COMPARISON OF ANALGESIC EFFICACY BETWEEN PREEMPTIVE INTRAVENOUS PARACETAMOL AND SINGLE SHOT CAUDAL BLOCK IN PAEDIATRIC INGUINAL HERNIA REPAIR

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ABSTRACT

Background:

There are various methods to obtain adequate analgesia post inguinal hernia repair in children. Caudal block has been generally preferred in paediatric lower abdominal surgery. Otherwise intravenous paracetamol became widely used for its safe and excellent analgesic in children. This study aim to compare analgesic efficacy of preemptive intravenous paracetamol and single shot caudal block following paediatric inguinal hernia repair.

Methods:

This is a prospective randomized study of a total of 40 children underwent elective unilateral inguinal hernia repair under general anaesthesia in Hospital Universiti Sains Malaysia. The patients who was consented by their guardian were randomized into two groups to receive intravenous paracetamol (group A) and caudal block (group B). Pain score of the patients was measured via FLACC score at 10 minutes, 30 minutes, 1 hour, 2 hour and 6 hour postoperatively and compared. Other outcomes that were measured and compared were mean blood pressure and heart rate intraoperatively, as well as mean time for first analgesic requirement, total fentanyl consumption intraoperatively and proportion of adverse effects between both groups.

Results:

The mean age of the patients was 30.48 months. Patients in B group has significantly lower pain score at 10 minutes ($p=0.018$), 30 minutes ($p=0.013$) and 1 hour ($p=0.05$) compared to group A. At 2 hour and 6 hour, no difference between groups was observed. No haemodynamic instability were recorded. No significant difference in time to first analgesic requirement ($p=0.079$) as well

as total fentanyl consumption (p=0.090) intraoperatively. Also, no significant major complications were observed in both groups.

Conclusions:

Caudal block is a better option compared to intravenous paracetamol in the first operative hour but gives no significant difference subsequently after that. Preemptive intravenous paracetamol is equipotent to caudal block for analgesic efficacy if we measure from the perspective of first analgesic requirement and total fentanyl usage.

ABSTRAK

Latar belakang:

Terdapat pelbagai kaedah untuk mencapai tahap keberkesanan analgesik yang mencukupi selepas pembedahan angin pasang di kalangan kanak-kanak. Pembiusan setempat ‘caudal block’ biasanya digemari dalam pembedahan bahagian bawah abdomen melibatkan kanak-kanak. Sebaliknya, paracetamol yang diberi melalui vena telah digunakan secara meluas kerana tahap keselamatan dan keberkesanan analgesiknya yang sangat baik. Kajian ini bertujuan untuk membandingkan tahap keberkesanan analgesic paracetamol yang diberi melalui vena dengan pembiusan setempat ‘caudal block’ selepas pembedahan angina pasang di kalangan kanak-kanak.

Kaedah:

Ini adalah satu kajian prospektif rawak melibatkan 40 orang kanak-kanak yang menjalani pembedahan elektif sebelah angin pasang di bawah pembiusan am di Hospital Universiti Sains Malaysia. Pesakit yang telah mendapat keizinan dari penjaga mereka dibahagi secara rawak kepada dua kumpulam yang menerima paracetamol melalui vena (kumpulan A) dan pembiusan setempat ‘caudal block’ (kumpulan B). Skor kesakitan diukur menggunakan skala FLACC pada 10 minit, 30 minit, 1 jam, 2 jam dan 6 jam selepas pembedahan dan dibandingkan. Keputusan lain yang diukur and dibandingkan adalah purata tekanan darah dan denyutan nadi semasa pembedahan, purata masa pertama untuk permintaan ubat tahan sakit, purata jumlah fentaniyl yang digunakan semasa tempoh pembedahan dan kadar kesan sampingan antara kedua-dua kumpulan.

Keputusan:

Purata umur pesakit adalah 30.48 bulan. Pesakit dalam kumpulan B mendapat keputusan skor kesakitan yang lebih rendah pada 10 minit (p=0.018), 30 minit (p=0.013) dan 1 jam (p=0.05) dibandingkan dengan kumpulan A. Pada 2 jam dan 6 jam, tiada perbezaan yang signifikan direkodkan. Tiada ketidakstabilan hemodinamik direkodkan. Tiada perbezaan signifikan dalam masa pertama untuk permintaan ubat tahan sakit (p=0.079) dan juga jumlah total penggunaan fentanyl (p=0.090) semasa tempoh pembedahan. Tiada komplikasi besar yang signifikan diperhatikan pada kedua-dua kumpulan.

