COMPARISON OF THE EFFECTIVENESS BETWEEN KATARIA AND PAEDFUSOR MODELS OF TARGET CONTROLLED INFUSION (TCI) DURING ANAESTHESIA IN ELECTIVE PAEDIATRIC SURGERY

By

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DISSERTATION SUBMITTED IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE DEGREE OF MASTER OF MEDICINE (ANAESTHESIOLOGY)

UNIVERSITI SAINS MALAYSIA

2017

ACKNOWLEDGEMENTS

I would like to thank all my lecturers from Department of Anaesthesia and Intensive Care, Hospital Universiti Sains Malaysia for their support and encouragement, particularly to Dr W Mohd Nazaruddin bin W Hassan, as my supervisor who has been giving me lots of advice throughout the entire process of accomplishing this study.

I would also like to express my thanks to my fellow colleagues who have assisted me in giving anaesthesia in the recruited patients. Without them, it was impossible for me to complete this study.

Not to forget, staff nurses in operation theatre for their willingness in helping me preparing the necessary equipment for my study.

Finally, I dedicate this dissertation to my husband, family and friends for their unconditional love.

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LIST OF ABBREVIATIONS

ASA	American Society of Anaesthesiologist
BIS	Bispectral index
Cp	Plasma concentration
Cpt	Target lasma concentration
CSHT	Context sensitive half time
HUSM	Hospital Universiti Sains Malaysia
MDPE	Multi-dimensional probability evolution
MDAPE	Median absolute percentage error
Pk	Pharmacokinetic
Pd	Pharmacodynamic
TCI	Target controlled infusion
TIVA	Total intravenous anaesthesia
Vd	Volume of distribution

Mengkaji keberkesanan dan perbezaan di antara Kataria dan Paedfusor model iaitu dua model pembiusan am menggunakan ubat propofol secara infusi kawalan sasaran semasa dan sejurus selepas pembiusan bagi kanak-kanak yang menjalani pembedahan elektif.

ABSTRAK

Latar belakang: Kataria dan Paedfusor adalah 2 model pembiusan am yang menggunakan ubat propofol secara infusi kawalan sasaran yang diiktiraf penggunaannya untuk tujuan pembiusan kanak-kanak. Tujuan kajian ini adalah untuk mengkaji keberkesanan dan perbezaan di antara model-model ini untuk pembiusan kanak-kanak yang menjalani pembedahan elektif.

Tatacara: 38 pesakit berumur 3 hingga 12 tahun yang mempunyai tahap kesihatan yang baik (ASA I atau II), menjalani pembedahan secara elektif dengan kaedah pembiusan penuh, dibahagikan secara rawak kepada 2 kumpulan: kumpulan Kataria (n=19) dan kumpulan Paedfusor (n=19). Semua pesakit diberikan infusi remifentanil pada dos 1mcg/kg selama 1 minit 15 saat diikuti infusi pada kadar 0.1 hingga 1mcg/kg/min. Kemudian, kedua-dua kumpulan dimulakan dengan infusi kawalan sasaran ubat propofol pada target konsentrasi plasma 6 mcg/ml menggunakan model kumpulan masing-masing semasa induksi dan ikuti pada target konsentrasi plasma 3 hingga 6 mcg/ml berdasarkan bacaan BIS semasa pembedahan. Masa untuk induksi, masa untuk pesakit sedar dan konsentrasi plasma ubat propofol ketika pesakit sedar direkodkan bagi tujuan analisis.

Keputusan: Kedua-dua kumpulan berjaya dibiuskan oleh model infusi kawalan sasaran dengan target konsentrasi plasma 6 mcg/ml. Tiada perbezaan di antara kedua model untuk masa induksi dan masa yang di ambil untuk bangun. Target konsentrasi plasma bagi kumpulan Kataria lebih rendah berbanding kumpulan Paedfusor [1.48 (0.11) minit vs 1.59 (0.14) minit, p=0.01].

Kesimpulan: Kedua-dua model infusi kawalan sasaran terbukti keberkesanannya dalam pembiusan. Tiada perbezaan masa yang diambil untuk induksi dan masa pesakit sedar. Didapati target konsentrasi plasma kumpulan Kataria lebih rendah.

Kata kunci: *Kataria model, Paedfusor model, infusi kawalan sasaran, propofol, remifentanil.*

Comparison of the effectiveness between Kataria and Paedfusor models of Target-controlled Infusion (TCI) during anaesthesia in elective paediatric surgery.

