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Original Research Paper

Epidemiology

DELIRIUM: NARRATIVE REVIEW

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ABSTRACT Delirium is a neuropsychiatric syndrome characterized by acute onset of deficits in attention and in multiple aspects of cognition. The prevalence of delirium varies considerably by patient group and setting, tending to be more common in hospitalized older adults or the critically ill. Three phenotypes of delirium are recognized depending on psychomotor activity (hyperactive, hypoactive, mixed). Its diagnosis is based on the criteria established in the DSM V, however we have diagnostic tools used in clinical practice such as 4A, CAM and ICDSC. The pharmacological management of delirium is still a matter of debate, treatments with antipsychotic drugs have been shown to reduce motor activity, but they do not seem to affect the dura

KEYWORDS : Delirium, clinical presentation, diagnosis, treatment.

INTRODUCTION

The term "delirium" derives from the Latin word delirare, whose meaning is "to get out of the groove" (to go crazy) (1). Delirium is a neuropsychiatric syndrome in which there is an acute onset of deficits in attention and in multiple aspects of cognition. Patients often have altered arousal, a spectrum ranging from coma to hypervigilance and severe confusion can be evidenced, not uncommonly also coexisting with hallucinations and mood disturbances. Delirium is triggered by multiple possible causes, including acute illness, drug use or withdrawal, trauma, and surgery.

Most causes originate outside the brain, however it is also recognized in primary neurological causes such as in stroke patients. Its duration is variable, but it has been seen that up to 20% of individuals can persist for months or weeks (2). It is worth noting the difference between delirium and acute encephalopathy, acute encephalopathy is not a clinical syndrome, but a rapidly developing pathological process that can manifest as delirium or a coma.

Thus, acute encephalopathy refers to the brain disorder underlying the delirium. For these reasons, an endorsed nomenclature has been created that helps to remove obstacles and confusion in favor of research and clinical care of these interrelated conditions (3).

METHODS

This narrative review was based on a search strategy that was carried out in databases such as PubMed/Medline, Lilacs and Redalyc, EBSCO. The MeSH and DeCS thesauri were used. Articles such as clinical trials, systematic reviews, topic reviews between the years of 1999 and 2022 were included (**Figure 1**).

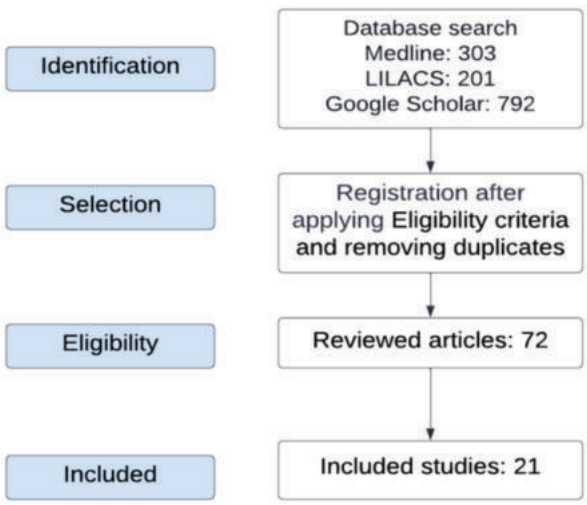

Figure 1: PRISMA

Epidemiology

The prevalence of delirium varies considerably by patient group and setting. It is known that delirium tends to be more common in hospitalized older adults. a meta-analysis by Gibb et al found an overall prevalence of delirium of 23% (4). Patients undergoing major surgery for emergency conditions have a prevalence of delirium >20% (5) (6). The prevalence of delirium is also substantial in palliative care settings, a

systematic review by Watt et al, reporting a prevalence of 4-12% in the community, 9-57% in hospitalized patients with a pooled prevalence of 35%. Regarding the youngest, it has been seen that the prevalence in seriously ill adolescents and children oscillates between 4-50% and it is said that in seriously ill children under 2 years of age, more than half presented delirium (7).

Definition

According to DSM V, delirium refers to the acute onset and fluctuating course of symptoms consisting of inattention, altered state of consciousness and cognition (loss of memory, disorientation or alteration in language). It is also accompanied by other alterations such as changes in the sleep cycle, visual or auditory hallucinations, inappropriate behavior and emotional lability (8).

Classification

Delirium can be classified according to psychomotor activity into 3 types:

1. Hyperactive delirium: the patient is hyperalert, restless, agitated and/or aggressive.

2. Hypoactive delirium: drowsiness with inattention predominates.

3. Mixed delirium: mixture of the 2 above.

Risk factor's

The risk of delirium is determined by predisposing factors (patient's condition) and triggering risk factors (injuries or drugs). The most recognized predisposing factors for delirium include advanced age, male sex, frailty, cognitive impairment (dementia, psychiatric illness), cardiovascular or renal disease, depression, disability, drug use, and poor nutritional status (9-11).

Pathophysiology

Delirium is triggered by a wide variety of acute medical conditions. The brain requires a great deal of energy, and with deficiency of oxygen or glucose its function can be severely limited.

There is then a hypothesis known as "cerebral metabolic insufficiency", it proposes that delirium is caused by lack of compliance with the energy requirements of the brain, which in turn is precipitated by an acute illness. 7 fundamental steps in its pathophysiology have been described:

First, respiratory distress produces hypoxemia and can cause cerebral hypoxia, limiting neuronal energy metabolism (12). This leads to impaired mitochondrial oxidative phosphorylation and insufficient energy generation, in the form of ATP. Under these conditions, the pyruvate generated by glycolysis, instead of being imported into the mitochondria, forms an excess of lactate, which can be measured in the extracellular fluid.

Second, septic shock reduces blood flow, leading to hypoxia and impaired glucose supply (13).

Third, even with adequate systemic blood flow, dysfunction of brain microcapillaries can lead to brain tissue hypoxia and neuroglycopenia.

Fourth, even with normal blood pressure, if neurovascular coupling is disturbed, the vessels may not meet the specific demands of regional neuronal activity and thus block higher-order brain functions (14).

Fifth, systemic hypoglycemia can lead to insufficient glucose supply to the brain, delirium, and coma.

Sixth, even with an adequate supply of glucose to the brain, insulin resistance can result in poor glucose utilization (15).

Seventh, altered expression of glucose transporters (GLUT1 and GLUT3), for example, in the degenerating brain, may limit glucose uptake by endothelium, astrocytes, or neurons, thereby limiting glucose-6-phosphate (G6P) necessary for glycolysis and limiting the generation of pyruvate required for the tricarboxylic acid cycle (16).

Evaluation

Although the diagnosis of delirium is based on the criteria established by the DSM V, it is common in clinical practice to have certain tools that help us clarify the diagnosis when we have suspicions, the choice of such tools varies depending on the clinical setting in which the patient is evaluated.

The 4A test is a 4-item tool, designed to be performed in 2 minutes, which does not require special training to perform, and is intended for patients in a general hospital setting. The four items are alertness, cognition (a brief orientation test), attention (reciting the months in reverse order), and the presence of a sharp change or fluctuating course. A meta-analysis carried out by Tieges et al, gives it a sensitivity and specificity of around 88% (17).

For intensive care patients, the utility of 2 similar tools has been demonstrated. The CAM tool (confusion assessment method) and the ICDSC (Intensive Care Delirium Screening Checklist). The first is designed to be used in intensive care patients, especially those undergoing mechanical ventilation. However, it can be used in other settings such as nursing homes, emergency rooms, or hospice homes, with a sensitivity of 80% and a specificity of 96% (18).

The ICDSC tool comprises eight features: level of consciousness, inattention, disorientation, psychosis, psychomotor changes, speech or mood changes, sleep-wake cycle disturbance, and symptom fluctuation. Each item is scored 0 (absent) or 1 (present) at the end of each nursing shift, and scores ≥ 4 are considered to indicate delirium. For this tool, a sensitivity of 74% and a specificity of 82% have been found (19).

Treatment

The pharmacological treatment of delirium has been a controversial issue for a long time, among the most relevant drugs are antipsychotic agents, however, in a review carried out by Cochrane in 2018, it was evidenced that antipsychotics had no effect on the severity of delirium, resolution of symptoms or mortality and that there was still a lack of information on the duration of the episode and the length of hospital stay (20), in the same way a review was carried out, this time in ICU patients which reached the same conclusions (21). Within this group of drugs, haloperidol and risperidone stand out , however, as mentioned before, their effectiveness is still debated given the low or very low quality evidence regarding their use.

Another group of drugs analyzed are cholinesterase inhibitors, but like antipsychotics they have a low quality of evidence. Another medication used to control motor symptoms refractory to haloperidol management in intensive care patients has been dexmedetomidine.

In a study carried out by Carrasco et al, a better effectiveness, safety and cost-benefit profile was demonstrated with respect to haloperidol (21). It is then concluded that there is still much to be investigated and that the management of delirium as a syndrome should not be limited only to ineffective pharmacological management, but should be given when there is intractable anxiety and other measures have been ineffective.

Table 1. Medication dosage

Daily use	Agitation
Risperidone 0,25 – 0,5 mg every 4 hours	Risperidone 0,25 – 0,5 mg every 4 hours
Olanzapine 2,5 – 5 mg/day	Olanzapine 20mg/day
Quetiapine 25-50 mg every 12 hours.	Quetiapine 25-50 mg every 4 hours (maximum 600 mg)
Ziprasidone 20-40 mg /day	Ziprasidone 10 – 20 mg IM
Haloperidol 1-20 mg/day	Haloperidol 5 mg IM

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