Kesimpulan:

Pembiusan setempat ‘caudal block’ merupakan pilihan yang lebih baik daripada paracetamol yang diberi melalui vena pada jam pertama selepas pembedahan namun tidak memberi perubahan yang signifikan selepas tempoh tersebut. Keberkesanan analgesik paracetamol yang diberi melaui vena adalah sama dengan pembiusan setempat ‘caudal block’ jika dikira dari perspektif masa pertama permintaan ubat tahan sakit dan juga jumlah penggunaan fentanyl.

LIST OF ABBREVIATION

ANOVA – Analysis of variance

ASA – American Society Anaesthesiologist

BP – Blood pressure

CB – Caudal block

COX – Cyclooxygenase enzyme

CO2 – Carbon dioxide

ECG – Electrocardiography

HR – Heart rate

IV – Intravenous

MAP – Mean arterial pressure

PCM – Paracetamol

p-value – Probability

CHAPTER 1: INTRODUCTION

1.1 Introduction

Inguinal hernia is a common pediatric condition. In boys, it occurs in about three to four times higher than in girls, with right side more affected than left side in both sexes. The incidence of hernia repair among boys was highest during the first year of life, but then decreased with age. However in girls, the incidence remained stable in the first six years of life.(1)

Thus inguinal hernia repair is a common surgical procedure among paediatric age group. Adequate analgesia is essential and may be obtained through various methods. These methods include administration opioids such as morphine, the administration of non-steroidal anti-inflammatory drugs such as ketorolac, administration of acetaminophen, and the use of regional anaesthetic techniques such as local anaesthesia and caudal anaesthesia or analgesia. Each of these technique has their advantages and disadvantages.

Preemptive analgesia is an antinociceptive treatment that prevents establishment of altered processing of afferent input, which amplifies postoperative pain (2) . In various studies of pre-emptive analgesia, local anaesthetics, opioids, paracetamol, non-steroid anti-inflammatory drugs, central and peripheral nerve blocks have been used for this purpose.(3) The preferred drug and its route of administration are still under investigation. It is still investigated which drugs and which route should be preferred for pre-emptive analgesic techniques.

Caudal block is a popular technique in conjunction with general anaesthesia for perioperative pain management in paediatric hernia repair. It is not only reduces dose of general anaesthetics but also attenuates the stress response to surgery. However it is often associated with side effects such as vomiting, urinary retention, delayed ambulation and rarely neurological deficits. There

are also few reports of systemic toxicity such as convulsions, hypotension and arrhythmias. Performing caudal block in anaesthetized child demands proper positioning, identifying proper space and the cumbersome manoeuvre of positioning and repositioning without compromising the airway.(4)

Paracetamol has been available in markets as oral and suppository forms for many decades, and the intravenous form has been introduced and received its approval in Europe at 2002 and in United States at 2010 (5). Currently intravenous (IV) form of paracetamol is widely used and its efficacy and safety has been established in paediatrics. It has been observed to be effective compared to rectal formulation due to the production of higher level of mean plasma concentration. The analgesic mechanism of paracetamol is not completely understood. Generally it is considered to be a weak inhibitor of prostaglandins (PGs) synthesis. In vivo, paracetamol effects are similar to selective COX-2 inhibitor. Although it reduces protaglandins synthesis, it does not reduce inflammation in rheumatoid arthritis as in other COX-2 inhibitors do. Moreover studies showed that it works as weak inhibitors of both COX-1 and COX-2 where concentration of arachidonic acid is low (6). Typically reported adverse reactions include hypotension, malaise, hypersensitivity reactions, elevated liver enzymes and thrombocytopenia. However, significant adverse effects with intravenous paracetamol are extremely rare, occurring at approximately 1:10000 (7).

This study aim to compare the the analgesic efficacy between pre-emptive intravenous paracetamol and caudal block in paediatric patients undergoing inguinal hernia repair.