Abstract

Background: Kataria and Paedfusor are two validated target controlled infusion (TCI) models for propofol in paediatric population. The aim of this study was to compare the effectiveness of these two different TCI models for propofol in paediatric age group during elective surgery.

Methods: 38 patients, aged 3-12 year-old, classified under ASA I and II, who underwent elective surgery under general anaesthesia, were randomised into two groups; Group Kataria (n=19) and Group Paedfusor (n=19). All patients received 1 mcg/kg loading dose of intravenous (IV) remifentanil over 1 minute 15 seconds and followed with infusion at 0.1 to 1 mcg/kg/min. Then, both groups were induced at plasma concentration (Cpt) propofol of 6 mcg/ml using respective model and maintained with Cpt between 3 to 6 mcg/ml guided by bispectral index (BIS) between 40-60. Remifentanil was maintained between 0.1 to 1 mcg/kg/min. Success rate of induction, induction time, recovery time and plasma concentration (Cp) at recovery were recorded for statistical analysis.

Results: Both groups were successfully induced with propofol Cpt of 6mcg/ml. There were no significant difference in induction and recovery time between these two groups. The plasma concentration at recovery in Kataria group was significantly lower than Paedfusor group [1.48 (0.11) mcg/ml vs 1.59 (0.14) mcg/ml, p=0.01].

Conclusion: TCI propofol for paediatric patients using Kataria and Paedfusor models were equally effective in success rate of induction, induction time and recovery time. Only plasma concentration at recovery was lower in Kataria group.

Keywords: *Kataria model, Paedfusor model, propofol, remifentanil, target-controlled infusion.*

SECTION 1

INTRODUCTION

1.0 Introduction

Total intravenous anaesthesia (TIVA) is a method of anaesthesia using only intravenous anaesthetic drugs. It can be delivered either in a conventional technique or in target controlled infusion (TCI) technique. TCI is a method of delivering intravenous (IV) drugs using a special infusion pumps which is incorporated with software consisted of a pharmacokinetics algorithm of the specific drugs .The properties of the drugs that are currently capable to be delivered by TCI methods are; fulfill the three compartmental models in distribution, short context-sensitive half-life and rapid in clearance. The only drugs that have validated pharmacokinetic models for TCI in adult at the moment are propofol and remifentanil [1].

Propofol is a substituted isopropylphenol (2,6-diisopropylphenol) that is administered intravenously as 1% solution in an aqueous solution of 10% soybean oil,2.25% glycerol, and 1.2% purified egg phosphatide (Figure 1) . This drug is chemically distinct from all other drugs that act as intravenous sedative-hypnotics. Administration of propofol, 1.5 to 2.5 mg/kg as a rapid injection (<15 sec), produces unconsciousness within about 30 seconds. Propofol is presumed to exert its sedative-hypnotic effects through a $GABA_A$ receptor interaction. The interaction of propofol with specific components of $GABA_A$ receptors appears to decrease the rate of dissociation of the inhibitory neurotransmitter, GABA from the receptor, thereby increasing the duration of the GABA-activated opening of the chloride channel with resulting hyperpolarization of cell membrane [2].

