A COMPARATIVE STUDY OF THE ANALGESIC EFFECT OF INTRAVENOUS PETHIDINE VS. KETOROLAC AFTER INGUINAL HERNIA SURGERY IN CHILDREN UNDER GENERAL ANESTHESIA

HAMID HAJIGHOLAM SARYAZDI*, OMID AGHADAVOUDI*, AMIR SHAVA**, AMIN MASOUMI*** AND PARNIAN SABERIAN****

Introduction: Postoperative pain due to tissue damage caused during surgery not only causes discomfort for the patients, but can also result in prolonged hospitalization, increased morbidity and respiratory disorders, and readmission to the hospital. For postoperative pain control, numerous methods and medications have been suggested, such as non-steroidal anti-inflammatory drugs (NSAIDs) and narcotics. Pethidine, as a narcotic analgesic, and ketorolac, as an NSAID, are widely used for pain control. Thus, in this study, the effects of these two drugs were studied and compared in terms of pain control after inguinal hernia surgery in children of 1-12 years of age.

Materials and Methods: Sixty-six children undergoing inguinal herniorrhaphy were selected and randomly divided into 2 groups. The first group received 0.5 mg/kg ketorolac and the second group received 1 mg/kg pethidine during extubation. Postoperative pain (using Wong Baker pain scale) and complications were measured until 24 hours after surgery.

Results: Mean and standard deviations of postoperative pain 1 hour after surgery in the pethidine and ketorolac groups were 5.06 ± 1.41 and 3.88 ± 0.93, respectively. The scale was significantly lower in the ketorolac group (P <0.001). Postoperative pain intensity 2 hours after surgery in these two groups was 4.48 ± 1.52 and 3.55 ± 1.15, respectively, and the difference between the two groups was significant (P = 0.006). The variation in postoperative pain intensity in the ketorolac group was statistically lower than the pethidine group (P = 0.020).

Conclusion

Keywords: Postoperative pain, ketorolac, pethidin, inguinal hernia surgery

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Introduction

Pain is a defense mechanism induced by tissue damage which causes individuals to react in order to resolve the pain stimulus. Nociceptors are free nerve endings and are stimulated by substances discharged from damaged tissues (such as bradykinin). Postoperative pain due to tissue damage caused during surgery can be the cause of much discomfort for patients. Pain not only affects the body, but also affects the mind and spirit. Prolonged hospitalization, increased morbidity in patients due to lack of mobility and respiratory disorders, and readmission to the hospital can be complications of inadequate postoperative pain control. In addition to having physical and psychological effects, pain also stimulates the sympathetic nervous system and causes side effects such as tachycardia, hypertension, myocardial infarction (MI), hypoventilation, and impaired wound healing.

Effective pain control increases patient satisfaction, reduces the length of hospitalization, and shortens the recovery time after surgery. Moreover, pain is an important criterion for patient satisfaction with physicians and provided treatment operations. Therefore, adequate postoperative analgesia is required and can be provided through different methods, notably prescription of opioids, non-steroidal anti-inflammatory drugs (NSAIDs), and local anesthetics.

Herniorrhaphy in children is associated with postoperative pain that can cause severe distress and complications. The present study aimed to compare the analgesic effect of intravenous pethidine or ketorolac after inguinal hernia surgery in children under general anesthesia.

Materials and Methods

This study was a double-blind clinical trial conducted in 2014 at Alzahra and Imam Hossein Hospitals in Isfahan, Iran. The target population consisted of 1-12 year old children undergoing elective inguinal hernia surgery at the abovementioned centers. Inclusion criteria included patients undergoing elective inguinal hernia surgery, age range of 1-12 years, willingness to participate in the study, lack of psychiatric problems, absence of coagulation disorders and chronic pain syndrome, no history of gastrointestinal bleeding and peptic ulcer, and no history of seizures. It was also decided that in case of any anesthetic and surgical complications that resulted in a change of surgical and anesthetic procedures, such as unexpected increase or decrease in blood pressure, and incidence of dysrhythmia in need of treatment, the patient would be excluded from the study. The required sample size for this study was calculated at 33 patients in each group. This amount was calculated using the sample size estimation formula to compare the two means, and considering the 95% confidence level, test power of 80%, standard deviation of postoperative pain of 1.17, and least significant difference between the two groups of 0.8.

After obtaining the approval of the proposal and the Medical University Ethics Committee, 66 patients, who met the inclusion criteria, were enrolled in the study. To ensure blinding, data was collected by one person and the intervention was conducted by another. Patients were initially administered premedication (intravenous midazolam 0.05 mg/kg), and then, transferred to the operating room, and were placed under general anesthesia using sodium thiopental 5 mg/kg, fentanyl 1-2 μg/kg, and atracurium 0.05 mg/kg. After intubation anesthesia was maintained with 1-2% isoflurane and a combination of oxygen and N2O (50%-50%).