CHAPTER 2: OBJECTIVES OF THE STUDY

2.1: GENERAL OBJECTIVE

To compare analgesic efficacy of preemptive intravenous paracetamol and single shot caudal block in paediatric patient undergoing inguinal hernia repair.

2.2: SPECIFIC OBJECTIVES

1. To compare the mean observational/ behavioural rating scale using Face, Legs, Activity, Cry and Consolability (FLACC) scale at 10 minutes, 30 minutes, 1 hour, 2 hours and 6 hours postoperatively between both groups.

2. To compare the mean blood pressure and heart rate intraoperatively between both groups.

3. To compare the mean time for the first analgesic demand and the mean total fentanyl consumption intraoperatively between both groups.

4. To compare the proportion of adverse reactions between both groups.

CHAPTER 3: MANUSCRIPT

3.1: Title page

Title:

Comparison of analgesic efficacy between preemptive intravenous paracetamol and single shot caudal block in paediatric inguinal hernia repair

Running head:

To compare analgesic efficacy of preemptive intravenous paracetamol and single shot caudal block in paediatric patient undergoing inguinal hernia repair.

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3.2: Abstract

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3.3: Introduction

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Caudal block is a popular technique in conjunction with general anaesthesia for perioperative pain management in paediatric hernia repair(8). It is not only reduces dose of general anaesthetics but also attenuates the stress response to surgery. However it is often associated with side effects such as vomiting, urinary retention, delayed ambulation and rarely neurological deficits. There are also few reports of systemic toxicity such as convulsions, hypotension and

arrhythmias. Performing caudal block in anaesthetized child demands proper positioning, identifying proper space and the cumbersome manoeuvre of positioning and repositioning without compromising the airway.(4)

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This study aim to compare the the analgesic efficacy between pre-emptive intravenous paracetamol and caudal block in paediatric patients undergoing inguinal hernia repair.

3.4: Methodology

Study design:

This is a stratified balanced randomized (1:1), single-blinded, parallel-group study conducted in Hospital Universiti Sains Malaysia.

Participants:

Eligible participants screened preoperatively were children undergoing elective unilateral hernia repair under general anaesthesia classified as ASA 1 and 2, age from 6 months old until five years old. Exclusion criteria were children less than 6 months or more than 5 years old, ASA 3 or 4 children, children who had allergy to the drugs used in the study that was paracetamol or levobupivacaine, children with kidney, liver, lung or heart dysfunction and children who had contraindication to caudal block.

Study settings:

The study took place at Hospital Universiti Sains Malaysia from June 2018 till August 2019 with estimated elective hernia repair about 4 cases per month.

Intervention:

Children who was consented by their guardian scheduled for unilateral hernia repair were randomized into 2 groups, Group A (paracetamol) and group B (caudal block) using computerized software randomization.

Group A children received intravenous infusion paracetamol of 15mg/kg (for those who weighed more than 10kg) or 7.5mg/kg (for those who weighed less than 10kg) given 15 minutes prior to induction of anaesthesia given by primary investigator or appointed trained doctor.

All children were induced either by inhalational technique by sevoflurane or by intravenous agent using propofol. Standard monitoring of non-invasive blood pressure, electrocardiogram (ECG) and pulse oximetry were applied. Appropriate size laryngeal mask were inserted and the concentration of sevoflurane were adjusted to deliver a minimum alveolar concentration of 1.0-1.2. Administration of intravenous fluids were given according to standard guideline (maintenance rates plus replacement of fluid deficits, third space fluid loss and blood loss).

Group B children received caudal block after induction of anaesthesia using 0.25% levobupivacaine at 0.75ml/kg. Caudal block was given by the primary investigator or appointed trained doctor using 22G branula after locating sacral hiatus and loss of resistance technique.

Blood pressure and pulse rate were recorded during skin incision and every 10 minutes intraoperatively. Children who had increase in heart rate of more than 20% of baseline were given a bolus of intravenous fentanyl 0.5mcg/kg and total consumption of intraoperative intravenous fentanyl were charted.