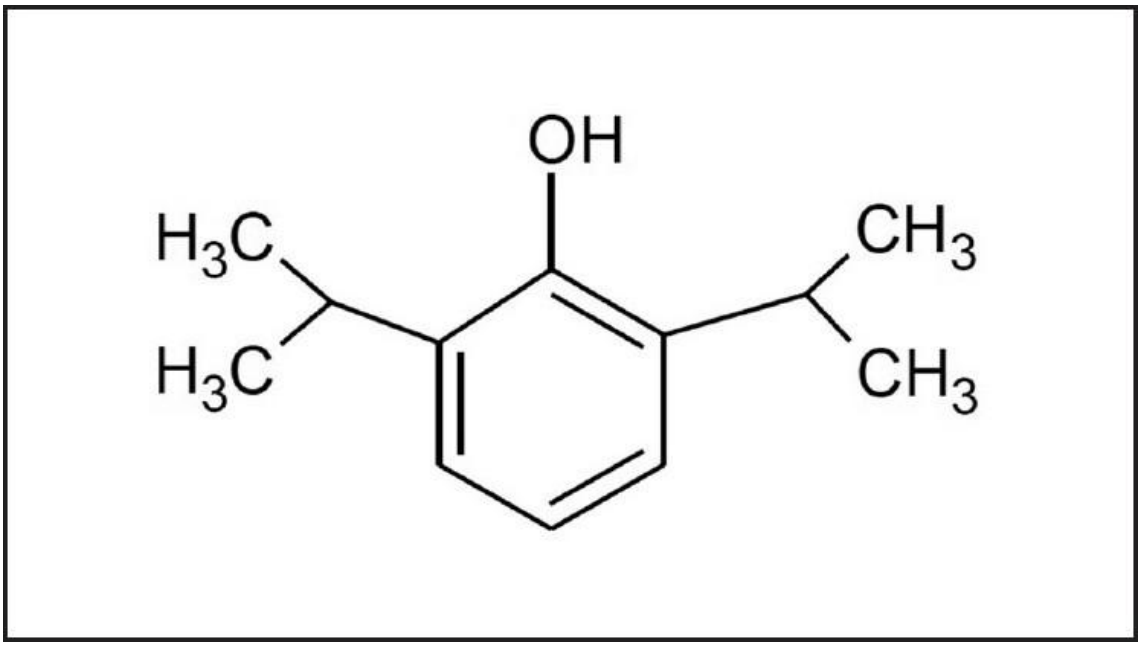

Figure 1: Structure of propofol (source: JAnaesth Clinical Pharmacology, 2011)

Propofol metabolism in humans is considered to be both hepatic and extrahepatic. Hepatic metabolism is rapid and extensive, resulting in inactive, watersoluble sulphate and glucuronic acid metabolites that are excreted by the kidneys. The fact that total body clearance of propofol exceeds hepatic blood flow is consistent with extrahepatic clearance (pulmonary uptake and first pass elimination, renal excretion) of propofol [3]. The context-sensitive half-time (CSHT) for propofol infusions lasting up to 8 hours is <40 minutes. The CSHT of propofol is minimally influence by the duration of the infusion because of rapid metabolic clearance when the infusion is discontinued [4]. This characteristic makes it suitable for TIVA. In addition, the general anaesthesia by propofol associated with minimal postoperative nausea vomiting, and awakening is prompt, with minimal residual sedative effect.

Nowadays, propofol is the commonest intravenous agent that has been used for induction and maintenance of anaesthesia, procedural and critical care sedation in children. In 1989, Federal Drugs and Administration (FDA) approved the use of

propofol for maintenance of anaesthesia in children 2 months old and above and for induction of anaesthesia in children 3 years old and above. The use of propofol for induction of anaesthesia in children less than 3 years old still remains off-label [4].

Remifentanil is a selective mu opiod agonist, short acting phenylpiperidine derivatives. Remifentanil is structurally unique because of ester linkage (Figure 2). This structure renders it susceptible to hydrolysis by nonspecific plasma and tissue esterases to inactive metabolites. This unique pathway of metabolism imparts to remifentanil brevity of action, precise and rapidly titratable effect due to its rapid onset and offset, noncumulative effects and rapid recovery after discontinuation of its administration. The pharmacokinetics of remifentanil are characterized by small Vd, rapid clearance and low interindividual variability compared to other IV anaesthetic drugs . CSHT for remifentanil is independent of the duration of infusion and is estimated to be about 4 minutes [5]. The combination of rapid clearance and small Vd responsible for the lack of accumulation even during prolonged periods of infusion. The facts that remifentanil has rapid clearance and rapid blood-brain equilibration, the changes infusion rates will be paralleled by changes in drug effect [5]. All these characteristics make it suitable for TIVA / TCI. Its rapid and consistent metabolism regardless of duration of infusion has made remifentanil a good choice for analgesia/anaesthetic option for paediatric care provider. Remifentanil has a CSHT that remains constant even in smaller children and neonates, which unique in paediatric practice [6].

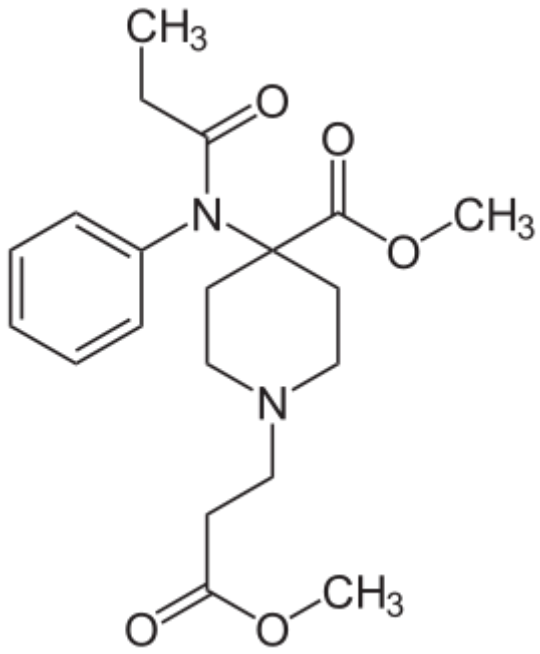

Figure 2: Structure of remifentanil (Source: PubChem, 2005)

