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Pain Relief after Strabismus Surgery in Children; Ketoprofen 'Pro Re Nata' or Scheduled Dosing?

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Abstract

Objective: Little is known about recovery, pain and analgesic requirements after discharge following pediatric day-case strabismus surgery. These data are essential in order to provide parents with appropriate instructions at discharge.

Methods: In this prospective, longitudinal, open study of 115 children who underwent strabismus surgery, ketoprofen tablets were prescribed at discharge to be used either as required (Group 1, n=59), or at scheduled times at a dose of 5 mg/kg in 24 h for the first 72 hours (Group 2, n=56). Paracetamol (acetaminophen) was allowed for rescue analgesia in Group 2. Parents recorded pain, pain relief, analgesic consumption, recovery and adverse effects for the first week after discharge in a diary that was returned in a prepaid envelope.

Results: The response rate was 98% (113 out of 115). After discharge 51/57 children in the Group 1 and 41/56 children in the Group 2 (p = 0.026) had pain for a median of 3 days (range 1-9). Most children had mild or moderate pain, but eight children (7%) reported severe pain. The pain relief was significantly better in those children scheduled ketoprofen tablets (p = 0.003) even though more children in Group 2 (39/56) had two muscles operated upon than in Group 1 (18/57). No serious or unexpected adverse events were reported, and no bleeding at the operative site was observed. All expect one child recovered to normal daily activities by the end of the first week.

Conclusion: Pain is a common outcome in children after strabismus surgery, and scheduled analgesic rather than 'Pro Re Nata' (PRN) treatment should be prescribed for 2-3 days after surgery.

Keywords: Pain; Ambulatory surgical procedures; Strabismus; Child; Ketoprofen; Paracetamol; Analgesia

Introduction

Strabismus surgery is the most common eye operation in childhood, one per thousand children in Finland undergoes strabismus surgery annually [1]. Strabismus surgery is associated with significant pain, and thus, postoperative routines should include appropriate analgesics therapy [2]. Non-steroidal Anti-inflammatory Analgesics (NSAIDs), such as ketoprofen, and paracetamol (acetaminophen) are highly effective and safe for short-term symptomatic treatment of mild and moderate pain in children [3-8]. For success in pediatric pharmacotherapy feasible dosage forms are important [9]. Paracetamol is available as an oral suspension, and ketoprofen as a small 25 mg tablet and oral syrup, both of which are feasible dosage forms in younger children [5].

Little is known about pain and recovery at home after strabismus surgery. This survey is a part of our Strabismus Surgery in Children-study and some results have already been published [1,6]. The aim of this study was to evaluate the recovery after discharge in 115 children with strabismus surgery. The primary outcome measure was to compare the pain relief achieved with two different treatment approaches, ketoprofen tablets on a required basis or a scheduled dosing for the first 72 hours after surgery.

Methods

Children, aged 1-15 years with American society of Anesthesiologists' physical status I-II, who were scheduled for day-case strabismus surgery at Kuopio University Hospital and had no contraindications for ketoprofen or paracetamol were enrolled. Children who had a known allergy to paracetamol, ketoprofen or other NSAIDs, asthma, any kidney or liver dysfunction or hemorrhagic diathesis were excluded.

The study was approved by the Ethics Committee of the Hospital District of Northern Savo, Kuopio, Finland, was conducted in accordance with the Declaration of Helsinki, and the National Agency for Medicines was notified of the study design. The parents gave a written informed consent, and those children old enough to understand gave an assent. The patient population was collected in two consecutive groups; the first group compromised 59 children [6] and the second 56 children [1].

The flow chart of the study is described in Figure 1. In brief, in the hospital a standardized anesthesia technique was used [1,6]. All children were given fentanyl 1 microg/kg i.v. during anesthesia, either ketoprofen 1-2 mg/kg i.v. (Orudis, Sanofi, Helsinki, Finland) or ketoprofen i.v. + paracetamol 24 mg/kg by mouth (Panadol 24 mg/ml, GlaxoSmithKline, Ballerup, Denmark) was given for background analgesia, and further doses of fentanyl were allowed for rescue analgesia in the post anesthesia care unit before discharge in the afternoon.

