**Kliiniline küsimus nr 4.**
Kas patsiendile ennetav (*preemptive, preventive*) valuvaigistite manustamine vs mittemanustamine mõjutab postoperatiivse ägeda valu tugevust?

Kriitilised tulemusnäitajad: *valu tugevus, lisavaluvaigisti vajadus, aeg esimese valuvaigistini (vajaduseni), valuvaigistitest tingitud kõrvaltoimed, postoperatiivsete tüsistuste esinemissagedus, ärkamisruumis viibimise aeg*

**Süstemaatilised ülevaated**

**LAMBERT P 2014:** 11 RCT-d, 742 pt: 4 uuringut võrdlesid preopratiivset **klonidiini vs platseebo** ; 6 uuringut klonidiin vs midasolaam ja 1 uuring klonidiin vs fentanüül.
Klonidiin preoperatiivselt vs platseebo:

- 4 mcg/kg:
  - **Lisavaluvaigisti vajadus väiksem** ( RR 0.24; 95% CI 0.11- 0.51; $I^2$ = 52%)
  - **Valu tugevus väiksem klonidiini grupis** ( SMD - 1.11 (95% CI - 1.46 -0.75)

- 2 mcg/kg:
  - **Vahet ei olnud lisavaluvaigisti vajaduses**

**SCHNABEL 2012:** 11 RCT, dexmedetomidine vs kontroll: 434 dexmedetomidiini; 219 platseebo;221 opiodi grupis. Operatsioonid : KNK; ambulatoorne kirurgia kõhukirurgia. Dexmedetomidiini manustati ühes uuringus enne nahalõiget, ülejäänutes peale induktsiooni 10 minuti jooksul.
**Dexmedetomidiin vs platseebo:**

- **Opiodi vajadus** ärkamisruumis ( 4 RCT, 249 pt): **madalam** dexmedetomidiini grupis RR 0.4 (95% CI 0.26 -0.62; P= 0.00001; $I^2$= 0 %)
- **Valu tugevus** ärkamisruumis ( 2RCT, 138 pt): tugeva ja mõõduka valuga lapsi **vähem** uuringugrupis RR 0.51 (95% CI: 0.32 -0.81; p= 0.004; $I^2$ = 0%)
- **Opiaadi vajadus** ( 2 RCT): **väiksem** uuringugrupis MD: -0.12 mg/kg; 95% CI: -0.25-0.01; P= 0.06, $I^2$= 86%)
- **Rahutus ärkamisel** (6 RCT, 385 pt): uuringugrupis **väiksem** arv lapsi, kel esines rahutus ärkamisruumis RR 0.41 ( 95% CI: 0.30-0.56; P< 0.00001; $I^2$ =0%)
- **Ekstubatsiooni aeg** (5 RCT): **pikem** 1,2 min ( 95% CI: -0.15 -2.64; p= 0.08; $I^2$ = 85 %)
- **Kõrvaltoimed:**
  - **Hüpotensioon ja bradükardia** ( 5 RCT, 240 pt): 1 bradükardia ja 2 hüpotensiooni juhtumit uuringugrupis
  - **Hingamisdepressioon** ( 5 RCT, 295 pt): 1 pt platseebogrupis
  - **PONV** (4 RCT, 249 pt): esinemissagedus **väiksem** uuringugrupis RR 0.76 ( 95% CI: 0.44- 1-30; p= 0.32, $I^2$= 0%)

**CHO 2014:** 24 RCT, 1257 pt, preoperatiivne ketamiin vs platseebo või kontroll ( opioid)

- **Postoperatiivne valu: statistiliselt** väiksem ketamiiini grupis 0 h (SMD= -1.7085; p= 0.0221), 1 h ( SMD = - 0.8660; p< 0.0001) ja 4 h ( SMD= - 0.7945; p< 0.0001); vahet ei ole 6h ( SMD = -0.4813; p= 0.1347), 12 h ( SMD = - 0.5600; p= 0.1219), 24 h ( SMD= - 0.8864; p= 0.1604)
- **Valuvaigisti vajadus: väiksem** ketamiini grupis ( SMD= -1.3361; p= <0.0001)
- **PONV**: esinemissagedus oluliselt **väiksem** ketamiini grupis ( p=0.0432)
- **Ärkamisaeg**: ketamiini grupis **pikem** ( SMD=0.3253; p= 0.0357), sedatsioon ei erinenud gruppide vahel
- **Psühhomimeetilised kõrvaltoimed**: olulist vahet ei ole gruppide vahel:
  - **Unehäired** ( SMD=- 0.4144; p= 0.4986)
  - **Halvad unenäod** ( SMD= 0.2885; p= 0.3658)
  - **Hallutsinatsioonid** ( SMD= 0.7374; p= 0.3795)

