

## Kliiniline küsimus nr 11 lapsed

Kas patsiendile valuvaigistite regulaarne skeemijärgne manustamine vs vajadusel manustamine mõjutab postoperatiivse ägeda valu ravi tulemust? (Does regular administration of pain killers vs administration of pain killers PRN (if needed) affect the outcome of postoperative acute pain treatment)

Kriitilised tulemusnäitajad: *valu tugevus, valu vähenemine, lisavaluvaigisti vajadus, aeg esimese lisavaluvaigisti vajaduseni, opiaadi vajadus, aeg valuvaigistava toime saabumiseni, postoperatiivsete tüsistuste esinemissagedus, rehospitalseerimine valu tõttu, patsiendi (eestkostja) rahulolu valuraviga, haiglaravi kestus*

### Kokkuvõte:

1 süstemaatiline ülevaade, 2 ülevaate artiklit, kõik korrektselt läbi viidud ja vormistatud. Lisaks Austraalia ja Uus-Meremaa valuravi juhend. Sarnaselt täiskasvanutele ei leidnud ülevaateid ega artikleid, mis oleksid otseselt käsitlenud valuvaigistite regulaarset või ebaregulaarset manustamist, kuid nagu ka täiskasvanute puhul kinnitasid ülevaated, et vajadus nn rescue medication'i (lisavaluvaigisti) järele tekkis sagedamini juhtudel, kui primaarselt manustatud valuvaigistite doosid olid väiksemad ja ravimeid manustati suuremate ajaintervallidega, s.t. ebaregulaarselt (*Wong et al, 2013*). See omakorda aga viitab sellele, et kui valuvaigistid olid manustatud enne uue valustiimuli teket (s.t regulaarselt), toimisid nad efektiivsemalt ja ei tekkinud vajadust lisavaluvaigisti manustamiseks. Näiteks *Tzortzopoulou et al (2011)* uurisid küll üksikdoosi Paracetamoli manustamise järgset efekti valustiimulile, kuid ka seal nähtus, et regulaarne Paracetamoli manustamine vähendab valutugevust 50% ning vajadus opioidi (lisavaluvaigisti) järele vähenes 30%. Ka *Michelet et al (2012)* viitavad, et perioperatiivne regulaarne NSAIDide manustamine vähendas lisavaluvaigisti kasutamise (opioidide) vajadust. Postoperatiivsete tüsistuste esinemissagedust, rehospitalseerimist valu tõttu ning haiglaravi kestust ei olnud neis ülevaadetes käsitletud.

### Viited:

**Authors** Wong I; St John-Green C; Walker SM.

**Title** Opioid-sparing effects of perioperative paracetamol and nonsteroidal anti-inflammatory drugs (NSAIDs) in children. [Review]

**Source** Paediatric Anaesthesia. 23(6):475-95, 2013 Jun.

**Abstract** BACKGROUND AND OBJECTIVES: Perioperative pain in children can be effectively managed with systemic opioids, but addition of paracetamol or nonsteroidal anti-inflammatory drugs (NSAIDs) may reduce opioid requirements and potentially improve analgesia and/or reduce adverse effects.

**METHODS:** A systematic literature search was conducted to identify trials evaluating postoperative opioid requirements in children and comparing NSAID and/or paracetamol with placebo. Studies were stratified according to design: continuous availability of intravenous opioid (PCA/NCA) vs intermittent 'as needed' bolus; and single vs multiple dose paracetamol/NSAIDs. Primary outcome data were extracted, and the percentage decrease in mean opioid consumption was calculated for statistically significant reductions compared with placebo. Secondary outcomes included differences in pain intensity, adverse effects (sedation, respiratory depression, postoperative nausea and vomiting, pruritus, urinary retention, bleeding), and patient/parent satisfaction.

**RESULTS:** Thirty-one randomized controlled studies, with 48 active treatment arms compared with placebo, were included. Significant opioid sparing was reported in 38 of 48 active treatment arms, across 21 of the 31 studies. Benefit was most consistently reported when multiple doses of study drug were administered, and 24 h PCA or NCA opioid requirements were assessed. The proportion of

positive studies was less with paracetamol, but was influenced by dose and route of administration. Despite availability of opioid for titration, a reduction in pain intensity by NSAIDs and/or paracetamol was reported in 16 of 29 studies. Evidence for clinically significant reductions in opioid-related adverse effects was less robust.

**CONCLUSION:** This systematic review supports addition of NSAIDs and/or paracetamol to systemic opioid for perioperative pain management in children.

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Publication Type Journal Article. Meta-Analysis. Research Support, Non-U.S. Gov't. Review.

Year of Publication 2013

**Authors** Michelet D; Andreu-Gallien J; Bensalah T; Hilly J; Wood C; Nivoche Y; Mantz J; Dahmani S.

**Title** A meta-analysis of the use of nonsteroidal antiinflammatory drugs for pediatric postoperative pain. [Review]

**Source** *Anesthesia & Analgesia*. 114(2):393-406, 2012 Feb.

**Abstract** **BACKGROUND:** Opioid side effects are a great concern during the postoperative period in children. Nonsteroidal antiinflammatory drugs (NSAIDs) have been shown to effectively decrease postoperative pain, but their opioid-sparing effect is still controversial. In this present meta-analysis, we investigated the postoperative opioid-sparing effect of NSAIDs in children.

