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Intensive care unit delirium

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Abstract
The Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, and the International classification of Diseases, 10th Revision, both provide detailed descriptions of delirium. These categorization systems are well recognized in the field of psychiatry. Delirium is characterized by an impairment of awareness and attention, alterations in cognitive function or perceptual abnormalities like hallucinations, a sudden onset, and the presence of an underlying medical reason. Delirium, sometimes known as 'acute confusional condition', 'metabolic or toxic encephalopathy', or 'acute brain failure'. An abrupt alteration in consciousness and attention occurs rapidly and is accompanied by other cognitive impairments, like memory loss, confusion, or perceptual problems.

Keywords: Unit delirium, psychiatry, confusional condition

Introduction
Delirium is an extremely serious form of brain dysfunction that is often seen in the intensive care unit (ICU). It is linked to greater rates of illness and death, prolonged hospitalizations, increased expenses, and long-lasting cognitive decline even after leaving the hospital [1].
Predisposing variables including smoking, hypertension, heart illness, sepsis, and pre-existing dementia. Precipitating variables involve respiratory distress and shock, metabolic problems, extended mechanical ventilation, discomfort, immobility, and the use of sedatives, as well as unfavorable surrounding conditions that hinder hearing, vision, and sleep [1].
Traditionally, antipsychotic medicines have been the primary therapy for delirium in critically sick patients. According to recent research, the current recommendations from the Society of Critical Care Medicine (SCCM) recommend regular usage of antipsychotics for delirium among individuals with critical conditions. Additional pharmacological therapies, such as dexmedetomidine, are currently being studied and their effects haven't yet been determined.
Non-pharmacologic therapies continue to be the fundamental aspect of delirium control [2].
The etiology of delirium remains uncertain and is likely a consequence of several pathways that are impacted throughout critical illness, leading to disturbances in cognitive function. Various pathogenic reasons have been suggested, including genetic abnormalities, exacerbation of brain inflammation, inadequate cerebral blood supply, and neurotransmitter imbalances. Managing ICU delirium has always been difficult due to the limited number of pharmaceutical interventions that have proven effective in managing delirium after its onset. For instance, antipsychotics have repeatedly demonstrated minimal efficacy in the treatment of the condition [3].

Manifestations and Outcomes of ICU Delirium
Manifestations
The prevalence of delirium may differ across specific studies but is a common diagnosis among all in-patient care conditions. Vasilevskis and colleagues estimated that about 33% of those admitted to hospitals eventually experienced delirium. Delirium is quite prevalent in the ICU, affecting around 75% of the individuals who need mechanical ventilation and up to 50% of those who do not require mechanical ventilation [4].
The symptoms of delirium also vary, especially in terms of its psychomotor presentations. Delirium is categorized into hypoactive, hyperactive, and mixed subtypes.

The most prevalent manifestations observed in the ICU are hypoactive and mixed delirium, which make up more than 90% of patients [5]. Individuals with hypoactive delirium exhibit mostly lethargy and decreased motor function, in contrast to those with hyperactive delirium who often display agitation and restlessness. Individuals diagnosed with mixed delirium suffer from symptoms of both hyperactive and hypoactive delirium, which may vary during the progression of the condition [6].

Outcomes

While critical care medicine has made tremendous progress in increasing survival rates, delirium continues to be a common and important cause of illness and death, leading to severe long-term impairments in both physical and mental abilities. individuals who experience delirium have a higher risk of death, both during their hospital stay and in the year after being discharged, contrasted with individuals who do not experience delirium [7].

Delirium occurring within 24 hours of admission to critical care is substantially correlated with higher rates of death throughout the hospital stay. individuals who need mechanical ventilation and have delirium have a higher risk of dying within 6 months and spend a much longer time in the hospital contrasted with individuals who do not have delirium [8]. There is an association between delirium and increased mortality in older critically sick patients up to one year after admission. It is important to note that hypoactive delirium has a greater mortality rate contrasted with mixed or hyperactive delirium [9].

