

Research Article

Delirium, The Geriatrics Ward Challenge

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ABSTRACT

Delirium or acute confusion state is a medical emergency, characterized by altered mental status with fluctuating deficits in attention and cognition. It's an important cause of morbidity and mortality. Even though most of the causes are secondary to medical conditions and after they are solved, the delirium disappear, there are cases that it can persist for weeks and months. Many risk factors are known, such as polypharmacy, restraint use, multiple illness, frailty, advanced age. Instruments like CAM (Confusion Assessment Method) can be useful to diagnose and non-pharmacological measures with low-dose antipsychotic drugs can be helpful in its resolution.

Keywords: Elderly, Delirium, Dementia, Confusion, Preventing, Anti-psychotic, CAM.

INTRODUCTION

Diagnosing delirium is a herculean task. Delirium is a non-benign clinical condition¹ with acute brain dysfunction¹⁻³ that is characterized by acute changes, in hours or weeks, in both attention and cognition. Diagnosis is made with clinical data, regarding to 4 criteria – acute onset and fluctuating course, inattention and change in the level of consciousness or disorganized thinking¹⁻¹³. These criteria are included in the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5)

and in the International Statistical Classification of Diseases and Related Health Problems, 10th Revision (ICD 10). From its first description in 1980, the importance of attention has risen, being the most important criteria^{7,10,11,13}. Many terms have emerged to describe delirium – “acute confusional state”, “acute brain syndrome”, “acute cerebral insufficiency” and “toxic-metabolic encephalopathy”¹¹. In 2004, it costed 2500 dollars per patient per hospitalization, increasing the indirect costs due to home health care, rehabilitation

services and informal caregiving^{11,13}. Already in 2011, it costed over 164 billion of dollars in the USA and over 182 billion dollars in 18 European countries¹⁰. Due to ethics, delirium may affect people's ability to consent, communicate or complete interviews^{12,13}.

DISCUSSION

Forms

Despite first being described over 2500 years ago, delirium remains frequently unrecognized and poorly understood^{10,13}. It's described two major psychomotor forms of delirium – hyperactive and hypoactive, that can be intermittent and be both present in the same patient in different evaluation times. Each one has different characteristics and consequently different prognoses^{4,10,11,12}. The hyperactive is more frequently found in acute alcohol withdrawal and the hypoactive in older patients and generally associated with a worse prognosis^{10,12}. Restlessness, irritability, agitation, combat is common in hyperactive delirium, and on the other side symptoms like lethargy, decreased learning, reduced mobility and social activity and increased sleep are present mainly in hypoactive delirium⁶. The earlier the prevention and the treatment are activated, the better are the prognosis⁹.

Screening and Diagnosis

Screening should be made daily in every environment of the elder (ward, emergency department, surgery, intensive care units [ICU]) by tools like CAM – Confusion

Assessment Method^{1,3,6,10,12} Pfeiffer index³ and Richmond Agitation and Sedation Scale (RASS). Note that the last one is for patients in the ICU and exclusively applied to patients with hyperactive delirium^{7,10,12} and it should not be used alone, but with the aid of tests of attention and cognition¹⁰. For measuring its severity, tools like Delirium Rate Scale (DRS and DRS-98) and Memorial Delirium Assessment Scale (MDAS) may be useful¹⁰.

Risk Groups

Delirium can affect both young and elder, being high risk groups. The first one because the brain networks are underdeveloped and the last because of the cumulate damage in the same network¹⁰.

Pathogenesis

The real pathogenic mechanisms are not well understood, but several of them were proposed, such as neurotransmitter imbalance with acetylcholine deficiency and dopamine excess, reduced cerebral blood flow and metabolism, dysregulation of stress response and the sleep-wake cycle and finally inflammation (due to infectious and non-infectious stimulus)^{1,5,9,10,11}. Histologically are found changes like apoptosis, activation of microglia and astrocytes^{1,8,9,10}. The development of delirium involves the complex inter-relationship between a vulnerable patient with multiple predisposing factors (including its genetics) and exposure to noxious insults or precipitating factors. In patients, very vulnerable with underlying dementia and multimorbid, the tiniest and

benign insult can precipitate delirium^{10,11}. Even though there are many theories, the final common pathway is still unknown¹⁰.

