Postoperative Pain Management in Children

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Objectives

• Describe the use of opioids for postop pain
• Discuss the limitations related to opioids, especially codeine for postoperative ENT patients
• Describe non-opioid multimodal analgesia options
INTRODUCTION

- Historical perspective
- Assessment
- Systemic analgesia
  - Opioids
  - Opioid side-effects
  - Non-opioid analgesics
- Sedation
  - Dexmedetomidine
Historical perspective

- Myth 1: Neonates are unable to experience pain

The Incidence of Postoperative Pain in Children

Laurence Mather and Josephine Mackie

75% describe mod to severe pain on post op day one
40% of those with opioid analgesia ordered, did not receive it
Most pain medication administered IM

Pain 1983
Myth 1: Don’t feel pain

- Infants with hx of prior surgery
- Subsequent surgeries
  - Same vs different dermatome
- Higher intra-op & post-op opioid requirements
- Higher catecholamine levels

Pain 2005
Assessment

FLACC Behavioral Pain Scale

<table>
<thead>
<tr>
<th>Categories</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Crying</td>
<td>Characteristic cry of pain is high pitched.</td>
</tr>
<tr>
<td></td>
<td>0 - No cry or cry that is not high-pitched</td>
</tr>
<tr>
<td></td>
<td>1 - Cry high pitched but baby is easily consolable</td>
</tr>
<tr>
<td></td>
<td>2 - Cry high pitched but baby is inconsolable</td>
</tr>
<tr>
<td>Requires $\text{O}_2$ for $\text{SaO}_2 &lt; 95%$</td>
<td>Babies experiencing pain manifest decreased oxygenation. Consider other causes of hypoxemia, e.g., oversedation, atelectasis, pneumothorax</td>
</tr>
<tr>
<td></td>
<td>0 - No oxygen required</td>
</tr>
<tr>
<td></td>
<td>1 - $&lt; 30%$ oxygen required</td>
</tr>
<tr>
<td></td>
<td>2 - $&gt; 30%$ oxygen required</td>
</tr>
<tr>
<td>Increased vital signs ($\text{BP}^<em>$ and $\text{HR}^</em>$)</td>
<td>Take BP last as this may awaken child making other assessments difficult</td>
</tr>
<tr>
<td></td>
<td>0 - Both HR and BP unchanged or less than baseline</td>
</tr>
<tr>
<td></td>
<td>1 - HR or BP increased but increase in $&lt; 20%$ of baseline</td>
</tr>
<tr>
<td></td>
<td>2 - HR or BP is increased $&gt; 20%$ over baseline</td>
</tr>
<tr>
<td>Activity</td>
<td>The facial expression most often associated with pain is a grimace.</td>
</tr>
<tr>
<td></td>
<td>A grimace may be characterized by brow lowering, eyes squeezed shut,</td>
</tr>
<tr>
<td></td>
<td>deepening naso-labial furrow, or open lips and mouth.</td>
</tr>
<tr>
<td></td>
<td>0 - No grimace present</td>
</tr>
<tr>
<td></td>
<td>1 - Grimace alone is present</td>
</tr>
<tr>
<td></td>
<td>2 - Grimace and non-cry vocalization grunt is present</td>
</tr>
<tr>
<td>Cry</td>
<td>Sleepless - Scored based upon the infant’s state during the hour preceding</td>
</tr>
<tr>
<td></td>
<td>this recorded score.</td>
</tr>
<tr>
<td></td>
<td>0 - Child has been continuously asleep</td>
</tr>
<tr>
<td></td>
<td>1 - Child has awakened at frequent intervals</td>
</tr>
<tr>
<td></td>
<td>2 - Child has been awake constantly</td>
</tr>
<tr>
<td>Consolability</td>
<td>Frequency to constant discomfort</td>
</tr>
<tr>
<td></td>
<td>0 - Frequent to constant discomfort</td>
</tr>
<tr>
<td></td>
<td>1 - Occasional discomfort</td>
</tr>
<tr>
<td></td>
<td>2 - Infrequent discomfort</td>
</tr>
<tr>
<td></td>
<td>3 - Rare discomfort</td>
</tr>
<tr>
<td></td>
<td>4 - None</td>
</tr>
</tbody>
</table>

Worst Possible Pain

- 10
- 9
- 8
- 7
- 6
- 5
- 4
- 3
- 2
- 1
- 0

No Pain
Systemic Analgesia
Someone once said
laughter is the best medicine - they're wrong.