Delirious individuals have not only increased mortality, but also significant physical consequences. Delirium has frequently been linked to increased duration of both ICU and hospitalizations. Individuals suffering from delirium have prolonged periods of mechanical ventilation and are more prone to respiratory problems, making the process of weaning them off the ventilator more challenging [10]. Delirium has also been linked to a higher probability of being transferred to a long-term care facility, and individuals with blood-borne infections were similarly less inclined to recover their previous functional level. Brummel and colleagues found that patients with critical illnesses who were on mechanical ventilation and developed delirium had significant difficulties in doing fundamental daily tasks. They also had worse sensory-motor function at the 3- and 12-month follow-up assessments [11]. Extended use of mechanical ventilation and the resulting impairment caused by delirium hinder patients from regaining their initial condition and diminishes their overall quality of life [12].

Risk Factors and Proposed Mechanisms

Predisposing Factors

Common factors that have consistently been associated with an increased risk of delirium in patients include being older, having existing cognitive impairment, and having a history of hypertension. Several studies have shown that cigarette smoking and alcohol consumption are related with an increased risk of delirium. However, the existing data is not enough to establish if they are independently linked to delirium in the ICU. Only uncontrolled hypertension, consuming alcohol, and cigarette smoking are among these risk factors that may be changed [13].

The risk of complications is believed to be higher in those with a significant number of comorbidities, heart illness, and frailty. However, the available information is not yet definitive. Individuals who have numerous coexisting medical conditions and are physically weak have a reduced ability to cope with the demands placed on their mental and physical health during a serious sickness. This may result in impaired brain function and might result in delirium [14].

Pharmacological Treatment

There are additional hazards that are linked to the treatments administered in the ICU. Research has demonstrated that the consumption of benzodiazepines, particularly lorazepam and midazolam, is directly linked to a higher likelihood of experiencing delirium. Furthermore, these investigations have shown a correlation that is dependent on the dosage, indicating that the risk increases as the benzodiazepine dosages increase. This is especially true when benzodiazepines are utilized as sedatives for mechanical breathing [15, 16].

Opiates, particularly morphine, have been associated with a higher risk of delirium. Additionally, there seems to be a connection between the use of opiates in combination with benzodiazepines and a longer period of delirium [17]. The association between these drugs and delirium may be attributed to the prolonged duration of their effects, which raises the likelihood of drug accumulate in the presence of impaired organ function [18]. In addition, the use of epidural analgesia and sedation with propofol has been shown to have some correlation, but the available information is not yet definitive [19].

Anticholinergic drugs may cause delirium, and there is strong evidence linking systemic corticosteroids to the development of delirium in individuals who were previously neither delirious or comatose [20]. The relationship between delirium and psychopharmacological agents is probably caused by their impact on neurotransmitters that seem to play a crucial role in the development of delirium, including acetylcholine, gamma-amino butyric acid (GABA), dopamine, and serotonin. An aberration in the production, release, and inactivation of these chemical transmitters appears to be one of the underlying causes of delirium [21].

Environment

Although sleep is crucial for healing, the quality of sleep in the ICU is often inadequate. Key factors that have a substantial impact include noise, frequent interruptions, the use of drugs that affect the structure of sleep, and disruption of the normal light-dark cycle owing to reduced exposure to sunlight [22]. The potential influence of low-quality sleep on delirium has been proposed as a modifiable risk factor. Although the relationship has not been definitively proven, the promotion of sleep is considered crucial and is included in the strategy for preventing delirium proposed by the Society of Critical Care Medicine (SCCM) [23].

In general, there seems to be an intricate relation between the elements that make someone more likely to develop delirium and those that trigger its onset. This connection involves the physical properties of the brain, various chemicals that convey signals in the brain, the immune system, the body's functions, hereditary factors, in addition to environmental and iatrogenic influences [24]. Therefore, even a patient who is severely fragile may have delirium from a relatively little physiological disturbance, whereas a patient with fewer underlying health conditions and excellent functional status may need a more significant

disturbance to develop delirium [25]. Comprehending these interconnected aspects is crucial for categorizing patients into various risk groups, enabling the development of preventative interventions that may effectively reduce the occurrence of delirium [26].

Pharmacological Management and Prevention

Dexmedetomidine

This compound is a specific α-2 adrenoreceptor agonist that has the potential to regulate the sleep-wake cycle and also induce anxiolysis and sedation. The administration of dexmedetomidine for delirium prophylaxis is a subject of controversy. Two double-blind, randomized controlled studies found that patients with mechanical ventilation who were sedated with dexmedetomidine had a 23% reduced risk of delirium contrasted to those who were sedated with midazolam. Additionally, participants sedated with dexmedetomidine had more than double the number of days without coma or delirium contrasted to those sedated with lorazepam [27].