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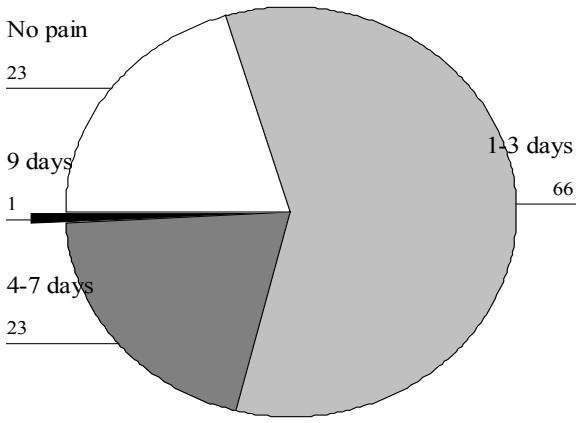

Figure 1: Flow diagram of patient distribution.

The present study was prospective, longitudinal and open. At discharge the children in the first group were prescribed ketoprofen 25 mg or 50 mg tablets to be taken 2-3 times per day to a maximum of 5 mg/kg in 24h as required. In the second group, ketoprofen tablets were instructed to be taken in scheduled times, two or three times a day to a dose of 4-5 mg/kg/24 h, for the first 72 postoperative hours, and after 72h as required. In the second group, if the pain relief achieved with ketoprofen tablets was insufficient, the children were instructed to be given paracetamol oral suspension 12 mg/kg/dose to a maximum of 72 mg/kg in 24h for the rescue analgesia.

At discharge all parents were given a diary which consisted both structured and open-ended questions dealing with pain, pain medication, recovery and adverse events during the first week after the surgery. The diary consisted four pages: three pages described the recovery for the first three postoperative days, and the fourth page the overall recovery during the first week after the discharge. Parents were asked to report how many days children experienced pain. Pain at home was evaluated with a 4-point verbal scale: 1=no pain, 2=mild, 3=moderate and 4=severe pain [10]. Pain at home was also evaluated by using a 100 mm visual analogue scale (VAS, left end=no pain, right end=most pain). Parents were asked to report the number of analgesic doses and if the pain medication was sufficient or not. The efficacy of pain medication was evaluated on a 5-point verbal rating scale: 1=complete, 2=significant, or 3=slight pain relief, 4=no pain relief, or 5=did not receive pain medication. The return to normal daily activities was evaluated by questions about drinking, eating, sleeping, playing and overall impression of child's activity compared to normal. Parents were asked to report all difficulties with pain management, administration problems and adverse events were specially asked for. The parents were asked to return the questionnaire on a prepaid envelope, and if it was not returned within 14 days, the parents were contacted by telephone.

Statistics

Differences between the two groups concerning continuous and nominal variables were analyzed by the Mann-Whitney U-test with two-sided significance, for categorical data the Pearson Chi Square-test was applied, and the Pearson correlation coefficient was used to analyze the correlation between different variables. Results are presented as number of cases (%) or median with range as appropriate. Differences between the groups were considered statistically significant for two-sided P-values under 0.05. All data were entered and analyzed using a statistical package for social sciences (IBM SPSS Statistics 19, Armonk, NY, USA).

Results

In the first group 57/59 diaries and in the second group all 56 diaries were returned, a response rate of 98%. No protocol deviations likely to interfere with the study variables were recorded. The patients' and surgical characteristics of the two group are presented in Table 1. In the first group the children were younger than in the second group (P=0.021, Mann-Whitney U-test), and in the first group two-thirds of the children underwent one muscle operation compared to the second group where two-thirds had two muscle operated upon (P=0.001, Pearson Chi Square-test).

In the first group 51/57 (90%) children and in the second group 41/56 (73%) children (P=0.026) had pain after discharge. Of those 92 children with pain, worst pain was severe in eight (9%), moderate in 30 (33%) and mild in 54 (59%) children with a similar incidence in the two groups. The number of operated muscles had a significant effect on the pain severity after discharge. All eight children with severe pain at home had two muscles operated upon, while 15/20 children with no pain had only one operated muscle (=0.004). The number of fentanyl doses before discharge for sufficient pain relief revealed a positive correlation with the pain severity at home (r=0.25, P=0.007, Pearson correlation coefficient). The median of pain cessation was 3 days (range 1- 9) with no difference between the two groups (Figure 2).

Ninety-seven (86%) children were provided analgesic treatment at home. A median of ketoprofen doses was less in the first group, 4 (0-16) tablets, than in the second group, 9 (0-16) tablets (mean difference 4.0 doses, 95% CI for the difference; 2.6 to 5.4 doses, P=0.001). In the second group 22/56 (39%) children were given paracetamol suspension for rescue analgesia, median 0 (0-13) doses. Two-thirds of the children still needed analgesic treatment on the third post-operative day.