TCI technique has been well established in adult patients for the past 15 years. In adult, pharmacokinetic models that can be used for TCI propofol is either Marsh or Schneider model whereas the only model can be used for TCI remifentanil is Minto model. The only validated paediatric models for TCI propofol are Kataria and Paedfusor models. TCI technique is different from conventional TIVA where it requires the user to set target plasma concentration or target-effect concentration of the drugs (the concentration of the drug at the brain level) that is aimed to be achieved based on key in data of patient's age, body weight, height and gender. Whereas, the conventional TIVA requires us to calculate the infusion rate based on the recommended dosage of the drugs [1].

In general, inhalational anaesthesia technique has been more common practice of general anaesthesia in paediatric for quite sometimes and it is still the more familiar technique nowadays. However, there are list of the surgeries or procedures that have more advantages of using TIVA/TCI technique than inhalational anaesthesia technique.

Indications for TIVA/TCI in children:

- Children undergoing frequent, repeated anesthesia (e.g.: radiation therapy)
- Brief radiologic or painful procedures where rapid recovery is needed (e.g. MRI, bone marrow aspiration, gastrointestinal endoscopy).
- During major surgery to control the stress response.
- During neurological procedures to assist with control of intracranial pressure and for cerebral metabolic protection.
- During spinal instrumentation surgery to provide controlled hypotension and when there is a need for evoked motor and auditory brain potentials or intraoperative wake-up test
- During airway procedures (e.g. bronchoscopy)
- Children at risk of malignant hyperthermia
- Children with increased risk of postoperative nausea and vomiting.

The advantages of TIVA/TCI over inhalational anaesthesia in paediatric:

- Induction is very rapid in onset
- Large keo in children result in very quick induction and rapid equilibration between plasma and effect site

- Rapid onset of action independent from alveolar ventilation
- Improved quality of emergence from anaesthesia
- Very smooth and peaceful recovery
- No risk of environment pollution
- Reduction in the incidence of postoperative nausea and vomiting
- Increased patient comfort, parental satisfaction in the postoperative period
- Propofol reduces brain metabolism and cerebral blood flow, hence used in reduction of intracranial pressure
- Method of choice in patients at risk of malignant hyperthermia
- Method of choice in some patients with congenital myopathies
- Useful method for spinal surgery using motor evoke potential (MEP) or somatosensory evoked potential (SSEP) monitoring because propofol does not suppress the wave form
- Can be reliably administered to maintain anaesthesia in patients undergoing airway procedures [1].

A three compartment model can be used to mathematical describe the behaviour of most anaesthetic drugs with reasonable accuracy (Figure 3).Central compartment,V1 is referred to as initial volume of distribution in which the drug is delivered and eliminated from a central compartment. In children, the volume of distribution are larger than adults. Hence, they need higher dose of drug for induction of anaesthesia.

The drug also distributes to and redistributes from two peripheral compartments, V2 representing well-perfused organs and tissues also called fast redistribution compartments. And V3 referred to as the vessel poor or slow compartment. The sum of V1,V2 and V3 gives the volume of distribution at steady state (Vdss). The rate of transfer between compartments and elimination can be describes using rate constants. By convention, k10 means rate constant for elimination, whereas k12,k21,k13 and k31 are used to denotes the rate constants for transfer between V1 and V2,V2and V1 and V1 and V3 and between V3 and V1 respectively. The term keo describes the rate of removal of drug from the effect site.keo is derived from Pk and Pd parameters from a study population. The other parameter t1/2keo is 0.693/keo is sometimes used to express this rate constant [1].