Postoperatively patient were monitored in recovery room for 30 minutes in the presence of one of the parents to reduce anxiety before discharged to ward. Intravenous fentanyl of 0.5mcg/kg were given if pain score more than 4 and time to first analgesic were recorded.

Outcome:

The main aim of this study was to compare analgesic efficacy between pre-emptive intravenous paracetamol and caudal block as well as their hemodynamic profiles. Observational/ behavioural rating scale using FLACC scale was used to assess pain score at 10 minutes, 30 minutes, 1 hour, 2 hour and 6 hours after surgery. The blood pressure and heart rate were recorded during skin incision and every 10 minutes intra-operatively. Total consumption of fentanyl used was

recorded as well. Besides, this study also aim to compare the proportion of adverse effects between the two groups, thus time to micturate, ambulate and other side effects such as hypotension, bradycardia, allergic reaction, nausea and vomiting were recorded. The investigator or appointed trained doctor or staff nurse were in charge of the recordings.

Sample size:

The sample size calculation is based on study by G.R. Khalili, A. Shafa, R. Yousefi, Comparison of the effects of preemptive intravenous and rectal acetaminophen on pain management after inguinal herniorrhaphy in children: A placebo-controlled study., Middle East J. Anaesthesiol. 23 (2016) 543–548.

Sample size estimation was calculated using two population means formula. Prior data indicated that the mean pain scores measured on the Face, Legs, Activity, Cry, and Consolability (FLACC) scale at six hours of the IV paracetamol group was 1.1 (standard deviation = 0.2) and the mean of acetaminophen suppository group was 1.3 (standard deviation = 0.2). Thus, a minimum sample size of 16 samples per group to be able to reject the null hypothesis with probability (power) 0.8. The Type I error probability associated with this test of this null hypothesis is 0.05. The independent t-test statistic used to evaluate this null hypothesis. **With an additional of 20% dropout rate, the sample size was 20 samples per group.**

Randomization:

The enrolment of participants were made one day prior to operation during the pre-assessment by investigator or by a trained assistant. For the allocation of the participants, a computer generated list of random numbers were used. Randomization sequence was created using statistical software and with 1:1 balanced allocation into 2 groups, Group PCM and Group CB. Only the participants were blinded throughout the trial.

Statistical methods:

The analyses were performed using IBM SPSS Statistics for Windows Version 24. Results were given as mean ± standard deviations. Comparison of Numerical Data between two independent groups that were normally distributed were analyzed using the Independent t-test. Assessments of the intensity of postoperative pain using FLACC scale at 10 minutes, 30 minutes, 1 hour, 2 hours, 6 hours post-surgery and hemodynamic data using the repeated measures ANOVA. All probability values were two-sided and a level of significance of less than 0.005 ($p<0.05$) were considered as statistically significant.

3.5: Results

Introduction

The purpose of conducting this study is to study the comparison of analgesic efficacy between preemptive intravenous paracetamol and single shot caudal block in paediatric inguinal hernia repair. Throughout this chapter, the results of the study were presented.

Participants Characteristic

A total of 40 participants were recruited for this study based on patients visiting the hospital.The data obtained was expressed as mean (SD=standard deviation) for numerical and n=frequency (%) for categorical variables as tabulated in Table 1. The result of the data showed that the mean age of the participants is 30.48 months, and the standard deviation is 20.23. Meanwhile, for the mean weight for the total of 40 participants were 11.87 kg, while the standard deviation is 4.38. The majority were male participants included in the study (n=35, 87.5%). Most of the participants were diagnosed with right inguinal hernia (n=27, 67.5%) compared to left inguinal hernia.

Comparison of mean observational/behavioural rating scale using Face, Legs, Activity, Cry and Consolability (FLACC) scale at 10 minutes, 30 minutes, 1 hour, 2 hours and 6 hours postoperatively within group (based on time).

There was a significant difference of mean pain score within group A (PCM) and B (CB) in repeated measure ANOVA($f=10.49, p<0.001$). Multiple analysis were performed with adjusted α based on Banferroni correction (Table 2). The results showed that there were some differences between pre and post results. For group CB, the results showed that there were differences between measurement of 30 minutes with 1 hour (mean difference=-0.70;95%CI: -1.11,-0.30;$p<0.001$) .