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Original Article

Ketorolac vs. tramadol for pain management after abdominal surgery in children

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Abstract

Background Tramadol is a pure analgesic widely used for postoperative treatment and well tolerated by children. However, it has only a 50% efficacy. Ketorolac, a non-steroid anti-inflammation drug (NSAID), is widely used in adults and has up to 85% clinical efficacy. Data supporting the use of ketorolac in children has been limited.

Objective To compare the clinical efficacies of intravenous ketorolac and tramadol for moderate-to-severe pain management after abdominal surgery in children.

Methods A double-blind controlled trial was conducted in Moh. Hoesin Hospital, Palembang, from January to June 2012. Subjects were postoperative children aged 1-7 years who met the inclusion criteria. They were randomized into two groups who received either intravenous ketorolac or tramadol. Subjects assessed their pain level using the *Face, Legs, Arms, Cry and Consolability* (FLACC) pain scale. The FLACC scores ≤3 were considered to indicate clinical success of the intervention. Data were analyzed by T-test, Chi-square test, and Fischer's exact test.

Results Of the 60 subjects who underwent abdominal surgery with general anesthesia, 31 (52%) were boys and 29 (48%) were girls. Subjects' mean age and body weight were 3.7 (SD 1.82) years and 12.6 (SD 2.85) kg, respectively. Mean duration of surgery was 71.7 (SD 21.11) minutes and mean post-operative FLACC score was 6.6 (SD 0.5). Eight subjects dropped out of the study. Efficacies of ketorolac and tramadol were not significantly different at 21/26 and 17/26, respectively (P=0.35). In addition, there was no significant difference in the number of patients experiencing a >3 FLACC score decline between ketorolac and tramadol groups (P=0.61).

Conclusion There is no significant difference in the efficacies of intravenous ketorolac and tramadol for moderate-to-severe pain management after abdominal surgery in children. **[Paediatr Indones. 2014;54:118-21.]**

Keywords: *intravenous, ketorolac,tramadol, FLACC*

About 75% children who undergo abdominal surgery experience moderate-to-severe pain and do not receive adequate pain management. The administration of adequate analgesics may minimize and prevent complications caused by pain, help the patient feel comfortable, and reduce morbidity and mortality rates.[1,2]

Tramadol has been used as a postoperative analgesic and is well tolerated in neonates and children.[2,3] However, several studies reported that the clinical efficacy of tramadol as an analgesic was only 50%.[3,4] In adults, ketorolac has been widely used as a postoperative analgesic for moderate-to-severe pain, with a clinical efficacy of up to 85%.[5] Data supporting the use of ketorolac for postoperative pain management in children is limited.

The purpose of this study was to compare the clinical efficacies of intravenous ketorolac and tramadol for moderate-to-severe pain management after abdominal surgery in children.

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Methods

This double-blind randomized controlled trial was conducted in Moh. Hoesin Hospital, Palembang, from January to June 2012, on 60 subjects who met the inclusion criteria. Inclusion criteria were subjects aged 1-7 years who underwent abdominal surgery with general anesthesia and had FLACC pain scores of ≥4 before the intervention. Level of pain was assessed by the FLACC pain scale.

We excluded patients with loss of consciousness, renal dysfunction, platelet count <150,000/mm^3, clotting time >9 minutes, history of asthma, liver dysfunction, peptic ulcers, as well as those who used tricyclic antidepressants, selective serotonin reuptake inhibitors (SSRI), monoamine oxide inhibitors (MAOI), antipsychotics, acetylsalicylic acid, oxpentafylline, probenecid, lithium salt, heparin, or regional anesthesia. Patients were considered to have dropped out of the study if they experienced loss of consciousness (GCS<15), adverse drug effects, or death.

Subjects were randomly assigned to 2 groups through sealed envelopes drawn by the anesthesiologist. For induction and maintenance of anesthesia we administered 2 μg/kg body weight intravenous fentanyl and 50% nitrous oxide (N_2O). For muscle relaxants, we used 0.5 mg/kg body weight intravenous atracurium and 2% volume volatile sevoflurane. Pain scoring was performed after the subject regained consciousness (GCS >14) and experienced pain. Analgesics were administered if they scored ≥4 on the pain scale.

Subjects in group I received 2mg/kg body weight intravenous tramadol every 6 hours, while those in group II received 0.5mg/kg body weight intravenous ketorolac every 6 hours. Oral or rectal paracetamol at a dose of 10-15mg/kg body weight was given every 6 hours to patients whose FLACC scores were <4. The analgesic intervention was replaced by 0.1 mg/kg body weight intravenous morphine sulfate every 12 hours as a rescue analgesic if the pain scale was still ≥4 at 24 hours of observation. FLACC scores ≤3 were considered to indicate clinical success of the intervention.

