



Thesis Submitted For Partial Fulfillment of the Master Degree in Anaesthesiology.

Presented by
Ayman Amin Abou Gabal
M.B,B.Ch
Faculty of Medicine
Cairo University

Supervisors

Prof. Dr. Azza Mohammed Ezzat

Professor of Anaesthesia, Surgical ICU and Pain Management Faculty of Medicine, Cairo University

Prof. Dr. Mohamed Farouk Youssef

Professor of Anaesthesia, Surgical ICU and Pain Management Faculty of Medicine, Cairo University.

Dr. Dalia Saad Abd EL Kader

Lecturer of Anaesthesia, Surgical ICU and Pain Management Faculty of Medicine, Cairo University.

Faculty of Medicine Cairo University 2014



Abstract

The current study was carried out on fifty two pediatric patients aged 6 months - 6 years old suffering from Acyanotic congenital heart disease scheduled for diagnostic or interventional cardiac catheterization. All patients received premedication 30 minute before induction of anesthesia via intramuscular route. Twenty six patients in Group (M) received intramuscular combination of 0.05mg/kg midazolam (Midathetic ,AmounPharmacetical CO), 2mg/kg ketamine (Ketamine ,Sigma Tec) and 0.02 mg/kg atropine while other twenty six patients in group (D) received intamuscular combination of 1ug/kg Dexmedetomidine (Precedex, Hospira, Lake Forest, Illinois) , 2mg/kg ketamine (Ketamine ,Sigma Tec), and 0.02 mg/kg atropine.

The results of this study showed no statistically significant differences between intramuscular dexmedetomidine and intramuscular midazolam as a premedication in pediatric Acyanotic cardiac patients with respect to blood pressure, sedation scores, easiness of parent separation, and acceptance of venous line. However, significant increase in heart rate was recorded with intramuscular midazolam compared to intramuscular dexmedetomidine.

Keywords: Intramuscular sedation – Dexmedetomidine – Midazolam – Cardiac catheter lab.



Acknowledgement

Foremost, I would like to express my sincere gratitude to my advisor **Prof. Dr. Azza Ezzat**, Professor of Anaesthesia, Surgical ICU and Pain Management, Faculty of Medicine, Cairo University, for the continuous support of my M.Sc. study and research, for her patience, motivation, enthusiasm, and immense knowledge. Her guidance helped me in all the time of research and writing of this thesis. I could not have imagined having a better advisor and mentor for my Ms.C. study.

Special thanks to **Prof. Dr. Mohammed Farouk Youssef**, Professor of Anaesthesia, Surgical ICU and Pain Management, Faculty of Medicine, Cairo University, for her encouragement, insightful comments, and very valuable questions and suggestions.

My sincere thanks also go to **Dr. Dalia Saad Abd EL Kader**, Lecturer of Anaesthesia, Faculty of Medicine, Cairo University, who was leading the experimental design, implementation of the research, testing the assumptions, and frame the overall structure and content of the study.

Special thanks to my Father god rest his soul, my Mother and my Aunt for supporting and helping me all through my life. Also special thanks to my brothers and sister for their support and their experience which helped me a lot to finish this work. Thanks to the parents who approved to me to conduct the study on their sick children's and pear the risk.

Ayman Amin Abou gabal



Aim of the work

The aim of the study is to compare the efficacy of intramuscular combination of Dexametomiditne and ketamine versus intramuscular combination of midazolam and ketamine as preoperative sedative and anxiolytic drugs in pediatric patients undergoing cardiac catheterization.



List of Abbreviations

ACEP The American College of Emergency Physicians

ANOVA Analysis of Variance

ASA The American Society of Anesthesiologists

ASD Atrial Septal Defect AR Adrenergic Receptors

BP Blood Pressure

CBF Cerebral Blood Flow
CCL Cardiac Catheter Lab
CNS Central Nervous System
CHD Congenital Heart Disease
CT Computed Tomography

DP Diastolic Pressure EEG Electroencephalogram

GABA Gama Amino Buytric Acid

HR Heart rate

IM Intra Muscular

ICP Intracranial Pressure ICU Intensive Care Unit

IV Intravenous KG Kilogram

MAP Mean Arterial Pressure

MRI Magnetic resonance imaging

NMDA N-methyl-D-aspartate

PCO2 Arterial Carbon Dioxide Tension PSA Procedural Sedation Anesthesia

PDA Patent Ductus Arteriosus
PO2 Arterial Oxygen tension
PS Pulmonary Stenosis
SD Standard Deviation
SP Systolic Pressure
Spo2 Oxygen Saturation

SVR Systemic Vascular Resistance TGA Transposition of great arteries VSD Ventricular Septal Defect



Table of Contents

Introduction	2
Chapter (1): Pediatric Cardiac Catheter Lab	6
Classification Of Congenital Heart Disease	
Cardiac Catheter laboratory (CCL):	
Orientation of cardiac catheter laboratory:	
Special Anesthetic Considerations:	
Procedures Performed in Our Study:	
Choice of Vessel Access:	
Common Complications of the Procedure:	
Future in anesthesia for interventional cardiology	
ruture in anestnesia for interventional cardiology	19
Chapter (2): Sedation In Pediatric Cardiac Patients	21
Role Of Pre-anesthetic Sedation In Pediatric Patients:	
Pediatric Sedation Required Professional Skills:	
Sedation Levels And Scales:	
Monitoring Patients During And After Sedation:	
Review of Some Medication Commonly Used For Pediatric Sedation:	
Adverse Sedation Events And Risks Related To Pediatric Sedation:	
Future of Pediatric Sedation:	30
Chapter (3-A): Pharmacology of Midazolam	33
History	
Physicochemical Characteristics	
Pharmacokinetics	
Pharmacology	
Uses	
Side Effects and Contraindications	45
Chapter (3-B): Pharmacology of dexmedetomidine	17
History	
Physicochemical Characteristics :	47
Pharmacokinetics:	
Pharmacodynamics:	
Side effects:	
	717