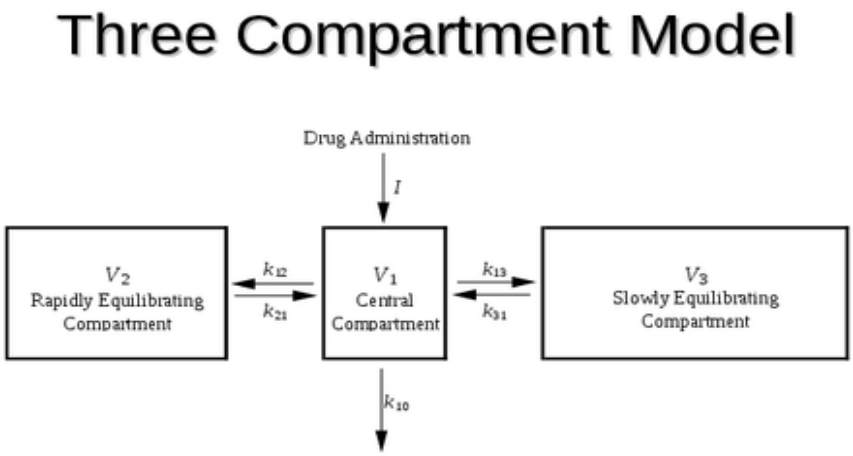

Figure 3: Schematic representation of a three compartment model (source: docslide.com).

The Pk concepts related to TIVA/TCI in children are differ from adults. Healthy children need a relatively high dose intravenous agent per unit of body weight and maintanance infusions rates need to be higher than the weight corrected dose for adult. This is because there are changes in regional blood flow, body composition, and body proportion in children. The clearance is very high in children, hence they need a higher maintenance infusion rate at steady state. At the age of 3 to 11 years old, the volume of distribution Vd is 9700mls/kg and clearance is 34ml/min/kg. Whereas in adult Vd is 4700ml/kg and clearance is 28ml/min/kg [1]. That is why adults TCI pump cannot be used in paediatric age group.

There are 2 validated TCI models in paediatric population which are Kataria and Paedfusor. The Paedfusor system was developed in the early 1990s as a variant of the Diprifusor (adult TCI software). The lower age limit for the use of Paedfusor is 1 year and the lower weight limit is 5 kg. Another validated TCI model for paediatric is Kataria model. This model was developed from the study over 600 plasma propofol samples from 53 children at various stages of induction, maintenance and recovery from anaesthesia. The lower age limit for the use of Kataria model is 3 years and the lower weight limit is 15kg (7). The two models of TCI are differ in PK profile. A study done by Munoz et al, in children aged 3-11,derived keo (keo is rate of removal of drug from the effect site) values for the Paedfusor model of 0.91/min (t1/2keo 0.8 min) and for Kataria models of 0.41/min (t1/2keo 1.7min) (8) . Table 1 summarizes the differences of PK between Kataria and Paedfusor for a 6 years old child, 20kg [9].

	Kataria	Paedfusor
V1 (L)	7.6	9.2
V2 (L)	17.4	19
V3 (L)	122.34	117.1
Cl 1 L/min	0.74	0.58
Cl 2 L/min	1.26	1.05
Cl 3 L/min	0.5	0.39
K10/min	0.097	0.063
K12/min	0.166	0.114
K13/min	0.066	0.042
K21/min	0.072	0.055
K31/min	0.0041	0.0033

From the data,we can see that the clearance and redistribution in Kataria model are faster than Paedfusor model. These Pk differences might lead to difference in clinical performance between this two group of TCI model. There was a study done by Coppen *et al* tested the performance of eight TCI models including Kataria and Paedfusor in heathy children from 3 to 26 months age. The study shown Kataria model performs poorly (Pk performance :MDPE 31.3%, MDAPE 34.1%) compared to Paedfusor model (MDPE 10.4% and MDAPE 19%) [10]. However, the study was performed in children less than 3 years old and the accuracy of models were measured based on the plasma concentration from arterial blood sampling. From our literature

search, there was no study previously comparing the clinical effectiveness between these two models. Our aims of the study are to compare the effectiveness of these two models during induction and recovery of anaesthesia.

Several factors that influence the patients selection in this study. The main factors are Pk and Pd of propofol. In this study, paediatric age group 3 to 12 years old was choosen because its fullfill the criteria for Kataria (for paediatric age 3 to 16 years old) and Paedfusor model (for paediatric age 1 to 16 years old). The other reason is to minimize the interindividual variability. This is because from birth to the age of 15,many changes influence Pk and metabolism. Three periods may be distinguisehed, the neonate, the infant and the prepubertal children. During neonatal period, anaesthetic doses have to be decreased to reach and maintain a target concentration because global immaturity and increased sensitivity to anaesthetic drugs. In infants (two-years of life), characterized by wide inter and intra variability because of progressive increase in distribution volume and fast maturational increase in clearance. From 3 years to puberty, volumes are nearly twice greater and inter-compartmental clearance 50% greater than adult [9].

