Comparison of perioperative ketoprofen 2.0 mg kg\(^{-1}\) with 0.5 mg kg\(^{-1}\) i.v. in small children during adenoidectomy

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**Summary**

We have investigated if ketoprofen 0.5 mg kg\(^{-1}\) i.v. provided as good analgesia with less adverse effects compared with ketoprofen 2.0 mg kg\(^{-1}\) i.v. in 107 children, aged 1–7 yr, after adenoidectomy, in a randomized, double-blind, parallel group study design. A standard anaesthetic method was used and all children received fentanyl 1 μg kg\(^{-1}\) i.v. during induction. Children in group 2.0 received ketoprofen 2.0 mg kg\(^{-1}\) and children in group 0.5, 0.5 mg kg\(^{-1}\) i.v. during induction. If the child was in pain, fentanyl 1 μg kg\(^{-1}\) was given i.v. as rescue analgesia. We found that ketoprofen provided good analgesia and only 49% of children required fentanyl in the post-anaesthesia care unit. There were no differences between the groups in the number of fentanyl doses, pain scores or frequency of adverse reactions. No serious adverse reactions occurred. (Br. J. Anaesth. 1997; 79: 606–608).

**Key words**


Postoperative pain is frequent in children, even after minor surgery. After myringotomy alone, more than 40%\(^{1}\) and after adenoidectomy at least 80% of children need analgesic treatment.\(^{2}\)

Adenoidectomy is performed frequently as a day-case operation and in most cases the patients are small children. It is important to find an effective and safe analgesic treatment for these patients. Opioids have been used because of their good analgesic effects, although adverse effects include emesis, excessive sedation and the risk of respiratory depression.\(^{3}\)

Non-steroidal anti-inflammatory drugs (NSAID) have been used for pain treatment in day-case surgery for mild and moderate pain and as a background analgesic for severe pain with good results.\(^{4}\) They also have known adverse effects such as gastrointestinal and renal dysfunction. NSAID increase perioperative bleeding by inhibiting cyclo-oxygenase and this leads to a prolonged bleeding time by inhibition of platelet thromboxane A\(_2\) production and platelet aggregation. Inhibition of cyclo-oxygenase depends on the blood concentration of the drug.\(^{5}\) Because these adverse effects are dose dependent it is important to find the smallest effective dose of the drug.

Ketoprofen is a NSAID with the chemical composition of 2-(3-benzophenyl)-propionic acid.\(^{6}\) It is available in i.v., i.m., oral and rectal formulations. In our previous study we showed that perioperative i.v. ketoprofen had a good analgesic effect in a dose of 2 mg kg\(^{-1}\) during adenoidectomy.\(^{6}\)

Ketoprofen has been recommended for administration in a dose of 2.5 mg kg\(^{-1}\) for acute pain in children.\(^{4}\) In an oral dose of 0.5 mg kg\(^{-1}\), ketoprofen has been shown to have a good antipyretic effect.\(^{7}\)

The aim of this study was to see if ketoprofen 0.5 mg kg\(^{-1}\) i.v. provided as good analgesia with less adverse effects compared with ketoprofen 2.0 mg kg\(^{-1}\) i.v. in children aged 1–7 yr after adenoidectomy.

**Patients and methods**

The study was approved by the Ethics Committee of Kuopio University Hospital and the parents of patients gave written informed consent. We studied 107 ASA I patients, aged 1–7 yr, undergoing adenoidectomy. Patients were excluded if they had a known allergy to ketoprofen or other NSAID, asthma, kidney or liver dysfunction, or haemorrhagic diathesis. A randomized, double-blind, parallel group study design was used. Children were allocated randomly to either group 2.0 (ketoprofen 2.0 mg kg\(^{-1}\)) \((n=54)\) or group 0.5 (ketoprofen 0.5 mg kg\(^{-1}\)) \((n=53)\).

A standard anaesthetic technique was used. Each child was premedicated with diazepam 0.5 mg kg\(^{-1}\) orally up to a maximum of 10 mg, 30–45 min before induction of anaesthesia. EMLA cream (Astra, Sweden) was applied to the skin 60 min before venepuncture. Anaesthesia was induced with thiopentone 5–7 mg kg\(^{-1}\) and fentanyl 1 μg kg\(^{-1}\) i.v. and tracheal intubation was facilitated with atracurium 0.5 mg kg\(^{-1}\). All children received fentanyl 1 μg kg\(^{-1}\) i.v. at induction and no more opioid was given during operation.
After induction of anaesthesia, children received ketoprofen (Orudis, Rhone-Poulenc-Rorer, Denmark) 2.0 or 0.5 mg kg⁻¹ dissolved in 10 ml of 0.9% saline injected i.v. over 10 min. Anaesthesia was maintained with 1–1.2% isoflurane (inspired concentration) and 65% nitrous oxide in oxygen with IPPV. On completion of the procedure, neuromuscular block was antagonized with neostigmine 50 μg kg⁻¹ and glycopyrronium 10 μg kg⁻¹.

All children were given 0.9% saline 10 ml kg⁻¹ h⁻¹ for intraoperative fluid maintenance. After surgery, children were transferred to the post-anaesthesia care unit (PACU) for continuous monitoring of vital signs and assessment of pain.