**Viited**

| **Kokkuvõtte (abstract või kokkuvõtlikum info)** | **Viide kirjandusallikale** |
|---|---|
| *Nt kokkulepitud struktuur võiks olla: Mitu uuringut, palju patsiente, tulemused*<br>*Uuringu kvaliteet*<br>*Lisada Grade tabel, juhul kui on* | . |
| Abstract<br>BACKGROUND AND OBJECTIVES:<br>The goal of this meta-analysis study was to perform a systematic review of the literature on the effects of ketamine on postoperative pain following tonsillectomy and adverse effects in children.<br>SUBJECTS AND METHODS:<br>Two authors independently searched three databases (MEDLINE, SCOPUS, Cochrane) from their inception of article collection to February 2014. Studies that compared preoperative ketamine administration (ketamine groups) with no treatment (control group) or opioid administration (opioid group) where the outcomes of interest were postoperative pain intensity, rescue analgesic consumption, or adverse effects (sedation, nausea and vomiting, bad dream, worsening sleep pattern, and hallucination) 0-24 hours after leaving the operation room were included in the analysis.<br>RESULTS:<br>The pain score reported by the physician during first 4 hours and need for analgesics during 24 hours postoperatively was significantly decreased in the ketamine group versus control group and was similar with the opioid group. In addition, there was no significant difference between ketamine and control groups for adverse effects during 24 hours postoperatively. In the subgroup analyses (systemic and local administration) regarding pain related measurements, peritonsillar infiltration of ketamine was more effective in reducing the postoperative pain severity and need for analgesics.<br>CONCLUSION:<br>Preoperative administration of ketamine systemically or locally could provide pain relief without side-effects in children undergoing tonsillectomy. However, considering the insufficient evaluation of efficacy of ketamine | PLoS One. 2014 Jun 30;9(6):<br><br>**Efficacy of ketamine in improving pain after tonsillectomy in children: meta-analysis.**<br><br>*Cho HK, Kim KW, Jeong YM, Lee HS, Lee YJ, Hwang SH* |
| | |
| BACKGROUND:<br>Postoperative pain remains a significant problem following paediatric surgery. Premedication with a suitable agent may improve its management. Clonidine is an alpha-2 adrenergic agonist which has sedative, anxiolytic and analgesic properties. It may therefore be a useful premedication for reducing postoperative pain in children.<br>OBJECTIVES:<br>To evaluate the evidence for the effectiveness of clonidine, when given as a premedication, in reducing postoperative pain in children less than 18 years of age. We also sought evidence of any clinically significant side effects.<br>SEARCH METHODS:<br>We searched the Cochrane Central Register of Controlled Trials (CENTRAL) in The Cochrane Library (Issue 12, 2012), Ovid MEDLINE (1966 to 21 December 2012) and Ovid EMBASE (1982 to 21 December 2012), as well as reference lists of other relevant articles and online trial registers.<br>SELECTION CRITERIA:<br>We included all randomized (or quasi-randomized), controlled | Cochrane Database Syst Rev. 2014 Jan 28;1:<br><br>**Clonidine premedication for postoperative analgesia in children.**<br><br>*Lambert P, Cyna AM, Knight N, Middleton P.* |

| | |
|---|---|
| trials comparing clonidine premedication to placebo, a higher dose of clonidine, or another agent when used for surgical or other invasive procedures in children under the age of 18 years and where pain or a surrogate (principally the need for supplementary analgesia) was reported.<br>DATA COLLECTION AND ANALYSIS:<br>Two authors independently performed the database search, decided on the inclusion eligibility of publications, ascertained study quality and extracted data. They then resolved any differences between their results by discussion. The data were entered into RevMan 5 for analyses and presentation. Sensitivity analyses were performed, as appropriate, to exclude studies with a high risk of bias.<br>MAIN RESULTS:<br>We identified 11 trials investigating a total of 742 children in treatment arms relevant to our study question. Risks of bias in the studies were mainly low or unclear, but two studies had aspects of their methodology that had a high risk of bias. Overall, the quality of the evidence from pooled studies was low or had unclear risk of bias. Four trials compared clonidine with a placebo or no treatment, six trials compared clonidine with midazolam, and one trial compared clonidine with fentanyl. There was substantial methodological heterogeneity between trials; the dose and route of clonidine administration varied as did the patient populations, the types of surgery and the outcomes measured. It was therefore difficult to combine the outcomes of some trials for meta-analysis.When clonidine was compared to placebo, pooling studies of low or unclear risk of bias, the need for additional analgesia was reduced when clonidine premedication was given orally at 4 µg/kg (risk ratio (RR) 0.24, 95% confidence interval (CI) 0.11 to 0.51). Only one small trial (15 patients per arm) compared clonidine to midazolam for the same outcome; this also found a reduction in the need for additional postoperative analgesia (RR 0.25, 95% CI 0.09 to 0.71) when clonidine premedication was given orally at 2 or 4 µg/kg compared to oral midazolam at 0.5 mg/kg. A trial comparing oral clonidine at 4 µg/kg with intravenous fentanyl at 3 µg/kg found no statistically significant difference in the need for rescue analgesia (RR 0.89, 95% CI 0.56 to 1.42). When clonidine 4 µg/kg was compared to clonidine 2 µg/kg, there was a statistically significant difference in the number of patients requiring additional analgesia, in favour of the higher dose, as reported by a single, higher-quality trial (RR 0.38, 95% CI 0.23 to 0.65).The effect of clonidine on pain scores was hard to interpret due to differences in study methodology, the doses and route of drug administration, and the pain scale used. However, when given at a dose of 4 µg/kg, clonidine may have reduced analgesia requirements after surgery. There were no significant side effects of clonidine that were reported such as severe hypotension, bradycardia, or excessive sedation requiring intervention. However, several studies used atropine prophylactically with the aim of preventing such adverse effects.<br>AUTHORS' CONCLUSIONS:<br>There were only 11 relevant trials studying 742 children having surgery where premedication with clonidine was compared to placebo or other drug treatment. Despite heterogeneity between trials, clonidine premedication in an adequate dosage (4 µg/kg) was likely to have a beneficial effect on postoperative pain in children. Side effects were minimal, but some of the studies used atropine prophylactically with the intention of preventing bradycardia and hypotension. Further research is required to determine under what conditions clonidine premedication is most effective in providing postoperative pain relief in children | |

