

Determination of the risk factors and delirium in the intensive care unit

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Received: 01/01/2024

Accepted: 30/01/2024

Published: 31.01.2024

Cite this article: Hacıömeroğlu A, Çıfci A. Determination of the risk factors and delirium in the intensive care unit. *Acad J Neurol Neurosurg.* 2024;1(1):11-13.

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ABSTRACT

Delirium is a pathology that most frequently affects elderly patients, is the result of an underlying condition, increases patient mortality and morbidity, and places a significant financial burden on clinics. Prevention of delirium is the simplest and most feasible approach. Despite all these, the clinical diagnosis of delirium is still inadequate and overlooked. In this review, current clinical practices for delirium, including etiology, pathophysiology, diagnosis, and treatment management, are reviewed.

Keywords: Delirium, geriatric, consciousness, attention

INTRODUCTION

Delirium is a clinical condition that often develops in later life. In delirium, the ability to focus and maintain focus generally decreases, and in addition, loss of attention, consciousness, and cognitive changes may develop. Delirium frequently occurs rapidly in a short period of time and fluctuates during the day.¹ In the clinical picture, psychomotor behavioral disorders are mostly observed together with restlessness. Psychomotor behavioral disorders may manifest themselves as hypoactivity or hyperactivity. This condition is usually accompanied by an increase or decrease in sleep duration and a deterioration in sleep quality.²

Delirium does not develop under normal conditions in many patients. Typically, an underlying medical condition is what causes it. In the etiology, there may be simple conditions such as constipation, pain, and local infections, or life-threatening conditions such as systemic infections, sepsis, and postoperative conditions.³

As a result of studies on delirium, the main feature that stands out in prevalence data is that it is frequently observed in the advanced age group. Incidence figures that can reach up to 25%, especially after major surgeries, and exceed 50% after risky surgical procedures have been found. In the postoperative period, the development of delirium has been found to be an independent predictor of mortality, causing an increase in mortality risk of approximately 10%. On the other hand, it was observed that the development of delirium increased mortality rates 2-4 times in patients followed up in intensive care units.^{4,5}

Delirium is a preventable clinical condition, and the most important approach is to prevent it before it develops. When it develops, it should be diagnosed early and rapidly, and its treatment should be performed carefully. Delirium is associated with increased morbidity as well as mortality risk. Consequently, it causes a serious cost increase for clinics.⁶ Possible consequences of delirium, especially in intensive care unit patients, are summarized in [Figure](#).

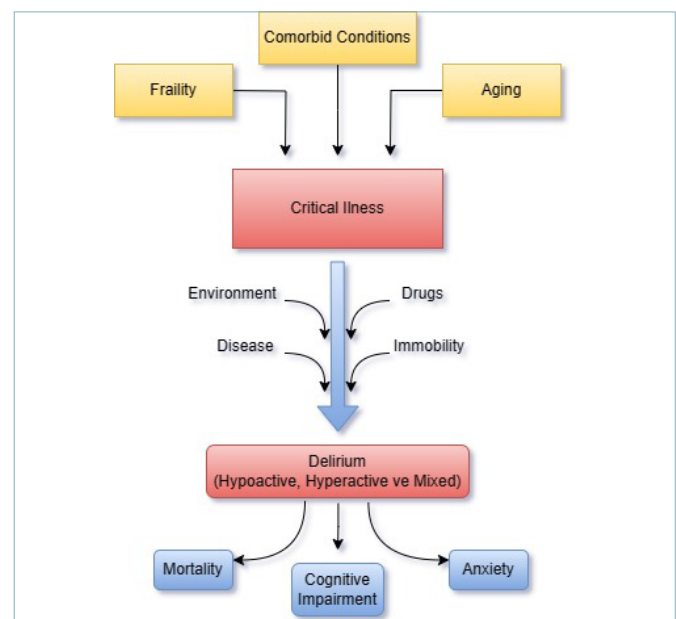


Figure. Risk factors and consequences of delirium in intensive care

ETIOLOGY AND RISK FACTORS

A new etiologic study in delirium is being added every day. However, the pathophysiology of many of the etiologic factors has not been fully elucidated. There are basically two groups of etiologies and risk factors related to delirium. These factors are roughly categorized as predisposing and accelerating factors. Delirium risk factors are summarized in **Table 1**.⁷

