Comparison between Single Dose of Dexmedetomidine and Midazolam for Prevention of Emergence Agitation after Sevoflurane Anesthesia in Children

Thesis

*Submitted for partial fulfillment of the **M.D. degree***
In Anesthesia

By

Amr Fouad Hafez Helmy
(M.B., B.Ch, M.Sc. Anaesthesia)

Under supervision of

Prof. Dr./Hoda Omar Mahmoud
Professor of Anesthesia, Intensive Care Medicine and Pain Management
Faculty of Medicine-Ain Shams University

Dr. /Mayar Hassan Sayed
Assistant Professor of Anesthesia, Intensive Care Medicine and pain management
Faculty of Medicine -Ain Shams University

Dr. /Hany Vector Zaky
Lecturer of Anesthesia, Intensive Care Medicine and pain management
Faculty of Medicine -Ain Shams University

Dr. /Mohammed Sayed Shorbagy
Lecturer of Anesthesia, Intensive Care Medicine and pain management
Faculty of Medicine -Ain Shams University

Faculty of Medicine
Ain Shams University
2016

﴿وَقُل رَّبِّ زِدْنِي عِلْماً﴾

سورة طه الآيـه رقم 114

Acknowledgement

First of all, all gratitude is due to **God** *almighty for blessing this work, until it has reached its end, as a part of his generous help, throughout my life.*

Really I can hardly find the words to express my gratitude to ***Prof. Dr./Hoda Omar Mahmoud,*** *Professor of Anesthesia, Intensive Care Medicine and Pain Management, for her supervision, continuous help, encouragement throughout this work and tremendous effort he has done in the meticulous revision of the whole work. It is a great honor to work under his guidance and supervision.*

I would like also to express my sincere appreciation and gratitude to ***Dr. /Mayar Hassan Sayed,*** *Assistant Professor of Anesthesia, Intensive Care Medicine and pain management, Ain Shams University, for his continuous directions and support throughout the whole work.*

Really I can hardly find the words to express my gratitude to ***Dr. /Hany Vector Zaky,*** *Lecturer of Anesthesia, Intensive Care Medicine and pain management, Faculty of Medicine -Ain Shams University for his continuous directions and meticulous revision throughout the whole work. I really appreciate their patience and support.*

Especially I am obliged to ***Dr./Mohammed Sayed Shorbagy,*** *Lecturer of Anesthesia, Intensive Care Medicine and pain management, Faculty of Medicine -Ain Shams University who offered his great help and his professional experience for completion of this work.*

Last but not least, I dedicate this work to the soul of my father, the struggle of my mother, the patience of my wife and my little children whom without them this work would not have ever been completed.

Amr Fouad Hafez Helmy

Contents

List of Abbreviations

ACTH	:	Adrenocorticotropic hormone
CNS	:	Central nervous system
CYP	:	Cytochrome P
EA	:	Emergence agitation
FA	:	Alveolar concentration
FI	:	Fraction inspired
FLACC	:	Face, Leg, Activity, Cry, Consolability
GABA	:	G-Aminobutyric acid
GFR	:	Glomerular filtration rate
HbF	:	Fetal haemoglobin
HFIP	:	Hexafluoroisopropanol
HR	:	Heart rate
LMA	:	Laryngeal mask airway
MAC	:	Minimal alveolar concentration
MAP	:	Mean arterial blood pressure

List of Abbreviations (Cont.)

$PaCO_2$	:	Arterial CO_2 tension
PaO_2	:	Arterial O_2 tension
PACU	:	Post-anesthesia care unit
PIFE	:	Pentafluoroisopropenyl fluoromethyl ether
SD	:	Standard deviation
SPSS	:	Statistical Program for Social Science
UDPG	:	Uridine diphosphate glucose

List of tables

List of Figures

Introduction

Emergence agitation (EA) in children early after sevoflurane anaesthesia is a common postoperative problem, with incidence ranging up to 80%, It is characterized by behavior that can include crying, disorientation, excitation and delirium ***(Abu-Shahwan, 2008).***

Symptoms of (EA) are worse for pediatric patients, they cry heavily and writhe to free themselves, pull on their IV line, and impose a heavy burden on the medical staff, they play a very big role in making their parents lose confidence and satisfaction in the anesthesia and surgery ***(Everett, 2008).***

Although EA is self-limiting and might not result in permanent sequelae, it carries the risks of self-injury and is a cause of stress to both caregivers and families ***(Kuratani and Oi, 2008).***

Sevoflurane in particular has been associated with an increased amount of agitation on emergence from anesthesia in children when compared with a more soluble anesthetic (halothane) even in the absence of any surgical intervention ***(Davis, 2004).***

Sevoflurane is used frequently in pediatric patients, when inhalational induction of anesthesia is required, because of its fast and non-irritating effects on the airway. The speed of emergence from sevoflurane anesthesia, however, sometimes presents a dilemma to both patient and anesthetist. Thesis show a higher incidence of postanesthetic agitation has been attributed to the use of this newer inhalational anesthetic. However, the exact etiology of restlessness after sevoflurane anesthesia is still not known ***(Aono et al., 1997).***

