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Intensive Care Unit
Optimum Sedation Guidelines

An Essay
Submitted For Partial Fulfillment of Master Degree in Intensive Care

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2012

Acknowledgement

*Before all, I would like to express my deep thanks to **ALLAH**, without his magnificent help; I would never accomplish this work.*

*I would like to express my sincere and deep appreciations and particular thanks to **Prof. Dr. Mervat Mohamed Marzouk,** Professor of Anaesthiology and Intensive Care , Faculty of Medicine, Ain Shams University, for her great help, constant encouragement, constructive guidance and maternal support which were the major factors behind the completion of this work.*

*I am indebted to **Assistant Prof. Dr. Reem Hamdy El-Kabarity,** Assistant Professor of Anaesthiology and Intensive Care, Faculty of Medicine, Ain Shams University, for her great help, remarkable effort, valuable advice and worthy remarks that have been of utmost help.*

*Many deepest thanks and appreciations to **Dr. Sanaa Farag Mahmoud,** Lecturer of Anaesthiology and Intensive Care, Faculty of Medicine, Ain Shams University, for her valuable instructions and rich guidance throughout this work.*

I would like to thank also my father and my beloved wife for all the help and support that they gave me in every step of my way.

Indications, contraindications and complications of sedation in the intensive care unit:

The formal definition of sedation is "the act of calming", especially by the administration of sedatives. In fact, sedation is a broad term often used to express sedative as well as analgesic treatment in the ICU ***(Egerod et al., 2006).***

Sedative and analgesic medications are administered to many patients who are critically ill in the ICU throughout the world. Patients in the ICU often require life saving procedures, to facilitate the use of life-support technology, and to relieve anxiety and pain, sedative drugs are commonly administered ***(Mehta et al., 2006).***

In spite of that, few guidelines are available to aid the clinician in this practice. Providing adequate sedation is an important, but often poorly managed component of critical care treatment and support. This aspect of critical care management is often lost in the myriad of hemodynamic, respiratory and metabolic derangements that are frequently encountered and often overwhelm the practitioner ***(Peruzzi and Hurt, 2005).***

In order to approach this issue properly, it is necessary to consider the key components of sedation regimen. The first step in all sedation protocols should be provision of adequate analgesia ***(Jacobi et al., 2002).***

The lack of appropriate analgesia may lead to hyperesthesia and paradoxical agitation inspite of other sedative drug administration. Attention to this aspect of sedation regimen will often eliminate the

need for more complex drugs combinations. Once adequate analgesia has been established, the reminder of the sedation regimen should be targeted at providing hypnosis, anxiolysis and an appropriate degree of amnesia ***(Peruzzi and Hurt, 2005).***

Heavy sedation in critical care to facilitate endotracheal tube tolerance and ventilator synchronization, often with neuromuscular blocking agents, was routine until relatively recently. The modern ICU ventilator is equipped with a wide range of ventilatory modes and, with the addition of electronic flow triggering, synchronization problems have largely disappeared. The replacement of an endotracheal tube by a tracheostomy reduces the discomfort associated with an artificial airway and may often remove the need for sedation entirely. Thus, modern day sedation involves more than tube tolerance and is now focused on the multifactorial individual needs of the patient ***(Tanios et al., 2009).***

The main principle of sedative administration is to define the specific problem requiring sedation and to rationally choose the drug and depth of sedation appropriate for the indication. Next, the clinician must recognize unpredictable effects of critical illness on drug pharmacokinetics. Failure to recognize these effects may lead initially to inadequate sedation and subsequently to drug accumulation. Drug accumulation may result in prolonged encephalopathy and mechanical ventilation and may mask the development of neurological or intra-abdominal complications ***(Gehlbach and Kress, 2002).***

Indications for sedation in the ICU:

1-Analgesia:

Analgesia is the act of blunting pain chiefly through administration of drugs which exert an effect on the peripheral or central nervous system (CNS), but also through positioning of the patient, stabilizing fractures and minimizing harmful physical stimulation ***(Jacobi et al., 2002).*** Pain is a common experience in critically ill patients. (about 45-82% of critically ill patients suffer from pain depending on their degree of activity) ***(Walder et al., 2002).*** It often originates from sources such as surgical incisions, vascular catheter placement and endotracheal suctioning.

