v. 5, n. 20, 2025

International Journal of Health Science

DELIRIUM IN OLDER ADULTS: PATHOPHYSIOLOGICAL MECHANISMS AND CURRENT PHARMACOLOGICAL APPROACHES

Acceptance date: 09/05/2025

Kelly Cristina de Amorim da Silva
National University of Rosario
Rosario, Argentina
https://orcid.org/0009-0008-7074-9638

Ana Victoria Frazao Corrêa Arrais
CET College, Teresina, Brazil
https://orcid.org/0009-0004-3425-5455

Leticia Sarah de Azevedo
Pontifical Catholic University of Rio Grande do Sul, Porto Alegre, Brazil
https://orcid.org/0009-0009-6785-8216

Fernanda Marques Cargnin
Federal University of Santa Maria
Santa Maria, Brazil
https://orcid.org/0009-0000-2538-7932

Julia Machado Simon de Carvalho
UNIDEP, Pato Branco, Brazil
https://orcid.org/0009-0002-0467-7521

Matheus Mendeleyev de Medeiros Borges
Estácio University Center of Ji-Paraná/ IDOMED, Ji-Paraná, Brazil
https://orcid.org/0009-0008-0749-9699

Jean Ricardo Oliveira dos Anjos
Jaguariúna University Center (UNIFAJ)
Jaguariúna, Brazil
https://orcid.org/0009-0007-0734-3857

Yanka Santana Frazão
Educational Foundation of the Municipality of Assis, Assis, Brazil
https://orcid.org/0009-0008-0116-0483

Marcelo Silva de Lima Júnior
Educational Foundation of the Municipality of Assis, Assis, Brazil
https://orcid.org/0009-0001-8654-3166

Maria Clara Cheraria Godinho
Educational Foundation of the Municipality of Assis, Assis, Brazil
https://orcid.org/0009-0007-6510-7094

Antonio Augusto Ribeiro Antunes
Educational Foundation of the Municipality of Assis, Assis, Brazil
https://orcid.org/0009-0007-9683-8308

Vitória Felisbino Ferrari
Positive University, Curitiba, Brazil
https://orcid.org/0009-0006-6355-5996

Abstract: Delirium is an acute neuropsychiatric syndrome characterized by a sudden and transient alteration in the state of consciousness, accompanied by global impairment of cognitive functions. It is a complex condition, with clinical manifestations ranging from difficulty maintaining attention to alterations in memory, language and perception. The clinical picture can vary widely, with fluctuations in the level of consciousness throughout the day, alternating between periods of drowsiness, restlessness and psychomotor agitation. These fluctuations make it difficult for the patient to interact with the environment and often confuse the diagnosis, especially in individuals with other neurological or psychiatric conditions. One of the most striking features of delirium is the alteration of the sleep-wake cycle, which often manifests itself as insomnia at night and excessive sleepiness during the day, and there can also be a complete reversal of these patterns. The fluctuation of symptoms, with worsening at night - a phenomenon known as "twilight" - is one of the clinical aspects that help differentiate delirium from other conditions, such as dementia, which has a more insidious and continuous evolution. This temporal variability of symptoms reinforces the importance of careful and repeated clinical assessment throughout the day, especially in at-risk populations. Delirium is particularly common in hospital environments, with a higher prevalence among the elderly and patients in intensive care units. Studies indicate that its occurrence can vary between 10% and 80%, depending on the population assessed and the criteria used for diagnosis. This high prevalence, coupled with the negative impact on clinical outcomes - such as increased morbidity and mortality, longer hospital stays and the risk of institutionalization - highlights the need for effective strategies for its early identification and appropriate management. Continuing education for healthcare teams, combined with systematic assessment

protocols, is a fundamental step towards reducing the incidence and complications associated with delirium. Delirium significantly affects the elderly population, mainly due to the greater brain vulnerability resulting from ageing and the presence of multiple comorbidities. In the elderly, delirium manifests itself with sudden changes in the state of consciousness and cognitive functioning, and it is common for symptoms to fluctuate throughout the day, alternating periods of drowsiness, agitation and disorientation. Alterations in the sleep-wake cycle, difficulty maintaining attention and perceptual alterations, such as illusions or hallucinations, are frequent manifestations in this age group. In addition, the presence of pre-existing conditions, such as dementia or other neurological diseases, can mask or aggravate the condition, making early diagnosis difficult.
Keywords: "Delirium", "Precipitating Factors", "Risk Populations", "Elderly", "ICU", "Hospitalized Patients", "Prevention", "Acute Confusion", and "Clinical Management"

INTRODUCTION

Population ageing is a worldwide phenomenon that has led to profound changes in health systems, requiring greater attention to common clinical conditions in the elderly [1-5]. Among these conditions is delirium, an acute neuropsychiatric syndrome characterized by disturbances in attention, consciousness and cognition, with a rapid onset and a generally reversible course [1-5].