It should be kept in mind that the most common cause of predisposing factors is advanced age, and the importance of drugs among accelerating factors should not be forgotten. On the other hand, accelerating factors may consist of clinically overlooked symptoms such as constipation. Therefore, especially elderly patients should be approached carefully and holistically in terms of delirium, and all complaints of the patient should be given equal importance.⁸

Table 1. Delirium risk factors

Predisposing Factors	Accelerator Factors
<ul style="list-style-type: none"> Advanced age (over 70 years) Dementia (usually undiagnosed) Functional disability Male gender Poor vision and hearing Mild cognitive impairment 	<ul style="list-style-type: none"> Medicines (especially anticholinergics) Postoperative period Anesthetic substance use Hypoxia Untreated pain Infections Acute exacerbations of chronic diseases Constipation Dehydration Insomnia Urinary retention, bladder catheterization

PATHOPHYSIOLOGY

Delirium occurs pathophysiologically as a result of various mechanisms, and all of these conditions have not been fully elucidated. In studies, it has been determined that many conditions should occur simultaneously for delirium to occur.⁸

Advanced age, which is one of the most important points in terms of pathophysiology, comes to the forefront primarily due to loss of physiologic reserve and increased sensitivity to diseases and stress situations.⁹ In addition, it has been demonstrated that inadequate perfusion of brain tissue with advanced age is effective in reducing the increase in neuronal degeneration and loss. It has been argued that the leading cause of neuron loss is the increase in endothelial permeability as a result of the loss of the effect of the endothelial barrier in the blood-brain barrier and the related increase in neuronal inflammation. In addition, it has been found that these cells are damaged at a higher rate than normal as a result of an increase in reactive oxygen species due to the high lipid content and low antioxidant capacity of central nervous system cells.¹⁰

One of the important factors in the development of delirium is sleep patterns. The function of the melatonin hormone has been determined as a result of many years of studies in order to elucidate hormonal mechanisms in this regard. Melatonin has many functions, including sleep-wake cycles, regulation of antioxidant defenses, and glucose metabolism. In cases of disruption of sleep duration, pattern, and structure, melatonin levels may be affected and lead to delirium.¹¹

CLINIC

The clinical course of delirium may vary in many different ways. As a result of the studies, it is generally analyzed in three subgroups and summarized in **Table 2**. Delirium may present as hypoactive, with increased sleep duration, somnolence,

and a depressive state, or hyperactive, with hallucinations, delusions, and an agitated general state. On the other hand, delirium may occur over a long period of time, such as days, or it may occur within hours. Therefore, the patient's general activity, condition, and mood must be evaluated in terms of delirium at each visit.¹²

Table 2. Delirium classification and clinic

Hyperactive Delirium	Hypoactive Delirium	Mixed Presentation
<ul style="list-style-type: none"> Increased agitation Hallucination Fighting aggressive behavior 	<ul style="list-style-type: none"> Sleepiness Increased sleep duration Depressive appearance Decreased excitability 	<ul style="list-style-type: none"> Clinical symptoms alternating between hyperactive and hypoactive

DIAGNOSIS

The starting point for the diagnosis of delirium is the suspicion of delirium. Clinical studies have shown that only 40% of all delirium cases are recognized, and many cases are not detected. It has been determined that most of the 60% of cases that are not recognized are in the picture of hypoactive delirium. Therefore, in patients with suspected delirium, the patient's companion or caregiver should be questioned in detail, and the presence of hypoactive symptoms should be detailed. It should be learned whether the patient has increased sleep, depressive appearance, and mood in recent days.¹³