Morphine is the best medicine.
Opioids

• Common opioids in acute pain:
  • Morphine 0.05-0.1 mg/kg IV q 2-4 hrs PRN
  • Dilaudid 5-10 mcg/kg IV q 2-4 hrs PRN
  • Fentanyl
  • Codeine 0.5-1 mg/kg PO q 4 hrs PRN
  • Oxycodone 0.1-0.2 mg/kg PO q 4 hrs PRN

• Less commonly used:
  • Methadone

• Routes:
  • Oral, Rectal, IM, IV, Transmucosal, Transdermal, SQ, neuraxial
Opioids

**Adverse events**
1. Respiratory depression
2. Nausea and vomiting
3. Constipation
4. Pruritus
5. Sedation
6. Dependence
7. Addiction
8. Opioid-Induced-Hyperalgesia
Codeine

- Not a very potent opioid
  - Prodrug metabolized to morphine
- Available as an elixir
- Usually combined with acetaminophen
- Schedule III - can phone in prescription
- Dose based on codeine
  - 0.5-1 mg/kg every 4-6 hours
- Polymorphisms
  - 5-10% poor metabolizers
  - 1-2% Ultra-rapid metabolizers (up to 30% in some African communities)
2 yo with OSA for T&A
Dead at home POD#2
Prescribed codeine 10 mg-12mg
Higher than therapeutic morphine plasma level
Cyt-P450 analysis-ultra rapid metabolizer
Codeine

February 2013
FDA Drug Safety Communication:
Codeine use in certain children after
tonsillectomy and/or adenoidectomy
may lead to rare, but life-threatening
adverse events or death

10 ped deaths, 3 resp depression
Letters to the Editor

<table>
<thead>
<tr>
<th>Medication</th>
<th>Frequency (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acetaminophen with hydrocodone</td>
<td>12 (25.5)</td>
</tr>
<tr>
<td>Acetaminophen</td>
<td>9 (19.1)</td>
</tr>
<tr>
<td>Ibuprofen</td>
<td>8 (17.0)</td>
</tr>
<tr>
<td>Acetaminophen with oxycodone</td>
<td>7 (14.9)</td>
</tr>
<tr>
<td>Acetaminophen with codeine</td>
<td>4 (8.5)</td>
</tr>
<tr>
<td>Hydrocodone</td>
<td>4 (8.5)</td>
</tr>
<tr>
<td>Oxycodone</td>
<td>2 (4.3)</td>
</tr>
<tr>
<td>None of the above</td>
<td>1 (2.1)</td>
</tr>
<tr>
<td>Codeine</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>47</td>
</tr>
</tbody>
</table>

When the editors read the manuscript of this report, they noted that the number of responses represents only around one-fifth of residents graduating this academic year, but it is important to emphasize that any use of codeine for postoperative tonsillectomy pain control should not be advised.

Adenotonsillectomy is an extremely common surgical procedure, with about half a million performed annually. Nearly all graduating otolaryngology residents are likely to perform this procedure during their training. Therefore, the findings of this study are likely to be relevant to other otolaryngology residents.

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Cheng, Otol-Head & Neck Surg 2013-letter
Other opioids

- Hydrocodone
  - CYP2D6
- Tramadol
  - CYP2D6
- Morphine
  - Glucuronidation
- Hydromorphone
  - Glucuronidation
Oxycodone

- More potent opioid than codeine
- Available as an elixir
  - Roxicodone
- Usually combined with acetaminophen
  - Percocet, roxicet
- More consistent analgesia than codeine
Retrospective Database

Relationship of preop oxygen saturation on postop MSO4 consumption in children with OSA for T&A

46 children, mean age 43 mo

Young age and low preoperative saturation --> decreased postop MSO4 requirement

Brown, Anesthesiology 2004
Prospective study

22 Children with OSA for T&A

2 groups

<85% O₂ sat nadir

>85% O₂ sat nadir

MSO₄ post-op to a behavioral score

Those <85% used HALF the MSO₄

Heightened sensitivity to opioids

Brown, Anesthesiology 2006
An Anesthetic Management Protocol to Decrease Respiratory Complications After Adenotonsillectomy in Children with Severe Sleep Apnea

Sreekrishna Raghavendra
Robert T. Brouillet

Retrospective evaluation
• New T&A mgt vs historical controls

New mgt:
1. Reduced morphine dose intraop & postop
2. Dexamethasone

Major resp interventions
• 11% vs 30% (historic)