Delirium affects up to 50% of hospitalized elderly people, especially those in intensive care units or undergoing surgical procedures [1-5]. Despite its high prevalence and association with negative outcomes, such as increased morbidity and mortality, prolonged hospitalization, risk of institutionalization and functional and cognitive decline, delirium remains underdiagnosed and is often confused with dementia or other psychiatric conditions [1-5].

The main characteristics of delirium include inattention, disorganized thinking, changes in the level of consciousness and disorientation, and can manifest in hypoactive, hyperactive or mixed forms [1-5]. In the elderly, factors such as pre-existing cognitive decline, multiple comorbidities, polypharmacy and prolonged hospitalizations significantly increase the risk of developing the syndrome [1-5].

From a clinical and social point of view, delirium in the elderly represents a serious public health problem [5-11]. It is associated with increased morbidity, hospital and post-discharge mortality, as well as longer hospital stays, early institutionalization and permanent functional decline [5-11]. The costs related to the treatment of delirium are significant, both for health systems and for families, resulting in a burden on caregivers and a significant economic impact [5-11].

Delirium is a multifactorial clinical condition that reflects acute brain dysfunction, usually transient, and represents an important challenge in the health care of the elderly [5-11]. In addition to predisposing and precipitating factors, the pathophysiological mechanisms are complex and not yet fully understood, but involve multiple related biological pathways [5-11].

Among the main pathophysiological hypotheses is an imbalance of neurotransmitters**, particularly a** reduction in cholinergic activity **and an** increase in dopaminergic activity, which impairs attention and cognition [5-11]. Other neurotransmitters such as serotonin, GABA and glutamate also play relevant roles, contributing to alterations in mood, sleep and sensory perception [5-11].

Early identification and appropriate management are essential for reducing complications [5-11]. Non-pharmacological strategies have been shown to be effective in preventing delirium, such as cognitive reorientation, encouraging early mobilization and family involvement in care [5-11].

Given its high prevalence and functional impact, delirium in the elderly should be recognized as a clinical emergency and an important marker of frailty, requiring preventive strategies and care focused on the elderly [5-11]. Due to the importance of the topic and the need to expand knowledge about caring for elderly people with delirium, this integrative review aimed to analyze studies addressing the prevalence, pathophysiological mechanisms, associated risk factors and the clinical, functional, cognitive and social impacts of delirium in the elderly [5-11].

OBJECTIVES

The main aim of the review is to provide an in-depth analysis of the pathophysiological mechanisms of delirium, with an emphasis on the more complex aspects surrounding the condition [12]. The review seeks to elucidate how neurotransmitter imbalances, neuroinflammation, oxidative stress, blood-brain barrier (BBB) dysfunction and neuroendocrine alterations contribute to the development and worsening of delirium [12]. This detailed understanding is essential to understand the biological basis behind this syndrome and the factors that make it so challenging in the clinical context [12].

In addition, the review aims to analyze the pharmacological approaches currently used in the management of delirium, with a focus on the most effective therapies for controlling acute symptoms and improving the patient's condition [12]. By addressing pharmacological strategies, the text aims to evaluate the available treatment options, their mechanisms of action, benefits and potential side effects, providing a more comprehensive understanding of the role of drugs in the management of this syndrome and directions for future research and clinical practice [12].

METHODOLOGY

This integrative review aimed to gather and analyze the best available evidence on precipitating factors and risk populations associated with the development of delirium, with an emphasis on early identification and prevention and clinical management strategies [12-13]. To this end, a systematic search was carried out in the PUBMED, VHL and MEDLINE databases, covering publications between the years 2020 and 2024 [12-13]. The search used the following descriptors in English and Portuguese, combined by Boolean operators (AND, OR): "Delirium", "Precipitating Factors", "Risk Populations", "Elderly", "ICU", "Hospitalized Patients", "Prevention", "Acute Confusion", and "Clinical Management" [12-13].

