Ain Shams University
Faculty of Medicine
Department of Anesthesia
Intensive Care & Algology

Managing the Agitated Patient in Intensive Care Unit

Essay Submitted for Partial Fulfillment of Master Degree in Intensive Care Medicine

By

Marwa Mohammed Abdo
M.B., B.Ch.

Under Supervision of

Prof. Dr. Ayman Mokhtar Kamaly
Professor of Anesthesiology & Intensive Care
Faculty of Medicine - Ain Shams University

Dr. Mostafa Gamal Eldin Maharan
Lecturer of Anesthesiology & Intensive Care
Faculty of Medicine - Ain Shams University

Dr. Assem Adel Moharram
Lecturer of Anesthesiology & Intensive Care
Faculty of Medicine - Ain Shams University

Faculty of Medicine
Ain Shams University
٢٠١٣

List of Abbreviations

ABC	**:**	Awakening and Breathing Controlled trial
ABD	**:**	Acute Behaviourial Disturbance
ACTH	**:**	Adreno-CorticosTropic Hormone
AMSS	**:**	Altered Mental Status Score
ARDS	**:**	Acute Respiratory Distress Syndrome
ASE	**:**	Attention Screening Examination
ATICE	**:**	Adaptation to Intensive Care Environment instrument
BARS	**:**	Behavioural Activity Rating Scale
BIS	**:**	Bispectral Index
BPS	**:**	Behavior Pain Scale
CAMICU	**:**	Confusion Assessment Method for the Intensive Care Unit
CNS	**:**	Central Nervous System
CPOT	**:**	Critical care Pain Observation Tool
CRF	**:**	Corticotropine-Releasing Factor
CT	**:**	Computed Tomography
DIS	**:**	Daily Interruption of Sedation
DSM	**:**	Diagnostic and Statistical Manual of Mental Disorders
ED	**:**	Emergency Department
EEG	**:**	Electroencephalogarm
EMG	**:**	Electro-myogram
GABA	**:**	Gamma-Amino Butyric Acid
ICDSC	**:**	Intensive Care Delirium Screening Checklist
ICP	**:**	Intracranial Pressure
ICU	**:**	Intensive Care Unit
IV	**:**	Intravenous
MAAS	**:**	Motor Activity Assessment Scale

MENDS	**:**	Maximinizing Efficacay of targeted sedation and reducing Neurological Dysfunction
MRI	**:**	Magnetic Resonance Imaging
MSAT	**:**	Minnesota Sedation Assessment Tool
NMBAs	**:**	Neuro Muscular Blocking Agents
NMDA	**:**	N-Methyl-D-Aspartate
NRS	**:**	Numerical Rating Scale
OASS	**:**	Overt Agitation Severity Scale
PRIS	**:**	Propofol Infusion syndrome
RASS	**:**	Richmond Agitation Sedation Scale
SAS	**:**	Sedation Agitation Scale
SBT	**:**	Spontaneous Breathing Trial
SCCM	**:**	Society of Critical Care Medicine
SEDCOM	**:**	Safety and Efficacy of Dexmedetomidine Compaired with Midazolam
SUPPORT	**:**	Study to Understand Prognoses and Preferences for Outcomes and Risks of Treatment
TOF	**:**	Train Of Four
VICS	**:**	Vancouver Interactive and Calmness Scale

List of Tables

List of Figures

Contents

Acknowledgement

*First of all praise and thanks to **ALLAH** providing me with time and effort to accomplish this essay.*

I wish to express my deep gratitude to Prof. Dr. Ayman Mokhtar Kamaly, *Professor of Anesthesiology and Intensive Care, Faculty of Medicine, Ain Shams University for his enthusiasm, meticulous guidance, precious remarks and follow up throughout this work. I had the honor to work under his supervision, and his scientific remarks are beyond acknowledgement.*

A special tribute and cordial thanks are paired to Dr. Mostafa Gamal Eldin Maharan, *Lecturer of Anesthesiology and Intensive Care, Faculty of Medicine, Ain Shams University for his authentic guidance, kind supervision and unlimited help in offering all facilities to accomplish this work..*

I am greatly indebted to Dr. Assem Adel Moharram, *Lecturer of Anesthesiology and Intensive Care, Faculty of Medicine, Ain Shams University, for his continuous encouragement and sincere contribution in this work with her time and effort.*

Introduction

Agitation has been identified as a psychomotor disorder and described as a continuum of varying patient behaviors and responses, including disorientation, restlessness, thrashing around in bed, pulling catheters and tubes and over-breathing the ventilator ***(Cohen et al., ٢٠٠٢)***.

