بسم الله الرحمن الرحيم

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

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Omar Sameh Goraba

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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

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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