Sedation in the Intensive Care Unit

Essay

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in Anesthesiology

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Abstract

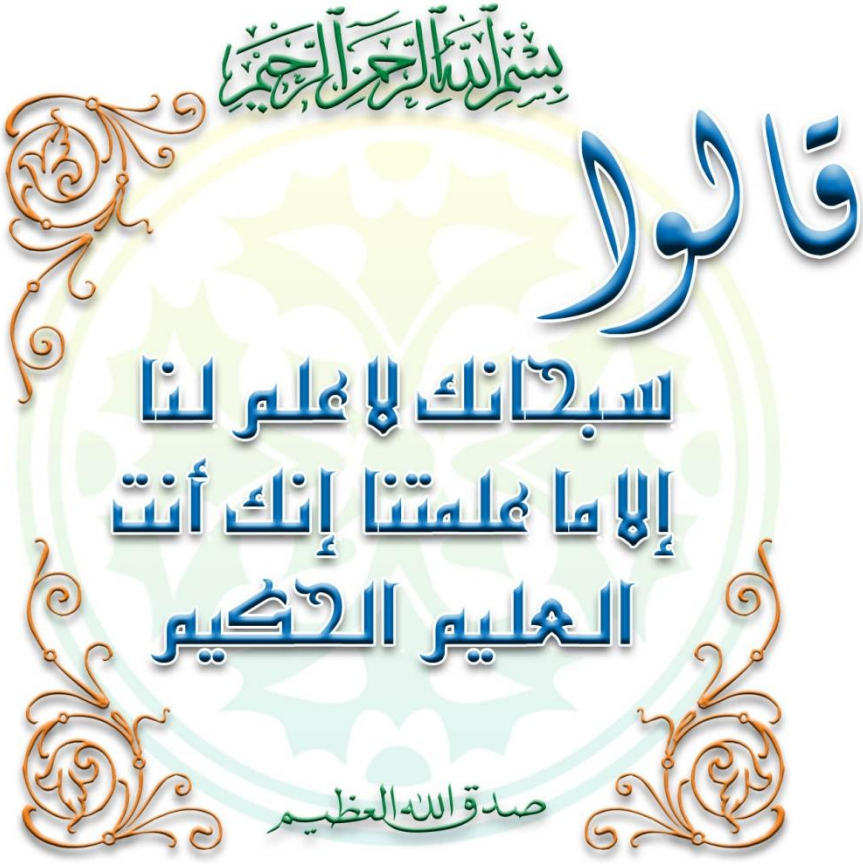
Background: Sedation is an integral component of ICU managements of critically-ill patients. Sedatives are prescribed to 42-72% of patients admitted to ICU. Sedation is required in intensive care units to control anxiety and agitation. Agitation and pain result in an increase in stress hormones, heart rate, blood pressure, oxygen consumption, and blood glucose. Agitation can also endanger the patient and make therapeutic maneuvers more difficult.

Aims: The purpose of this essay is to provide an overview of the pharmacology of commonly prescribed sedatives, and their complications.

Methodology: Critical illness can be a frightening experience for a variety of reasons, and adequate sedation may reduce this. It plays a pivotal role in the care of the critically ill patient, and encompasses a wide spectrum of symptom control that will vary between patients, and among individuals throughout the course of their illnesses.

Conclusion: Sedation protocols should be standard in every critical care, and followed by nursing and medical staff. Such protocols should be regularly updated. Titration of individual patients' sedation throughout their ICU admission should reduce over-sedation and side-effects, and contribute to reduced duration of mechanical ventilation and length of stay.

Keywords: Sedation, Intensive Care Unit, pharmacology, prescribed sedatives



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List of Abbreviations

Abbreviation	Meaning
AEPs	: Auditory evoked potentials
BIS	: Bispectral Index
CABG	: Coronary artery bypass graft
CPOT	: Critical-Care Pain Observation Tool
CPP	: Cerebral perfusion pressure
EEG	: Electroencephalogram
ETT	: Endotracheal Tube
FEMG	: Fast frontalis EMG
GABA	: α-amino butyric acid
ICP	: Intracranial pressure
ICU	: Intensive Care Unit
MAAS	: Motor Activity Assessment Scale
NI	: Narcotrend Index
NSAIDS	: Non-Steroidal Analgesics
PRIS	: Propofol infusion syndrome
PSI	: Patient State Index
PTSD	: Post-traumatic stress disorder

RASS : Richmond Agitation-Sedation Scale

RE : Response Entropy

RSS : Ramsay Sedation Scale

SAS : Sedation Agitation Score

SE : State entropy

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Introduction

Sedation is an integral component of ICU managements of critically-ill patients ***(Devabhakthuni et al., 2012).*** Sedatives are prescribed to 42-72% of patients admitted to ICU ***(Salgado et al., 2011).*** Sedation is required in intensive care units to control anxiety and agitation ***(Barr et al., 2013).*** Agitation can occur in over 70% of ICU patients and can have many causes, e.g., anxiety, lack of sleep, excess stimulation (alarms and the constant noise within an ICU), dyspnea and pain ***(Burk et al., 2014).*** Agitation and pain result in an increase in stress hormones, heart rate, blood pressure ***(Grap et al., 2014)*** *and* ***(Stites, 2013),*** oxygen consumption, and blood glucose ***(Jung and Cho, 2015).*** Agitation can also endanger the patient and make therapeutic maneuvers more difficult ***(Granja et al., 2008).***

