

### بسم الله الرحمن الرحيم

 $\infty\infty\infty$ 

تم رفع هذه الرسالة بواسطة / هناء محمد علي

بقسم التوثيق الإلكتروني بمركز الشبكات وتكنولوجيا المعلومات دون أدنى مسئولية عن محتوى هذه الرسالة.

		4534		
\ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \	(m) (m)		\$	ملاحظات:
		حامعتهت		
	since	1992	1.53	

بركات وتكنولوجياراه

# THESIS FOR PARTIAL FULFILMENT OF MASTER DEGREE IN ANESTHESIA

#### Title:

A Comparison between Intravenous Ketamine and Magnesium Sulphate for Prevention of Intraoperative Shivering in Patients Undergoing Spinal Anesthesia

**Postgraduate Student:** Omar Ahmed Sameh Mahmoud Ghoraba **Degree:** (M.B. B.Ch) Cairo University

**DIRECTOR:** Dr. Ayman Mokhtar Kamaly **Academic Position:** Professor

**Department:** Anesthesia, Intensive care and Pain Medicine **Ain Shams University** 

Co-DIRECTOR: Dr. Rami Mounir Wahba Academic Position: Lecturer

**Department:** Anesthesia, Intensive care and Pain Medicine **Ain Shams University** 

**Co-DIRECTOR:** Dr. Reham Fathy Galal **Academic Position:** Lecturer

**Department:** Anesthesia, Intensive care and Pain Medicine **Ain Shams University** 

FACULTY OF MEDICINE AIN SHAMS UNIVERSITY 2022

### Acknowledgments:

S would like to express my deepesr gratitude and respect to Sr. Ayman Mokhtar Kamaly. Sr. Ramy Mounir and S. Reham Sathy Sor their careful supervision and assistance throughout this study. And their guidance through every step, with patience and helpful feedback added much needed experience that would benefit me in the rest of my career.

The am also thankful for all the support and assitance provided by the staff of the anesthesia department, without which this study could have never been completed.

Tam thankful for my mother, family and friends for their continous support.

Omar Bameh Goraba

### **Contents**

	<b>Page</b>
Acknowledgments	3
Contents	4
Abbreviations list	5
Figures list	8
Tables list	11
Introduction	<i>13</i>
Literature review	<i>15</i>
Anatomical considerations	<i>16</i>
Pharmacology	<i>22</i>
Physiologic Effects of Neuraxial Block	<i>31</i>
Technique of Neuro-axial Blockade	41
Patients and Methods	<i>49</i>
Statistical Analysis	<i>55</i>
Results	<i>56</i>
Discussion	<i>79</i>
Summary	95
References	99
Arabic Summary	<i>110</i>

### **List of Abbreviations**

°C Celsius degree

**5-HT** 5-Hydroxy Tryptamine

**ANOVA** Analysis of variance

**ASA** American society of anesthesiologists

**ATP** Adenosine triphosphate

**CBC** Complete blood picture

**CNS** Central nervous system

**CS** cesarean section

**CSF** Cerebrospinal fluid

**DM** Diabetes mellitus

**DNA** Deoxy Ribo-Nucleic Acid

**ECF** Extracellular fluid

**ECG** Electrocardiogram

**EEG** Electroencephalography

**HR** Heart rate

**HTN** Hypertension

**I.V** Intravenous

**ICP** Intra-cranial pressure

**INR** Internation normalized ratio

**ISS** Inova sedation scale

**Kg** Kilogram

**LV** Left - Ventricular

MAP Mean arterial blood pressure

**mEq** milliequivalent

Mg Milligram

Mg Magnesium

MgSo4 Magnesium Sulphate

**NIBP** Noninvasive blood pressure

NMDA N-Methyl-d-aspartate

**PACU** post-anesthetic care unit

**PONV** postoperative nausea and vomiting

**Pre-op** Pre-operative

**PT** Prothrombin time

**PTT** Partial thromboplastin time

**RNA** Ribonucleic Acid

**SD** Standard deviation

**SPO2** Saturation of Peripheral Oxygen

**TURP** Transurethral prostatectomy

## **List of Figures**

Figure	Subject	Page
Figure 1	Normal curvature of the vertebral column	17
Figure 2	Lumbar vertebra	18
Figure 3	Sagittal section of the lumbar region	19
Figure 4	Schematic illustration of thermoregulation.	33
Figure 5	Surface landmarks for identifying spinal levels.	42
Figure 6	Sitting position for neuroaxial blockade.	43
Figure 7	The effect of flexion on adjacent vertebrae.	43
Figure 8	Lateral decubitus position for neuroaxial blockade.	44
Figure 9	Lumbar epidural anesthesia; midline approach.	45

