

Delirium in the Intensive Care unit

Essay

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Summary

Delirium is defined as a transient, usually reversible, cause of cerebral dysfunction and manifests clinically with a wide range of neuropsychiatric abnormalities.

Although historically dismissed as an inconvenient and transient problem, recent studies have reported that delirium is associated with more complications, increased length of hospital stay, and higher mortality. Although delirium is a prevalent condition in the intensive care unit (ICU), the condition appears to be largely underdiagnosed.

Risk factors for delirium can be divided into predisposing factors (host factors) and precipitating factors. Although predisposing factors are present before ICU admission and are difficult to alter, precipitating factors occur during the course of critical illness, these factors represent areas of risk that are potentially modifiable by preventive or therapeutic intervention.

The first obligation of the caregiver, before giving sedation, is to insure that underlying illness isn't manifesting as agitation or delirium. Life-threatening illness, such as hypoglycemia, hypoxia, or sepsis, may masquerade first as agitation or an altered mental status.

Almost all patients who are mechanically ventilated receive continuous infusions of sedatives and analgesics; usually these are generally administered with the aim of reducing pain and stress and improving compliance with treatment. It was found that there is an association between sedative drugs and delirium. Daily wake-up tests and sedation scoring are recommended, as they allow dose titration on an individual patient basis.

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LIST OF ABBREVIATIONS

ABG:	Arterial blood gases
ACA:	Anterior cerebral artery
ACTH:	Adrenocorticotrophic hormone
APOE:	Apolipoprotein E
ATICE:	Adaptation to Intensive Care Environment
BIS:	Bispectral index
CAD:	Coronary artery disease
CAM-ICU:	Confusion Assessment Method for the Intensive Care Unit
CHF:	Congestive heart failure
CNS:	Central nervous system
COPD:	Chronic obstructive pulmonary disease
CSF:	Cerebrospinal fluid
CT:	Computed tomography
CVA:	Cerebrovascular accident
CXR:	Chest x-ray
CYP:	Cytochrome P
DIS:	Daily interruption of sedative infusions
ECG:	Electrocardiography

EEG:	Electroencephalogram
GABA:	<i>Gamma</i>-Aminobutyric acid
ICDSC:	Intensive Care Delirium Screening Checklist
ICU:	Intensive Care unite
MCA:	Middle cerebral artery
MRI:	Magnetic resonance imaging
MSAT:	Minnesota Sedation Assessment Tool
NMDA:	N-methyl-D-aspartate
NPS:	Numeric Pain Scale
NSAIDs:	Nonsteroidal anti-inflammatory drugs
PCA:	Posterior cerebral artery
PCP:	Phencyclohexyl piperidine
RASS:	Richmond Agitation Sedation Scale
REM:	Rapid eye movement
RSS:	Ramsay Sedation Scale
US:	Ultrasound
VICS:	Vancouver Interactive and Calmness Scale

INTRODUCTION

The term delirium stems from the Latin word "delirare." In common usage it meant to be "crazy" and was derived from two other Latin words, "de" and "lira" ("the ridge between furrows"). The literal translation is "to go out of the furrow" while plowing. In the first century AD, Celsus used the term delirium to distinguish a constellation of symptoms from that of hysteria, depression, and mania. It corresponded to "phrenitis" (English derivative--"frenzy"), which was known to Hippocrates (460-366 BC), who observed the appearance of cognitive and sleep disturbances and agitated behavior in patients with febrile illnesses. **(Clements et al, 2003)**

Delirium or acute confusional state is a transient global disorder of cognition. The condition is a medical emergency associated with increased morbidity and mortality rates. Early diagnosis and resolution of symptoms are correlated with the most favorable outcomes. Therefore, it must be treated as a medical emergency. **(Kannayiram and Patricia, 2011)**

Delirium is not a disease but a syndrome with multiple causes that result in a similar constellation of symptoms. Delirium is defined as a transient, usually reversible, cause of cerebral dysfunction and manifests clinically with a wide range of neuropsychiatric abnormalities. The clinical hallmarks are decreased attention span and a waxing and waning type of confusion. It's often unrecognized or misdiagnosed and commonly is mistaken for dementia, depression, mania, an acute schizophrenic reaction, or part of old age. **(Kannayiram and Patricia, 2011)**

Recent advances in critical care medicine have improved survival in patients admitted in intensive care units (ICUs) worldwide, and in doing so they

have revealed a major public health concern that previously had been under-appreciated. Critical care clinicians have historically been attuned to pulmonary, cardiac, and renal dysfunction as a source of morbidity and mortality in ICU patients but have underestimated the impact of brain dysfunction. **(Timothy et al, 2008)**

Although historically dismissed as an inconvenient and transient problem, recent studies have reported that delirium is associated with more complications, increased length of hospital stay, and higher mortality. Although delirium is a prevalent condition in the intensive care unit (ICU), the condition appears to be largely underdiagnosed. **(Van Eijk and Slooter, 2010)**

Risk factors for delirium can be divided into predisposing factors (host factors) and precipitating factors. Although predisposing factors are present before ICU admission and are difficult to alter, precipitating factors occur during the course of critical illness. They may involve factors of the acute illness or be iatrogenic; these factors represent areas of risk that are potentially modifiable by preventive or therapeutic intervention. **(Timothy et al, 2008)**