The indications of sedation in the intensive care unit (ICU) include; prevention of anxiety and/or fear, maintenance of normal sleep, decrease metabolism, protection against organ ischemia, control of recall, facilitation of mechanical ventilation, and control of agitation ***(Brush and Kress, 2009).***

While under-sedation has many deleterious effects, over-sedation is serious. This is highlighted by research that has shown that sedative medications can themselves contribute to increased morbidity and mortality in the critically ill patients ***(Xing et al., 2015)*** *and* ***(Girard et al., 2008).***

The ideal sedative drug in the ICU will be; inexpensive, have minimal hemodynamic effects, minimal respiratory depression, no drug interactions, produce no active metabolites, cause no organ toxicity, have a short context sensitive half-life and have elimination independent of organ function ***(Barr et al., 2013)*** *and* ***(Mesnil et al., 2011).*** Unfortunately no sedatives to date possess all the properties described above.

Opioids have been an integral part of caring for critically ill patients since the early days of intensive care. Morphine is widely used in ICUs, and its sedative effects, especially at higher doses, may seem attractive in combining pain relief and sedation (analgo-sedation) ***(Strøm et al., 2010).*** Fentanyl is a shorter-acting opiate with no active metabolites; however, like morphine, it has a long context-sensitive half-life and accumulates in renal failure ***(Pypendop et al., 2014).*** Although fentanyl has less-sedating effects than morphine, it potentiates the effects of sedative drugs and in

high doses can produce somnolence and sedation ***(Choi et al., 2016).***

Benzodiazepines remain the most commonly used ICU sedative agents around the world. Their unpredictable accumulation, however, with prolonged sedation as a consequence, has been recognized for a long time ***(Fraser et al., 2013).*** It was, therefore, natural that the short-acting anesthetic propofol would be introduced for ICU sedation with great enthusiasm and expectations. Though allowing rapid awakening after short-term use, propofol also appeared to unpredictably accumulate after long-term use and to cause prolonged sedation ***(Srivastava et al., 2014).*** Unfortunately, a serious adverse effect, the propofol infusion syndrome (PRIS), was recognized ***(Roberts et al., 2009).***

Dexmedetomidine, a sedative with high α2-adrenoreceptor affinity and agonist action in the locus ceruleus, was recently introduced for ICU sedation. It has been shown to be non-inferior to both midazolam and propofol in maintaining light to moderate sedation ***(Srivastava et al., 2014).*** It appears to shorten time to extubation and enhance arousability and patients' ability to communicate with caregivers ***(Ahmed and Murugan, 2013).*** Dexmedetomidine may reduce delirium after long-term sedation as compared with midazolam and also reduce the overall neurocognitive adverse events of sedation, such as

agitation, anxiety, and delirium, when compared with propofol ***(Jakob et al., 2012).***

Inhaled anesthetic agents such as sevoflurane and isoflurane have been advocated for ICU sedation ***(Jerath et al., 2015).*** To avoid repeating the etomidate story, safety assessment according to current drug development standards is mandatory before introducing new drugs for ICU sedation ***(Bracco and Donatelli, 2011).***

Sedation, when administered to the ICU patient, should be considered a goal-directed therapy. What this goal is will vary from patient to patient and will be affected by physician preference. It has been shown that regular assessment of sedation level facilitates the dosing of sedatives to help achieve the targeted therapeutic goal ***(Shehabi et al., 2013).***

Sedation assessment can be performed using subjective sedation scales or objective monitors that are based on processed EEG monitoring. A variety of scales ***(Lacoske, 2015)*** *and* ***(Patel et al., 2009)*** have been developed to monitor sedation and agitation but the commonest in widespread use are the Ramsay Scale, Riker Sedation Agitation Score (SAS) and the Richmond Agitation-Sedation Scale (RASS). Practice guidelines suggest that objective measures of brain function (e.g.,

auditory evoked potentials [AEPs], Bispectral Index [BIS], Narcotrend Index [NI], Patient State Index [PSI], or state entropy [SE]) be used as an adjunct to subjective sedation assessments in adult ICU patients who are receiving neuromuscular blocking agents, as subjective sedation assessments may be unobtainable in these patients ***(Barr et al., 2013)*.**

Sedation in ICU should follow evidence-based practical guidelines to achieve the best results. Sedation protocols are now routinely used in ICUs and provide health care providers with a structural framework to initially choose the appropriate sedative and analgesic and then in conjunction with sedation scales, to modify treatment plans based on clinical changes ***(Shehabi et al., 2013)*.** Studies have shown that nurse-implemented sedation protocol has better results compared to physician-directed sedation ***(Quenot et al., 2007)*.** In addition, daily interruption of sedation paired with early mobilization was found to decrease delirium rates and improve functional outcomes ***(Mehta et al., 2012)*.**

Aim of the Work

The purpose of this essay is to provide an overview of the pharmacology of commonly prescribed sedatives, and their complications.