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Cost-effectiveness comparison between caudal block and intravenous ketorolac as an early post-operative analgesic in pediatric patients underwent surgery below umbilicus segment

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ABSTRACT

Post-operative pain treatment in pediatric is frequently inadequate that could lead to psychological, physiological and behavioral changes. Therefore, adequate pediatric pain management is needed. Some analgesics such as ketorolac and regional anesthesia techniques such as caudal block have been applied to relieve pain. Ketorolac and caudal block have its own advantages and disadvantages. The aim of study was to compare the cost-effectiveness of ketorolac and caudal blok as a post-operative analgesic in pediatric. This was double blind randomized controlled clinical trial with parallel design conducted in Dr. Sardjito General Hospital. The subjects were children who underwent surgery below umbilicus segment. Seventy patients were randomly divided into two groups with 35 patients in each group. Group I (Caudal block Group) was given caudal block with bupivacaine 0.12% 1 mL/kg body weight (BW) whereas Group II (Ketorolac Group) was given ketorolac 0.5 mg/kg BW intravenously (IV). The patient's pain was scored at 0, 15, 30, 45 minute and 1, 2, 3 hours after the conscious patients using modified Children's Hospital of Eastern Ontario Pain Scale (mCHEOPS). Furthermore, the cost-effectiveness the both interventions was also compared. The caudal block was more effective in reducing pain than the ketorolac at minutes 0 (27/8 vs 10/25) and 15 (34/1 vs 18/17) ($p<0.05$). However, at third hour the ketorolac revealed more effective than the caudal block (29/6 vs 32/3) ($p<0.05$). The cost of the caudal block was higher than the ketorolac (IDR 95.860 ± 5.745 vs IDR 7.200 ± 14.886) ($p<0.05$). However, the length of stay after the caudal block was shorter than the ketorolac (40.43 ± 13.899 vs 48.57 ± 14.068) ($p<0.05$). Morphine was more needed for rescue analgesic in the ketorolac ($p < 0.05$) in first hour of operation, whereas after three hour operation paracetamol was more needed in caudal block ($p < 0.05$). In conclusion, the caudal block is not more cost-effective than ketorolac in reducing post-operative pain in pediatric patients underwent surgery below umbilicus segment.

ABSTRAK

Pengobatan nyeri setelah operasi pada anak sering tidak memadai sehingga dapat menyebabkan perubahan psikologis, fisiologis dan perilaku. Oleh karena itu, penatalaksanaan nyeri pada anak yang memadai diperlukan. Beberapa analgesik seperti ketorolak dan tindakan anestesi regional seperti blok kaudal telah digunakan dalam meredakan nyeri. Ketorolak dan blok kaudal masing-masing mempunyai kelebihan dan kekurangan. Tujuan penelitian ini adalah untuk membandingkan efektivitas biaya ketorolak dan blok kaudal sebagai analgesik setelah operasi pada pasien anak. Penelitian ini adalah penelitian uji klinik acak tersamar ganda yang dilakukan di RSUP Dr. Sardjito.

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Subjek penelitian adalah anak yang menjalani operasi segmen umbilikus bawah. Tuju puluh pasien dibagi secara random menjadi dua kelompok dengan masing-masing kelompok 35 pasien. Kelompok I (Kelompok Blok kaudal) diberi blok kaudal dengan 0.12% bupivakain 1 mL/kg berat badan (BB), sedangkan Kelompok II (Kelompok Ketorolak) diberi ketorolal 0.5 mg/kg BB secar intravena. Nyeri pada pasien diukur pada menit ke 0, 15, 30, 45 dan 1, 2, 3 jam setelah pasien sadar menggunakan Children's Hospital of Eastern Ontario Pain Scale (mCHEOPS) yang dimodifikasi. Selanjutnya efektivitas biaya setelah blok kaudal dan pemberian ketorolak juga dibandingkan. Kaudal blok dengan bupivakain lebih efektif menurunkan nyeri pada menit ke 0 (27/8 dibanding 10/25) dan menit ke 15 (34/1 dibanding 18/17) ($p<0.05$). Namun demikian, pada jam ke 3 ketorolak lebih efektif daripada kaudal blok (29/6 dibandingkan 32/3) ($p<0.05$). Biaya kaudal blok lebih tinggi dibanding keltorolak (Rp. 95,860 ± 5,745 vs Rp 17,200 ± 14,886) ($p<0,05$). Namun demikian lama tinggal setelah kaudal blok lebih pendek dibandingkan ketorolak (40,43 ± 13,899 vs 48,57 ± 14,068) ($p<0,05$). Morfin lebih banyak dibutuhkan untuk analgesik pemeliharaan banyak dibutuhkan pada ketorolak pada jam pertama ($p<0.05$), seangkan pada jam ke 3 parasetamol banyak dibutuhkan pada blok kaudal ($p<0.05$). Dapat disimpulkan, efektivitas biaya blok kaudal tidak lebih baik dari ketorolak dalam menurunkan nyeri setelah operasi pada anak yang menjalani operase segmen umbilikus bawah.