Data was analyzed using the SPSS program version 15 (*SPSS Inc.*, 2007). Continuous data was analyzed using *t*-test and categorical data was analyzed

Table 1. Characteristics of subjects by analgesic group (n=52)

Characteristics	Ketorolac group (n=26)	Tramadol group (n=26)
Gender, n		
• Males	14	14
• Females	12	12
Mean age (SD), years		
• 1 – <5 years old	2.3 (1.07)	2.5 (0.92)
• 5 – 7 years old	5.4 (0.3)	5.9 (0.53)
Mean body weight (SD), kg	12.3 (2.74)	13 (2.86)
Nutritional status, n		
• Well-nourished	5	8
• Undernourished	21	18
Indications for abdominal surgery, n		
• Intra-abdominal tumor	2	4
• Perforated appendicitis	2	3
• Visceral rupture	4	5
• Incarcerated inguinal hernia	5	5
• Obstructive ileus	6	4
• Reducible inguinal hernia	7	5
Mean duration of surgery, minutes (SD)	71.7 (23.15)	69.6 (19.33)
Mean interval between end of surgery and onset of pain after regaining consciousness (SD), minutes	22.3 (6.36)	22.5 (7.11)
Mean FLACC score after regaining consciousness (SD)	6.5 (0.51)	6.5 (0.51)

using Chi-square and Fischer's exact tests.

This study was approved by the Board of Ethics of Sriwijaya University Medical School and subjects' parents provided informed consent.

Results

Sixty children aged 1 to 7 years participated in this study but only fifty-two subjects completed the study. Reasons for dropping out were death within 18-24 hours after surgery (3 children), loss of consciousness within 6-12 hours after surgery (2 children), transfer to another hospital (2 children), or gastrointestinal hemorrhage before completing 4 doses of analgesic (1 child). Characteristics of the subjects by analgesic group are shown in **Table 1.**

At 1 hour after drug administration, the mean FLACC score decline in the ketorolac group was 3.1 (SD 1.05) compared to 2.6 (SD 1.03) in the tramadol group. Twenty-five subjects in the ketorolac group and 23 subjects in the tramadol group had ≥3 decline of FLACC score in 1 hour observation. This proportion was not significantly different between the two groups (P=0.61).

Rescue analgesic was given to 5/26 children in the ketorolac group and 9/26 in the tramadol group. Based on the need for rescue analgesics, ketorolac and tramadol was deemed effective for 21/26 and 17/26 of the subjects, respectively, not a statistically significant difference (P=0.35).

At 2 hours after drug administration there were 38 subjects, 21 in the ketorolac group and 17 in the tramadol group, who did not require rescue analgesics. Mean baseline pain scores in the ketorolac and tramadol groups were 6.4 (SD 0.51) and 6.2 (SD 0.44), respectively. Unpaired T-test between groups showed no significant difference between groups (P=0.22). All subjects experienced declines in FLACC score ≥3 in 2-24 hours after drug administration.

Discussion

The first dose of medication was efficacious in 21/26 of the ketorolac group and in 17/26 of the tramadol group. This result is similar to another study reporting that ketorolac efficacy was 85%,[5] while other study reported that tramadol efficacy was only 50%.[4] However, a study found that intravenous tramadol was more effective (90%) than intravenous ketorolac for pain management of inguinal herniotomy.[6] Their subjects all underwent similar surgeries, herniotomy.[6] One limitation of our study was the lack of homogenity in the types of surgery our subjects underwent, some of which take longer durations. Further study with more homogenous subjects, in terms of indications for surgery, is needed to limit the variability in degree of pain caused by surgery.

A previous study showed that there was a significant decline in pain scale score after intravenous administration of ketorolac at the 30-minute, post-operative observation.[7] In contrast, we observed that the decline in FLACC score took a longer time and there was no significant difference in the time required to lower the mean pain score to ≤3. This difference might be due to the type of surgery, tonsillectomy in their subjects,[7] with less tissue damage and less induced pain, than abdominal surgery in our subjects.

We clinically monitored the following adverse effects: gastrointestinal (GI) disturbance such as nausea, vomiting, or GI bleeding, as well as skin bleeding, petechiae, bradycardia, urinary retention, seizure and respiratory depression. During the observation, one subject in the ketorolac group experienced GI bleeding, so the analgesic administration was stopped and replaced with morphine sulfate. This patient was excluded due to this severe adverse effect. Nausea and vomiting were observed in 2 subjects in the ketorolac group and 5 subjects in the tramadol group. Gastrointestinal tract complaints in our tramadol group were more frequent than in Barsoum's study which reported that 4% subjects experienced nausea and vomiting.[8] Another study also reported that as much as 7% of the subjects in the ketorolac group complained of nausea and vomiting.[9]

In conclusion, there is no significant difference between intravenous ketorolac and intravenous tramadol efficacy for moderate-to-severe pain management after abdominal surgery in children.

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