Pain management in the ED: Review of Available Therapies

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Key Learning Points

- IV titratable, not IM
  - Treat early, front-load
- No more demerol
- Hydrocodone, not codeine
- NSAIDs are not benign
- Anxiolysis plays an important role

Why do we Under Treat Pain? Myths vs Reality

- Fear of adverse reactions
  - *Proven very rare in multiple studies*
  - *2.3%, none serious. Ann Emer Med.1999*
- Masking of exam findings
  - *6 prospective studies have disproven this*
- Inducing addiction to opioids
  - *Rate of 1/3,000 pts in Boston study*
- Patients will tell us if they are in pain
  - *70% of pts will not request Tx despite pain*

Pain Therapy: Simple Improvements

- Routine, early treatment
  - Protocols that identify painful conditions
- Treat moderate/severe pain IV
  - Pts rate IM injections as very painful
  - IM Tx rarely truly saves time or money
  - *53% IM in 1993, vs. 5% in 1997, using an RN protocol*

Kelly. J Accid Emer Med.2000

Many Therapeutic Options for Pain Control

- Stimulate CNS opiate receptors: opiates
- Block inflammatory mediators: NSAIDs
- Block transmission to the CNS: local anesthetics
- Stimulate descending 5-HT paths: TCAs
- "Close gates" at dorsal horn: TENS, acupuncture
- Interpretation of pain: anxiolytics

Consider Combination Therapy

- Different pathways
- Different half-lives
- Less toxicity of individual agents
- Most serious medical conditions are not treated with single therapy
  - Severe asthma or hypertension
  - Serious infections
- Not logical to treat severe pain with only one drug

Opioids

"Among the remedies which it has pleased Almighty God to give to man to relieve his sufferings, none is so universal and so efficacious as opium."

—Sir Thomas Sydenham, 1680

Opioid Potency: Rule of 10

Relatively equivalent potencies:

- 0.1mg fentanyl (100ug)
- 1 mg hydromorphone
- 10 mg morphine
- 100 mg meperidine

Opioids: Meperidine (Demerol)

Many EDs no longer stock it

- A "messy" drug
- Metabolism prolonged in renal or hepatic disease
- Metabolite (normeperidine) is a CNS toxin
- Can induce the Serotonin Syndrome

Highest rate of associated euphoria

- Problematic pts often request it

Opioids: Morphine

The "gold-standard" agent, but:

- Potent respiratory depressant
- Active metabolites, can accumulate with renal impairment
- Highest association with histamine release
- High prevalence of nausea

Opioids: Fentanyl

- Quickest onset and elimination
  - Onset = 1 minute, peaks at 3-5 minutes
  - Half-life = 30-90 minutes
- A very "clean" drug
  - No histamine release
  - No hemodynamic instability
  - No active metabolites
  - *Glottic spasm and chest rigidity seen only with very high doses (>10 µg/kg)*
- Dosage: 1 – 3 µg/kg
  - *Can accumulate in fat with repeated doses*

Opioids: Hydromorphone (Dilaudid)

- Kinetics like morphine
- Very potent and highly soluble
  - Smaller injection volumes
  - Very well tolerated
- No active metabolites
- No accumulation with repeated doses
  - Dosage: 1 – 2 mg per dose
  - No clear maximum dose

Opioids: New strategies

- Less meperidine and morphine
- Early, rapid control with fentanyl
  - Titrate IV
  - Limit total dose
- Maintenance with hydromorphone
  - Start 5 -30 minutes later
  - Well tolerated
  - No maximum dose

Oral Opioids: Codeine vs Hydrocodone

- Similar half-lives: 3 – 4 hours
- Codeine efficacy is much less
  - Questionably better than APAP alone
- Much more GI upset with codeine
- P450 pathway converts codeine to morphine
  - 2% to 15% of patients lack this pathway
- Should preferentially use hydrocodone

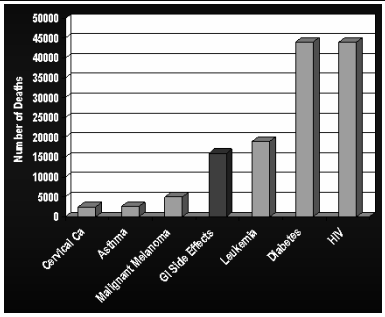
Opioids: Other Points

- Propoxyphene (Darvon)
  - High respiratory depression and dysphoria rates
  - Elderly especially at risk!
- Mixed analgesics / antagonists
  - Nalbuphine, Butorphanol, Pentazocine (Talwin)
  - High dysphoria rates, can induce withdrawal, limits other options

NSAIDs Mechanism of Action

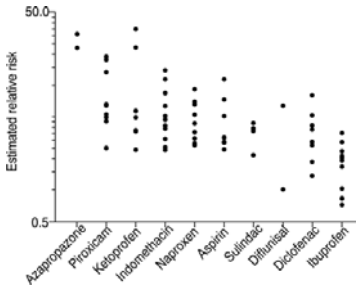
- Anti-inflammatory and antipyretic
- Decrease synthesis of prostaglandins
  - Anti-inflammatory effect may decrease function of neutrophils and have other (undesirable) effects
- Have primarily peripheral effects
  - Limited central nervous system effects seen with some agents
  - In contrast, acetaminophen acts in CNS

Selected Leading Causes of Death, 1994



Singh G. *Am J Med*. 1998:105(1B):31S-38S.