Keywords: caudal block – ketorolac – post-operative pain – cost – effectiveness

INTRODUCTION

The pediatric patients is frequently at risk of inadequate pain treatment. It is because inability of pediatric patients to describe location and severity of the pain, lack physician's knowledge about pathology of pain and pharmacology of analgesic in pediatric as well as variability in assessing pain. In addition, the choice inappropriate therapy as well as fears of adverse effects of analgesic medications play a role in the emergence of inadequate pain treatment in pediatric patients.[1-3]

Barriers to adequate pain treatment in pediatric patients causes its clinical outcomes relatively low. Study conducted on post-operative pain of 127 pediatric patients showed only 25% of the patients had no early post-operative pain and 40% of those experienced moderate to severe pain.[4] Other study reported that 15-30% of pediatric patients experienced post-operative chronic pain which not properly treated.[5]

Pain treatments are unfamiliar and un-pleasent environments for children. Inadequate pain treatment in pediatric patients can affect their emotional, psychological and physical, behavioral changes.[6,7] Pediatric patients having strong analgesia is associated with a significant decrease in post-operative response parameter, metabolic asidosis incident, sepsis, disseminated intravascular coagulation (DIC) and mortality.[8]

Several analgesic drugs are frequently used in pediatric pain management. Acetaminophen, narcotic analgesics such as fentanyl, morphine and pethidine, and nonsteroidal anti-inflammatory drug (NSAID) such as ketorolac have been used in pain treatments in children.[9] Moreover, regional anesthesia techniques such us local or caudal anesthesia have also been apllied to relieve pain in children.[10] Each intervention in the pain managements has its own advantages and disadvantages in relation to their efficacy and adverse effects. However, study comparing the cost-effectiveness of each the pain intervention has not much been conducted.

Caudal block is the most administered regional anesthesia to pediatric patients particularly infants, since easier to do when the exact landmark is identified. Caudal anesthesia is recommended for almost all lower body section surgery particularly below umbilicus,

including herniorapy, tractus urinarius and rectal surgery, and orthopaedic procedure on pelvis and lower extrimities.[10,11] However, recently the safety of the caudal block for pediatric patients is debateble due to its complication.[12]

Ketorolac is a NSAID with a potent analgesic effects and a moderate anti-inflammation. It can be given through intra-muscular (IM) or intravenous (IV). It is useful for post operative analgesia both as a single agent and an opioid supplement. Thirty miligrams ketorolac IM has equal analgesic potency to that of 10 mg morphine or 100 mg meperidine. Moreover, ketorolac has no effects on respiratory and cardiovascular systems.[9,13]

This study was conducted to compare the cost-effectiveness of the caudal block and the ketorolac as an early post-operative analgesia in pediatric patients underwent surgery below umbilicus segment with moderate post-operative pain.

MATERIALS AND METHODS

Subjects

This was randomized double blind randomized controlled clinical trial with parallel design conducted in Dr. Sardjito General Hospital, Yogyakarta from October 2010 to January 2011. The subjects were 2-6 years old pediatric patients who underwent surgery below umbilicus segment by general anesthesia and the surgical duration shorter than 120 minutes with moderate post-operative pain, and had a physical status of ASA I and II. Seventy patients who fulfilled the inclusion and exclusion criteria were randomly divided into two groups with 35 patients in each group. Group I as caudal block group was given caudal block with bupivacaine 0.12% 1 mL/kg body weight (BW) whereas Group II as ketorolac group was given 0.5 mg/kg BW intravenously (IV). The protocol of this study was reviewed and approved by the Medical dan Health Research Ethics Committee, Faculty of Medicine, Universitas Gadjah Mada Yogyakarta.