Brown, Anesth Analg 2010
Non-opioid analgesia

**Acetaminophen**

- **Safe**
  - Reduction in APAP-glucuronide formation
    - Tanaka, J Clin Pharm Ther 1998
- **Reduces opioid requirements**
  - Korpela, Anesthesiology 1999
- **Dosing**
  - ORAL 10-15 mg/kg Q 6 hrs
  - RECTAL 40 mg/kg Q 6 hrs
  - IV 10-15 mg/kg Q 6 hrs
Acetaminophen

1. 40 mg/kg rectal recommended

2. 10-30 mg/kg inadequate serum levels

- Birmingham, Anesthesiology 1997

Birmingham, Anesthesiology 2001

**Initial and Subsequent Dosing of Rectal Acetaminophen in Children**

Background: Recent studies have determined that an initial rectal acetaminophen dose of approximately 40 mg/kg resulted in children to achieve target antipyretic serum concentrations. The timing and amount of subsequent doses, after a 40 mg/kg dose has been cleared by the route of administration, have not been determined. This is important because additional acetaminophen dosing may be desired in the postoperative period for analgesia or anxiolysis, and has been reported after multiple dosing. Based on previous studies, in which doses of 40-50 mg/kg were given, we determined the dosing regimen and serum concentrations.

**Subsequent dose - 20 mg/kg every 6 hours**

Maintains serum concentrations

With Institutional Review Board approval (Children's Memorial Hospital, Chicago, IL) and parental informed consent, patients received an initial dose of 40 mg/kg rectal acetaminophen after induction of anesthesia and between zero and three subsequent 20 mg/kg doses at 6-h intervals. This dosing regimen was determined using previous pharmacodynamic parameter estimates. Fever-Melody suppositories (Eugene, OR) were used. In this suppository formulation, acetaminophen is suspended in a hydrophilic vegetable oil base. Combinations of the four commercially available doses (80, 120, 180, and 250 mg) were used to deliver a dose for each patient as close as possible to the desired dose. Suppositories were not cut, because acetaminophen may not be distributed evenly throughout the suppository.

Children aged 2-12 yr undergoing elective orthopaedic surgery were eligible if they were to be hospitalized after surgery, weighed more than 12 kg, were classified as American Society of Anesthesiologists' physical status 1-3, and had a preoperative hemoglobin more than 90%. Children were excluded if they had received acetaminophen within 24 h before the study.
IV Tylenol

- 36 studies
- 3896 patients
  - Adults & Peds
- 50% pain reduction in 1/3
- 30% reduction in opioid req’s
- Safe
IV Tylenol

- FDA approved 2011
- Not < 2yo
- 10 x dose error
- Ordered in $MG$
- Given in $ML$

PEDIATRICS
OFFICIAL JOURNAL OF THE AMERICAN ACADEMY OF PEDIATRICS

Intravenous Acetaminophen in the United States: Iatrogenic Dosing Errors
Richard C. Dart and Barry H. Rumack
Pediatrics 2012;129:349; originally published online January 23, 2012;
DOI: 10.1542/peds.2011-2345

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://pediatrics.aappublications.org/content/129/2/349.full.html

Pediatrics 2012;129
**NSAID**

**Ketorolac**
- 0.5-1 mg/kg every 6-8 hours
- Reduces opioid requirements

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*Ketorolac Reduces Postoperative Narcotic Requirements*

By David E. Carney, Linda A. Nicolette, Michael H. Ratner, Anita Miner, and Thomas J. Baesl
Syracuse, New York

![Graph showing morphine requirements over postoperative days](image)

J Ped Surg 2001
Ketorolac

- 120 children
- Four Groups
  1. Tyl 10 mg/kg
  2. Tyl & cod 1 mg/kg
  3. Butorphanol 25 mcg/kg (nasal)
  4. Ketorolac 1 mg/kg (IM)

Ketorolac
  - Lower pain scores
  - Less PONV

Postoperative Analgesia in Children Undergoing Myringotomy and Placement Equalization Tubes in Ambulatory Surgery

Ana Lucia Pappas, MD, Elaine M. Flader, RN, CCRN, Steve Creech, MD,
Andrew Hotaling, MD, and Albert Park, MD

*Department of Anesthesiology, †Department of Otolaryngology-Head and Neck Surgery, Loyola University Medical Center, Maywood, Illinois

We enrolled 120 children, undergoing bilateral myringotomy and tube placement in this prospective, randomized, double-blind study. Patients were randomized into one of four groups: Group 1 = control, placebo = 10 mg/kg; Group 2 = acetaminophen 10 mg/kg with 1 mg/kg of ondansetron; Group 3 = transtracheal butorphanol 25 mcg/kg given immediately after the induction of anesthesia; and Group 4 = ketorolac 1 mg/kg given IM immediately after the induction of anesthesia. All children received oral midazolam (10 mcg/kg) before surgery. A nurse blinded to the analgesics before the study assessed the child’s behavior at the induction of anesthesia and in the post-anesthesia care unit (PACU) every hour. Analgesic effectiveness was determined by assessing the child’s pain of human interest using a modified 1-10 point objective pain scale. The post-anesthesia care unit (PACU) nurse pain medication was administered as needed. A pain score of 5 or behavior score ≥ 5. On data showed that DM hemietra was a promising analgesic in pediatric cases. Time to first rescue analgesics was longer in the ketorolac group, and there was no associated postoperative vomiting or nausea. Delays in ketorolac during surgery was the best practice regimen for these procedures.

