ACETAMINOPHEN

N-acetyl-p-aminophenol or (APAP) or paracetamol (PARA)

Mechanism of Action

1. COX-associated peroxidase hypothesis
   A reducing agent inhibiting a step in prostanoid synthesis by COX enzymes
2. Cannabinoid Hypothesis
   Acetaminophen metabolite (AM404) inhibits COX, activates TRPV1 and TRPA1 channels, pain receptors that are also sensitive to cannabinoids

25 Billion doses used annually as a non-prescription medication

Dosing

- <50 kg: 12.5 mg/kg every 4 hours or 15 mg/kg every 6 hours; maximum daily dose: 75 mg/kg/day (≤3.75 g/day)
- ≥50 kg: 650 mg every 4 hours or 1,000 mg every 6 hours; maximum single dose: 1,000 mg/dose; maximum daily dose: 4 g/day
- Caution in hepatic disease/cirrhosis, limit therapy to ≤2 g/day

IV vs. Oral?

- 2015 Meta-analysis of 6 randomized clinical trials comparing IV and oral acetaminophen
- No clinically significant difference in efficacy between the two formulations
- These studies however looked at patients who could tolerate oral formulation. IV acetaminophen may be best used for our patients with poor GI absorption at baseline or post-surgically.

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181,640 adults who underwent colectomy at 602 hospitals, retrospective between 2011 and 2016

Wasserman et.al Anesthesiology July 2018

References:
