Comparison between Dexmedetomidine and Propofol for sedation in mechanically ventilated intensive care patients

Thesis

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Mohamed Atef Ahmed Ebrahim

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List of Abbreviations

Abb.	Meaning
AAI	Alaris Auditory response index
AEP	Auditory Evoked potential
APGAR score	(Appearance, pulse, grimace, activity and respiratory effort) score
AR	Adrenergic receptor
ASA	Accelerated Safety Assessment
ATICE	Adaptation to intensive care environment
AVP	Arginine vasopressin
BE	Base excess
BIS	Bispectral index
BPS	Behavior pain scale
CABG	Coronary artery bypass graft
cAMP	Cyclic Adenosine Monophosphate
CNS	Central Nervous System
CPOT	Critical-Care Pain Observation Tool
CSI	Cerebral State Index
CT	Computed Tomography
CK	Creatine Kinase
DBP	Diastolic blood pressure

List of Abbreviations

Abb.	Meaning
ECG	Electrocardiogram
EDTA	Ethylenediaminetetraacetic acid
EEG	Electroencephalogram
EMG	Electromyogram
FDA	Food & Drug Administration
FiO_2	Fraction of inspired oxygen
FLACC	Face, leg, activity, cry and consolability
GABA	gamma-aminobutyric acid
ICU	Intensive Care Unit
IM	Intramuscular
IV	Intravenous
IVRA	Intravenous regional anaesthia
LOS	Length of stay
MAP	Mean arterial pressure
Mcg	Microgram
MOASS	Modified Observer's Assessment of Alertness/Sedation Scale
MOC Etomidate	Methoxy-Carbonyl-Etomidate
MRI	Magnetic Resonance Imaging

List of Abbreviations

Abb.	Meaning
MSAT	Minnesota sedation assessment tool
NPS	Numeric pain scale
PAD	Pain, agitation and delirium
PaO_2	Partial pressure of oxygen in arterial blood
PaO_2 / FiO_2	An index of arterial oxygenation efficiency that corresponds to ratio of partial pressure of arterial O2 to the fraction of inspired O2
$PaCO_2$	Partial Pressure of Carbon Dioxide in Arterial Blood
PH	Potential of Hydrogen
pK	Pharmacokinetics
PRIS	Propofol infusion syndrome
PSI	Patient State Index
PTSD	Posttraumatic stress disorder
RASS	Richmond Agitation-Sedation Scale
SPO_2	Oxygen saturation
RSS	Ramsay Sedation Scale
SAS	Sedation Agitation Scale
SBP	Systolic blood pressure
SCCM	Society of Critical Care Medicine

List of Abbreviations

Abb.	Meaning
SUPPORT	Study to Understand Prognoses & Preferences for Outcomes & Risks of Treatments
t ½ α	distribution half-life
t ½ β	elimination half-life
TCI	Target Controlled Infusion
TMN	Tuberomamillary nucleus
TRPA 1	Transient Receptor Potential Ankyrin 1
VICS	Vancouver interactive and calmness scale
VLPO	Ventrolateral Preoptic Area

Abstract

Background:

Critically ill patients are submitted to several interventions that can lead to distress and pain, like endotracheal intubation, mechanical ventilation, and central venous and arterial catheterization. Indeed, pain is one of the most common memories from patients admitted to intensive care unit (ICU) and can lead to agitation and its consequences, as accidental extubation, and removal of intravascular devices. Accordingly, one of the most used drugs for patients in the ICU are sedatives and analgesics

Objectives:

The aim of the study is to compare dexmedetomidine and propofol for sedation in mechanically ventilated intensive care patients according to vital data and laboratory findings during sedation to figure out efficacy and safety profiles between both drugs in sedation, weaning and facilitating extubation in intensive care unit

Patients and Methods:

This study was performed on 40 patients divided into 2 groups equally one group received propofol and the other group received dexmedetomidine as a sedative during mechanical ventilation. We collected vital and heamodynamics data and laboratory findings during the time of sedation in ICU.

Results:

All the 40 patients completed the study. The demographic profiles of both the groups were comparable. These groups were also comparable with respect to baseline vital parameters and baseline investigations. The study groups included both surgical and medical patients.

There were no statistically significant differences between the two patient groups with respect to age, weight, gender and APACHE II score.