Additional filters were applied to restrict the selection to studies published in English and Portuguese, with full-text access and peer-reviewed [12-13]. Narrative review articles, editorials, studies with pediatric populations, and those that did not clearly address the triggering factors of delirium or the characteristics of the populations most susceptible to its development were excluded [12-13]. The inclusion criteria prioritized observational studies, clinical trials and systematic reviews that explored the relationship between acute clinical conditions (such as infections, metabolic imbalances and medication use), the hospital environment and the occurrence of delirium, as well as research that discussed the prevalence and impact of the syndrome in vulnerable populations, especially the elderly and patients in intensive care units [12-13].

The selection process was carried out in two stages [12-13]. In the first phase, 278 titles and abstracts were analyzed, of which 52 studies were selected for full reading. In the second phase, after a detailed evaluation of the texts, 27 articles met the established methodological and thematic criteria and were included in the final analysis [12-13]. The data extracted was

organized into thematic categories, focusing on the main precipitating factors of delirium (infections, metabolic disorders, sensory deprivation, medication use), the population groups most at risk (the elderly, hospitalized patients, neurological comorbidities), and the preventive and therapeutic strategies addressed in the studies [12-13]. This approach enabled a critical synthesis of the available evidence, contributing to an understanding of the mechanisms underlying delirium and to the formulation of more effective clinical approaches aimed at its prevention and management [12-13].

RESULTS AND DISCUSSION

NEUROTRANSMITTER IMBALANCES IN THE PATHOPHYSIOLOGY OF DELIRIUM

Neurotransmitter dysfunction plays a central role in the pathophysiology of delirium, directly affecting neuronal activity, cognitive function and the state of consciousness of patients [13-16]. This condition is marked by complex alterations in the brain's main neurotransmitter systems, such as acetylcholine, dopamine, glutamate and GABA [13-16]. Imbalances in these systems contribute to the manifestation of the classic symptoms of delirium, including mental confusion, psychomotor agitation, visual hallucinations and changes in the level of consciousness [13-16].

Among the neurotransmitters most studied in the context of delirium is acetylcholine. Its deficiency has been widely associated with impaired attention, disorientation, difficulty concentrating, slow thinking and memory lapses [13-16]. The cholinergic hypothesis proposes that impaired cholinergic activity in the central nervous system is one of the main pathophysiological mechanisms of delirium, especially in elderly patients or those taking anticholinergic drugs [13-16]. Thus, support for cholinergic neurotransmission may represent a promising avenue for therapeutic interventions [13-16].

Dopamine, in turn, is linked to a dopaminergic hyperactivity often observed in patients with hyperactive delirium [13-16]. An excessive increase in dopamine release or a reduction in inhibitory modulation of this system can cause symptoms such as hallucinations, delusions and disorganized behaviour [13-16]. This mechanism is especially relevant in situations of acute stress, substance withdrawal or severe metabolic dysfunction [13-16]. Understanding the role of dopamine in the pathophysiology of delirium opens the way for therapeutic approaches aimed at reducing its excessive activity, such as the judicious use of antipsychotics [13-16].

Glutamate, the brain's main excitatory neurotransmitter, also has a significant influence on the genesis of delirium [13-16]. Under conditions of metabolic stress, hypoxia or neuronal injury, there is an exacerbated release of glutamate, resulting in overstimulation of NMDA receptors [13-16]. This process can trigger excitotoxicity, neuronal damage and acute cognitive alterations [13-16]. This pathway has been particularly associated with delirium in critically ill and neurological patients, indicating that regulating the glutamatergic system may be a relevant therapeutic strategy [13-16].

In addition, gamma-aminobutyric acid (GABA), the main inhibitory neurotransmitter in the central nervous system, also plays a role in the pathophysiology of delirium [13-16]. The reduction in GABAergic activity compromises neuronal inhibition, favoring cortical hyperactivity and symptoms such as agitation, insomnia and anxiety [13-16]. Patients with alcohol withdrawal, for example, have marked GABAergic dysfunction and are more susceptible to severe delirium tremens [13-16]. Therefore, modulating GABAergic transmission can be an effective approach, especially in the most hyperactive cases of the syndrome [13-16].