The pain relief was significantly better in the second group (P=0.003) (Figure 3). The satisfaction with the analgesic treatment was similar and high in both groups. Two patients reported that the pain relief was not sufficient; both were in the first group and neither used ketoprofen as prescribed; the other who could have used 15 doses had used ten doses of ketoprofen in five days and the other who could have used nine doses used three doses in three days.

In *a post hoc* analysis the effect of age on pain and recovery was evaluated. In the first group 23 children were aged 2-4 years, 27 were 5-11 years and 7 were 12-14 years old, and in the second group 11 children were aged 2-4 years, 35 were 5-11 years and 10 were 12-15 years old. In the first group school age children, 5-11 years, reported more pain than younger children or adolescents (P=0.028) but in the second group age did not correlate with pain or recovery after strabismus surgery.

	pro re nata dosing group n=57	**scheduled dosing group n=56**
Age median (months)	66	88
Range	24- 166	35-184
Weight median (kg)	24	25
range	Oct-45	Dec-64
Height median (cm)	120	124
range	87-156	87-171
Gender (Male/Female)	23/34	27/29
Number of muscles operated (one/two)	39/18	17/39

Data are presented as median and range, or number of cases (n=113)

Table 1: Patient demographics and surgical data of the two study groups.

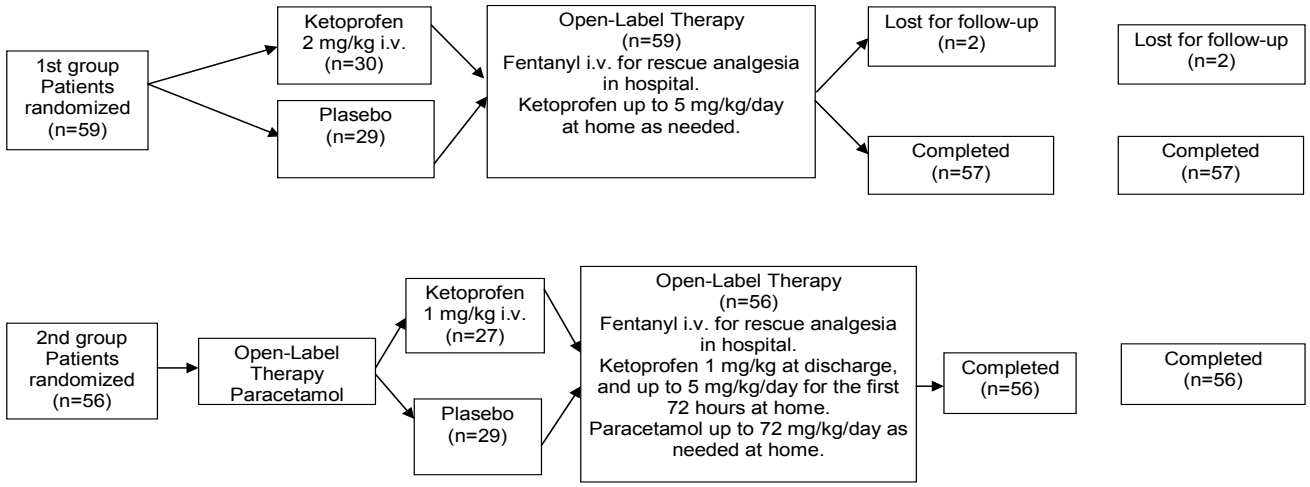

Figure 2: A: Duration of pain after strabismus surgery in the "pro re nata" dosing group (n=57). B: Duration of pain after strabismus surgery in the scheduled dosing group (n=56).

	pro re nata dosing group n=57	scheduled dosing group n=56
Somnolence	51 (89 %)	39 (70%)
Vomiting	7 (12 %)	13 (23%)
Nausea	12 (21 %)	16 (29%)
Epigastric pain	7 (12 %)	5 (9%)
Abdominal pain	7 (12 %)	10 (18%)
Headache	11 (19 %)	13 (23%)
Dizziness	18 (32 %)	18 (32%)
Fever	5 (9 %)	4 (7%)
Other*	1 (1 %)	7 (13%)
Total number of adverse-events	120	125
Number of children with one or more adverse events	52 (91%)	44 (79%)

Data are presented as number of cases (%), n=113.

*diplopia (n=3), diarrhoea (n=2), throat sore (n=2), upper respiratory track infection (n=1), nervousness (n=1).

