults when they are admitted for chemo or surgery.
• During surgery they will likely have regional anesthesia unless contraindicated.
• Neurontin dose escalated day of surgery
• They will be discharged on gabapentin and a PRN oral opioid
• Rarely on long acting opioid
• Gabapentin will be weaned off prior to gabapentin
• These gabapentin will be appropriate
• Typically 3-4 months post operative.

Gabapentin Protocol

Patients are seen by the APS APRN during outpatient and inpatient admissions
We see roughly 13 pediatric limb salvage patients per year

Supporting literature

A meta-analysis of the preoperative use of gabapentinoids for the treatment of acute postoperative pain following spinal surgery
Bo Liu, MD, Ruihe Liu, MD, and Lifeng Wang, MD
Ketamine

- Ketamine is a fast acting N-methyl-D-aspartate (NMDA) receptor antagonist
- In lower doses ketamine is a powerful analgesic
- Can prevent the development of pain sensitivity and opioid tolerance

Ketamine mediates pain at the dorsal horn of the spinal cord.

A variety of drugs act at different anatomic locations along the pain signaling pathway. Ketamine modulates pain at the dorsal horn of the spinal cord.

https://www.researchgate.net/publication/302915005_Intravenous_sub-anesthetic_ketamine_for_perioperative_analgesia
Molecular action of Ketamine

- Mixture of both anti- and pro-nociceptive actions
- Supraspinal blockade of the NR2B NMDA sub-unit
- Direct effect on delta opioid receptor
- Acts to augment opioid mu-receptor function
- May be attributable to a reduction in NMDA-mediated "wind-up"


How we started the journey – Literature Review

Clinical trials mostly in adults report up to 30% reduction in opioid requirement when used for post-operative pain management

Typically used as part of a multimodal regimen for severe pain

Situations in which low dose ketamine may be of benefit:
- Suspected or potential opioid induced hyperalgesia
- Acute pain in patients on chronic high dose opioids
- Post operative pain management
- Neuropathic pain resistant to standard treatments
- Patients with cancer and chronic opioid requirements
- As a component of palliative or end of life care for analgesia
- Burn patients on high dose opioids
Finding out what others are doing
Pediatric pain list serve responded with 15 pediatric institution protocols

Ketamine

Nationwide Children’s Hospital Protocol
- Started process in 2013
- Organized a group of key stakeholders
  - Nursing leadership
  - Anesthesia Pain Team & Palliative Care physician
  - PICU team – MD, fellow, nursing
  - Nurse manager and Nurse educator
  - Pharmacy – Pharm D, leadership, and IS QI
  - QI Team
  - Professional Development
- Verified with the Ohio Board of Nursing – RNs are allowed to administer ketamine for analgesic purposes only (not for sedation)

Ketamine Protocol
- Analgesic dosing
  - Continuous infusion:
    - 0.025-0.1 mg/kg/hr recommended starting dose
    - 0.025-0.4 mg/kg/hr dosing range
  - Higher doses are more likely to produce side effects
  - 40 mg/hr max suggested dose non palliative care patients
  - Infusions for > 5 days may require slow taper
Ketamine Protocol

• Side effects
  • Minimal side effects with low doses
  • Fatigue, drowsiness, vivid dreams, misperceptions or confusion, feeling of inebriation or hallucinations
    • Dysphoria or hallucinations-reduce dose of ketamine and give a benzodiazepine
  • Excessive oral secretions
    • Glycopyrrolate

Ketamine infusion monitoring

<table>
<thead>
<tr>
<th>Frequency</th>
<th>Monitor</th>
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<tbody>
<tr>
<td>Baseline</td>
<td>Baseline assessment RR, HR, sedation level, O2 Saturation, and pain</td>
</tr>
<tr>
<td>Start of infusion</td>
<td>Every 30 minutes: RR, Every 2 hours: X2 hours, then Every 4 hours and PRN</td>
</tr>
<tr>
<td>Change in dose or patient status</td>
<td>Every 30 minutes: RR</td>
</tr>
<tr>
<td>Routine</td>
<td>Continuous Pulse Oximetry (O2 saturation)</td>
</tr>
<tr>
<td>Routine</td>
<td>Every 2 hours Sedation level Infusion documentation in EPIC</td>
</tr>
<tr>
<td>Routine</td>
<td>Every 4 hours HR, BP and Pain Assessment</td>
</tr>
</tbody>
</table>

Implementation/Education

EPIC order set was created
EPIC nursing documentation
Nursing education Mandatory learning center module was created
Ketamine

- Nationwide Children's Hospital Protocol
- Implemented in 2014
- Patients with low dose ketamine will be managed by the Acute Pain Service or Palliative Care Service
- The infusion is locked in a PCA pump
- RNs must have completed the IV opioids/hypnotic/sedative class to administer low dose ketamine

