Opioid use for chronic nonmalignant pain in children and adolescents

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June 12, 2015
Agency Medical Directors’ Group, Seattle, WA
Disclosures

• Special Government Employee, United States Food and Drug Administration, Anesthetic and Analgesic Drug Products Advisory Committee
• Chair, Pediatric Research Network for Pain (PRN-Pain)
• Consultation to
  • Pfizer
With very rare exception, opioids have not been labeled for use in individuals less than 18 years of age.

Persistent, recurrent, and chronic pain in infants, children, and adolescents are often qualitatively different than chronic pain problems in adults.

Children are not little adults BUT adults are big children.
Pediatric drug development: Choices for pediatricians

- Do not treat children with potentially beneficial medications because they are not approved for use in children.

- Treat with medications based on adult studies with limited data or anecdote (off label use).
Medications used in pediatrics labeled for indications in children

- Labeled: 20%
- Off label: 80%
Drug labeling for children

• Limited or no data on safety
  • Pharmacokinetics (PK)
  • Pharmacodynamics (PD)
  • Serious adverse events (SAE)

• Limited or no efficacy data
• Limited or no data on long-term use
• Limited or no data on long-term sequelae
1994: survey data to establish sufficiency for pediatric use and labeling
1997: FDAMA (FDA Modernization Act): pediatric studies lead to patent extension
1998: Pediatric Rule (challenged in 2000, enjoined by the Court in 2002)
2002: Best Pharmaceuticals for Children Act (BPCA)
2003: Pediatric Research Equity Act (PREA) replaced Pediatric Rule
2007: FDAAA (FDA Amendments Act): reauthorization of BPCA and PREA
2012: FDASIA (FDA Safety and Innovation Act)
  • Makes BPCA and PREA permanent
  • Pediatric development plans submitted earlier during drug development
FDA: CDER

FDAMA, BPCA, PREA impact (through April 30, 2015)

• 522 new pediatric trials

• Pediatric information in product labeling in >160 drugs

Analgesics with pediatric indications

Note: for the 0 to 6 month age group, there are 0

Acetaminophen, Aspirin, NSAIDs
- APAP (>2 y)
- ASA
- Ibuprofen (> 6 m)

Opioids (non-combination products)
- Fentanyl transdermal (>2 y)
- Buprenorphine injection
- Fentanyl citrate injection
- Meperidine
Extrapolation

- Expert consensus: the effectiveness of opioids may be extrapolated from studies on adults and older children down to those 2 years of age and older
- Lacking sufficient data on drug metabolism, dose response, and toxicity
Chronic pain and development

- Acute pain problems in pediatrics have many characteristics in common with adult presentations.
- Persistent, recurrent, and chronic pain in infants, children, and adolescents are often qualitatively different than chronic pain problems in adults.
- It is a corollary that treatment approaches may vary accordingly.
Chronic pain in pediatrics

- Common pediatric chronic pain
  - Headache
  - Abdominal pain
  - Musculoskeletal pain

- Common adult chronic pain
  - Neuropathic
  - Related to aging and degeneration

- Opioid use not indicated
  - Rare exceptions when pain has clearer nociceptive origin and defined endpoint
Children are not little adults, but adults are big children

- Adults with chronic pain often recall having had difficulties in their earlier years
- Prospective longitudinal or cross-sequential studies show contiguity or continuity between pediatric and adult chronic pain
  - Abdominal pain
  - Headaches
  - Back pain
Clinical recommendations

- Prescribe opioids for acute pain in infants and children only if knowledgeable in pediatric medicine, developmental elements of pain systems, and differences in pharmacokinetics and pharmacodynamics in young children.

- Avoid opioids in the vast majority of chronic non-malignant pain problems in children and adolescents, as evidence shows no indication.

- Opioids are indicated for a small number of persistent painful conditions, including those with clear pathophysiology and when an endpoint to usage may be defined.
Clinical recommendations

- Opioids may be indicated for some chronic pain conditions in children and adolescents, when there is *clear pathophysiology*, and no definable endpoint
- Utilize safety guardrails when prescribing opioids to younger patients
  - Limiting total dispensed
  - Educating parents about dosing, administration, storage and disposal (minimizing risks of diversion or accidental ingestion)
  - Adolescents should undergo screening for risk of substance abuse
- Consult or refer to a pediatric pain specialist when chronic pain problems in children and adolescents are complicated or persistent