Table 2: Adverse events after discharge in the two study groups.

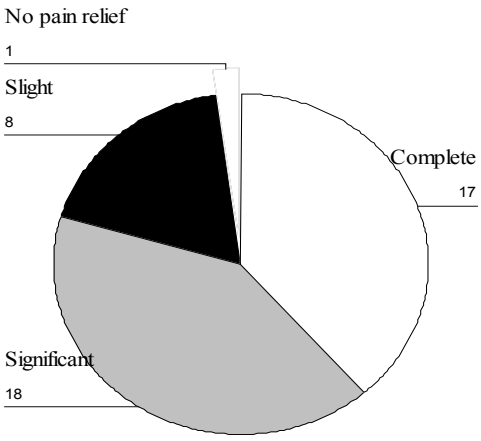

Figure 3a: The pain relief achieved with ketoprofen tablets in the "pro re nata" dosing group (n=44).

Seven of the 56 (13%) children in the first group had problems to take ketoprofen tablets, but none refused to take the medicine. In the second group no cases of analgesic administration was reported.

One hundred (88%) children developed adverse effects, and 96 (85%) reported more than one adverse event (Table 2). However, no serious or unexpected adverse events were reported and the frequency of adverse effects reduced significantly after the operation day (data not shown). Somnolence, reported in 90 (80%) children on the operation day evening, was the most common complaint. Thus, most of the adverse effects were unlikely related to the study medication, and more likely remaining effects of anesthesia. No case of postoperative bleeding was reported.

Most children, 107/113 (95%), returned to normal daily activities within three days after the operation, and only three children had problems beyond the first week. Already on the first postoperative day four-fifths of the children were able to drink, eat and sleep normally, and two-fifths were overall normal. There were no differences between the two groups on the return to the normal daily activities.

Discussion

In the present study less children reported pain after discharge and the pain relief achieved with non-opioid analgesics was significantly better with the scheduled use of ketoprofen (NSAID) tablets for three days after surgery than in the first group were ketoprofen was given only to an established pain. This agrees with a present report in adults, patients having endoscopic sinus surgery prescribed scheduled non-opioid analgesics after discharge used significantly more doses of paracetamol and the recovery was significantly more straightforward than that among those who were prescribed analgesic to be used only as needed [10]. The present study emphasized that strabismus surgery is associated with significant pain in some children [2]. Although the majority of the children had just mild or moderate pain there were almost 10% of children who reported severe pain after discharge. Therefore postoperative routines in children with eye surgery should include scheduled analgesic treatment as long as pain is expected to last, which was 2-3 days in the present study. This approach is supported also by a recent systematic review indicating more consistent analgesic efficacy when multiple doses of NSAID are administered during the

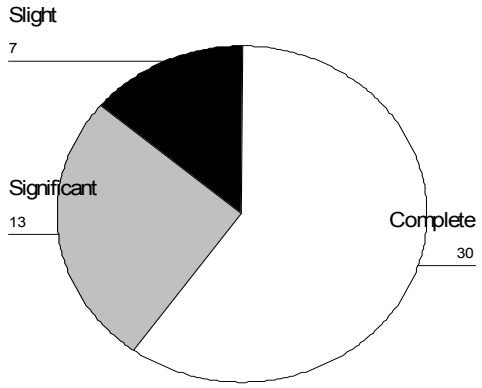

Figure 3b: The pain relief achieved with ketoprofen tablets with/without paracetamol mixture in the scheduled dosing group (n=50).

early perioperative period. In that review NSAIDs proved to be superior compared to paracetamol in acute postoperative pain [7]. However, whether the combination of NSAID with paracetamol may perform better than NSAID alone needs further confirmatory studies [1,8,11].

Severe pain is a significant factor affecting behavioral changes in children [12]. Our experience shows that with scheduled analgesic treatment with non-opioid analgesics major negative consequences after surgery may be prevented [13]. For effective pain management parents counseling is important, because appropriate instructions improve both pain management and recovery after discharge [14]. In the present study most parents followed the instructions given at discharge and all children with pain were provided pain medication at home. The analgesic treatment with non-opioid analgesic was effective and only two children were reported to have achieved no or insufficient pain relief with ketoprofen tablets; both children were provided less analgesic doses than prescribed.