**METHODS:** A comprehensive literature search was conducted to identify clinical trials using NSAIDs and opioids as perioperative analgesic compounds in children and infants. Outcomes measured were opioid consumption, pain intensity, postoperative nausea and vomiting (PONV), and urinary retention. All outcomes were studied during postanesthesia care unit (PACU) stay and the first 24 postoperative hours. Data from each trial were combined to calculate the pooled odds ratios (ORs) or standardized mean difference (SMD) and their 95% confidence interval.

**RESULTS:** Twenty-seven randomized controlled studies were analyzed. Perioperative administration of NSAIDs decreased postoperative opioid requirement (both in the PACU and during the first 24 postoperative hours; SMD = -0.66 [-0.84, -0.48] and -0.83 [-1.11, -0.55], respectively), pain intensity in the PACU (SMD = -0.85 [-1.24, -0.47]), and PONV during the first 24 postoperative hours (OR = 0.75 [0.57-0.99]). NSAIDs did not decrease pain intensity during the first 24 postoperative hours (OR = 0.56 [0.26-1.2]) and PONV during PACU stay (OR = 1.02 [0.73-1.44]). Subgroup analysis according to the timing of NSAID administration (intraoperative versus postoperative), type of surgery, or coadministration of paracetamol did not show any influence of these factors on the studied outcomes except the reduction of pain intensity and the incidence of PONV during the first 24 postoperative hours, which were influenced by the coadministration of paracetamol and the type of surgery, respectively.

**CONCLUSION:** This meta-analysis shows that perioperative NSAID administration reduces opioid consumption and PONV during the postoperative period in children.

Publication Type Journal Article. Meta-Analysis. Review.

Year of Publication 2012

**Authors** Tzortzopoulou A; McNicol ED; Cepeda MS; Francia MB; Farhat T; Schumann R.

**Title** Single dose intravenous propacetamol or intravenous paracetamol for postoperative pain. [Review]

**Source** *Cochrane Database of Systematic Reviews*. (10)CD007126, 2011.

**Abstract** **BACKGROUND:** Paracetamol (acetaminophen) is the most commonly prescribed analgesic for the treatment of acute pain. It may be administered orally or intravenously. The efficacy and safety of intravenous (IV) formulations of paracetamol, IV paracetamol and IV propacetamol, compared with placebo and other analgesics, is unclear.

**OBJECTIVES:** To assess the efficacy and safety of IV formulations of paracetamol for treatment of postoperative pain in both adults and children.

**SEARCH STRATEGY:** We searched the Cochrane Central Register of Controlled Trials (CENTRAL) (The Cochrane Library 2010, Issue 2), MEDLINE (1950 to May 2010), EMBASE (1980 to 2010, Week 18), LILACS (1992 to May 2010) and reference lists of retrieved articles.

**SELECTION CRITERIA:** Randomized, double-blind, placebo- or active-controlled single dose clinical trials of IV propacetamol or IV paracetamol for acute postoperative pain in adults or children.

**DATA COLLECTION AND ANALYSIS:** Two review authors independently assessed the risk of bias and extracted data. We contacted study authors for additional information. We collected adverse event information from the studies.

**MAIN RESULTS:** Thirty-six studies (3896 participants) were included. Thirty-seven percent of participants receiving IV propacetamol/paracetamol experienced at least 50% pain relief over four hours compared with 16% of those receiving placebo (number needed to treat to benefit (NNT) = 4.0; 95% confidence interval 3.5 to 4.8). The proportion of participants in IV propacetamol/paracetamol groups experiencing at least 50% pain relief diminished over six hours, as reflected in a higher NNT of 5.3 (4.2 to 6.7). Participants receiving IV propacetamol/paracetamol required 30% less opioid over four hours than those receiving placebo. However, this did not translate to a reduction in opioid-induced adverse events. Meta-analysis of efficacy comparisons between IV propacetamol/paracetamol and active comparators (opioids or nonsteroidal anti-inflammatories (NSAIDs)) were either not statistically significant, not clinically significant, or both. Adverse events occurred at similar rates with IV propacetamol or IV paracetamol and placebo. However, pain on infusion occurred more frequently in those receiving IV propacetamol versus placebo (23% versus 1%). Meta-analysis did not demonstrate statistically significant differences between IV propacetamol/paracetamol and active comparators for any adverse event except a reduction in the rate of hypotension versus NSAIDs and a reduction in the rate of gastrointestinal disorders versus opioids.

**AUTHORS' CONCLUSIONS:** A single dose of both IV propacetamol and IV paracetamol provides around four hours of effective analgesia for about 37% of patients with acute postoperative pain. Both formulations are associated with few adverse events, although patients receiving IV propacetamol have a higher incidence of pain on infusion than both placebo and IV paracetamol.

Publication Type Journal Article. Meta-Analysis. Review.

Year of Publication 2011