(Anesth & Analg 2003;98:S241-4)

Butorphanol myringotomy with placement of pressure equalization tubes (BMT) is one of the most common outpatient surgical procedures in children. Despite the broad spectrum of the procedure, the need for preoperative analgesia is still recognized. More than 90% of children undergoing BMT who do not receive preoperative analgesics will require pain medication in the early postoperative period (1). At this institution, BMT is most often performed without IV sedation, and therefore, pain relief by an alternate route is required. In this study, we compared the efficacy of preoperatively administered IM ketorolac, intranasally administered butorphanol, and orally administered acetaminophen plus codeine in each other and in the post-anesthesia care unit (PACU) every hour. Ketorolac 1 mg/kg was scheduled to reduce the pain for the scheduled amyolocytic BMT in the children. Written, informed consent was obtained in all cases. Children who received analgesics within 8 h before surgery or had an upper respiratory infection were excluded. Also excluded were children who required IV induction (e.g., malignant hyperthermia, history of opioid, aspiration, or nonsteroidal anti-inflammatory drug allergy, renal insufficiency, bleeding disorders, or active ulcer disease). All children were kept nothing by mouth after midnight for solids. Liquids were permitted until 6 h before expected operating room time. Each child received oral midazolam 0.5 mg/kg maximum dose 20 mg for preoperative sedation 30–60 min before surgery. The children were randomized into one of four groups by a computer-generated numbers table. The treatment groups were as follows: Group 1 (control) = acetaminophen 10 mg/kg; Group 2 (AC) = acetaminophen 10 mg/kg with oxycodone 1 mg/kg; Group 3 (B) = transtracheal butorphanol 25 mcg/kg. The IV preparation of butorphanol was used. If the volume to be administered was >8 mL, a preservative-free saline solution was added to achieve a total volume of 10 mL to increase surface area contact. Group 4 (K) =

Anesth & Analg 2003
Ketorolac

- **Meta-analysis, 7 studies, 505 patients**
- **Increased rate of re-operation with NSAIDS, 0.8% vs 4.2%**
- **Odds ratio = 3.8, NNH = 29**
Ketorolac

Criticism
1. Too small: Only included 7 studies
2. Too Variable: Surgical skill, technique
3. Short 1/2 life of ketorolac
   • Some patients rec’d just one dose
4. Cox II’s not included
5. Cochrane Database 2005
   • No increased bleeding if ketorolac removed from analysis
NSAIDS & T&A

- 15 studies
- 1101 children
- Bleeding req surgery; OR = 1.69
- Bleeding req med mgt; OR = 0.99
- Less PONV with NSAIDS

Cochrane Review 2013
Cox II

- Prospective, randomized
- 60 children s/p tonsillectomy
- Rofecoxib vs hydrocodone/tyl for 3 days postop
- Better analgesia with cox II
- No increased bleeding

OBJECTIVE: The goal of the study was to evaluate the effects of rofecoxib on postoperative pain in children after tonsillectomy. The study was a single-center, randomized, controlled trial comparing rofecoxib with hydrocodone/tyl in children undergoing tonsillectomy.

STUDY DESIGN: A single-center, randomized, controlled trial comparing rofecoxib with hydrocodone/tyl in children undergoing tonsillectomy.

RESULTS: There were no significant differences between the two groups in terms of pain scores or other analgesic requirements.

CONCLUSION: Rofecoxib is an effective analgesic for children undergoing tonsillectomy.
Sedation & Analgesia
Dexmedetomidine Infusion for Analgesia and Prevention of Emergence Agitation in Children with Obstructive Sleep Apnea Syndrome Undergoing Tonsillectomy and Adenoidectomy

Anuradha Patel, MD, FRCA, Melissa Davidson, MD, Minh C. J. Tran, MD, MPH, Huma Quraishi, MD, Catherine Schoenberg, BSN, Manasee Sant, MD, Albert Lin, MD, and Mary Sun, MS

**BACKGROUND:** Dexmedetomidine, a specific α2 agonist, has an analgesic sparing effect and reduces emergence agitation. We compared an intraoperative dexmedetomidine infusion with bolus fentanyl to reduce perioperative opioid use and decrease emergence agitation in children with obstructive sleep apnea syndrome undergoing adenotonsillectomy (TA).