Protocol of study

In the preparation room, the patients were inserted an intravenous line on the right or left hand. The patients were administered a premedication of midazolam 0.05 mg/kg BW. After sedated, the patients were delivered to the operation room. Standards for patients monitoring during anesthesia i.e. electro-cardiogram (ECG), blood pressure, mean atrial blood pressure (MAP), heart rate (HR) and oxugen saturation (SpO_2) were initiated. The patients were then inducted with sevoflurane or propofol 2 mg/kg BW IV and intubated without muscle relaxant (i.e. apnea non-muscle relaxant). Anesthesia was maintaned using 50% N_2O in 50% O_2 and isoflurane. In Group I, after the operation finished, the intubated patients were positioned left lateral decubitus and given caudal block with bupivacaine 1 mL/kg BW 0.125%, whereas in Group II, 30 minutes before operation finished or the time when the skin was closed, the patients were injected with ketorolac 0.5 mg/kg BW.

After the anesthesia finished, the patients were delivered to the recovery room. The parents accompanied the patients until fully conscious. The pain was scored in the recovery room every 15 menit for the first hour continued every 1 hour until the third hour using modified Children's Hospital of Eastern Ontario Pain Scale (mCHEOPS). The patients experienced pain score > 4 was given a morphine 50 µg/kg BW. Ondansentron IV was given to the patients experiencing vomiting. The other outcomes observed in this study were the length of stay in the recovery room (the time needed until the Aldrete score 10), side effect of drug i.e. vomiting, rescue analgesic given i.e. morphine and paracetamol and antiemetic given. The cost-

effectiveness after caudal block and ketorolac interventions was also evaluated and compared.

Statistical analysis

Characteristics of pediatric patients were presented as mean ± standard deviation (SD) or number (n) and analyzed using Chi-square or t-test depend on its variables. The effectiveness and rescue analgesic between caudal block intervention and ketoralac intervention were compared using Mann-Whitney U test, whereas their cost-effectiveness were compared using t-test. A p value of <0.05 was concidered significant.

RESULTS

The patients characteristics of Caudal block Group and Ketorolac Group are presented in TABLE 1. All variables observed in both groups were not significantly difference indicating that these both groups were similar.

TABLE 1. Baseline characteristic of patients

Variables	Caudal block Group	Ketorolac Group	p
Age (years)	3.89 ± 1.491	4.17 ± 1.636	0.448
Gender			
• Male	23	25	0.607
• Female	12	10	
Weight (kg)	15.49 ± 3.673	15.51 ± 3.936	0.975
Diagnosis			
• Hipospadia	9	9	
• Hernia	5	7	
• Fraktur	6	3	
• Undescenceus testis	3	2	0.361
• Atresia ani	8	7	
• Other	4	7	
Type of operation			
• Chordectomy	5	2	
• Orchidopeksi	3	2	
• Uretroplasty	4	6	
• Hernia repair	5	7	
• Stump cut	1	5	
• Pull through	1	1	0.441
• ORIF	2	1	
• Reposition	1	1	
• STSG	3	1	
• PSARP	5	3	
• Other	5	6	
Initial pulse rate	104.74 ± 8.665	105.43 ± 8.590	0.741
Initial CHEOPS			
• 2	31	32	0.690
• 3	4	3	
ASA			
• I	19	25	0.138
• II	16	10	
Operation duration	71.91 ± 25.168	69.74 ± 23.99	0.771

*Data shown as mean ± SD or n (%)

The effectiveness caudal block and ketorolac interventions are presented in TABLE 2. The caudal block intervention showed more effective in reducing pain than the ketorolac intervention at minutes 0 and 15 after operation (p=0.000). However, at hour 3 after operation, the ketorolac intervention revealed more effective than the caudal block intervention (p=0.031).

TABLE 2. Comparison of effectiveness between Caudal block and Ketorolac Groups

Effectiveness at a time observed	Caudal block Group	Ketorolac Group	p
Minute 0			
• Effective	27	10	0.000*
• Non effective	8	25	
Minute15			
• Effective	34	18	0.000*
• Non effective	1	17	
Minute 30			
• Effective	34	33	0.555
• Non effective	1	2	
Minute 45			
• Effective	34	35	0.314
• Non effective	1	0	
Hour 1			
• Effective	32	34	0.303
• Non effective	3	1	
Hour 2			
• Effective	30	32	0.452
• Non effective	5	3	
Hour 3			
• Effective	26	32	0.031*
• Non effective	9	3	

* significantly different p<0.05

The cost-effectiveness analysis showed that cost of the caudal block intervention was higher than the ketorolac intervention (p = 0.000) (TABLE 3). However, the length of stay of patients in the recovery room after the caudal block intervention was shorter than the ketorolac intervention (p = 0.017). In addition, the incidence of side effects e.g. vomiting was not significantly difference between two groups (p = 0.555) and an antiemetic was not be required for patients having vomiting. In this study, some patients underwent intra-operative urinary catheterization during operation and most other patients normally were voiding immediately or two hours after surgery. Furthermore, ambulatory could be conducted as soon as after conscious patients.