International Journal of Health Science ISSN 2764-0159 DOI https://doi.org/10.22533/at.ed.15952025240413

An integrated understanding of these imbalances in neurotransmitter systems is essential in order to elucidate the mechanisms underlying delirium and propose more targeted treatments [13-16]. By recognizing the impact of alterations in the cholinergic, dopaminergic, glutamatergic and GABAergic systems, it becomes possible to develop more effective pharmacological and non-pharmacological strategies [13-16]. This knowledge also reinforces the importance of prevention, especially in at-risk populations, with the aim of minimizing the occurrence of acute episodes and improving the clinical outcomes of affected patients [13-16].

INFLAMMATORY RESPONSE AND COGNITIVE DYSFUNCTION IN DELIRIUM

Neuroinflammation plays a central role in the pathophysiology of delirium and is a dynamic process that contributes significantly to the onset and progression of this condition [13-16]. Stressful events, such as systemic infections, trauma, cerebral ischemia and surgical procedures, are capable of activating an inflammatory cascade in the central nervous system (CNS) [13-16]. This process is mediated mainly by the brain's resident immune cells, such as microglia and astrocytes, which release pro-inflammatory cytokines when activated [13-16]. These cytokines increase the permeability of the blood-brain barrier, facilitating the entry of peripheral immune cells into the CNS and promoting a neurotoxic and dysregulated environment [13-16].

Among the main mediators involved are interleukins (IL-1β, IL-6), tumor necrosis factor alpha (TNF-α) and other pro-inflammatory molecules, which directly interfere with neurotransmission and synaptic plasticity [13-16]. In addition, intracellular pathways such as the activation of nuclear factor kappa B (NF-κB) and the inflammasome complex are fundamental in perpetuating the inflammatory state [13-16]. These mechanisms lead to neuronal dysfunction, contributing to the cognitive deficits observed in delirium, such as inattention, disorientation and altered level of consciousness [13-16].

Another relevant aspect is the activation of the hypothalamic-pituitary-adrenal (HPA) axis by neuroinflammation, resulting in the increased release of cortisol, a hormone that regulates the stress response [13-16]. In excess, cortisol can negatively modulate brain activity, potentiating neurotoxicity and exacerbating symptoms typical of delirium, such as sleep disorders, autonomic instability and circadian rhythm changes [13-16]. This interaction between inflammatory processes and the HPA axis reveals the neuroendocrine complexity underlying the condition [13-16].

In addition to the HPA axis, neuroinflammation interacts with systems such as the vagus nerve, the autonomic nervous system and the endocrine system [13-16]. These interactions contribute to the heterogeneity of the clinical manifestations of delirium, which can range from neuropsychiatric symptoms - such as psychomotor agitation, delusions and hallucinations - to physiological instabilities, such as tachycardia, hypertension or hypotension [13-16]. This clinical complexity makes early diagnosis difficult and highlights the need for a comprehensive approach to understanding and managing the syndrome [13-16].

Given the importance of inflammatory mechanisms, interest is growing in therapies that modulate the neuroimmune response in delirium [13-16]. Current strategies are still limited and focus on supportive approaches and treatment of the underlying cause [13-16]. However, advances in knowledge about the specific inflammatory pathways involved in delirium pave the way for the development of more precise interventions capable of reducing the impact of neuroinflammation and improving the cognition of affected patients [13-16].

International Journal of Health Science ISSN 2764-0159 DOI https://doi.org/10.22533/at.ed.15952025240413

OXIDATIVE STRESS AND ITS CONTRIBUTION TO THE PATHOPHYSIOLOGY OF DELIRIUM

Oxidative stress is a fundamental component in the pathophysiology of delirium and is triggered by different clinical conditions that favor the exacerbated production of reactive oxygen species (ROS) [16-18]. During episodes of delirium, factors such as cerebral hypoxia, ischemia, tissue reperfusion, increased cerebral metabolism and intense inflammatory processes increase the levels of ROS in the central nervous system [16-18]. These highly reactive molecules promote oxidative damage to essential structures such as lipids, proteins and DNA, which significantly compromises neuronal function and cellular integrity [16-18].