NSAID GI Toxicity Generally Varies with Half-life of the Agent



Henry, et al. BMJ.2000;312:1563

NSAIDs Limitations

- GI distress, ulceration / bleeding
- Renal impairment or failure
- Increase in incidence and severity of CHF
- Interfere with aspirin benefits
- Platelet inhibition may cause bleeding

Is Ketorolac Contraindicated in Perioperative or Trauma Patients?

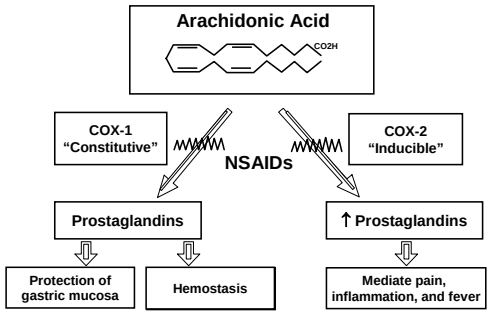
- Toradol is contraindicated as prophylactic analgesic before any major surgery, and intraoperatively whenever hemostasis is critical[1]
  - Does have significant antiplatelet effects in clinical trials[2]
- Large case-control study did not show increased bleeding when given peri-op to surgical patients[3]

[1]*Physicians' Desk Reference (PDR®)*, ed. 56. Montvale, NJ: Medical Economics Co. 2002.
[2]Noveck RJ, et al. *Clin Drug Invest*. 2001;21:465-476.
[3]Strom BL, et al. *JAMA*. 1996;275:376-382.

NSAIDs in Perspective

- No NSAID has been proven significantly more efficacious than another, when given in equivalent doses
  - Select agents based on toxicity profiles?
  - Side-effect rates generally parallel half-life profiles
- Pt. response can vary between agents
  - Multiple categories of agents
- No difference in efficacy by mode of administration

Mechanism of Action of NSAIDs



Cyclooxygenase (COX) Enzymes

COX-1

- Always active
- Maintains normal function of stomach, intestines, kidneys, and platelets (blood clotting)

COX-2

- Activated by injury
- Expressed at site of injury
- Mediates pain, inflammation, and fever

COX-2 Specific Inhibitors

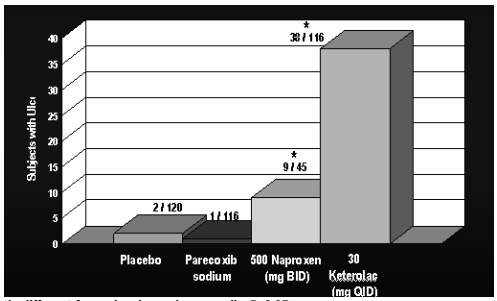
- Celecoxib
  - Celebrex
- Rofecoxib
  - Vioxx
- Valdecoxib
  - Bextra
- Parecoxib
  - Dynastat in Europe (parenteral)

COX-2 Agent Indications

All have OA and RA FDA indications

- Celecoxib
  - Also has acute pain indication
- Rofecoxib
  - Acute pain and dysmenorrhea (gout)
- Valdecoxib
  - Dysmenorrhea (acute pain, LBP)

Combined Incidence of Gastroduodenal Ulcers



Significantly different from placebo and parecoxib; *P*<0.05.
Data on file. Pharmacia Corporation.

COX-2 Efficacy vs Opioids

- Celecoxib 200 mg equivalent to Vicodin in post-orthopedic patients, but with less dosing frequency and fewer side effects
- Valdecoxib at least equal to Tylox in oral surgery patients
- Valdecoxib decreased need for morphine in hip-surgery patients

Do NSAIDs or Coxibs Interfere with Bone Healing?

"No good evidence that NSAIDs or coxibs inhibit bone healing, with the possible exception of long-term use. Use appears to increase bone density, and does not increase fracture risk"

- *Only evidence is animal studies of questionable relevance*
- *Shown to inhibit deleterious heterotopic calcification*

NSAIDs, coxibs, smoking and bone? Bandolier Library Web site. http://www.jr2.ox.ac.uk/bandolier/booth/painpag/wisdom/NSAIbone.html. Accessed May 5, 2004

Pain Therapy: Point Injections

"Trigger" or other point injections may represent an attractive and viable option in selected patients

- Lower cervical injections for headache relief.
  Mellick GA, Mellick LB. Headache 2001.41(10): 992
- Pericranial injection of local anesthetics in the ED management of resistant headaches
  Brofeldt, Panacek. Acad Emer Med. 1998.

Pain Therapy: Other Options

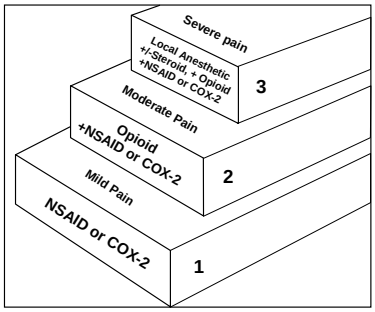
- Patient controlled analgesia (PCA)
- Nitrous oxide
- Moderate procedural sedation
- Deep procedural sedation

Pain Therapy: Anxiolysis

- Catecholamines and other stress responses play and important role in the experience of pain
- Anxiolytics can have independent benefits, as well as decreasing total opioid requirements

Do not underestimate the benefits of physician reassurance

WHO: Acute Pain Ladder



Pain Therapy: Key Learning Points

- Treat early, front load, maintain
  - IV titratable, not IM
  - Combination therapy
- Dilaudid, not demerol
- Hydrocodone, not codeine
- Beware NSAIDs complications
- Consider anxiolysis therapy

Questions?

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