

Summary Statement of Evidence on Codeine

Use of oral analgesia for the management of moderate to severe pain in children

Issue

- Codeine and codeine products will no longer be available on the hospital Formulary as of July 1, 2010

Context

- Pain management is a high priority at SickKids
- The SickKids Pain Management Clinical Practice Guideline states that oral morphine is preferred to codeine for the management of moderate to severe pain
- Some units have already removed codeine from their ward stock supply

Summary of the Literature

- Codeine is dependent on hepatic metabolism (CYP2D6) for conversion to its active form, morphine
- This metabolism is subject to genetic variability such that analgesic and adverse effects of codeine are unpredictable in a significant proportion of the population
- The genetic polymorphism of this metabolic pathway results in:
 - Slow metabolizers (insufficient morphine resulting in ineffective analgesia in up to 10% of population)
 - Ultra-rapid metabolizers (excessive morphine resulting in toxicity in 10-30% of population)

Implications for Practice for the Treatment of Moderate to Severe Pain

- Scheduled acetaminophen and non-steroidal anti-inflammatory drugs are recommended if no contraindications exist
- Use physical (ice/heat) and psychological (distraction/relaxation) techniques of pain control if appropriate
- Codeine should not be used for children with moderate to severe pain when alternative, more reliable medications are available

Recommendations

Drug	Dosing
Morphine	0.2-0.5mg/kg/dose po q4-6h, max 15mg/dose
Hydromorphone	0.04-0.08mg/kg/dose po q3-4h max 2-4mg/dose
Oxycodone	0.05-0.15mg/kg/dose po q4-6h, max 5-10mg/dose

Selected References:

Madadi P, Koren G. Pharmacogenetic insights into codeine analgesia: implications to pediatric codeine use. *Pharmacogenomics* 2008;9:1267-84.

Ciszkowski C et al. Codeine, Ultrarapid-Metabolism Genotype, and Postoperative Death. [Letter to the Editor]. *NEJM* 2009; 361;8: 827-8.

Gasche Y, Daali Y, Fathi M, et al. Codeine intoxication associated with ultrarapid CYP2D6 metabolism. *N Engl J Med* 2004;351:2827-31.

FOR FURTHER INFORMATION PLEASE CONTACT

Drug Information: 416-813-6703 or druginfo@sickkids.ca