Clinical uses	52
Chapter (3-C): Pharmacology of Ketamine	57
History:	
Physicochemical Characteristics:	57
Pharmacokinetics:	
Pharmacology:	
Uses:	
Side effects & Contraindications:	64
Chapter (4) Patients and Methods	
Chapter (5): Results	/4
Chapter (6): Discussion:	85
Summary	92
References	96
Arabic Summary	110



List of tables

Table 1.1: Common complication of interventional cardiology	15
Table 2.1: ASA Definitions of General Anesthesia and Levels of	2.2
sedation/Analgesia	23
Table 2.2: Ramsay score	26
Table 4.1: Ramsay scale	71
Table 4.2: Study statistical tests procedure	72
Table 5.1: Age in months, gender distribution and weight in kilogram of the	7.4
two groups	74
Table 5.2: Procedural detail and time of procedure in minutes	75
Table 5.3: Heart rate of the two groups.	76
Table 5.4: Heart rate within each group	77
Table 5.5: Mean Arterial Pressure in mmHg for all groups	78
Table 5.6: Blood pressure within each group.	79
Table 5.7: Sedation assessment of the two groups	80
Table 5.8: Easiness of patient separation from parents between two groups	82
Table 5.9: Venous line insertion between two groups	83



List of figures

Figure 1.1: Orientation of cardiac catheter laboratory	9
Figure 3.1: Benzodiazepine action on GABA receptor	37
Figure 5.1: Demographic data of the two groups	75
Figure 5.2: Mean heart rate overtime	77
Figure 5.3: column chart representing effect of two drugs on mean arterial blood pressure	79
bioou pressure	
Figure 5.4: Sedation assessment of the two groups	81
Figure 5.5 : percentage of patient easily separated from parents	82
Figure 5.6: percentage of patient who accepted venous line insertion	83



Introduction



Introduction

The preoperative period is a stressful event that faces the majority of individuals undergoing surgery or interventional procedure. Pharmacological and behavioral interventions are used to treat preoperative anxiety in children and their parents. (1)

Among the different results that may be achieved with premedication such as amnesia, optimization of preoperative conditions, and prevention of physiological stress, the primary aim in children is anxiolysis. (1) It has been reported that there are correlations between heart rate, blood pressure, and behavioral ratings of anxiety. (2)

In order to alleviate physiological and psychological effects of preoperative anxiety in children, most anesthesiologists use either parental presence or sedative premedication, since separation from parents and induction of anesthesia are considered the most perioperative stress inducing phases. Both approaches are considered appropriate choice of interventions. (3)

The ideal premedication agent in children should be readily acceptable and should have a rapid and reliable onset with minimal side effects. Choosing



the appropriate agent or combination is crucial in order to alleviate noxious stimuli, stress and anxiety, while minimizing the risk of adverse effects. The desired goals of each pediatric patient's sedation should be identified and carefully considered by the practitioner before initiation of any drug therapy. (4)

Non pharmacologic-based methods may be used to initially allay anxiety in the child and parents before the procedure, including the involvement of child-life practitioners followed by a discussion of the planned procedure, duration, and plan for provision of sedation and analgesia. Careful attention to patient and parental preferences is important, and prior adverse experiences with certain drugs or methods of drug administration should be discussed and clarified, along with any drug allergies. Most patients with congenital heart disease (CHD) have had multiple hospital experiences and, as a result, not infrequently have definitive preferences in these areas. ⁽⁵⁾

A highly selective $\alpha 2$ -adrenoreceptor, dexmedetomidine has been found to have sedative, anxiolytic, and analgesic effects without respiratory impairment. ⁽⁶⁾⁽⁷⁾ Dexmedetomidine induced sedation through alpha 2 receptor in the locus coeruleus in the central nervous system, the quality of sedation simulate normal deep sleep that is to say you can arousal the child easy. ⁽⁸⁾⁽⁹⁾



One of the main advantages of dexmetedomidine over other sedative agents used in children is intact upper air way reflex and minimal effect on the respiratory center derives. (10)



Chapter (1) Pediatric cardiac catheter lab



Chapter (1): Pediatric Cardiac Catheter Lab

In the last 2 decades the number of infants, children, and adults who survived with congenital heart disease (CHD) has continued to grow substantially. (11) Several investigations will be needed for defining the anatomy, subsequent to echocardiography, primarily for evaluation of thoracic venous and arterial anomalies. Complete angiographic definition of aortopulmonary collateral arteries, complex aortic arch anomalies, and pulmonary arterial and venous anomalies optimizes surgical planning and intervention. (12)

Classification of Congenital Heart Disease

Congenital heart disease is a problem with the heart's structure and function that is present at birth.

Congenital heart disease is often divided into two types: non-cyanotic and cyanotic. The following lists cover the most common congenital heart diseases.

Non-cyanotic Heart Disease:

- Aortic stenosis
- Atrial septal defect (ASD)