Agitation in the ICU patient jeopardizes the immediate safety of the patient and may signify a potentially unidentified pathologic process. Delirium is the most frequent cause of agitation and is associated with poorer outcomes across multiple facets of patient care **(Jason, 2008)**

Delirium is a common, underestimated, multi-factorial problem in ICU that requires a multidisciplinary approach for assessment, management, and treatment. Although more pharmacological trials are awaited, the mainstay of treatment remains minimizing and correction of risk factors along with regular screening of patients using simple checklist. **(Jennifer and Andrew, 2009)**

RISK FACTORS OF DELIRIUM

Delirium is a syndrome with a wide range of presentations. It was thought that a delirious patient is that one who is aggressive, agitated, pulling out lines, and possibly hallucinating. This is hyperactive delirium and occurs in only 5–22% of such patients. The majority of critically ill patients with delirium have either the hypoactive form or a mixed picture where they fluctuate between hyperactivity and hypoactivity. Patients with hypoactive delirium are most commonly missed. They often wake up from sedation peacefully, smile, nod, and say yes to all questions. Closer questioning will, however, reveal signs of inattention and decreased awareness of the environment. **(Jackson et al, 2007)**

Delirium is a psychiatric disorder and as such, it's subdivided according to etiology:

- i. delirium due to a general medical condition;
- ii. substance induced delirium—including medication side-effects;
- iii. delirium due to multiple etiologies;
- iv. delirium not otherwise specified.**(Jennifer and Andrew, 2009)**

Risk factors for delirium can be divided into three broad categories: Properties of the illness (acute physiologic), preexisting properties of the patient (chronic physiologic) and properties of the environment (iatrogenic) **(Ely et al, 2001)**

Classification of common risk factors for delirium:

Properties of Illness (Acute Physiologic)	Properties of Patient (Chronic Physiologic)	Properties of Environment/Treatment (Iatrogenic)
Hyper- or hyponatremia	Age >70 years	Administration of psychoactive medication
Hyper- or hypoglycemia	Transfer from a nursing home	Tube feeding
Hyper- or hypothyroidism	History of depression	Urinary catheter
Hyper- or hypothermia	History of dementia	Rectal catheter
BUN/creatinine ratio >18	History of stroke	Central venous catheter
Renal failure (creatinine >2.0 mg/dL)	History of seizure	Physical restraints
Liver disease (bilirubin >20 mg/dL)	Alcohol abuse within one month	
Cardiogenic shock	Drug overdose	
Septic shock	History of congestive heart failure	
Hypoxia	Human immunodeficiency virus infection Malnutrition	

Table (2-1) Risk Factors for Delirium (Timothy et al, 2008)

Although predisposing factors (Properties of Patient) are present before ICU admission and are difficult to alter, precipitating factors (Properties of Illness &

iatrogenic factors) occur during the course of critical illness. They may involve factors of the acute illness or be iatrogenic; these factors represent areas of risk that are potentially modifiable by preventive or therapeutic intervention. **(Timothy et al, 2008)**

Only a few studies have examined risk factors for delirium in the ICU, but numerous delirium risk factors have been identified in non-ICU patients. Table (2-1) highlights factors that have been identified in both ICU and non-ICU studies. In a large study that examined risk factors for ICU delirium, 820 general ICU patients were studied, and determined that hypertension, alcoholism, severity of illness, and exposure to sedatives and analgesics (when used to induce coma) increased the likelihood of delirium. **(Ouimet et al, 2007)**

There is a genetic predisposition to ICU delirium in some patients, the association between apolipoprotein E (APOE) genotype and duration of delirium among 53 mechanically ventilated medical ICU patients was evaluated. Patients with the APOE4 polymorphism (a risk factor for Alzheimer's disease) were delirious for twice as long as those without the APOE4 polymorphism. **(Ely et al, 2007)**

Other factors associated with delirium in the ICU include older age, baseline cognitive impairment, metabolic disturbances (for instance, derangements in sodium, calcium, and blood urea nitrogen), acute infection, respiratory disease, acidosis, anemia, and hypotension. **(McNicol et al, 2003)**

Critically ill patients are typically exposed to numerous factors that may precipitate delirium. Two delirium risk factors nearly universally experienced by ICU patients are exposure to sedative and analgesic medications and sleep

deprivation. The risk associated with both of these factors is potentially modifiable, as is discussed in greater detail below. **(Ely et al, 2004)**

Patients treated with benzodiazepines were found to be more likely to have postoperative delirium than were those not treated with benzodiazepines. Meperidine also increased the likelihood of postoperative delirium. **(Marcantonio et al, 2004)**

Treatment with fentanyl, morphine, and propofol were not significantly associated with transition to delirium. Midazolam was shown to increase the likelihood of transition to delirium in a study of trauma and surgical ICU patients. **(Pandharipande et al, 2007)**

Sedative agents that are GABA receptor sparing, such as opioids and Dexmedetomidine (a novel α_2 -receptor agonist), may reduce the risk for delirium in ICU patients as compared with the risk attributable to benzodiazepines. Although studies have consistently identified Lorazepam and midazolam as risk factors for delirium, the data regarding opioids are less consistent. For example, mean daily opioid doses noted to be higher among ICU patients without delirium than among ICU patients with delirium. Treatment with Meperidine was an exception, because this drug increased the risk for delirium as compared with other opioids. These investigations point to the importance of judicious use of these psychoactive medications, with focus on adequate analgesia. **(Morrison et al, 2003)**