A randomized controlled study, conducted with an open-label design, compared the use of dexmedetomidine with usual care as the primary sedation option for patients with mechanical ventilation. The trial also observed a modest augmentation in the number of days without coma or delirium in the dexmedetomidine group. Nevertheless, there was no disparity in the 90-day death rate across the groups. This research was constrained by the fact that a substantial proportion of the participants in the dexmedetomidine group subsequently got additional medications, like fentanyl and propofol [28].

Ketamine

It is a substance that blocks the N-methyl-D-aspartate (NMDA) receptors in the body when administered via an intravenous route. It has the ability to induce anesthesia, relieve pain, treat depression, and reduce inflammation. The use of ketamine during surgery leads to a considerable reduction in postoperative levels of interleukin-6 and the amount of pain medication needed after the surgery [29]. Hudetz *et al.* [30] discovered that giving ketamine near the beginning of a medical procedure was also linked to a positive effect on cognitive impairment that occurs after cardiac surgeries. The concentration of C-reactive protein was substantially reduced in the ketamine group compared to the control group (median: 7.9 vs. 11.6 mg/dL, $p< 0.01$). These findings indicate that ketamine has potential as a preventive or curative medication for postoperative or critical illness delirium. However, randomized controlled research that compared a single dosage of ketamine given after surgery to a placebo didn't find any difference in the occurrence of postoperative delirium. However, the groups who received ketamine had a higher incidence of hallucinations and nightmares. While the Hudetz trial and this study both utilized comparable dosages of ketamine, they diverged in terms of time and premedication methods [31].

Non-pharmacologic Interventions

Non-pharmacologic therapies have been the primary focus of delirium treatment and management for many years. Interventions such as fostering consistent sleep-wake patterns, minimizing unnecessary intrusive sensory stimulation, and regularly reorienting patients have been improved throughout time and are now considered the standard of care in ICUs across the globe. The ABCDEF bundle, which is always changing, has been the basis for the conceptualization of these therapies. Enhancements in adherence to the ABCDEF bundle are linked to a decrease in mortality rates, as well as a decrease in the number of days spent in the ICU without experiencing coma or delirium [32].

Early Mobility and Exercise

Early mobility encompasses a variety of activities, ranging from gentle movement of joints to walking with assistance. Administering this treatment to critically sick patients is both secure and practical, resulting in reduced occurrences of delirium, shorter periods of mechanical ventilation, decreased length of stay in the intensive care unit, and overall reduced hospitalization duration. Early mobility may be performed by any member of the care team, with the amount of activity regulated according to the patient's state of sedation. In a study including critically sick patients on mechanical ventilation, it was shown that early mobility throughout SATs significantly increased the chances of returning to independent functional status by discharge. The odds ratio was 2.7, with a 95% CI: 1.2-6.1. Research is presently being conducted to examine the feasibility and results of early combined cognitive and physical therapies in a comparable group [33].

Implications for clinical practice

Reliable research indicates that a minimum of 30% of instances of delirium in older persons who are admitted to the hospital may be avoided. This can be achieved by implementing treatments carried out by a team of healthcare professionals from many disciplines, including nursing, medicine, and allied health clinicians [34]. There is reliable data indicating that these therapies, which comprise of many components, are beneficial in reducing delirium in both general wards and aged care settings. Nevertheless, the data regarding the efficacy of therapies aimed at alleviating the impact of delirium in critical care settings has been equivocal. Although tiny single-site, non-pharmacological multi-component interventional trials have shown encouraging outcomes, greater studies conducted among high-risk patients have not provided conclusive evidence of a significant advantage. Specifically, elderly patients undergoing cardiothoracic surgery seem to exhibit resistance to treatment in the intensive care unit, despite the fact that other surgical individuals of the same age may be at risk for decreased post-operative delirium. Several substantial organizational and design modifications have been suggested for the critical care environment, with the aim of addressing the problem of delirium and ensuring that it no longer remains a concern in the future [34].

Conflict of Interest

Not available.

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