TABLE 3. Comparison of length of stay in the recovery room (RR), cost and side effect between caudal block and ketorolac group

Variables	Caudal block Group Mean ± SD	Ketorolac Group Mean ± SD	p
Length of stay in RR (hours)	40.43 ± 13.899	48.57 ± 14.068	0.017**
Cost (IDR)*	95.860 ± 5.745	17.200 ± 14.886	0.000**
Side effect (vomiting) (n)	1/34	2/33	0.555

*IDR = Indonesian Rupiah; **significantly different p<0.05

The need of rescue analgesic was significantly different between two groups (TABLE 4). In the first hour of operation, morphine was more required for rescue analgesic in the Ketorolac Group (p = 0.000), whereas after three hour operation paracetamol was more required in Caudal block Group (p = 0.017).

TABLE 4. Rescue analgesic comparison between Caudal block and Getorolac Groups

Variables	Caudal block Group	Ketorolac Group	p
Morphine	8/27	25/10	0.000*
Paracetamol	11/24	3/32	0.017*

*significantly different p<0.05

DISCUSSION

In this study, the caudal block intervention was more effective than ketorolac intervention at minute 0 and 15. However at the third hour, the ketorolac intervention was more effective than the caudal intervention in reducing post-operative pain. It was indicated that the caudal block with bupivacaine can provide adequate analgesia in the early post-operative period. The duration of action bupivacaine at dose 2 to 2.5 mg/kg BW is 2-4 hours.[13,14] As a result, systemic analgesia is usually required to maintain of the analgesia effect. In this study, no patient in both of the groups was found not requiring rescue analgesic. However, the rescue analgesics required in both groups was different. In the first hour of operation, morphine was more required in the Ketorolac, whereas after three hour operation paracetamol was more required in Caudal block Group.

Studies to compare effectiveness between caudal block with biopivacaine and ketorolac in reducing post-operative pain have been conducted previously. Splinter *et al*.[15] reported that ketorolac 1 mg/kg BW IV was comparable with caudal bupivacaine 0.125% in reducing post-operative pain and side effects. In addition, the ketorolac had a better recovery profile, including lower incidence of vomiting and rapid urinating. Cyna and Middleton[16] showed that the caudal block and parenteral analgesia were not significantly different in the requiremet for rescue analgesia. Shi *et al*.[17] showed that the pain score and the incidence of agitation as well as emergence delirium on the caudal block and ketorolac groups after sevoflurane anesthesia in children were lower than the control group. However, it was not significantly different between the caudal block and the ketorolac group.

The cost in the Caudal block Group was higher than the Ketorolac Group in this study. The cost consisted of the cost of drugs used and rescue analgesia. In the early post-operative pain period, the caudal block was more effective than the ketorolac. The rescue analgesia was not required in this period. However, 3 hours after surgery, the rescue analgesia was required due to the duration of action bupivacaine as well as ketorolac alost finished. Furthermore, although the length of stay in the recovery room of the Caudal block Group was statistically shorter than the Ketorolac Group, however it did not affect cost for the recovery room. The cost in the recovery room of Dr. Sardjito General Hospital used basic range, i.e. < 6 hours and > 6 hours. Moreover, no significant differences were found in the incidence of vomiting between two groups, therefore additional anti-emetic was not required. It is mean that no additional cost for anti-emetic was not necessary.

In addition, some patients underwent urinary catheterization during operation and the most other patients were voiding immediately or 2 hours after surgery. Furthermore, ambulatory could be conducted as soon as after conscious patients. This result was consistent with the study conducted by Wolf *et al.*[18] that bupivacaine 0.125% provides adequate analgesia with minimum motoric blockage.

Cost-effectiveness analysis compares all the costs both of direct and indirect costs with the clinical outcome assessment for different therapeutic regimens.[19] A therapeutic regimen is considered to be better if its clinical improvement is comparable with the increase of the price per unit.[20,21] This study showed that the Caudal block Group and Ketorolac Group had similar effectiveness in reducing post-operative pain in children. Moreover, the cost of Caudal block Group was higher than Ketorolac Group. Therefore, it can be stated that caudal block with bupivacaine is not more cost-effective than ketorolac.

CONCLUSION

In conclusion, the caudal block with bupivacaine is not more cost-effective than ketorolac in reducing early moderate post-operative pain in pediatric patients underwent surgery below umbilicus segment.

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