After completion of surgery and before extubation, the patients were divided into groups A and B through randomized block method. Group A received 0.5 mg/kg intravenous ketorolac and group B received 1 mg/kg intravenous pethidine. After extubation patients were transferred to the recovery room. In the recovery room, the children’s pain was measured using a standard pediatric pain scale. Based on the Wong Baker pain scale, if the pain intensity was higher than 4, analgesics were prescribed for the patient (preferably 0.5 mg/kg pethidine). In addition, the level of patient’s consciousness was examined after being brought to the recovery room and at 1, 2, 6, 12, and 24 hours after surgery. Hemodynamic parameters
including blood pressure, pulse rate, all used medications and their possible side effects, such as gastrointestinal bleeding, respiratory apnea, respiratory depression (respiratory rate less than 12 per minute), body rash, and time of first additional analgesic dose administration were recorded. Patients were discharged from the recovery room after regaining full consciousness based on the modified Aldrete score. Furthermore, the incidence of vomiting at the mentioned times were evaluated, and in case of its incidence, 0.07 mg/kg dose of metoclopramide was administered. The total dose of metoclopramide administered in 24 hours in both groups was determined and recorded.

After data collection, the codes were opened by the main executor of the research and the data were analyzed using SPSS software (version 22; SPSS Inc., Chicago, IL, USA). In order to compare the mean of qualitative variables between the groups, independent t-test, and if necessary, Mann-Whitney test were used. To compare the frequency distribution of qualitative variables between the two groups chi-square test was used. Repeated measures analysis of variance (ANOVA) was used to analyze the variation in hemodynamic parameters and pain after surgery. Statistical Significance was considered at P <0.05.

Results

Sixty six children undergoing inguinal hernia operation were randomly divided into two groups of 33 patients each. The mean ages of the groups receiving pethidine and ketorolac were 4.95 ± 2.58 and 4.86 ± 2.59 years, respectively. There was no significant difference between the two groups (P = 0.89). The gender ratios (female/male) in the two groups were, respectively, 28/5 and 30/3, and was not significantly different (P = 0.71). The variation in hemodynamic parameters before surgery until 24 hours after surgery in both groups are illustrated in figs. 1 to 4. Variations in systolic and diastolic blood pressure, mean arterial blood pressure, and pulse showed no significant difference before surgery and until 24 hours after surgery in both groups (P >0.05).
Table 1 shows the mean and standard deviation of consciousness level and postoperative pain intensity in both groups. The level of consciousness on admission to the recovery room and at 1 hour after the operation in the group receiving ketorolac was significantly higher ($P<0.05$). However no significant differences were observed in the consciousness level until 24 hours after surgery in the two groups ($P=0.091$). Pain intensity and additional analgesics received in both groups are presented in Table 2. The intensity of pain was only different between the two groups at 6 hours after surgery and being lower in the Ketorolac groups. No differences were seen in the additional analgesics received between the two groups.

The time to first narcotic adminisration, dose of narcotics and metoclopramide were not different between the two groups (Table 3). However, the length of stay in the recovery room was higher in the ketorolac group (Table 3). No postoperative complications were observed in both groups.

### Discussion

In the present study, administration of ketorolac reduced pain and the length of stay in the recovery room. In this study, although no significant difference was observed between narcotic dose and the first time of receiving analgesics in the two groups, patients receiving ketorolac used significantly less narcotics and their first analgesics administration time was shorter.

NSAIDs have fewer complications compared to narcotics. Postoperative complications were not observed in any of the patients of the present study. Ketorolac is an NSAID and its anti-inflammatory effect is due to the inhibition of prostaglandin synthesis. Like other cyclooxygenase inhibitors, ketorolac inhibits platelet aggregation, and thus, can increase the risk of bleeding; however, this effect was not observed in the present study. Various

### Table 1

The mean and standard deviation of the level of consciousness and postoperative pain intensity in the two groups.

<table>
<thead>
<tr>
<th>Time variable</th>
<th>Level of consciousness</th>
<th>Postoperative pain intensity</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pethidine (n =33)</td>
<td>Ketorolac (n =33)</td>
</tr>
<tr>
<td>Into Recovery</td>
<td>2.37 ± 0.98</td>
<td>3.63 ± 1.08</td>
</tr>
<tr>
<td>1 hour after surgery</td>
<td>1.72 ± 0.52</td>
<td>1.67 ± 0.5</td>
</tr>
<tr>
<td>2 hours after surgery</td>
<td>1 ± 0.01</td>
<td>1.60 ± 0.24</td>
</tr>
<tr>
<td>6 hours after surgery</td>
<td>1 ± 0.01</td>
<td>1 ± 0.01</td>
</tr>
<tr>
<td>12 hours after surgery</td>
<td>1 ± 0.01</td>
<td>1 ± 0.01</td>
</tr>
<tr>
<td>24 hours after surgery</td>
<td>1 ± 0.01</td>
<td>1 ± 0.01</td>
</tr>
<tr>
<td>P (between the two groups)</td>
<td>0.091</td>
<td></td>
</tr>
</tbody>
</table>
articles have declared different findings regarding the use of ketorolac and its effect on increasing the risk of bleeding during or after surgery. However, in the majority of these studies, no difference was observed between ketorolac and other narcotics regarding increased risk of bleeding\textsuperscript{15,16}. For example, ketorolac use in endoscopic sinus surgery is without complications and does not increase the risk of bleeding or anemia due to acute blood loss\textsuperscript{17}. In addition, the use of ketorolac in pediatric osteotomy in the lower extremities, pediatric cardiac surgery, scoliosis surgery, and urology surgery has been announced to be without complications and safe\textsuperscript{7,8,18-20}. Although some articles showed increase in bleeding\textsuperscript{21} during or after surgery\textsuperscript{22,23}, the effectiveness of ketorolac in controlling acute pain after abdominal surgery has been well documented. It has rapid effectiveness and can be used as an analgesic during the surgery and for pain control after surgery\textsuperscript{24}. In the study by Kay et al., the use of ketorolac for children undergoing surgery due to bone fracture was without complications; no observations were reported regarding infection and wound problems, or increased risk of delayed bone repair or lack of bone repair\textsuperscript{25}.