Studies indicate that pain severity after surgery during the first hours of recovery may be used as a guess for analgesic need after discharge [13,15,16]. In the present study, accordingly, children who needed more opioid doses for rescue analgesia at hospital had more severe pain at home. The intensity and cessation of pain are affected also by the extent of surgery; the children with two muscles operated upon had more pain and needed more analgesic doses after the discharge than the children with one operated muscle. This is also the case after throat surgery where children with adenoidectomy have significantly less pain than children with tonsillectomy, which is more extensive procedure [15,16].

There were not serious or unexpected adverse events. Although more doses of ketoprofen were used and more muscles were operated upon in the second group less children were reported to have developed any untoward symptoms after discharge than in the first group children. The most common adverse event was somnolence on the operation day evening. This was considered to be rather a residual effect of the anesthetics than a ketoprofen-related adverse effect [17]. All indicators of discomfort diminished after the operation day, and most children had returned to normal daily activities on the third day after surgery.

It is concluded that pain is a common outcome in children after strabismus surgery, and therefore children should be prescribed scheduled non-opioid analgesics treatment for the first two-three days after discharge to allow a calm recovery.

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References

1. Kokki H, Purhonen S, Teräsvirta M, Ylönen P (2004) Ketoprofen for add-on pain treatment to paracetamol after strabismus surgery in children. Clin Drug Investig 24: 237-244.
2. Finley GA, McGrath PJ, Forward SP, McNeill G, Fitzgerald P (1996) Parents' management of children's pain following 'minor' surgery. Pain 64: 83-87.
3. Anderson BJ (2004) Comparing the efficacy of NSAIDs and paracetamol in children. PaediatrAnaesth 14: 201-217.
4. Alam K, Takrouri MS (1999) Analgesic effects of intra-muscular ketoprofen (Profenid) and pethidine for squint surgery in children. Middle East J Anesthesiol 15: 31-38.
5. Kokki H, Nikanne E, Ahonen R (2000) The feasibility of pain treatment at home after adenoidectomy with ketoprofen tablets in small children. PaediatrAnaesth 10: 531-535.
6. Kokki H, Homan E, Tuovinen K, Purhonen S (1999) Peroperative treatment with i.v.ketoprofen reduces pain and vomiting in children after strabismus surgery. ActaAnaesthesiolScand 43: 13-18.
7. Wong I, St John-Green C, Walker SM (2013) Opioid-sparing effects of perioperative paracetamol and nonsteroidal anti-inflammatory drugs (NSAIDs) in children. PaediatrAnaesth 23: 475-495.
8. Hiller A, Meretoja OA, Korpela R, Piiparinen S, Taivainen T (2006) The analgesic efficacy of acetaminophen, ketoprofen, or their combination for pediatric surgical patients having soft tissue or orthopedic procedures. AnesthAnalg 102: 1365-1671.
9. Kankkunen P, Vehviläinen-Julkunen K, Pietilä AM, Kokki H, Halonen P (2003) Parents' perceptions and use of analgesics at home after children's day surgery. PaediatrAnaesth 13: 132-140.
10. Kemppainen TP, Tuomilehto H, Kokki H, Seppä J, Nuutinen J (2007) Pain treatment and recovery after endoscopic sinus surgery. Laryngoscope 117: 1434-1438.
11. Kokki H (2010) Ketoprofen pharmacokinetics, efficacy, and tolerability in pediatric patients. Paediatr Drugs 12: 313-329.
12. Kotiniemi LH, Ryhänen PT, Moilanen IK (1997) Behavioural changes in children following day-case surgery: a 4-week follow-up of 551 children. Anaesthesia 52: 970-976.
13. Tuomilehto H, Kokki H, Ahonen R, Nuutinen J (2002) Postoperative behavioral changes in children after adenoidectomy. Arch Otolaryngol Head Neck Surg 128: 1159-1164.
14. Sepponen K, Kokki H, Ahonen R (1999) Training of medical staff positively influences postoperative pain management at home in children. Pharm World Sci 21: 168-172.
15. Nikanne E, Kokki H, Tuovinen K (1999) Postoperative pain after adenoidectomy in children. Br J Anaesth 82: 886-889.
16. Salonen A, Kokki H, Nuutinen J (2002) The effect of ketoprofen on recovery after tonsillectomy in children: a 3-week follow-up study. Int J PediatrOtorhinolaryngol 62: 143-150.
17. Kotiniemi LH, Ryhänen PT, Valanne J, Jokela R, Mustonen A, et al. (1997) Postoperative symptoms at home following day-case surgery in children: a multicentre survey of 551 children. Anaesthesia 52: 963-969.