Response

- Low dose ketamine drips for analgesia are commonly used at Nationwide Children’s Hospital as an adjunct for pain control – 357 encounter and 265 unique patients
- Sickle Cell Pain
- Intra operative pain management
- Post operative pain management
- Chronic pain and end of life management
- RNs and other staff have been receptive to the implementation of the protocol
- Patients with severe pain have benefited from the use of low dose ketamine as a modality
- Currently conducting IRB retrospective review for future publication

Lidocaine for Acute and Chronic pain

Lidocaine is a local anesthetic that blocks both initiation and conduction of nerve impulses by decreasing ionic flux through the neuronal membrane by blocking Na channels.
Role of lidocaine with central sensitization

First try 2015

How we started the journey: take 2
A thorough literature review was completed and reviewed by the group.

- **Lidocaine workgroup**
  - Multidisciplinary group met to develop the protocol. The disciplines include:
    - Pharmacy
    - Heme/Onc nursing leadership and educators
    - Pain service
    - Anesthesia
  - The workgroup reviewed protocols from other institutions including St. Jude, St. Louis Children's, Children's Mercy

- **Lidocaine for acute and chronic pain**
  - IV lidocaine hydrochloride is useful when administered systemically for pain resistant to standard therapies
  - This protocol does not apply to lidocaine for cardiac arrhythmias
  - Examples of circumstances where IV lidocaine may be used:
    - Intractable neuropathic pain
    - Chronic pain not responsive to multiple other therapies
    - Suspected or potential opioid induced hyperalgesia
    - Pain resistant to standard treatments
    - Patients with cancer and chronic opioid requirements
    - As a component of palliative or end of life care for analgesia
**Lidocaine**

- IV Lidocaine is used as a part of a multimodal regimen for severe pain.
- IV Lidocaine infusion for pain control will be managed by the Pain or AIM (Advanced Illness Management) service.

**Dosing**

- Infusions may be prescribed at a rate range of 1-3mg/kg/hr. (max 3mg/kg/hr. or 200 mg/hr.)
- The duration of infusion will vary depending on the indication.
- Loading doses may be administered if indicated.
- Dose recommendation is 2mg/kg (max of 300mg).

**Contraindications**

- History of cardiac arrhythmia
- Seizure
- Heart failure
- Electrolyte disturbances
- Hepatic failure
- Known sensitivity to lidocaine

- The protocol was first used on the Hematology/Oncology inpatient unit and infusion clinic.
- Started March 2020.
- Started using this protocol hospital-wide 9/2020.
- As of 4/21/2021 have used this modality 71 times on 49 different patients.
Monitoring

- Patient will have a baseline ECG (within 30 days of initial administration)
- Follow up ECG as needed
- During infusion
  - Patient will be on a continuous pulse oximetry monitor
  - Vital signs (BP/HR/RR), sedation/LOC, pain assessment
  - At initiation of the infusion
  - 30 min after initiation
  - 1 hr. after initiation
  - 2 hrs. after initiation
  - Every 4 hrs. for the remainder of the infusion
  - If an increase in dose or bolus is given, then Vitals every 30 min x 2 then resume previous vital sign monitoring
- End of infusion
  - Vital signs at discontinuation and then 2 hrs. post discontinuation
  - Pulse oximetry monitoring can be discontinued 2hrs post lidocaine infusion discontinuation

Nursing Education

1. Education will include:
   - Indications and benefits of lidocaine for analgesia
   - Common dosage ranges
   - Potential adverse effects

2. Education will be provided in the IV opioid/sedative/hypnotic course for incoming RNs

3. RNs will need to complete The Learning Center module
Technology Updates

- Infusion pump library changes
  - Lidocaine for arrhythmia vs. analgesia
- Epic
  - Order set build
  - Flowsheet build
  - Update Lexicomp for use for analgesia

Case Study
Gabapentin w/ Spinal Fusion

16yr M
52.1kg
H/o scoliosis and autism
S/p T4-L2 spinal fusion
Pre-op:
- 600 mg PO gabapentin
POD0:
- 800mg IV acetaminophen q6h
- 15mg ketorolac q6h
- 300mg PO gabapentin TID
- 2mg PO diazepam q6h prn
- naloxone gtt 0.25mcg/kg/hr.
- hydromorphone NCA 0.2mg/dose every 12 minutes
### Gabapentin for Post Op Analgesia Case Study

**POD 0**
- Lumbar epidural placed
- 0.2% ropivacaine and clonidine 1 mcg/ml IV

**POD 1**
- Acetaminophen 650mg PO Q6H
- Gabapentin 300mg PO TID
- Ketorolac 2mg/kg/hr IV
- Oxycodone 5mg PO q4HR
- Hydromorphone 0.2mg 1Q2H PRN