Recent studies have reported agitation to be particularly common in intensive care unit (ICU) patients, with its incidence ranging between ٥٢٪ and ٧٠٪ ***(Jabber et al., ٢٠٠٥).***

This variation may be partly attributed to differences among studies regarding patient inclusion criteria (i.e. mechanically ventilated or not), to difficulties in the definition and differential diagnosis of agitation and to the use of different scales developed for monitoring agitation ***(Fraser & Riker, ٢٠٠١)***.

Agitated behavior has been associated with potentially dangerous complications, such as unplanned self-intubation, removal of arterial or venous catheters and increased systemic and myocardial oxygen consumption, as well as adverse patient outcomes, including prolonged mechanical ventilation and ICU stay and increased nosocomial infection rate ***(Fraser & Riker, ٢٠٠١)***.

Numerous scales and tools to monitor the degree of agitation in clinical practice are described

in the literature. Most commonly used are Ramsay Sedation Scale **,** Sedation Agitation Scale (SAS), motor activity assessment scale, Vancouver Interactive and Calmness Scale (VICS), Richmond Agitation-Sedation Scale (RASS) **,** Adaptation to Intensive Care Environment instrument (ATICE) and the Minnesota Sedation Assessment Tool (MSAT). Among all of these, Ramsay and RASS are the most commonly employed ***(Patel et al.,* ٢٠٠٩*)***.

Treatment of agitation includes non pharmacologic and pharmacologic therapy. Before administration of sedation and analgesia, potentially life-threatening problems that require specific solutions must be investigated. ***(shyoko et al.,* ٢٠١٠*).***

Both pharmacologic agents and physical restraints have been used for treating agitation. However, considering prevention is superior to treatment, identification and timely treatment of factors predisposing to agitation are important. These factors can generally be divided into patient characteristics (high clinical severity and neurological damage), metabolic disorders (acidosis), drugs administered or devices used (nasogastric tube and Foley catheter) and the ICU environment (circadian disruption) ***(shyoko et al.,* ٢٠١٠*).***

Aim of the Work

This study is designed to understand the etiology, physiology of agitation in ICU, review objective assessment tools that may used at the bedside, explore available therapeutic modalities, and provide a practical approach for management of sedation, analgesia for agitated patient in ICU.

Agitation physiology, causes and complication

Agitation is a psychomotor disturbance characterized by a marked increase in both motor and psychological activities, often accompanied by a loss of control of action and a disorganization of thought. This problem is driven by frequently occurring situations in the intensive care unit (ICU), such as anxiety and delirium. Therefore, it is fairly common in the ICU setting, particularly in older patients, and it may be caused by numerous factors, linked both to the disease itself (metabolic disorders, medications, sepsis-associated encephalopathy, and others) and to external factors [e.g., noise, discomfort, pain] **(Pandharipande *et al.*, ٢٠٠٥).**

Agitation per se may be dangerous in the ICU: its occurrence may compromise care, raise metabolic requirements and, finally, increase morbidity and mortality. Length of stay in the ICU as well as in the hospital may also be increased, in turn leading to an increase in costs. In addition, compared to that of similar but non-delirious patients, the post-hospital mortality rate may be higher in patients having presented with agitation and delirium. For all these reasons, these mental disorders should be a source of serious concern and, therefore, vigorously managed through a systematic approach. It is generally accepted that these symptoms represent a marker of acute cerebral insufficiency **(Chevrolet *et al.*, ٢٠٠٧).**

Significance of agitation and delirium in the ICU

Besides agitation, several mental disturbances may be observed in the ICU, in particular anxiety and delirium. It is not presently known if these mental states express different types of brain dysfunction, or if they represent some sort of spectrum in the severity of the cerebral insult **(Pandharipande *et al* .,٢٠٠٥).**

Anxiety is a diffuse sensation of fear, which is not related to a real and actual external danger. This sensation is expected to occur in the ICU due to the numerous stressful situations occurring in this setting (pain, noise, and loss of body control, among others) .If a certain degree of anxiety seems to be 'normal' in the ICU environment, some authors have described a 'pathological' anxiety when this sensation appears to be disproportionately high considering its cause, and when it is associated with other severe signs, such as severe dysautonomia, loss of self-control, and cannot be appropriately treated due to a complete lack of patient cooperation **(Chevrolet *et al.*,٢٠٠٧).**