The subjects of this study must be healthy children (ASA 1 and ASA 2) since the effects of propofol particularly to the cardiovascular system. Propofol can cause bradycardia and hypotension produced by inhibition of symphathetic vasoconstrictor nerve activity and negative inotropic effect [11] . The patients with heart disease are excluded in this study because they might not tolerate with this cardiovascular changes.

Bispectral index (BIS) was used in this study to monitor depth of anaesthesia. Its prevent overuse of propofol and avoid awareness during anaesthesia. The BIS reading should be maintained between 40 to 60 for anaesthesia. A study done by Agnes *et al*,

regarding the relationship between BIS and propofol during TCI anaesthesia comparison between prepubertal subjects and young adults, concluded that good relationship between propofol concentration and BIS in children as in adult [12]. In children, the predictibility of plasma propofol concentration with the classical Pk/Pd model is limited. Therefore, a cerebral Pd feedback, such as BIS may be useful in this population .

1.1 Rationale of Study

This study was to compare the effectiveness of Kataria and Paedfusor TCI models in providing anaesthesia in paediatric age group. This study was focus on successful rate of induction with TCI propofol 6 mcg/ml, induction time, and time of recovery and plasma concentration of propofol during recovery. Up to now, there was no study done to determine the effectiveness of Kataria TCI model and comparing Kataria and Paedfusor TCI models. This research is necessary to determine which one is the most effective between these 2 validated TCI models in paediatric population.

SECTION 2

OBJECTIVES OF THE STUDY

2.1 Primary objectives:

- To compare the effectiveness of Kataria versus Paedfusor models of target controlled infusion (TCI) propofol during anaesthesia for paediatric patients.

2.2 Secondary objectives:

- To compare the success rate of induction at initial induction target plasma concentration of 6 mcg/ml between the two models.
- To compare the induction time between the two models at target plasma concentration of 6 mcg/ml
- To compare plasma concentration at emergence between the two models
- To compare the time of recovery during emergence between the two models.

SECTION 3

BODY CONTENT

3.1 Title page

Title:

Comparison of the Effectiveness between Kataria and Paedfusor Models of Target-Controlled Infusion (TCI) during Anaesthesia in Elective Paediatric Surgery.

Short title:

Comparison of Kataria and Paedfusor Models of Target-controlled Infusion Propofol in Paediatric Anaesthesia.

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Conflict of interest: None

Acknowledgement:

I would like to acknowledge Miss Faza Ayunnie for her assistance on statistical analysis.

3.2 Main document

Title:

Comparison of the Effectiveness between Kataria and Paedfusor Models of Target-Controlled Infusion (TCI) during Anaesthesia in Elective Paediatric Surgery.

Abstract

Background: Kataria and Paedfusor are two validated target controlled infusion (TCI) models for propofol in paediatric population. The aim of this study was to compare the effectiveness of these two different TCI models for propofol in paediatric age group during elective surgery.

Methods**:** 38 patients, aged 3-12 year-old, classified under ASA I and II, who underwent elective surgery under general anaesthesia, were randomised into two groups; Group Kataria (n=19) and Group Paedfusor (n=19). All patients received 1 mcg/kg loading dose of intravenous (IV) remifentanil over 1 minute 15 seconds and followed with infusion at 0.1 to 1 mcg/kg/min. Then, both groups were induced at plasma concentration (Cpt) propofol of 6 mcg/ml using respective model and maintained with Cpt between 3 to 8 mcg/ml guided by bispectral index (BIS) between 40-60. Remifentanil was maintained between 0.1 to 1 mcg/kg/min. Success rate of induction, induction time, recovery time and Cpt at recovery were recorded for statistical analysis.

Results**:** Both groups were successfully induced with propofol Cpt of 6 mcg/ml. There were no significant differences in induction and recovery time between these two

groups. The plasma concentration at recovery in Kataria group was significantly lower than Paedfusor group [1.48 (0.11) mcg/ml vs 1.59 (0.14) mcg/ml, p=0.01].

Conclusion: TCI propofol for paediatric patients using Kataria and Paedfusor models were equally effective in success rate of induction, induction time and recovery time. Only plasma concentration at recovery was lower in Kataria group.