**POD 2**
- Acetaminophen 650 mg PO q6 hrs.
- Gabapentin 300mg PO TID
- Ketorolac 2mg/kg/hr IV transitioned to ibuprofen after 8 doses of ketorolac
- Naloxone gtt 0.25 mcg/kg/hr.
- Hydromorphone NCA 0/0.2 mg q12min
- Add oxycodone 5 mg PO q4 HR

**POD 3**
- D/C Naloxone gtt
- D/C hydromorphone NCA

**POD 4**
- Pain well controlled
- Epidural removed at 4/15
- No PRN opioids needed

**POD 5**
- Pain well controlled
- No PRN opioids needed
- Epidural removed
- Increased gabapentin to 300 mg TID

**POD 6**
- Pain well controlled on oral oxycodone

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**Case Study: Gabapentin w/ Spinal Fusion**

- **9 yr. old M**
- **39.1kg**
- **H/o R distal femur osteosarcoma**
- Admitted for total knee reconstruction with oncologic distal femur replacement
  - **Day of surgery 5/10/20**
Gabapentin for post op analgesia

• Further gabapentin weaning in oncology clinic

Ketamine for Analgesia Case Study

10yr old M
30.9kg
h/o SCN9 gene mutation with related inherited erythromelalgia, with recent onset of bullous lesions presented with Hypothermia and AMS. Bilateral LE pain

Hospital day #0:
• Fan blowing on bilateral feet for comfort
• Gabapentin started 5mg/kg BID
• Ketamine drip started at 0.15mg/kg/hr.
• Ketorolac 15mg q 6hr

Hospital day #1:
• Pain better today
• Continued with current doses of meds

Hospital day #2:
• Pain continues to be controlled
• Continued with current doses of meds
• Hospital day #3:
• Pain continues to be controlled
• Having some jitteriness
• Decreased ketamine to 0.1mg/kg/hr.
• Continue gabapentin at current dose

Hospital day #4:
• Jitteriness better today
• Ketamine d/c'd
• Ketorolac and gabapentin continued at current doses

Hospital day #5:
• D/C'd home

Lidocaine for Analgesia Case Study

7 yr. old male
32.8kg
h/o sickle cell disease and functional asplenia
Admitted for vaso-occlusive crisis and R arm pain

Home meds: Tramadol 25mg q 6hr PRN, Ibuprofen 10mg/kg q 6hr PRN, acetaminophen 10mg/kg q6hr PRN
• h/o severe pruritus with opioids

Inpatient pain plan:
• Tramadol 30 mg q 4hr
• Fentanyl PCA 0.5mcg/kg q 10 min-no basal
• Naloxone 0.5mg/kg IV q 6hrs x 12 doses then Ibuprofen 10mg/kg q 6hr
• Acetaminophen 15mg/kg q 6hr
• Lidocaine drip 2mg/kg/hr
• Ondansetron q 6hr scheduled
• Hydroxyzine 15mg q 6hr
Lidocaine for Analgesia Case Study

- Hospital day #0
  - Started on pain plan listed above
- Hospital day #1
  - Lidocaine drip increased to 1.5mg/kg/hr.
- Hospital day #2
  - Lidocaine and fentanyl pain pump d/c'd. Scheduled oxycodone 5 mg q 4hr added. Patient discharged home later that day

*Since the addition of lidocaine to this patient’s pain plan his opioid requirement is much less than previous admissions

Questions?

- Please email with any questions:
  - Sharon.Wrona@nationwidechildrens.org
  - Lauren.Renner@nationwidechildrens.org

- Thank you for your time!

PCSS Mentoring Program

- PCSS Mentor Program is designed to offer general information to clinicians about evidence-based clinical practices in prescribing medications for opioid addiction.
- PCSS Mentors are a national network of providers with expertise in addictions, pain, evidence-based treatment including medication-assisted treatment.
- 3-tiered approach allows every mentor/mentee relationship to be unique and catered to the specific needs of the mentee.
- No cost.

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PCSS is a collaborative effort led by the American Academy of Addiction Psychiatry (AAAP) in partnership with:

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- American Society of Addiction Medicine
- Addiction Technology Transfer Center
- American Academy of Pain Medicine
- American Academy of Pediatrics
- International Nurses Society on Addictions
- American College of Emergency Physicians
- American Psychiatric Nurses Association
- American College of Physicians
- National Association of Community Health Centers
- American Dental Association
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- American Osteopathic Academy of Addiction Medicine

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Funding for this initiative was made possible (in part) by grant no. 1H79TI081968 from SAMHSA. The views expressed in written conference materials or publications and by speakers and moderators do not necessarily reflect the official policies of the Department of Health and Human Services; nor does mention of trade names, commercial practices, or organizations imply endorsement by the U.S. Government.