Neurons, due to their high metabolic activity and the abundance of unsaturated fatty acids in their membranes, are particularly sensitive to the damaging effects of oxidative stress [16-18]. This vulnerability makes them primary targets for oxidative aggression, which can result in loss of structural integrity, synaptic dysfunction and cell apoptosis [16-18]. These effects culminate in impaired cognitive functions, such as memory and attention, which are hallmarks of delirium and various neurodegenerative diseases [16-18].

Oxidative stress, in addition to causing direct damage to neuronal cells, acts as an intracellular signaling agent, activating molecular pathways such as NF-κB and the inflammasome [16-18]. These pathways promote the transcription of pro-inflammatory genes and the release of cytokines, creating an even more aggressive neurotoxic environment [16-18]. Thus, there is a constant interaction between oxidative stress and neuroinflammation, forming a vicious cycle that intensifies neuronal dysfunction and the progression of delirium [16-18].

The body's natural response to oxidative stress is the activation of endogenous antioxidant systems, which include enzymes such as superoxide dismutase (SOD), catalase and glutathione peroxidase [16-18]. These mechanisms act by neutralizing free radicals and restoring the cellular redox balance [16-18]. However, when the production of ROS exceeds the body's neutralization capacity, the antioxidant response becomes insufficient [16-18]. This failure leads to irreversible damage to neuronal cells and worsens the patient's clinical condition [16-18].

The limitations of the antioxidant response in extreme stress scenarios highlight the need for interventions that strengthen these natural defenses [16-18]. Studies show that antioxidant compounds, both endogenous and exogenous, can play a relevant role in the prevention and treatment of delirium [16-18]. The inclusion of antioxidants in therapy, in addition to protecting neurons against oxidative damage, can contribute to a significant improvement in the clinical outcomes of patients affected by the condition [16-18].

Therefore, understanding the impact of oxidative stress in the context of delirium is essential for designing more effective and targeted therapeutic strategies [16-18]. Clinical management can benefit from the use of antioxidant agents, the reduction of metabolic and inflammatory insults, and the prevention of precipitating factors that amplify oxidative stress [16-18]. In this way, it is possible to mitigate neurological damage, improve cognition and reduce the morbidity and mortality associated with delirium [16-18].

BLOOD-BRAIN BARRIER DYSFUNCTION AND ITS CONTRIBUTION TO DELIRIUM

Alterations in the blood-brain barrier (BBB) play a crucial role in the pathophysiology of delirium, since this structure regulates communication between the circulatory system and the central nervous system (CNS) [16-18]. The BBB acts as a functional boundary between blood and brain tissue, strictly controlling the exchange of substances in order to protect the brain against potentially harmful agents and maintain neural homeostasis [16-18]. In the context of delirium, any impairment of this barrier can trigger a cascade of neuroinflammatory and neurodegenerative events [16-18].

The function of the BBB depends on its semi-permeable properties, which allow the selective entry of essential nutrients and block the passage of toxins, pathogens and inflammatory molecules [16-18]. This selectivity is guaranteed by complex junctions between the endothelial cells of the cerebral capillaries, associated with astrocytes and pericytes [16-18]. This structure is vital for preserving the stability of the cerebral microenvironment, which is fundamental for proper synaptic transmission and cognitive function [16-18]. When this system fails, the balance of the CNS is threatened [16-18].

In situations of metabolic stress, such as hypoxia, trauma, systemic infections or extensive surgery - conditions often associated with delirium - the integrity of the BBB can be compromised [16-18]. This leads to an increase in its permeability, allowing the entry of substances that would normally be blocked [16-18]. This weakening of the barrier facilitates the penetration of toxic and inflammatory elements into brain tissue, making the neuronal environment vulnerable to damage [16-18].

During delirium, this impairment of the BBB favors the passage of pro-inflammatory cytokines, reactive oxygen species (ROS) and other inflammatory mediators into the brain [16-18]. The presence of these substances in the CNS activates microglia and astrocytes, promoting local inflammation, synaptic dysfunction and changes in neuronal metabolism [16-18]. This inflammatory environment is a determining factor in the manifestation of symptoms typical of delirium, such as confusion, disorientation, fluctuations in consciousness and agitation [16-18].

Ultimately, the breakdown of the BBB in delirium intensifies the neuroinflammatory process and contributes to the neuronal dysfunction and cognitive impairment observed in these patients [16-18]. Understanding this mechanism is essential for the development of therapeutic strategies aimed at protecting the integrity of the BBB, attenuating brain inflammation and effectively preventing or treating delirium [16-18]. Furthermore, preserving the BBB may be a key to improving clinical outcomes in critically ill patients [16-18].