Keywords*: Kataria model, Paedfusor model, propofol, remifentanil, target-controlled infusion.*

Introduction

Total intravenous anaesthesia (TIVA) is a method of anaesthesia using only intravenous anaesthetic drugs. It can be delivered either in a conventional technique or on target controlled infusion (TCI) techniques. TCI is an advanced method of delivering intravenous (IV) drugs using a special infusion pump which is incorporated with software consisted of an algorithm based on pharmacokinetics (PK) profile of the specific drugs and age appropriate parameters. The properties of the drugs that are currently capable to be delivered by TCI methods are; fulfill the three compartmental models in distribution, short context-sensitive half-life and rapid in clearance. The only drugs that have validated pharmacokinetic models for TCI at the moment are propofol and remifentanil [1].

The PK concepts related to TIVA/TCI in children are differ from adults. Healthy children need a relatively high dose intravenous agent per-unit of body weight and maintenance infusions rates need to be higher than the weight corrected dose for adults. This is because there are changes in regional blood flow, body composition, and body proportion of children. The clearance is very high in children. Hence, they need a higher maintenance infusion rate at steady state. At the age of 3 to 11 years old, the volume of distribution (Vd) is 9700mls/kg and clearance is 34ml/min/kg. Whereas in adult Vd is 4700ml/kg and a clearance is 28ml/min/kg [1]. That is why adults TCI models cannot be used in paediatric age group.

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Kataria model. This model was developed from the study over 600 plasma propofol samples from 53 children at various stages of induction, maintenance and recovery from anaesthesia. The lower age limit for the use of Kataria model is 3 years and the lower weight limit is 15kg [2].

The two models of TCI differ in PK profile. A study done by Munoz *et al*, in children aged 3-11, derived keo (keo is the rate of removal of drug from the effect site) values for the Paedfusor model of 0.91/min (t1/2keo 0.8 min) and for Kataria models of 0.41/min (t1/2keo 1.7min) [3]. Other differences are initial volume of distribution, Paedfusor: 9.2L whereas Kataria: 7.6L, clearance in Paedfusor: 0.58L/min whereas Kataria: 0.74L/min [4]. Although there are differences between these two TCI models, both are validated and performed well clinically.

From our literature search, there is no study at the moment comparing the effectiveness between these two models. Our aims are to compare the effectiveness of these two models during induction and recovery of anaesthesia.

Materials and Methods

This study was a prospective, double-blinded, randomised controlled trial, conducted in the university hospital (Hospital Universiti Sains Malaysia).

After approval from the university ethics committee and written inform consent from all patient's parents, 38 patients undergoing elective surgery under general anaesthesia, with age between 3 to 12 years old and American Society of Anaesthesiologists (ASA) class I-II, were randomized into two groups; Group Kataria (n=19) and Group Paedfusor (n=19). Those patients with a history of allergies to study drugs, co-morbidities related to the heart and history of inborn error metabolism of lipid which are risky for propofol infusion syndrome were excluded from the study. Patients were withdrawn from the study if not cooperative during intravenous line insertion, severe hypotension or bradycardia after starting infusion of study drugs that required optimisation with rescue drugs (atropine/ ephedrine).

Randomisation

A study number of 01 to 38 was prepared. These numbers were being labelled as Group A (Kataria) or Group B (Paedfusor) and the randomization was done through the internet, at the website of www.randomization.com. 38 subjects were randomised and divided into 2 groups equally, Group A (Kataria) and Group B (Paedfusor). The study was completed after 38 patients successfully recruited. Initial 38 subjects for randomisation were based on a calculation of a 10 % drop out rate.

Blinding

This study was a double blinded study where the patient and the second medical officer who assessed the patient in the OT did not know which model of TCI propofol was being used. All patients used a standard Alaris™ PK TCI pump for TCI propofol and manual infusion pump for remifentanil. TCI pump setting up was performed by anaesthesiology registrar based on randomisation. The conduct of anaesthesia was performed by a second medical officer and data collection was done by the first investigator.

Study protocol

After approval from Ethics committee, patients were selected according to inclusion and exclusion criteria during the preoperative assessment round. Study procedures were explained and written consents were obtained from parents. In all children, eutectic mixture of local anesthetic cream was applied on both hands during pre-operative visit and intravenous (IV) cannula was inserted after an hour in the ward. No premedication was prescribed in the morning of the surgery. All consented patients were randomized using computer generated randomization into two groups: Group A (Kataria model) and group B (Paedfusor model). In OT, all of the patients monitored for non-invasive blood pressure, pulse oxymeter, electrocardiogram, capnography and bispectral index monitoring (BIS). After pre-oxygenation for 3 minutes, all patients received a slow bolus of intravenous infusion of remifentanil 1 mcg/kg for 1 minute 15 seconds as initial analgesia. During induction, Group A was induced with the Kataria model of TCI propofol at 6 µg/ml, whereas Group B was induced with a Paedfusor model of the TCI propofol also at Cpt of 6 µg/ml. After successful induction, the supraglottic device (laryngeal mask airway) was inserted to aid the respiration. The subject was breathing

