Incidence of bleeding in children undergoing circumcision with ketorolac administration

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Abstract

Introduction: Circumcision is the most common surgical procedure performed by pediatric urologists. Ketorolac has been shown to have an efficacy similar to morphine in multimodal analgesic regimens without the commonly associated adverse effects. Concerns with perioperative bleeding limit the use of ketorolac as an adjunct for pain control in surgical patients. As such, we sought to evaluate our institutional outcomes with respect to ketorolac and postoperative bleeding.

Methods: We retrospectively reviewed all pediatric patients undergoing circumcision from January 1, 2014 to December 31, 2015 at the Alberta Children’s Hospital. Demographics, perioperative analgesic regimens, and return to emergency department or clinic for bleeding were gathered through chart review.

Results: A total of 475 patients undergoing circumcisions were studied, including 150 (32%) who received perioperative ketorolac and 325 (68%) who received standard analgesia. Patients receiving ketorolac were more likely to return to the emergency department or clinic for bleeding (ketorolac group 19/150 [13%], non-ketorolac group 16/325 [5.0%]; p=0.005). Patients receiving ketorolac were more likely to have postoperative sanguineous drainage (ketorolac group 96/150 [64%], non-ketorolac group 150/325 [46%]; p<0.001). There was no significant difference in the number of patients requiring postoperative admission or further medical intervention.

Conclusions: Although a promising analgesic, ketorolac requires additional investigation for safe usage in circumcisions due to possible increased risk of bleeding.

Introduction

Circumcision is a common surgical intervention in pediatric urology indicated in instances of refractory balanitis, pathological phimosis, or paraphimosis. The control of postoperative pain is essential in order to decrease patient morbidity and to improve patient and parent satisfaction. Methods to reduce postoperative morbidity in circumcision include the use of general anesthesia combined with regional block. Common regional blocks include dorsal penile nerve blocks (DPNB) or caudal epidural blocks (CB). Neither has been shown to be more effective than the other in terms of the need for rescue or other analgesia.1,2 DPNB may be preferred over CB in the case of ambulatory children, as CB carries the risk of temporary leg weakness after use.

Even with current analgesia standards, pediatric surgical patients are often at risk of being undertreated for postoperative pain when the regional anesthesia resolves.3 Pain is by far the most common complaint of parents after circumcision2 and a common reason for parents to avoid pursuing circumcision for their child.4 Ketorolac is an effective non-steroidal anti-inflammatory drug (NSAID) that provides an analgesic effect through inhibition of COX-1 and COX-2 within the body.5 Compared to opioids, ketorolac offers equivalent levels of pain relief with a decreased incidence of postoperative nausea and vomiting.6,7 A single dose of systemic ketorolac has been demonstrated to be an effective adjunct in multimodal analgesia regimens in order to reduce postoperative pain.8

Although ketorolac is a promising analgesic, trials for tonsillectomies have suggested an increased risk of postoperative bleeding.9,10 This finding, however, is not consistent.6 The fear of bleeding has led many otolaryngologists and anesthesiologists to avoid ketorolac in tonsillectomies and other conditions that may have an increased risk of bleeding. Bleeding, although uncommon, is the most common complication suffered by children receiving ketorolac.10 Overall, the favourable side effect profile of ketorolac is balanced by concerns of postoperative bleeding. With circumcision being a high-volume pediatric urological procedure, we sought to evaluate the bleeding outcomes of children receiving ketorolac for circumcision.

Methods

We conducted a retrospective study of pediatric patients (<18 years old) at the Alberta Children’s Hospital who underwent circumcision for refractory balanitis, pathologi-
After the procedure, children were observed in the PACU by a nurse. If necessary, analgesics (acetaminophen) were given by a member of the anesthesia team. Children were discharged from the hospital after a period of observation and spontaneous micturition. Statistical analysis via chi-square was performed using SPSS analytical software.

Results

Patient demographics are shown in Table 1. Between the two-year period (January 1, 2014 to December 31, 2015), 475 children aged five days to 17 years (mean age 5.3±4.2) underwent circumcision at the Alberta Children’s Hospital. A general analgesic regimen was used in 325 children (68%), while perioperative ketorolac was used in 150 children (32%). There was no significant difference in age between groups (ketorolac group 5.6±4.1 years, non-ketorolac group 5.2±4.2 years; 𝑝=0.496) and perioperative ketorolac was administered in the ketorolac group (0.44±0.14 mg/kg; range 0.11–1.14).

Results of data analysis are displayed in Table 2. There was a significantly higher incidence of postoperative sanguineous drainage for ketorolac patients: 64% ketorolac vs. 46% non-ketorolac (odds ratio [OR] 2.07; 95% confidence interval [CI] 1.39–3.09; 𝑝<0.001). There was a significantly higher return to the emergency department or clinic for bleeding for ketorolac patients: 13% ketorolac vs. 5% non-ketorolac (OR 2.63; 95% CI 1.30–5.32; 𝑝=0.005). There was no difference in postoperative admission between the groups: 0% ketorolac vs. 0.9% non-ketorolac (OR 0.991; 95% CI 0.98–1.00; 𝑝=0.238).