HPA AXIS, CORTISOL AND THE STRESS RESPONSE IN DELIRIUM

Neuroendocrine dysfunction is a key element in the pathophysiology of delirium, particularly alterations in the hypothalamic-pituitary-adrenal (HPA) axis, which regulates the stress response [18-20]. This axis plays a fundamental role in maintaining homeostasis, but in critical situations, such as infections, surgeries or serious illnesses - factors often associated with delirium - it can become hyperactivated [18-20]. This exacerbated activation leads to the excessive release of cortisol, the main glucocorticoid hormone, which has a direct impact on the brain and immune system [18-20].

The HPA axis works like a hormonal feedback loop: the hypothalamus releases corticotrophin-releasing hormone (CRH), which stimulates the pituitary gland to secrete adrenocorticotrophic hormone (ACTH) [18-20]. This, in turn, acts on the adrenal glands, inducing the production of cortisol [18-20]. Under normal conditions, cortisol regulates inflammation and metabolism [18-20]. However, in delirium, the persistent and elevated release of this hormone contributes to a state of systemic inflammation and neuroinflammation, aggravating the cognitive dysfunction and altered behavior characteristic of the condition [18-20].

Excess cortisol in the central nervous system has neurotoxic effects and can directly damage sensitive areas such as the hippocampus, which is responsible for memory and learning [18-20]. In addition, high cortisol levels compromise neurogenesis and synaptic plasticity - crucial processes for cognition [18-20]. In the long term, this hormonal imbalance can contribute to cognitive deterioration, anxiety, sleep disorders and mood swings, symptoms often observed in patients with delirium, especially the elderly or critically ill [18-20].

In addition to the HPA axis, other hormones are also altered in delirium [18-20]. Dysregulated secretion of antidiuretic hormone (ADH) can lead to electrolyte disturbances, such as hyponatremia, which in itself can trigger or aggravate an episode of delirium [18-20]. Changes in thyroid hormone levels have also been described, which can affect cerebral metabolism and neuronal function [18-20]. These combined hormonal changes contribute to a state of metabolic and functional instability in the central nervous system [18-20].

Therefore, recognizing neuroendocrine dysfunction as a component of delirium broadens our understanding of its pathophysiology and opens up avenues for more targeted therapeutic approaches [18-20]. Strategies aimed at restoring the balance of the HPA axis, modulating cortisol levels and correcting other hormonal alterations could represent significant advances in the treatment and prevention of delirium, especially in hospital and intensive care settings [18-20].

PHARMACOLOGICAL MANAGEMENT OF DELIRIUM

Pharmacological interventions play a fundamental role in the management of delirium, especially in cases where the symptoms are intense, with psychomotor agitation, hallucinations or risk of injury to the patient or staff [18-20]. However, the use of medication should always be judicious and individualized, respecting the particularities of each case [18-20]. The approach should take into account the etiology of delirium, the presence of comorbidities, the patient's age, as well as the expected response to the desired effects and possible adverse reactions [18-20].

Among the pharmacological options available, antipsychotics are the most commonly used to control the psychotic symptoms of delirium [18-20]. Drugs such as quetiapine, risperidone, haloperidol and olanzapine are often indicated, with preference given to those with less potential for extrapyramidal effects, such as quetiapine, especially in the elderly [18-20]. These drugs act by blocking dopaminergic and serotoninergic receptors, reducing disorganized thinking and the distorted perception of reality [18-20]. Even so, they should be used with caution, as they can cause excessive sedation, hypotension and even prolongation of the QT interval [18-20].

Benzodiazepines, on the other hand, have a more limited indication in delirium and are generally reserved for cases of delirium induced by alcohol withdrawal or sedatives [18-20]. In these contexts, drugs such as lorazepam and diazepam are effective in preventing seizures and controlling intense agitation

[18-20]. Outside of these scenarios, benzodiazepines should be avoided as they can aggravate confusion, increase the risk of falls and prolong the duration of delirium, especially in elderly and frail patients [18-20].