Delirium is defined as an acute change in mental status, or a fluctuation of mood, associated with impaired attention, disorganized thinking, confusion and an altered level of consciousness. It is often referred to as a state of acute confusion **(Meagher *et al.*, ٢٠٠٠).**

Most cases of delirium have an acute onset, particularly in the ICU. Typically, this cognitive alteration varies throughout the day, and achieves peak intensity during the night. This symptom is usually

reversible within a period of days or weeks, whereas some patients can progress to permanent brain failure. Illusions and hallucinations may also occur. Florid delirium with intense agitation in a combative patient (active delirium) is easy to detect, but delirium can also be present in a calm and quiet patient (hypoactive delirium), the succession of both types being possible **(Meagher *et al.*, ٢٠٠٠).**

Despite the fact that delirium is frequent in the ICU (occurring in ١٥٪ to ٤٠٪ of patients), it seems that critical care physicians' performance in detecting it remains poor; around two-thirds of these patients are not identified. Fortunately, simple tools that can be used by non-psychiatrists at the bedside have been developed to detect delirium in the ICU **(Pandharipande *et al.*, ٢٠٠٥).**

Many difficult but interesting questions regarding agitation and delirium in the ICU remain unanswered. First, it is not known precisely if the prevention or the timely detection and treatment of this condition can favorably influence a patient's outcome. Second, the exact relationships between agitation and delirium, on the one hand, and mortality and cerebral dysfunction, on the other, are poorly understood **(Riker *et al.*, ٢٠٠٥).**

In particular, it would be of great interest to understand if the brain is just a passive victim, one of many organs to dysfunction in critical illness, expressing its injury through agitation and delirium, or if it is an active player, participating and contributing to the extra cerebral organ dysfunction. The indication and

type of treatment for agitation and delirium are clearly related to the answers to these questions **(Sharshar *et al.*, ٢٠٠٥).**

The exact mechanisms causing the mental problems described above in ICU patients have not been fully characterized, except when a metabolic cause is obvious, such as hypoglycemia, or hypoxemia. Nevertheless, these disturbances are believed to have an organic basis. The generalized electroencephalographic abnormalities observed during this condition represent an argument in favor of such a diffuse neurological dysfunction **(Milbrandt *et al.*, ٢٠٠٥).**

Several hypotheses are actively discussed today. First, the role of abnormalities at the level of the central neurotransmission process is debated; these abnormalities are characterized by an excess in dopaminergic activity consecutive with adepletion in cholinergic stores **(Chevrolet *et al.*, ٢٠٠٧).**

Importantly, many drugs prescribed in the ICU have an anti cholinergic activity and some of them have been clearly associated with delirium, such as anti arrhythmic medications, antibiotics (penicillin, rifampin), and so on. These drugs should be avoided in delirious patients when possible. Interestingly, an 'inflammatory reflex' has recently been observed, leading to a real cooperation between the central nervous system and the inflammatory pathways **(Czura *et al.*, ٢٠٠٥).**

More precisely, an anti-inflammatory action exerted by vagus nerve endings located at the vicinity

of macrophages in inflammatory foci, through nicotinic receptors at the surface of these cells, has been demonstrated. These observations could provide some explanation as to the origin of delirium caused by a neuronal dysfunction, as well as a substrate for the causal role of the brain in immune modulation **(Sharshar *et al.*, ٢٠٠٥).**

Other central neurotransmitters have been thought to play a role in delirium, such as dopamine, serotonin, or gamma-amino butyric acid (GABA). This probably represents the substrate for the delirium occasionally associated with benzodiazepines or propofol (so-called 'paradoxical reactions'). Note also that benzodiazepines and opioids have been clearly shown to be independent factors for the occurrence of delirium **(Pandharipande, ٢٠٠٦).**

Inflammatory mediators (that cross the blood brain barrier and alter blood flow and vascular permeability) and alterations in brain metabolism are other factors that may play a role in the development of delirium. Better understanding of the physiological consequences of and biological mechanisms that fuel agitated behaviors may lead to novel therapeutic approaches in the future and ultimately improve the delivery of care in the ICU **(Shyoko *et al.*, ٢٠١٠).**

The second group of hypotheses to explain the mental dysfunction observed in the ICU relates to the presence of potential organic cerebral lesions not detectable by currently available technology (computed tomography (CT) scan, magnetic resonance imaging, and so on **(Orlikowski *et al.*, ٢٠٠٣).**