Different strategies have been suggested to decrease the incidence and severity of EA, such as administrating sedative medication before induction, a change in the maintenance technique of anaesthesia, or pharmacological agent administration at the end of anesthesia **(*Koner et al., 2011).***

The side effects of sedatives used in management of EA are potentially harmful and lead to an increased length of stay in the postanesthesia care unit (PACU), resulting in patient discomfort and increased perioperative costs ***(Joseph et al., 2003).***

Midazolam is considered the most popular benzodiazepine in clinical use. It may be used for short-term sedation of intubated and mechanically ventilated ICU patients, as it is valuable for short-term procedures; it is used as a preoperative sedative anxiolytic ***(Mcintoch et al., 2004*****).**

Dexmedetomidine is a potent selective α2-adrenergic agonist, is frequently used in children because of its efficacy and lack of respiratory depression ***(Mason and Lerman, 2011).***

Because dexmedetomidine has sedative, hypnotic and analgesic properties, it can reduce the dose of hypnotics, opioids, analgesics, and anesthetics required to be concomitantly administered. Intraoperative administration of dexmedetomidine reduced sevoflurane requirements in children undergoing various surgeries ***(Lili et al., 2012).***

Aim of the work

This study will be performed to compare the effect of dexmedetomidine and midazolam administrated intraoperatively on emergence agitation in children receiving sevoflurane.

Pediatric Anesthesia

Pediatrics has unique anatomic, physiologic and pharmacological consideration. So they need specific care with respect to these differences from adults ***(Morray et al., 2000).***

Physiologic considerations

Physiological differences between pediatrics and adults are important determinants when planning management of anesthesia in pediatric patients. Monitoring vital signs and organ function during the preoperative period is especially important, as neonates and infants have decreased physiologic reserves ***(Stoelting and Dierdorf, 2002).***

Cardiovascular system

The process of growth demands a high metabolic rate. Thus, a higher cardiac index (compared with adult) is required to increase oxygen delivery to tissue. The main determinate of cardiac output is heart rate since the ventricle of neonates is poorly developed. Infants tolerate heart rates of 200 beats min^{-1} with ease at birth (Table 1), resting cardiac output is approximately 200ml/kg/minute, after which it declines gradually to approximately 100ml/kg/minute by adolescence, so that drugs are distributed to and from their sites of action more rapidly ***(Holzman et al., 2008).***

Age	**Mean value** (beat / min)	**Normal range** (beat / min)
Neonate	140	100-180
1 year	120	80-150
2 years	110	80-130
6 years	100	70-120

Table (1): Variation in heart rates (beat / min) with age *(Aitkenhead et al., 2001).*

Bradycardia may occur rapidly in response to hypoxemia and vagal stimulation. Immediate termination of the stimulus and treatment with oxygen and atropine are absolutely crucial. A heart rate of 60 beats/min in an infant is considered a cardiac arrest and requires cardiac massage. Usually cardiac arrest occurs in the form of electromechanical dissociation and asystole, not ventricular fibrillation, Systemic vascular resistance is lower in infants due to the abundance of vessel-rich tissues in spite of having high cardiac index and this account for lower arterial blood pressure. The pressure increases from approximately 80/50mmHg at birth to the normal adult value of 120/70mmHg by the age of 16 years. Central neural block at start of anesthesia tends to produce no decrease in blood pressure in Children under the age of 8 years. Also fluid preload isn't crucial like adults, because venous pooling tends not to occur as venous capacitance cannot increase much. The reasons for this is the ill-developed sympathetic nervous system and so infants tend to be venodilated at rest, and so vasoconstrictive responses to hemorrhage are less in neonates than adults ***(Aitkenhead et al., 2001).***

Caudal anesthesia altered neither heart rate nor mean arterial blood pressure. However, significant increases in descending aortic blood flow and in stroke volume were associated with a decrease in lower body vascular resistance. These results propose that caudal anesthesia results in arterial vasodilation in the anesthetized location. The local anesthetic-induced sympathetic block is the probable cause of this vasodilation ***(Larousse et al. 2002).***

Respiratory system

Control of respiration in newborn infants, especially premature neonates is ill-developed. The incidence of central apnea (defined as a cessation of respiration for 15 second or longer) is not uncommon in newborn infants especially with a drug with a sedative effect. Unlike the adult, hypoxia in the neonate and small child appears to inhibit rather than stimulate respiration. The newborn has between 20 and 50 million terminal air spaces. At 18 months of age, the adult level of 300 million is reached by a process of alveolar multiplication. Subsequent lung growth occurs by an increase in alveolar size. The lung volume in infants is disproportionately small in relation to body size. Their metabolic rate is nearly twice that of the adult, and therefore ventilator Pediatric anesthesia requirement per unit lung volume is increased. Thus they have far less reserve for gas exchange ***(Aitkenhead et al., 2001).***

Before the age of 8 years, the diameter of the airway is relatively narrow. The cricoid cartilage is the narrowest point of the airway in children less than 5 years of age, in adults; the narrowest point is the glottis. One millimeter of edema will have a proportionately greater effect in children because of their smaller tracheal diameters ***(Morgan et al., 2006).***

Airway resistance is therefore relatively high. Small decreases in the diameter of the airways as a result of edema formation or respiratory secretions increase the