Despite the widespread use of antipsychotics and benzodiazepines, the scientific evidence supporting their effectiveness in treating delirium is still limited [18-20]. For this reason, clinical guidelines recommend that non-pharmacological interventions should always be considered as the first line of treatment [18-20]. Measures such as maintaining a quiet environment, adequate lighting, temporal and spatial orientation, sleep management and hydration, as well as the presence of family members or caregivers, are strategies that can significantly reduce the incidence and duration of delirium [18-20].

The management of delirium therefore requires a broad and integrated vision, which values both pharmacological resources and environmental and behavioral interventions [20-27]. The introduction of medication should always be accompanied by rigorous monitoring, with constant reassessment of efficacy and safety [20-27]. In addition, the gradual withdrawal of drugs should be planned as soon as the acute symptoms are controlled, in order to avoid late adverse effects [20-27].

In conclusion, the pharmacological treatment of delirium is a valuable tool, but it should be used with caution and good clinical judgment [20-27]. Prioritizing non-pharmacological approaches, associated with the judicious use of medication, can result in better functional recovery and shorter hospital stays [20-27]. Thus, a balance between drug interventions and humanized care is essential for therapeutic success and patient well-being [20-27].

CONCLUSION

The findings of this integrative review reinforce the complexity of delirium as a multifactorial condition whose occurrence is strongly related to acute precipitating factors and the clinical vulnerability of specific populations, such as the elderly and hospitalized patients, especially in intensive care units. Early identification of these factors is essential for the development of preventive strategies and the implementation of effective interventions that can minimize the incidence and complications associated with the syndrome. The analysis of the selected studies highlighted the importance of systematic and continuous assessment of patients' mental state, as well as the need for special attention to aspects such as polypharmacy, infections, metabolic disorders and sensory deprivation.

The literature reviewed indicates that delirium prevention should be a priority in healthcare, focusing on multifaceted interventions adapted to each patient's risk profile. Measures such as optimizing the hospital environment, promoting sleep, adequate pain control, early mobilization and careful review of the medications used have proved effective in various clinical contexts. In addition, training multi-professional teams to recognize early signs of the syndrome is an indispensable strategy for improving prognosis and reducing length of stay and hospital costs.

It can therefore be concluded that dealing with delirium requires a proactive, patient-centered and evidence-based approach. Integrating the knowledge produced by recent studies with daily clinical practice can make a significant contribution to the quality of care provided and patient safety. Thus, this integrative review not only deepens understanding of the factors related to the development of delirium, but also supports the formulation of care protocols aimed at its prevention and appropriate clinical management, with a focus on humanization and effective health care.

International Journal of Health Science ISSN 2764-0159 DOI https://doi.org/10.22533/at.ed.15952025240413

REFERENCES

1. Inouye SK, Westendorp RG, Saczynski JS. Delirium in elderly people. Lancet. 2014;383(9920):911–22.

2. Oh ES, Fong TG, Hshieh TT, Inouye SK. Delirium in older persons: advances in diagnosis and treatment. JAMA. 2017;318(12):1161–74.

3. Bolelli G, Morandi A, Di Santo SG, Mazzone A, Cherubini A, Mossello E, et al. "Delirium Day": a nationwide point prevalence study of delirium in older hospitalized patients using an easy standardized diagnostic tool. BMC Med. 2016;14(1):106.

4. Neto AS, Nassar AP Jr, Cardoso SO, Manetta JA, Pereira VG, Esposito DC, et al. Delirium in intensive care unit patients: a systematic review and meta-analysis. Rev Bras Ter Intensiva. 2012;24(3):245–53.

5. Maldonado JR. Neuropathogenesis of delirium: review of current etiologic theories and common pathways. Am J Geriatr Psychiatry. 2013;21(12):1190–222.

6. Boettger S, Breitbart W. Delirium in elderly patients: diagnosis, prevention and treatment. Oncol Ther. 2021;9(2):255–71.

7. Souza MT, Silva MD, Carvalho R. Revisão integrativa: o que é e como fazer. Einstein (São Paulo). 2010;8(1 Pt 1):102–6.

8. Cerejeira J, Firmino H, Vaz-Serra A, Mukaetova-Ladinska EB. A hipótese neuroinflamatória do delírio. Acta Neuropathol. 2010;119(6):737–54. doi:10.1007/s00401-010-0674-1.

9. Mendes KDS, Silveira RCCP, Galvão CM. Revisão integrativa: método de pesquisa para a incorporação de evidências na saúde e na enfermagem. Texto Contexto Enferm. 2008;17(4):758–64.