Figure 10	Technique of paramedian approach.	45
Figure 11	Sensory dermatomes.	47
Figure 12	Sex precentage	58
Figure 13	Age mean	58
Figure 14	Height mean	59
Figure 15	. Weight mean	59
Figure 16	ASA II and III percentage	60
Figure 17	Incidence of Hypertension (HTN)	60
Figure 18	Neuropathy grade comparison	61
Figure 19	Spinal Level comparison	65
Figure 20	Hypotension incidence	68

Figure 21	Sedation scores	68
Figure 22	Hallucination incidence	69
Figure 23	Incidence of Shivering	71
Figure 24	Requirement of rescue pehtidine	71
Figure 25	Time elapsed to the start of shivering	72
Figure 26	Mean arterial pressure chart every ten minutes	74
Figure 27	Heart rate chart every ten minutes	76
Figure 28	Body temperature chart every ten minutes	78

## **List of Tables**

Table	Subject	Page
Table 1	Grades of shivering.	53
Table 2	Inova sedation scale	53
Table 3	Demographic data	57
Table 4	Pre-operative data	61
Table 5	Operative data comparison	64
Table 6	Side effects	67
Table 7	Shivering results among groups	70
Table 8	Mean arterial pressure measurements	73

Table 9	Heart rate measurements	75
T 11 10		77
Table 10	Body temperature measurements	77

### **Introduction**

Shivering is a physiological function described as involuntary, repetitive and spontaneous muscle contractions in response to a drop in core body temperature. It aims to combat hypothermia through skeletal muscle contraction and expenditure of energy. It is regulated by the primary motor center for shivering, located in the posterior hypothalamus near the wall of the third ventricle which has a thershold value, below which will lead to responses in the skeletal muscles. (*Chan et, al. 1999*)

Shivering is a very common complication during and following spinal anesthesia triggered by hypothermia. Hypothermia or the drop in core temperature is due to decreased sympathetic tone -and subsequent vasodilatation- caused by subarachnoid block, which leads to quick heat loss and redistribution of body heat to the periphery. The drop of core temperature is also compounded by temperature loss to the cold atmosphere of the operating theater, or body cavity exposure plus systemic release of pyrogens due to surgery. (*Crowley et al. 2008*)

While not causing severe morbidity in healthy patients, shivering aims to raise core temperature. This is achieved through raising the metabolic activity and oxygen consumption (up to 400%) leading to arterial hypoxemia. In addition this leads to increase cardiac output, carbon dioxide production and lactic acidosis. In susceptible patients (patients with poor cardiopulmonary reserve) this may result in increased risk of myocardial ischemia, increased intracranial tension and intraocular pressure. It also impedes monitoring the patient by interfering with ECG, blood pressure and pulse oximetry readings, thus compromising patient safety. And lastly shivering causes patient discomfort and distress and also potentially worsens wound pain. (*Frank et, al.* 2000)

Shivering is one of the common problems after spinal anesthesia with an incidence of up to 56.7%.

At present, there are many clinical treatments available for patients to control shivering after spinal anesthesia. This includes nonpharmacological methods and pharmacological methods.

Nonpharmacological methods using equipment to maintain a normal temperature of the body through limiting heat loss are effective, but expensive. These include for example; operating theater temperature control, fluid

warmers, surgical drapes, blankets, forced air warmers and active circulating water mattresses.

However, pharmacological methods are easier to carry out and more reasonable financially. These include using drugs, such as opioids (Pethidine, Tramadol), Alpha agonists (Clonidine), neostigmine, magnesium sulphate and ketamine. (*Peng et, al 2018*)

Ketamine is a competitive NMDA (N-Methyl-d-aspartate) receptor antagonist that has a role in thermoregulation at various levels. NMDA receptors modulates noradrenergic and serotoninergic neurons in the locus ceruleus. Ketamine increases arterial blood pressure, heart rate and cardiac output due to direct sympathetic stimulation and reduction of noradrenaling reuptake into the postganglionic sympathetic nerve endings, thus in effect decrease peripheral redistribution of heat. Ketamine is used as an antishivering agent in the dose of 0.5- 0.75mg/kg. (*Dal et, al. 2005*)

Meanwhile, trials showed that there is sufficient data to conclude that intravenous magnesium reduces shivering in perioperative patients. The drug not only exert a central effect, but is also a mild muscle relaxant and may thus simultaneously reduce the gain of shivering (incremental shivering intensity with progressing hypothermia). ( *Kawakami et, al. 2019*)

This is randomized placebo-controlled clinical trial that aims to evaluate and compare the relative efficacy and safety of low dose ketamine (0.5mg/kg) versus magnesium sulphate (30 mg/kg) in the inhibition of shivering during/post anesthesia in patients undergoing diabetic foot debridement surgeries under spinal anesthesia. The primary outcome is the prevention of shivering and the secondary outcomes are the effect of studied drugs on hemodynamics and level of consciousness plus the effect of chronic diabetes on the incidence of shivering under spinal anesthesia.

### **Literature Review:**

#### **Anatomical considerations**

#### **Pharmacology**

Physiological effects of central neuroaxial blockade

**Technique of Neuroaxial blockade**