In many studies, the use of ketorolac after abdominal or pelvic surgery, urological surgery, lumbar decompression surgery, and cesarean section had significant analgesic effects and reduced the need for narcotics\textsuperscript{5-10}. In some studies, only a reduction in the need for narcotics was reported. Nevertheless, it did not decrease the duration of hospitalization and returning to oral intake of nutrition\textsuperscript{26}. In some studies, in addition to the effectiveness of a single dose of ketorolac in reducing post-operative pain, they also showed that ketorolac reduced nausea and vomiting\textsuperscript{27}. Numerous studies have been conducted on the use of analgesics for inguinal hernia surgery. For example, in the study of Lau et al., ketorolac IV before inguinal hernia repair surgery had the same analgesic effect as that of diclofenac suppository\textsuperscript{28}. In another study conducted by Splinter et al., in

\textbf{Table 2}

<table>
<thead>
<tr>
<th>Time variable</th>
<th>Severe pain (higher than 4)</th>
<th>Additional analgesic dosage received</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pethidine (n = 33)</td>
<td>Ketorolac (n = 33)</td>
</tr>
<tr>
<td>Into Recovery</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>1 hour after surgery</td>
<td>15 (45.5%)</td>
<td>13 (39.4%)</td>
</tr>
<tr>
<td>2 hours after surgery</td>
<td>6 (18.2%)</td>
<td>3 (9.1%)</td>
</tr>
<tr>
<td>6 hours after surgery</td>
<td>10 (30.3%)</td>
<td>3 (9.1%)</td>
</tr>
<tr>
<td>12 hours after surgery</td>
<td>2 (6.1%)</td>
<td>3 (9.1%)</td>
</tr>
<tr>
<td>24 hours after surgery</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
</tbody>
</table>

\textbf{Table 3}

<table>
<thead>
<tr>
<th>Groups variable</th>
<th>Pethidine (n = 33)</th>
<th>Ketorolac (n = 33)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>First narcotic administration</td>
<td>1.79 ± 0.42</td>
<td>1.33 ± 0.42</td>
<td>0.45</td>
</tr>
<tr>
<td>Narcotic dosage</td>
<td>8.64 ± 5.53</td>
<td>6.82 ± 5.84</td>
<td>0.20</td>
</tr>
<tr>
<td>Metoclopramide dosage</td>
<td>1.89 ± 0.94</td>
<td>1.62 ± 0.55</td>
<td>0.47</td>
</tr>
<tr>
<td>Length of stay in the recovery room</td>
<td>71.52 ± 12.4</td>
<td>83.48 ± 9.96</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

\textsuperscript{M.E.J. ANESTH 23 (5), 2016}
inguinal hernia repair surgery, the intravenous use of ketorolac was preferred to caudal analgesia\textsuperscript{11}. In addition, in the study of Hong et al., preoperative administration of ketorolac for pain relief was effective in inguinal hernia repair in children\textsuperscript{29}. In the study by Lieh-Lai et al., the analgesic effects of morphine and ketorolac in children after surgery were compared. They found that the analgesic effect of ketorolac was comparable with morphine, and a single dose of ketorolac did not have an abnormal effect on postoperative bleeding\textsuperscript{30}.

In the study by Eberson et al., the effects of ketorolac were examined after pediatric orthopedic surgery. In this study, the ketorolac group had shorter hospitalization length and showed no bleeding complications. Therefore, they announced that ketorolac was a safe and effective method of reducing postoperative pain\textsuperscript{31}. Some studies suggest that narcotics, compared to NSAIDs, have better analgesic effects. In addition, adding ketorolac to narcotics reduced complications and the need for narcotics\textsuperscript{32}.

Therefore, based on the results of this study and their comparison to other studies, it can be concluded that ketorolac is effective for pain relief and reduction of complications after inguinal hernia surgery and it is superior to pethidine, and thus, its use is recommended.
References


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* Train-of-four
† Post-tetanic count
‡ Second twitch

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