Conclusion:

This study evaluated dexmedetomidine versus propofol for sedation in mechanicaly ventilated patients in ICU. We conclude that adequate level of sedation can be achieved by both dexmedetomidine and propofol

Keywords: Vancouver interactive and calmness scale, Transient Receptor Potential Ankyrin 1, Ventrolateral Preoptic Area

INTRODUCTION

Critically ill patients are submitted to several interventions that can lead to distress and pain, like endotracheal intubation, mechanical ventilation, and central venous and arterial catheterization. Indeed, pain is one of the most common memories from patients admitted to intensive care unit (ICU) and can lead to agitation and its consequences, as accidental extubation, and removal of intravascular devices. Accordingly, one of the most used drugs for patients in the ICU are sedatives and analgesics **(*Reade and Finfer, 2014*).**

For a long time, sedation of mechanically ventilated patients was based and guided by practices of anesthesiologists during surgical procedures. Indeed, until recently, the evidence regarding sedation in critically ill patients was scarce, and many physicians believed that the deepest sedation was the best option for patients admitted to the ICU under mechanical ventilation **(*Shehabi et al., 2013*).**

As one of the main reasons was the fact that mechanical ventilation was delivered by machines incapable of synchronizing with the respiratory pattern and efforts of the patient. Consequently, deep sedation was necessary to adapt the patient to the mechanical ventilator **(*Shehabi et al., 2013*).**

Maintenance of lighter levels of sedation is associated with improved clinical outcomes in critically ill patients, such as shorter duration of mechanical ventilation and ICU length of stay ***(Barr et al., 2013).***

Maintaining ideal analgesia while at the same time promoting early extubation and ICU discharge can be difficult to achieve. Different algorithms and recommendations have been proposed for short- and long-term extubation goals in the ICU. The decision to use a specific agent is also based on the patient's hemodynamic/respiratory status, the physiologic rationale, severity of the disease, the desired level of sedation, and the potential for adverse effect ***(Larson et al., 2013).***

The World Health Organization's analgesic ladder classifies pain in three categories: mild, moderate, and severe. Nonopioids should be considered with mild to moderate pain or as an adjuvant agent for moderate to severe pain to reduce the need for opioids. Intermittent IV opioids and benzodiazepines could be used for minor bedside procedures or in mechanically ventilated patients. However, continuous infusions of sedatives and analgesics such as dexmedetomidine, morphine, or midazolam may be more practical for long-term use. Propofol should be used only for procedural sedation and short-term sedation because of the risk for propofol infusion syndrome (PRIS) ***(Diedrich and Brown, 2011).***

Among Intensive Care unit (ICU) patients who require continuous sedation therapy, the pain, Agitation and Delirium (PAD) guidelines recommend that either dexmedetomidine or propofol should be considered as a replacement for benzodiazepine therapy ***(Hoy et al., 2011).***

Dexmedetomidine is a potent alpha-2-adrenergic agonist, more selective than clonidine, with widespread actions on the mammalian brain that include sedation, anesthetic-sparing, analgesia and sympatholytic properties. A large body of recent work supports its favorable profile in improving outcome and long-term brain function in the critically ill. The source of these benefits may lie in the neuroprotective properties that are seen in experimental models and in the clinical setting, in which it can attenuate delirium, preserve sleep architecture, preserve ventilatory drive and decrease sympathetic tone and inflammatory response. Dexmedetomidine may also be a valuable adjuvant when regional anesthesia is used. Future research should aim at establishing the risk/benefit ratio when used at the bedside ***(Mantz et al., 2011).***

Propofol (Diprivan) is a phenolic derivative with sedative and hypnotic properties but is unrelated to other sedative/hypnotic agents. Formulated as an oil-in-water emulsion for intravenous use, it is highly lipophilic and rapidly crosses the blood-brain barrier resulting in a rapid onset of action. Emergence from sedation is also rapid because of a fast redistribution into peripheral tissues and metabolic clearance ***(McKeage et al., 2003)***.

AIM OF STUDY

The aim of the study is to compare dexmedetomidine and propofol for sedation in mechanically ventilated intensive care patients according to vital data and laboratory findings during sedation to figure out efficacy and safety profiles between both drugs in sedation, weaning and facilitating extubation in intensive care unit.

Chapter (1)

SEDATION IN ICU

Critically ill patients are routinely provided analgesia and sedation to prevent pain and anxiety, permit invasive procedures, reduce stress and oxygen consumption, and improve synchrony with mechanical ventilation. Regional preferences, patient history, institutional bias, and individual patient and practitioner variability, however, create a wide discrepancy in the approach to sedation of critically ill patients. Untreated pain and agitation increase the sympathetic stress response, potentially leading to negative acute and long-term consequences ***(Christopher et al., 2012).***

Ensuring patient comfort and safety is a universal goal that has been endorsed by national medical societies and oversight bodies. In critically ill patients, pain and anxiety contribute to an already prominent sympathetic stress response that includes increased endogenous catecholamine activity, increased oxygen consumption, tachycardia, hypercoagulability, hypermetabolism and immunosuppression ***(Jacobi et al., 2002).***

Furthermore, unrelieved pain and anxiety can lead to severe agitation and the removal of lifesaving medical devices (e.g., endotracheal tubes and intravascular lines), placing both the patient and health care providers at risk. This may also contribute to significant physical and psychological stress