10. Zhang J, Bloom I, Dennison E, Ward KA, Robinson SM, Barker M, et al. Understanding influences on physical activity participation by older adults: a qualitative study of community-dwelling older adults from the Hertfordshire Cohort Study, UK. PLoS One. 2022;17(1):e0263050. doi:10.1371/journal.pone.0263050.

11. Lima BR, Nunes BKG, Guimarães LCC, Almeida LF, Pagotto V. Incidência de delirium após internação de idosos com fraturas: fatores de risco e mortalidade. Rev Esc Enferm USP. 2021;55:e20200467. doi:10.1590/1980-220X-REEUSP-2020-0467.

12. Lee, Sangil et al. "Delirium and Delirium Prevention in the Emergency Department." *Clinics in geriatric medicine* vol. 39,4 (2023): 535-551. doi:10.1016/j.cger.2023.05.006

13. Liu, Si Bo et al. "Delirium in the ICU: how much do we know? A narrative review." *Annals of medicine* vol. 56,1 (2024): 2405072. doi:10.1080/07853890.2024.2405072

14. Jaqua, Ecler Ercole et al. "Delirium in Older Persons: Prevention, Evaluation, and Management." *American family physician* vol. 108,3 (2023): 278-287.

15. Khaing, Kay, and Balakrishnan R Nair. "Melatonin for delirium prevention in hospitalized patients: A systematic review and meta-analysis." Journal of psychiatric research vol. 133 (2021): 181-190. doi:10.1016/j.jpsychires.2020.12.020

16. Alexander, Sian K, and Edward Needham. "Diagnosis of delirium: a practical approach." *Practical neurology* vol. 23,3 (2023): 192-199. doi:10.1136/pn-2022-003373

17. Smith, Camryn J et al. "The Pathophysiology and Biomarkers of Delirium." Seminars in neurology vol. 44,6 (2024): 720-731. doi:10.1055/s-0044-1791666

18. Umoh, Mfon E et al. "The Relationship between Delirium and Dementia." *Seminars in neurology* vol. 44,6 (2024): 732-751. doi:10.1055/s-0044-1791543

19. Bellelli, Giuseppe et al. "Delirium and frailty in older adults: Clinical overlap and biological underpinnings." *Journal of internal medicine* vol. 296,5 (2024): 382-398. doi:10.1111/joim.20014

20. Martínez-Arnau, Francisco Miguel et al. "Incidence of delirium in older people with cancer: Systematic review and meta-analysis." *European journal of oncology nursing : the official journal of European Oncology Nursing Society* vol. 67 (2023): 102457. doi:10.1016/j.ejon.2023.102457

21. Agar, Meera R. "Delirium at the end of life." *Age and ageing* vol. 49,3 (2020): 337-340. doi:10.1093/ageing/afz171

22. Andrews, Patricia S et al. "Delirium, depression, and long-term cognition." *International psychogeriatrics* vol. 35,8 (2023): 433-438. doi:10.1017/S1041610221002556

23. He, Steven et al. "Does delirium prevention reduce risk of in-patient falls among older adults? A systematic review and trial sequential meta-analysis." *Australasian journal on ageing* vol. 41,3 (2022): 396-406. doi:10.1111/ajag.13051

24. He, Steven et al. "Does delirium prevention reduce risk of in-patient falls among older adults? A systematic review and trial sequential meta-analysis." *Australasian journal on ageing* vol. 41,3 (2022): 396-406. doi:10.1111/ajag.13051

25. Rushani, Dinela et al. "Commentary: Finding delirium: It's harder than you think!." *The Journal of thoracic and cardiovascular surgery* vol. 163,2 (2022): 737-738. doi:10.1016/j.jtcvs.2020.07.023

26. Ista, Erwin et al. "Factors Associated With Delirium in Children: A Systematic Review and Meta-Analysis." Pediatric critical care medicine : a journal of the Society of Critical Care Medicine and the World Federation of Pediatric Intensive and Critical Care Societies vol. 24,5 (2023): 372-381. doi:10.1097/PCC.0000000000003196

27. Gallie, Louise. "Delirium: name it, say it-loud and clear." *Intensive care medicine* vol. 50,2 (2024): 314-316. doi:10.1007/s00134-023-07279-2