A detailed physical examination must be performed on patients with suspected delirium. First of all, vital signs should be evaluated; if necessary, a complete blood count, blood biochemistry, electrolytes, urinalysis, and, if possible, arterial blood gas should be performed. If deemed necessary in line with the patient's clinical condition, chest radiography and an ECG should be ordered. The aim of all these tests is not to diagnose delirium but to determine the underlying etiologic cause. Although there is data showing that values such as CRP, some interleukins, and cortisol are correlated with delirium in clinical trials, they have no place in the diagnosis and are not recommended for follow-up.¹³ The diagnosis of delirium is made according to DSM-5 criteria. These criteria are summarized in **Table 3**, and the presence of all criteria is required for diagnosis.¹⁴

Table 3. DSM-5 diagnostic criteria for delirium

<p>Attention and discrimination disorder</p> <p>a. Decreased ability to direct, focus, maintain, and shift attention. Decreased orientation to the environment.</p> <p>b. Develops over a short period of time (hours to a few days) with fluctuations in severity during the day.</p> <p>c. Additional impairment in cognition, memory, orientation, language, visuospatial competence, or perception</p> <p>Impairment in criteria A and C;</p> <ul style="list-style-type: none"> Is not better explained by another pre-existing, established, or developing neurocognitive disorder. It does not occur in the context of a severely reduced level of alertness, such as a coma.
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TREATMENT APPROACH

In the treatment of delirium, primarily non-pharmacologic steps are applied. Identifying patients at risk for delirium in the foreground is seen as the most important intervention that can be done to prevent the emergence of delirium. The critical points to prevent delirium in these high-risk patients are to ensure that their rooms get enough sunlight, are frequently ventilated with enough fresh air, and are have a competent caregiver or a knowledgeable companion. In addition, unnecessary intravenous treatments

and urinary catheters that will tie the patient to the bed and prevent mobilization should be avoided. In addition, no medical agent that will not clearly benefit the patient should be started.¹³

In patients in whom delirium occurs, other causes that may lead to a similar picture should be rapidly ruled out. It should be ensured that the patient is not in sepsis, is not hypoxic, is not hypoglycemic, has no electrolyte imbalance, and all vital signs are stable.

After excluding all these causes, medical treatment can be administered to patients who are sure of the diagnosis of delirium. Especially due to the advanced age and patients with comorbid conditions, the qualities of the medical agents to be selected have been determined. The agent to be preferred must have a short half-life, low toxicity risk, no effect on seizure threshold, and minimal effect on the cardiovascular and respiratory systems.⁷

Any pharmacological agent is not recommended in hypoactive delirium since the agents in the treatment generally have the effect of reducing agitation and sedation. In hyperactive delirium, antipsychotics should be preferred as first-line treatment in the absence of contraindications. Frequently used agents can be listed as haloperidol, quetiapine, and risperidone.¹⁵

Haloperidol is used as the first-choice agent in the treatment of delirium and may cause mild hypotension in patients. It is available in oral, intramuscular, and intravenous forms. Because of the risk of QT interval prolongation, ECG monitoring is recommended. Prolongation in the QT interval is observed more frequently in the elderly, female gender, and patients with endocrine disorders such as diabetes mellitus.¹⁶

CONCLUSION

Although results are obtained with haloperidol and other agents in almost all patient groups, no response to these agents can be obtained in rare patient groups. This is called resistant delirium, and benzodiazepines, anesthetic drugs, and even electroconvulsive therapies are recommended in this group of patients.

In recent years, studies, especially on sleep patterns, have shown that melatonin treatment leads to a decrease in the frequency of delirium by providing sleep patterns. However, it has not been fully utilized due to controversial publications in the literature.¹⁷

ETHICAL DECLARATIONS

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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