The adenoids were removed using indirect currettization. Haemostasis was controlled with nasopharyngeal packs with or without electrocautery. Surgeons estimated the amount of bleeding using a five-point scale (1 = “no bleeding”, 2 = “less than normal”, 3 = “normal”, 4 = “more than normal” and 5 = “profuse”). Postoperative pain was assessed by the Maunuksela score, which is an observer assessment based on facial expression, vocalization, movement or rigidity of the limbs and body, response to handling and irritability, together with measured cardiorespiratory variables. In the modified score, 0 = “no pain”, 1–3 = “mild pain”, 4–6 = “moderate pain”, 7–9 = “severe pain” and 10 = “worst possible pain”.

Specially trained research nurses assessed the pain expressed by the child at rest and during swallowing. If the child was in pain (pain score at rest was 3 or more) fentanyl 1 μg kg⁻¹ was given i.v. for rescue analgesia. The dose was repeated at 5-min intervals until the child was comfortable. No more than three doses of fentanyl were allowed in 1 h. No other analgesic medication was permitted during the study. The children were monitored closely after each dose of fentanyl in the PACU. On leaving hospital, pain was assessed by a specially trained research nurse at rest and during swallowing. All adverse reactions were recorded and summarized for each patient.

Analysis of variables was performed using the two tailed Student’s t-test and chi-square test. *P = 0.56 (chi-square test) was considered statistically significant. Results are presented as number of patients (%) or mean (SD) where appropriate.

## Results

Sex distribution, age, weight and type of surgery performed were similar in the two groups (table 1).

There were no differences in the number of fentanyl doses needed in the PACU. In group 2.0, 27 (50%) and in the group 0.5, 25 (47%) children needed supplementary doses of fentanyl. The number of fentanyl doses needed in the PACU was 0.7 (SD 0.8) in both groups.

There were no differences between the groups in the Maunuksela pain scores (table 2).

In the PACU there was no difference in the frequency of adverse reactions between the groups (table 3). In group 2.0, seven (13%) and in the group 0.5, nine (17%) children had one or more adverse reactions. There were no serious adverse reactions but one patient who received ketoprofen 2.0 mg kg⁻¹ developed minor urticaria and conjunctivitis.

The surgeon estimated the amount of intraoperative bleeding using a five-point scale. There was no difference between the groups in the amount of bleeding (table 4). One child in group 2.0 had postoperative bleeding and was transferred to the ward. The bleeding stopped without any intervention. He was observed for a few hours before being discharged.
Discussion

We have found that i.v. ketoprofen at a dose of 2.0 mg kg\(^{-1}\) did not provide better analgesia than a dose of 0.5 mg kg\(^{-1}\) in small children during adenoidectomy. The Maunuksela pain scores were at acceptable levels throughout the study in both groups.

In the PACU only 49% of all children needed supplementary doses of i.v. fentanyl and there was no difference between the groups in the need for supplementary analgesia. In 31% of patients, one dose and in 17% of patients, two doses of fentanyl were given. We found that the need for supplementary doses of fentanyl was smaller than expected, possibly because of the analgesic effects of i.v. ketoprofen during operation.

The incidence of adverse reactions was 15%. In previous studies on the use of ketoprofen the incidence varied from 0% to approximately 50% of patients.\(^5\) There were no serious adverse effects in this study but one patient in group 2.0 had an allergic reaction after injection of ketoprofen and developed urticaria and conjunctivitis. The child was treated with an antihistamine, which alleviated his symptoms in a few hours, but he was observed in a ward overnight. The cause of this allergic reaction was possibly ketoprofen. On the other hand, atracurium is known to release histamine and this may have been a possible cause for the urticaria and conjunctivitis. The incidence and scale of adverse reactions in our study were comparable with other reports of short-term use of NSAID in children.\(^3\)\(^9\)

Epigastric distress is a known adverse effect of NSAID but did not occur in this study. This may be because of the small dose of ketoprofen used and also because it was administered i.v. Oral ketoprofen may cause epigastric distress by local irritation of the gastric mucosa. In our previous study, one child in the ketoprofen group and one child in the placebo group experienced epigastric distress.\(^6\)

Increased perioperative bleeding has been shown to occur with ketorolac 1 mg kg\(^{-1}\) \(^{10}\)\(^{11}\) Gunter and colleagues even suggested that ketorolac is contra-indicated in children undergoing adenotonsillectomy.\(^11\) In their study ketorolac was used in a dose of 1 mg kg\(^{-1}\). In our opinion this dose is rather excessive because in a previous study a dose of 0.2 mg kg\(^{-1}\) had a good analgesic effect after major surgery in children.\(^9\)

We found no difference between the groups in the amount of intraoperative bleeding and none of the children needed further treatment because of bleeding. Only one child in group 2.0 experienced postoperative bleeding. This child was observed for a few hours before discharge. In our previous study, intraoperative bleeding estimated by the surgeon proved to be greater if children received ketoprofen 1 mg kg\(^{-1}\) during operation instead of placebo.\(^6\) In that study none of the children experienced bleeding which required intervention or delay in discharge from hospital.

In our opinion, based on this and our previous study, i.v. ketoprofen is a useful analgesic in children undergoing day-case surgery. It provided good analgesia after adenoidectomy in children and we found no major problems with adverse effects or perioperative bleeding. In our two studies, only one of 271 children required an overnight stay in hospital and none needed treatment for bleeding.

References