



بسم الله الرحمن الرحيم

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Efficacy of Intraoperative Magnesium Sulphate versus Ketamine on Emergence Agitation in Pediatric Patients under Sevoflurane Anesthesia

Thesis

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بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

قَالَ

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List of Abbreviations

Abb.	Full term
ASA.....	American Society of Anesthesiologists
AV	Atrioventricular
Bpm	Beats per Minute
CBC	Complete Blood Count
CNS	Central Nervous System
EA	Emergence Agitation
EA.....	Emergence Agitation
ECG	Electrocardiography
ED	Emergence Delirium
ENT	Ear, Nose, Throat
ETT.....	Endotracheal tube
FPS-R	Faces Pain Scale – Revised
HFIP	HexaFluoroIsoPropanol
HR.....	Heart rate
IQR	Interquartile range
IV	IntraVenous
K	Ketamine
M.....	Magnesium Sulphate

List of Abbreviations *cont...*

Abb.	Full term
MAC	Minimum Alveolar Concentration
Mg	Magnesium
mLS	Milli-liter solute
mmHg.....	Millimeter Mercury
NaCl.....	Sodium Chloride
NIBP	Non-Invasive Blood Pressure
NMB	Neuromuscular Blockade
NMDA	N-Methyl-D-aspartate
OIH.....	Oblique Inguinal Hernia
PACTR.....	Pan-African Clinical Trial Registry
PACU	Post-Anaesthetic Care Unit
PAED	Pediatric Anesthesia Emergence Delirium
SD	Standard Deviation
SPO2.....	Pulse oximetry
TFA	TriFluoroAcetic acid

INTRODUCTION

Emergence agitation (EA) is a postoperative phenomenon which is observed in children after Sevoflurane anesthesia, with an occurrence rate of up to 80%. (*Abdelhalim and Alarfaj, 2013*). It presents with behavioral changes as irritability, agitation, inconsolable sobbing, mental confusion, some psychotic traits such as hallucinations and delusions, and cognitive impairment (*Abu- Shahwan and Chowdary, 2008*). Emergence agitation is diagnosed by a final composite score of greater than or equals 10 on the Pediatric Anesthesia Emergence Delirium Scale (PAED), a scale which measures 5 emergence behaviors in children, and each of which is assessed on a 5-point Scale (*Stamper et al., 2014, Sikich and Lerman, 2004*).

Although its exact causes are unknown, the cause of EA may be multifactorial with patient-related, anesthesia-related, and surgical factors (*Lee and Sung, 2020*). One of the postulated anesthetic causes of EA is Sevoflurane use (*Vlajkovic and Sindjelic, 2007*). Sevoflurane is a volatile anesthetic agent preferred in the initiation and maintenance of general anesthesia in pediatric patients due to its rapid onset

and termination of action as well as its low pungency and non-irritating effect on the airways (*Kawai et al., 2019*).

Effective treatment of EA due to Sevoflurane use requires an understanding of all the possible mechanisms underlying its causation (*Bae et al., 2010*). One of the proposed treatments for EA is the use of opioids, however, it carries the risk of an extended Post Anesthetic Care Unit (PACU) stay resulting in parents' discomfort and added costs (*Alghamdi et al., 2020*). Therefore, analgesic adjuvants with NMDA (N-methyl-D-aspartate) receptor antagonist functions, such as Ketamine (*Chen et al., 2013*) and Magnesium Sulphate (*Abdulatif et al., 2013*), have been tried to control this phenomenon in children.

As a sedating analgesic, Ketamine was found to be successful in the management of EA in children but was associated with a delay in recovery (*Chen et al., 2013*). Also, according to *Ng et al (2019)*, the recommendations for Ketamine use for the prevention of EA in children may be limited by lack of confidence in the evidence.

AIM OF THE WORK

The aim of this work was to investigate the effectiveness of intraoperative Ketamine versus Magnesium Sulphate infusions on reducing the incidence as well as the severity of emergence agitation that follows anesthesia using Sevoflurane immediately and after 30 minutes in PACU.

We hypothesized that the intraoperative Magnesium Sulphate would be superior to Ketamine in reducing the incidence and severity of emergence agitation in pediatric patients undergoing pelvic and abdominal operations under Sevoflurane anesthesia.

EMERGENCE AGITATION IN CHILDREN

Definition and assessment tools of emergence agitation

Emergence delirium (ED) is defined by anesthesia literature as a state of mental confusion, agitation, hallucinations, delusions, and disinhibition which may be associated with some degree of hyperexcitability, moaning, restlessness, and involuntary physical activity during recovery from general anesthesia (*Stamper et al., 2014*).

Agitation can be also defined as “a behavioral symptom of physical or emotional distress that includes any of the following behaviors alone or in combination: crying, restlessness, thrashing, verbal out-bursts, kicking, or biting; purposeful and non-purposeful behaviors in children that may be coherent or incoherent” (*Ringblom et al., 2018*).

This phenomenon is found to be predominantly seen in preschool children aging from 3-5 years. It may lead to lost intravenous catheters, as well as disconnected cables and monitoring instruments. The greatest incidence of agitation is observed during the first 30 minutes after emergence, and duration is generally limited, and recovery is spontaneous. However, prolonged episodes of agitation lasting for up to 2 days have been described and there is no definitive explanation for emergence agitation (*Lerman, 2004*).

Possible causes of postanesthetic problematic behavior in children include physiologic compromise such as metabolic disturbances, hypoxemia or bladder distension. The occurrence of such complications is however possible to recognize. Among the confounding variables that might pose a diagnostic dilemma, pain remains the most problematic. Behavioral signs of emergence agitation often mimic those of postoperative pain (*Costi et al., 2014*).

The Pediatric Anesthesia Emergence Delirium (PAED) scale, illustrated in **Table 1**, was developed with the objective of minimizing errors in the clinical assessment of agitation in children (*Przybylo et al., 2013*).

Table 1: PAED scale.

Behavior	Frequency of behavior				
	Not at all	Just a little	Quite a bit	Very much	Extremely
The child makes eye contact with the caregiver	4	3	2	1	0
The child's action is purposeful	4	3	2	1	0
The child is aware of his/her surroundings.	4	3	2	1	0
The child is restless	0	1	2	3	4
The child is inconsolable	0	1	2	3	4

It is possible that the adoption of an age-based pain scale in combination with the PAED scale could be useful for defining diagnosis and assessment of emergence agitation. The Pediatric Anesthesia Emergence Delirium Scale (PAED); the total PAED is the sum of the scores (i.e., the values shown in the table) for the five behaviors listed. EA is indicated by a total PAED score of >10 (*Sikich and Lerman, 2004*).

Pathophysiology and risk factors:

The exact mechanism of EA after general anesthesia is still not known. The occurrence of EA in children is thought to be multifactorial. Suggested causes of EA in children include patient-related, anesthesia-related, and surgical factors (*Lee and Sung, 2020*).

A. Patient related risk factors:

1. Age and Sex:

A high incidence of EA was described in **preschool-aged boys (3-6 years)** who underwent minor urological surgery under sevoflurane anesthesia. Preschool-aged children of both genders are at risk of EA and children aged 2-6 years are mostly the target group for several studies. This is caused by their emotional lability when exposed to stressful or unfamiliar environment. Also, the hippocampus is still underdeveloped at this age (*Lee and Sung, 2020*).