Ketamine-Dexmedetomidine versus Ketamine-Midazolam in anesthesia of burn Pediatric Patients

Thesis

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Haitham Mohammad Shafeek Ahmad Rizk

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List of Abbreviations

Abbr.	Full-term
ASA	: American society of anesthesiology
AVP	: Arginine vasopressin
BZDs	: Benzodiazepines
CAMP	: Cyclic adenosine monophosphate
CNS	: Central nervous system
FDA	: Food and Drug Administration
FLACC	: Faces, Legs, Activity, cry and consolability
FPS-R	: Revised Faces Pain Scale
GABA	: Gamma amino butyric acid
HR	: Heart rate
ICP	: Intracranial pressure
MAP	: Mean arterial pressure
MRI	: Magnetic resonance imaging
NMDA	: N-methyl-D-aspartate
NO	: Nitric oxide
PCA	: Patient controlled Analgesia
PCP	: Phenyl-cyclohexyl piperidine
PONV	: Postoperative nausea and vomiting
SD	: Standard deviation
SpO2	: Peripheral oxygen saturation
SPSS	: Statistical Program for Social Science
TMN	: Tuberomamillary nucleus
VAS	: Visual Analogue Scale
VLPO	: Ventrolateral preoptic nucleus

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Introduction

Burn injury causes severe pain and anxiety and leads to many physical and psychological effects. Pain control is an important problem that needs to be solved in burn units. For this purpose, different pharmacological and non-pharmacological methods have been used to provide patient comfort and pain relief for pediatric burn dressing changes. Pharmacological treatment is the primary approach, and several categories of drugs have been used to manage burn pain ***(Stoddard et al., 2002).***

Ketamine is a phencyclidine derivative, primarily used for the induction and maintenance of general anesthesia, usually in combination with a sedative. Other uses include sedation in intensive care, analgesia (particularly in emergency medicine), and treatment of bronchospasm. Ketamine has a wide range of favorable effects in humans, including analgesia, anesthesia, bronchodilatation and some side effects as hallucinations, elevated blood pressure. The effect of ketamine is thought to be the result of N-methyl-D-aspartate (NMDA) receptor antagonism, opioid mu receptor agonism, and voltage-sensitive sodium channel interactions ***(Peck et al., 2008).***

Midazolam is a short-acting drug in the benzodiazepine class used for treatment of acute seizures, moderate to severe

insomnia, and for inducing sedation and amnesia before medical procedures. It possesses profoundly potent anxiolytic, amnestic, hypnotic, anticonvulsant, skeletal muscle relaxant, and sedative properties ***(Olkkola et al., 2008).***

Midazolam seems to somewhat help alleviate discomfort arising from emergence phenomena caused by Ketamine ***(Doenicke et al., 1992).***

Alpha 2 receptors are found in the peripheral and central nervous systems, platelets, and many other organs, including the liver, pancreas, kidney, and eye. Stimulation of the receptors in the brain and spinal cord inhibits neuronal firing, causing hypotension, bradycardia, sedation, and analgesia. The responses from other organs include decreased salivation, decreased secretion, decreased bowel motility and inhibition of renin release ***(Gertler et al., 2001).***

Dexmedetomidine is the S-enantiomer of medetomidine and an alpha $_2$-adrenoreceptor agonist agent that has sedative, analgesic, and anxiolytic properties. Endomorphine-1 is an endogenous u-opioid agonist peptide and has synergistic antinociceptive interaction with dexmedetomidine and/or *S*-(+)-ketamine at the NMDA receptor level. Therefore, the combination of both these drugs has potent antinociceptive activity and may result in a decrease in the total drug dose. The mechanism of action of dexmedetomidine differs from

clonidine as it possesses selective alpha 2-adrenoceptor agonism especially for the 2A subtype of this receptor, which causes it to be a much more effective sedative and analgesic agent than clonidin ***(Horvath et al., 2001).***

Aim of the Work

This study aims to compare the effects of Ketamine – Dexmedetomidine versus Ketamine- Midazolam in anesthesia of pediatric burn patients.

Burn

Introduction

Children are naturally curious. As soon as they are mobile, they begin to explore their surrounding environment and play with new objects. By this way, they acquire the skills they need to survive in the world. At the same time, they come into contact with objects that can cause severe injuries. Playing with fire or touching hot objects can result in burns, which is a debilitating condition accompanied by intense pain and often by longer-term illness that creates suffering not only for the child but for their family and community. Fortunately, the prevention, acute care and rehabilitation of burns have improved greatly over the past decades. There is now an evidence that a number of measures are effective in preventing burns. These include the introduction and enforcement of items such as smoke alarms, residential sprinklers and fire-safe lighters, and laws regulating the temperature of hot-water taps. Nonetheless, considerable disparities exist between countries in the extent of their prevention, care and rehabilitation of burns. It is estimated that over half a million children are hospitalized with burn injuries per year in the world, with the majority occurring in low to middle income countries in Asia and Africa ***(Burd and Yuen, 2005).***

Low socio-economic status of the family and low educational level of the mother are the main demographic factors associated with a high risk of burn injury ***(Ahuja and Bhattacharya, 2004)***.

Other factors associated are: high population density, high levels of household crowding, absence of water supply and psychological stress within the family. Children who were not the biological son or daughter of the head of the household are also at increased risk for burns ***(Delgado et al. 2002)***.

Non-accidental burn injury (i.e., abuse) is present in a higher proportion of families with a single parent, a younger mother, a low income or an unemployed parent ***(Brown et al., 1997).***

Many children with non-accidental burns have a higher incidence of previous notifications for suspected abuse or neglect to child protection agencies ***(Andronicus et al., 1998).***

The developmental progress of a child between the ages of 0 to 15, at both a neurocognitive and physical level, influences the type of burn injury most frequently sustained, as well as the child's ability to remove him/herself from a dangerous situation ***(Robert et al., 2007)***.

Parents can inadvertently contribute to the mismatch between their child's developmental skills and the demands