**METHODS:** One hundred twenty-two patients with obstructive sleep apnea syndrome undergoing T&A ages 2 to 10 years, completed this prospective, randomized, U.S. Food and Drug Administration-approved study. After mask induction with sevoflurane, group D received IV dexmedetomidine 2 μg · kg⁻¹ over 10 minutes, followed by 0.7 μg · kg⁻¹ · h⁻¹, and group F received IV fentanyl bolus 3 μg · kg⁻¹. Anesthesia was maintained with sevoflurane, oxygen, and nitrous oxide. Fentanyl 0.6 to 1 μg · kg⁻¹ was given to subjects in both groups for an increase in heart rate or systolic blood pressure ≥30% above preinduction values that continued for 5 minutes. Observers in the postanesthesia care unit (PACU) were blinded to treatment groups. Pain was evaluated using the objective pain score in the PACU on arrival, at 5 minutes, at 15 minutes, then every 15 minutes for 120 minutes. Emergence agitation was evaluated at the same intervals by 2 scales: the Pediatric Anesthesiology Emergence Delirium Scale and a 5-point scale described by Cole. Morphine 0.05 to 0.1 mg · kg⁻¹ was given for pain (score > 4) or severe agitation (score 4 or 5) lasting more than 5 minutes.

**RESULTS:** In group D, 0.6% patients needed intraoperative rescue fentanyl in comparison with 36% in group F (P = 0.001). Mean systolic blood pressure and heart rate were significantly lower in group D (P < 0.05). Minimum alveolar concentration values were significantly different between the 2 groups (P = 0.015). The median objective pain score was 3 for group D and 5 for group F (P = 0.001). In group D, 10 (16.6%) patients required rescue morphine, in comparison with 26 (47.5%) in group F (P = 0.002). The frequency of severe emergence agitation on arrival in the PACU was 18% in group D and 46.9% in group F (P = 0.004); at 5 minutes and at 15 minutes it was lower in group D (P = 0.028). The duration of agitation on the Cole scale was statistically lower in group D (P = 0.004). In group D, 10% of patients and 40.9% in group F had an episode of SPO₂ below 95% (P = 0.001).

**CONCLUSIONS:** An intraoperative infusion of dexmedetomidine combined with intravenous anesthetics provided satisfactory intraoperative conditions for T&A without adverse hemodynamic effects. Postoperative opioid requirements were significantly reduced, and the incidence and duration of severe emergence agitation was lower in fewer patients having desaturation episodes. (Anesth Analg 2010;111:1004–10)

**PATIENT DATA:**

- **Prospective, randomized**
- **120, 2-10 yo**
- **Dex 2 mcg/kg then gtt vs fent 1 mcg/kg**
- **Rescue MSO4 – 16% vs 45%**
- **Emergence Agitation – 18% vs 46%**
- **Sats < 95% – 18% vs 41%**

Patel, Anesth Analg 2010
• Prospective, blinded, randomized
• Dexmedetomidine gtt vs saline gtt
• Results:
  • Decreased HR, MAP
  • Less “subjective” bleeding
  • Less isoflurane use
  • Less post-op analgesic use

Durmus, Eur J Anaesthesiol 2007
Case report
Prolonged infusion of dexmedetomidine for sedation following tracheal resection

GREGORY B. HAMMER MD*, BRIDGET M. PHILIP MD*, ALAN R. SCHROEDER MD, FREDERICK S. ROSEN MD† and PETER J. KOLTAS MD‡

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- 4 yo with subglottic stenosis
- Failed midazolam & fentanyl sedation
- Dexmedetomidine 0.2-0.5 mcg/kg/hr X 4 days
- Improved analgesia & cooperation, less sedation

* Correspondence to Gregory B. Hammer MD, Department of Anesthesia, Perioperative Care, and Critical Care, Stanford University School of Medicine, 300 Pasteur Drive, Stanford, CA 94305-5084, USA (email: ghammer@stanford.edu)

2005 Blackwell Publishing Ltd

Hammer, Peds Anesth 2005
Conclusions

• Many options
• Acute Pain Service
• Multimodal approach is best
  • Non opioid analgesics
  • Use less Opioid analgesics
  • Avoid codeine
QUESTIONS?