Discussion

Circumcision is the most common surgical procedure performed by pediatric urologists. Ketorolac has been shown to have an efficacy similar to morphine in multimodal analgesic regimens without the commonly associated adverse effects.6,7 Unfortunately, the most common side effect of ketorolac is increased bleeding.5 As such, the objective of this study was to retrospectively evaluate bleeding outcomes in children under-
going circumcision with ketorolac. In addition, any serious adverse events would help in the design of future randomized trials involving ketorolac in pediatric surgeries.

Overall, there was a significantly higher incidence (p<0.001) of postoperative sanguineous drainage for ketorolac patients (96/150, 64%) compared to the non-ketorolac group (150/325, 43%). In other words, the surgical site of ketorolac patients looked bloodier than those of standard analgesia patients. With ketorolac patients exhibiting a bloodier surgical site, surgeons may be called to the PACU more frequently. In addition, patients receiving ketorolac were found to be more likely to return to the emergency department or clinic for bleeding (ketorolac group 19/150 [13%), non-ketorolac group 16/325 [5%]; p=0.005). This suggests a possible safety concern towards ketorolac administration in pediatric patients. Furthermore, additional visits to a physician increase the burden to our healthcare system. There was no significant difference for postoperative admission between groups. Although promising, the low incidence of admissions makes this result inconclusive.

An attempt was made to evaluate a dose-response relationship between ketorolac and risk of bleeding; however, anesthetists at the Alberta Children’s Hospital tended to use an average 0.5 mg/kg dosage of ketorolac for each patient and, therefore, no dose response was seen. Furthermore, the number of patients with postoperative bleeding requiring return to medical attention was low, making this a small sample size to evaluate.

There are currently no studies regarding circumcision and ketorolac in previous literature to our knowledge. That being said, pediatric tonsillectomy studies have demonstrated increased risk of bleeding with ketorolac.9,10 This finding, however, is not consistent.6 Although findings in literature are conflicting, the fear of bleeding has led many otolaryngologists and anesthesiologists to avoid ketorolac in tonsillectomies and other conditions that may have an increased risk of bleeding. The results of this circumcision study raise concerns about bleeding and supports the findings of most pediatric tonsillectomy studies.

As a retrospective cohort study, this study was limited in a few areas. Firstly, key outcomes, such as postoperative pain control, were not recorded. This means that although ketorolac resulted in more bleeding events, we have no indication of whether the pain control may have been worth the risk. To further explore this area, a randomized, controlled trial of pain control in ketorolac and non-ketorolac patient is currently underway. In addition, rare outcomes, such as postoperative admission or additional surgical intervention, were difficult to evaluate. A meaningful conclusion for these outcomes would require a much larger sample size than the number of studies we had for review at the Alberta Children’s Hospital.

Another limitation was that patients could have presented to hospitals other than the Alberta Children’s Hospital for bleeding. As a result, some bleeding cases could have been missed. To reduce this effect, patients were given a standardized sheet that instructed them to come back to Alberta Children’s Hospital given any concerns; however, this may not have always been followed by patients. In addition, patients were instructed to take ibuprofen and acetaminophen for postoperative pain and, unfortunately, adding an NSAID could have increased the anticoagulation effect. With this database, it was not possible to tell which patients took ibuprofen or how much they took. An ongoing prospective study with postoperative home phone calls aims to evaluate this parameter further.

Overall, ketorolac patients had significantly more bleeding events requiring medical attention than patients receiving standard analgesia during circumcision. In addition, surgeons may be called to the PACU more frequently with more sanguineous ooze noted in ketorolac patients. Although a promising analgesic, ketorolac requires additional investigation for safe use in circumcisions due to possible increased risk of bleeding. We have launched a randomized, controlled trial evaluating the pain control and safety of ketorolac in pediatric circumcisions and hope to provide more answers on this topic.

Competing interests: Dr. Weber has participated in a clinical trial supported by Allergan. The remaining authors report no competing personal or financial interests.

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References


Table 2. Comparative analysis with chi-square for children undergoing circumcision with or without ketorolac administration

<table>
<thead>
<tr>
<th>Absolute count without ketorolac</th>
<th>Absolute count with ketorolac</th>
<th>Odds ratio (95% CI) p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Postoperative sanguineous drainage</td>
<td>150/325 (46.2%)</td>
<td>96/150 (64.0%)</td>
</tr>
<tr>
<td>Return to ED or clinic for bleeding</td>
<td>16/325 (4.9%)</td>
<td>19/150 (12.7%)</td>
</tr>
<tr>
<td>Postoperative admission within 30 days</td>
<td>3/325 (0.9%)</td>
<td>0/150 (0.0%)</td>
</tr>
</tbody>
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CIs: confidence interval; ED: emergency department.


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