In addition of suffering adverse effects of pain in critically ill patients may include increased endogenous catecholamine activity, myocardial ischemia, induction of hypermetabolic states and anxiety. Also, pain may cause altered gastrointestinal motility, impaired urinary tract function, changes in blood viscosity, clotting time and platelets aggregation, diminished immune function and impaired wound healing. So, achieving adequate analgesia is the first priority when administering sedation in the ICU ***(Jacobi et al., 2002).***

Pain is the root cause of distress experienced by many ICU patients, but anxiety, dyspnea, delirium, sleep deprivation and other factors such as mechanical ventilation, indwelling tubes and catheters, iatrogenic illness, medication side effects, nursing interventions contribute and are often additive or synergistic. Thus, improving the patient's tolerance of these common issues that contribute to a state of relative discomfort or outright distress is important ***(De Wit et al., 2009).***

2-Anxiety :

About 71% of critically ill patients have been shown to suffer from anxiety, confusion and agitation ***(Fraser et al., 2000).*** Anxiety and agitation may arise from innumerable psychological and physical sources and may be more commonly recognized than pain. Anxiety that is difficult to be explained may be a result of inadequately treated pain ***(Gehlbach and Kress, 2002).***

Anxiety and agitation is usually associated with potentially dangerous complications such as self-extubation, removal of arterial and venous catheter, increased systemic and myocardial oxygen consumption and failure to participate in therapeutic interventions. The agitation syndrome may be caused by many factors, including the underlying illness itself, discomfort associated with invasive catheter and tube and many stimuli common in the ICU environment. Agitation develops regardless of age, sex or underlying diseases. The syndrome complicates management in the ICU, often leading to further morbidity and complications ***(Cohen et al., 2002).***

The agitated patient will often exaggerate complains of pain, in actually other factors such as the need to urinate or have a bowel movement are the cause of complaints ***(Cohen et al., 2002).***Vital signs are generally abnormal in the agitated patient. Arterial blood pressure (ABP) may increase to dangerously high ranges, respiratory rate (RR) may be elevated and heart rate (HR) may increase, with potential for ischemia. An elevated basal metabolic rate (BMR) results in an increase in overall oxygen requirements and if left to continue for a protracted period of time, an increase in caloric

demand. The agitated patient with a rapid respiratory rate may not be able to synchronize respiration with the mechanical ventilators, resulting in high airway pressures, inadequate ventilation and decrease in PaO2 with either increases or decreases in PaCO2, all of which further propagate the tendency toward agitation. These physiologic changes frequently vary over 24 hours depending on the chronicity or intermittency of the agitation. Agitated patients generally can not concentrate or pay attention to caregivers around them, making the ability to follow requests or demands exceeding difficult ***(Cohen et al., 2002).***

3- Delirium:

Delirium in the ICU is a common disorder, with an estimated rate of 20% ***(Mehta et al., 2006).*** A more specific definition of delirium is "an acute, reversible organic mental syndrome with disorder of attention and cognitive function, increased or decreased psychomotor activity and disordered sleep-awake cycle". The estimated prevalence of delirium in the ICU is escalating as a result of increases in the number of elderly and more severely ill patients admitted to the ICU. In this setting, delirium contributes to increased morbidity and is associated with a poorer prognosis and a mortality rate of 10% to 33% ***(Roberts, 2001).***

Predisposing factors for delirium include advanced age, underlying primary cerebral illness such as dementia and Alzheimer's disease and a history of alcohol or substance abuse. Underlying chronic systemic illness accentuated by metabolic and homodynamic instability, hypoxemia, acidosis and electrolytes imbalances, severe infections and intra-cerebral abnormalities such as brain tumours can

also precipitate delirium. ICU-related factors contributing to the development of delirium include sleep deprivation, sensory overload, lack of meaningful verbal or cognitive stimulation and immobilization. Withdrawal of drugs such as opioids, sedatives and several other pharmacologic agents can also contribute to the development of delirium ***(Roberts, 2001).***

Delirious patients are restless and agitated. Conversely, those with hypoactive variant exhibit decreased consciousness and psychomotor activity. A mixture of hyperactive and hypoactive delirium is also seen in some patients ***(Roberts, 2001).*** An interesting characteristic of delirium is that the behaviors of the patient can change dramatically within hours or even minutes. Drowsiness and lethargy can change to alertness and lucidity for a time and then can quickly change to agitation and aggression ***(Justic, 2000).***

ICU delirium represents a form of brain dysfunction as in many organ dysfunction is grossly under recognized because a majority of patients have hypoactive or "quiet" delirium characterized by "negative" symptoms. This inattention and flat effect not alarming the treating team. Hyperactive delirium, formerly called ICU psychosis, stands out because of symptoms such as agitation that may cause harm to self or staff, but is actually rare relative to hypoactive delirium and associated with a better prognosis ***(Meagher and Trzepacz, 2000).***

4-Respiratory Failure and Patient Ventilator Asynchrony:

The subjective sense of dyspnea is common in ICU patients and may be a source of sever anxiety and distress. Appropriate sedation is especially important in patients with respiratory failure. When sufficient doses are administered, sedatives can diminish patient struggle against mechanically supported breaths, improve chest wall compliances and allow manipulation of inspiratory to expiratory ratio and other ventilators variables to maximize oxygenation ***(Gehlbach and Kress, 2002).***

Patients undergoing MV (mechanical ventilation) are likely to breath out of synchronization with the ventilator when agitation (resulting from fear and anxiety) causes tachypnea. Because agitation leads to an increase in CO2 and lactic acid production, life-threatening respiratory and metabolic acidosis may occur. This desynchronization causes ineffective oxygen delivery and CO2 elimination. Some of the signs of respiratory distress are tachypnea, diaphoresis and cardiovascular abnormalities ***(Yagan et al., 2000).***

5-Weaning from Mechanical Ventilation:

Managing agitation and pain in mechanically ventilated patients who are ready for weaning requires a through understanding of the available pharmacologic agents, because their manifestations can profoundly influence the outcomes of weaning. It is now well known that patients being weaned from MV require appropriate sedation for a successful outcome with respect to extubation and release from the ICU ***(Cohen et al., 2002).***

Non pharmacologic intervention at the time of the weaning may relieve mild anxiety. Such interventions include changing the

environment, using relaxation techniques, reassuring the patients and providing adequate rest and psychological support. However, for patients who do not respond to this intervention, pharmacological therapy should be given on a regularly scheduled basis to promote stable blood levels ***(Carroll and Margruder, 2001).***

Sedative agents that can contribute to significant respiratory depression should be avoided when a patient is being weaned from MV ***(Dattani and Wong, 2000).***

6-To decrease excess oxygen consumption:

Sedatives are commonly used to decrease the volume of oxygen utilization associated with anxiety, dyspnea and delirium. Minimizing the volume of oxygen utilization is particularly important in patients with acute hypoxemic respiratory failure and shock ***(Gehlbach and Kress, 2002).***

7-Reduction of seizure:

Seizures are a frequent complication in the neurointensive care unit (NICU) ***(Bladin et al., 2000).*** Convulsive and non convulsive seizures occurred in 22% of traumatic brain injury and in 15% of patients with intracerebral hemorrhage (ICH) or subarachnoid hemorrhage (SAH) ***(Kraus et al., 2002).*** Sedation appears to be an attractive option in reducing seizures in the NICU ***(Citerio and Cormio, 2003).***

8-To achieve amnesia:

Although this seems intuitively desirable for critically ill patients, data supporting this point are lacking. Rather, there are reports of adverse psychological sequele in patients unable to recall factual memories from their illness**.**The only circumstance in which amnesia is mandatory is when neuromuscular blocking (NMB) agents are being administrated ***(Gehlbach and Kress, 2002).***

9-To facilitate care:

Sedative are often used to facilitate the delivery of nursing care (dressing wounds, administering baths and so on) ***(Gehlbach and Kress, 2002).*** The care of patients in the ICU is highly challenging. Not only because of differences between patients that can significantly affect the outcome of management, but also, age, personal characteristics, underlying disease and the nature of the insult leading to admission to the ICU. All profoundly affect the decision-making process for patient management including sedation which is a key part of treatment in the ICU. So, sedation must be individualized to the patient ***(Peruzzi and Hurt, 2005).***

10-Alcohol withdrawal:

Alcohol withdrawal symptoms can progress over a period of 24-72 hours to delirium, which is the most serious manifestation of the alcohol withdrawal spectrum. It is seen in approximately 5% of

hospitalized patients with history of alcohol abuse and has a mortality rate ranging from 1% to 15% ***(Cohen et al., 2002).***

Whenever possible, treatment of alcohol withdrawal should be initiated before the onset of agitated delirium. Patients with deteriorating conditions and those with concomitant medical problems always require admission to the ICU where control of seizure, maintenance of hemodynamic stability, arrhythmia management, airway protection and correction of nutritional and metabolic deficiencies are carried out with initiation of pharmacologic therapy for withdrawal ***(Mirski et al., 2000).***

Once heavy alcohol use has been identified, proper prophylaxis should be started, both by maintaining optimal electrolytes levels through potassium, magnesium, phosphorus replacement and by administration of thiamine, vitamin B12 and folate together with an appropriate sedative ***(Cohen et al., 2002).***

The most important pharmacologic treatment is the use of agents that are cross-tolerant with alcohol, therapy providing prophylaxis against seizure and relieving the frequently intense agitation and hallucination. The most widely administered pharmacologic agents for the treatment of alcohol withdrawal are benzodiazepines ***(Mirski et al., 2000).***