spontaneously throughout the surgery. During the maintenance of anaesthesia, both groups were maintained at target plasma concentration propofol of 3-8 µg/ ml with either using Kataria model in group A or Paedfusor model in group B and were guided with BIS index of 40-60. All patients received continuous infusion of remifentanil 0.1-1.0 µg/kg/min as main intraoperative analgesia. Supplement analgesia was provided appropriately with suppository paracetamol 20 mg/kg and/or suppository diclofenac sodium 1 mg/kg. The regional block was given to patients if no contraindication. After completion of the surgical procedure, TCI propofol and remifentanil infusion were discontinued and patients were extubated when they were fully recovered. The success rate of induction at Cpt of 6 µg/ml, induction time, plasma concentration at recovery and the recovery time were recorded. The success rate of induction was defined as successful loss of consciousness and verbal response at initial Cpt. The induction time was defined as the time taken from starting of infusion of propofol to loss of consciousness/verbal response. The plasma concentration at recovery was defined as the concentration of propofol at the plasma level, which was displayed on the TCI pump monitor at extubation. The recovery time was defined as the time taken from discontinuation of propofol to extubation.

Sample size calculation

The sample size calculation was based on the study by Agnes Rigouzzo which resulted a significant difference in time of emergence was 0.4, standard deviation 0.35 with a power of 0.8 and α=0.05 [5]. The calculated sample size was 17 per group. We used Power and Sample size software version 3.0.10 for the calculation version 3.1.2. After considered 10% drop out. Therefore, the total samples were 38 patients.

Statistical analysis

All measurement data were analysed for normal distribution and homogeneity variance. Measurement of data that showed a normal distribution was presented as mean (standard deviation). The non-normal distribution was presented as median. Variables between groups were analysed with independent tests. The statistical analysis was performed by SPSS version 22 software and $P < 0.05$ was considered as a significant difference.

Results

38 patients were enrolled in the study, with 19 patients in Group Kataria and another 19 patients in Group Paedfusor. The types of surgery underwent by the study subjects included general surgery (84.2%) and orthopaedic surgery (15.8%). There was no significant difference in terms of age, height, weight, genders, types of surgery and ASA health status between the two study groups (Table 1).

All study subjects were successfully induced with TCI propofol at Cpt 6 mcg/ml. There was no significant difference in time of successful induction between the two groups (Table 2). There was also no significant difference in time of recovery. In terms of plasma concentration of propofol at emergence, there were differences between the two groups (Table 2) in which Kataria group was significantly lower than Paedfusor group [1.48 (0.11) mcg/ml vs 1.59 (0.14) mcg/ml, p=0.01].

Discussion

Total intravenous anaesthesia (TIVA) has become more popular and possible in recent times because of the PK and pharmacodynamics properties of propofol and the availability of short acting opioids such as remifentanil. The propofol anaesthesia has been especially focused on TCI anaesthesia taking into account its well known advantages in adults. A study done by Russel *et al* comparing manual infusion with TCI propofol in adult shown that more rapid induction and haemodynamic stability in TCI group [6].

A UK survey on paediatric total intravenous use revealed that about 25% of paediatric anaesthetists use TIVA at least monthly, 40% rarely and the remaining anaesthetists never. Over the last year 13% of anaesthetists used TIVA in children under 1 year of age, and the two most common surgical specialties with which TIVA used are ENT and orthopaedics. Lastly, TCI is still uncommonly used in children [7]. Eventhough it was the only European survey, it highlights that TIVA and TCI is still not a common practice for paediatric anaesthetist, but they perceive the anaesthetic and surgical benefits. The recent knowledge on Pk in childhood together with sophisticated devices have increased the perception of TIVA safety.

The Kataria and Paedfusor were validated TCI models in paediatric population. The Alaris Pk is a commercially available infusion pump that has both Kataria and Paedfusor TCI models that can be chosen by the user for induction and maintenance of anaesthesia. An algorithm based on population pharmacokinetics, patient's age and weight was used to estimate plasma concentrations of propofol and adjusted the infusion rate to achieve a set target. In the adult devices, to achieve rapid induction, improvement has been made to target directly on the effect site. This approach required the knowledge of the rate constant called ke0 between plasma and effect site. In