| | |
|---|---|
| BACKGROUND:<br>Aim of the current meta-analysis was to assess the effects of intraoperative dexmedetomidine on postoperative pain, analgesic consumption, and adverse events in comparison with placebo or opioids in children undergoing surgery.<br>METHODS:<br>This meta-analysis was performed according to the recommendations of the PRISMA statement and the Cochrane collaboration. For dichotomous and continuous outcomes of efficacy and adverse events, the Revman(®) (The Nordic Cochrane Centre, Copenhagen, Denmark) statistical software was used to calculate relative risk (RR), mean difference (MD), and 95% confidence intervals (CI).<br>RESULTS:<br>We included 11 randomized controlled trials - 434 children received dexmedetomidine, 440 received control. In comparison with placebo, children receiving dexmedetomidine showed a reduced RR for postoperative opioids (0.4; 95% CI: 0.26-0.62; P < 0.00001) and postoperative pain (0.51; 95% CI: 0.32-0.81; P = 0.004). Similar results were obtained for the comparison with intraoperative opioids: reduced RR for postoperative pain (0.49; 95% CI: 0.25-0.94; P = 0.03) and the need for postoperative opioids (0.77; 95% CI: 0.60-1.09; P = 0.05).<br>CONCLUSIONS:<br>This meta-analysis revealed a lower risk for postoperative pain and the need for postoperative opioids following intraoperative dexmedetomidine in comparison with placebo or opioids in children undergoing surgery; however, the influence of dexmedetomidine on postoperative opioid consumption is less clear. Although there were only a limited number of adverse events, further studies focusing on procedure specific dexmedetomidine dosing and adverse events are urgently needed | Paediatr Anaesth. 2013 Feb;23(2):170-9. doi: 10.1111/pan.12030. Epub 2012 Oct 9.<br>**Efficacy and safety of intraoperative dexmedetomidine for acute postoperative pain in children: a meta-analysis of randomized controlled trials.**<br><br>*Schnabel A, Reichl SU, Poepping DM, Kranke P, Pogatzki-Zahn EM, Zahn PK.* |

**Ravijuhendid**

**Good Practice in Postoperative and Procedural Pain Management 2nd Edition, 2012 (PEDI-12)**

Küsimusele vastavaid soovitusi ei ole, tekstis on mainitud paratsetamooli: *Paratsetamool on efektiivsem p/o preoperatiivselt kui rektaalselt peale anesteesia induktsiooni. Vähendab opioidi vajadust ja PONV-i.*

Põhineb kolmel uuringul, 1 hindab paratsetamooli farmakokineetikat, teine viide ei ole paratsetamooli uuring.

Anderson 1996 a: 100 last, tonsillektoomiad, preoperatiivne paratsetamool 40mg/kg p/o vs rektaalne paratsetamool 40 mg/ kg peale anesteesia induktsiooni.

- p/o paratsetamooli kontsentratsioon kõrgem ( p < 0.001)
- VAS madalam p/o grupis ( 5 vs 7, p< 0.02)
- Morfiini vajadus väiksem (10 vs 23; p < 0.001)
- PONV sama mõlemas grupis

Recent queries in pubmed

Search,Query,Items found,Time

#3,"Search ((((""postoperative pain"") OR ""postsurgical pain"") OR ""pain"")) AND (((preventive) OR preemptiv

#7,"Search ((((""potoperaive pin"") OR ""postsurgical pin") OR ""pain"")) AND (((preventive) OR preemptiv published in the last 10 years Humans Child: birth---18 years",88,04:56:44

#6,"Search ((((""potoperaive pin"") OR ""postsurgical pain"") OR ""pain"")) AND (((preventive) OR preemptiv published in the last 10 years Humans",517,04:47:19

#5,"Search ((((""potoperaive pain"") OR "postsurgical pain"") OR ""pain"")) AND (((preventive) OR preemptiv published in the last 10 years",524,04:47:13

#4,"Search ((((""postoperative pain"") OR ""postsurgical pain"") OR ""pain"")) AND (((preventive) OR preemptiv

#2,"Search ((""postoperative pain"") OR ""postsurgical pain"") OR ""pain""",522743,04:46:27

#1,"Search ((preventive) OR preemptive) OR prevention",1407821,04:45:23