Treating alcohol withdrawal usually includes the substitution of an agent with effects on the gamma amino butyric acid (GABA) receptors. Benzodiazepines have been successfully used to reduce the signs and symptoms of withdrawal. Propofol may be an alternative to benzodiazepines for controlling alcohol withdrawal symptoms, but

there is limited data available supporting its use in non intubated patients ***(Jacobi and Farrington, 2002).*** Also, with the exception of a few case reports, there have been limited studies of propofol for the treatment of patients with delirium in the ICU ***(Coomes and Smith, 2000).***

11- Other withdrawal and intoxication syndromes:

Another complicating factor in the management of ICU patient is the presence of symptoms related to either the withdrawal of drugs or drug intoxication resulting from adverse effects or drug-drug interactions. These symptoms may arise with drugs used therapeutically in the ICU or with licit or illicit drugs that the patient used before hospital admission ***(Cohen et al., 2002).***

Withdrawal symptoms are a frequent problem in the ICU and it confuses the clinician management of such patients and may be extremely difficult to diagnose. So, it is often lethal if not discovered immediately. The principle of most withdrawal therapy is supportive care and treatment with appropriate sedative (i.e., benzodiazepine or propofol). In consideration of the high rate of multiple intoxications present in trauma patients, withdrawal can occur from multiple agents in a single patient, further compounding the difficulties inherent in managing this patient population ***(Justic, 2000).***

For example, withdrawal as a result of the use of benzodiazepines in the ICU includes an abstinence syndrome, which is marked by anxiety, fear, confusion and agitation. In addition, the possibility of tachycardia and panic attacks may occur as the patient emerges from sedation. Severe withdrawal symptoms including refractory seizures

may be seen when benzodiazepines are discontinued in critically ill patients who had been received treatment with these agents before their hospital admission. Treatment with benzodiazepine such as oral lorazepam is appropriate for withdrawal symptoms with slow tapering of the dose. Intravenous (IV) agents such as lorazepam or midazolam can be used in itubated patients. Also, alpha blocker (αB) and beta blocker (BB) can be administrated to modify symptoms and improve tolerance to benzodiazepines withdrawal ***(Durbin, 2001).***

Another example is narcotic withdrawal which is common in patients receiving long-term therapy with opioids for palliative care of cancer or chronic pain syndromes, as well as in patients with a history of narcotic abuse. Replacement of narcotic occurs with continuous infusions of fentanyl or morphine sulphate or administration of methadone which is commonly used in the ICU. Also, cocaine which is sympathetic stimulating drug, increase the release of presynaptic norepinephrine and blocks its reuptake ***(Cohen et al., 2002).*** This hypercatecholomic state causes various cardiopulmonary and neuropsychiatric effects including tachycardia, hypertension, respiratory depression, anxiety, tremors, seizures and hyperthermia. When initiating sedation in patients who are in hypercatecholamine state, it is important to determine both the patient history of cocaine use and evidence of withdrawal symptoms. Benzodiazepines are commonly used for sedation of patients with suspected or known cocaine abuse ***(Cohen et al., 2002).***

12- Acute severe asthma:

Patients presenting with status asthmatics or severe asthma that not responsive to standard therapy, usually require MV and sedation until respiratory functions improve. Benzodiazepine were the most

commonly used sedatives in these patients, but propofol may be the most appropriate for asthmatic patients as it has recently been shown that it has bronchodilator properties at high doses which is not demonstrated with other sedatives or analgesic ***(Mazzeo, 2000).*** These bronchodilator properties are explained by the fact that propofol reduces the pulmonary vascular resistance (PVR) in patients with chronic obstructive pulmonary disease (COPD) who were undergoing MV ***(Conti et al., 2001).***

Propofol containing di sodium edetate (EDTA) is commonly used in patients at risk of status asthmaticus for its bronchodilator properties and its lack of a trigger in extrinsic asthma. Other agents with bronchodilator properties such as ketamine and halothane have undesirable side effects ***(Zaloga et al., 2001).***

13-Terminal weaning:

In recent years, there has been a greater awareness of the importance of providing maximum comfort to terminally ill patients who are being weaned from MV. After ICU interventions are discontinued, patient comfort becomes the most important objective. This must be assessed frequently and signs of discomfort should be treated with adequate doses of sedatives and opioids. If terminal weaning is chosen, a limited time course should be agreed on to prevent prolongation of the dying process ***(Ramelet and Eusebio, 2009).***

Hall et al., (2000) compared the use of sedation and pain relief to prevent and treat discomfort during the dying process in the end of life care of the ICU patients who were or were not withdrawn from