Mediators

Mediators like cytokines (IL1, IL6 and TNF α)^{1,3} and prostaglandins are pointed. C-reactive protein (CRP) was also studied but it is not consensual. Some studies showed the elevation of IL6 and IL8 in older patients that developed delirium and with patients with schizophrenia^{1,9}. Other markers were also pointed such as s100B (calcium-binding protein B), IL1 β ^{3,9}, and TNF receptors serum levels, the last two independent of on course sepsis³. Insulin-like growth factor (IGF)-1, IL1 β and IL1 receptor antagonist (RA), interferon (IFN) γ have been also associated with delirium. Literature point that low levels of IGF1 were associated with the delirium severity⁹.

Etiology

The etiology is commonly multifactorial^{8,9,10,11,13} organic and most of them modifiable^{5,6,8,9}. On the other hand, there are no modifiable risk factors like dementia and cognitive impairment, advanced age, history of previous delirium, stroke, neurological disease, falls or gait disorder, multiple comorbidities, male sex, chronic or hepatic disease¹¹.

There are some risk factors and conditions such advanced age (≥ 60 years old)^{1,3,4,10} hospitalization itself^{8,10,11} and medical conditions such as acute illness like hypoxia cerebral ischemia^{1,9,10,11} infections and

sepsis^{1,3,9-12} trauma, cancer, post-surgery^{1,6,11,12} moderate or severe hydro electrolyte changes, organ dysfunction such as kidney and liver failure, drugs consumption or withdrawal^{3,4} sleep deprivation, endocrine and metabolic conditions, frailty, restraint use, polypharmacy, especially when corticosteroids and anti-cholinergic are part of the habitual medication^{4,9,11,12} dementia^{1,4,6-8,10-12} anemia⁶ pain⁷ hypoglycemia⁹ alcohol dependence/abuse^{10,11} and depression¹⁰.

Infection is the common cause of infection in the elderly, especially the ones located on the urinary tract⁴. Most of the causes of delirium need medical hospitalization and that's the main reason that it's more frequent in hospitals and medical facilities^{12,13}.

Clinical History and Physical Examination

A good clinical history may be essential. Obtaining it from an informed observer (e.g. family member, caregiver or staff member) and performing a brief cognitive assessment may simplify the diagnosis work-up. This is fundamental because it allows to establish the patient's baseline^{9,10}. The physical examination of the delirious patient should be a comprehensive effort to find clues as to the cause of delirium. Commitment to a systematic and thorough examination may provide a key piece of data to aid rapid diagnosis. Examination begins with the vital signs, which can be critical for determine the underlying cause¹².

Work-Up

Analytical

Routine blood work-up includes electrolytes, glucose, arterial blood gas, calcium, phosphate and magnesium. Infection work-up may also be helpful – if there is a suspicion on urosepsis use urine analysis, if it's pneumonia use X-ray, if it's bacteremia take blood cultures and if it's procedure infection, make imaging on the surgical site. Clinical manifestations of infection are subtle in this group. Review the patient medication specially the one with anticholinergic activity and exclude substance abuse as alcohol and benzodiazepines^{6,12}.

Non-Analytical

Neuroimaging: Some neuroimage studies have been made and changes like brain atrophy⁹ impaired total and regional perfusion¹⁰ and ventricular dilatation and white matter lesions¹¹ were found. Magnetic Resonance Imaging (MRI) or computed tomography (CT) scans are recommended for acute neurological findings, history of or signs of recent fall or head trauma, fever with suspicion of encephalitis or decreased level of consciousness with no identified etiology. Patients with delirium can have normal CT scan in almost 98%. Lumbar puncture can be also useful when the delirium is persistent or no etiology has been pointed¹⁰ MRI may be used to study the integrity of blood-brain barrier and its role in the development of delirium. New studies with PET and SPECT imaging have been made to study cholinergic receptors and

dopaminergic activity¹¹. Even so more studies need to be made, because the ones available are limited for small samples sizes, inadequate control groups and lack of baseline scans prior to delirium^{9,10}.

Electroencephalogram (EEG)

EEG has limited sensivity and specificity in the diagnosis of delirium, however it is the result of a characteristic pattern of diffuse slowing with increased theta and delta activity and poor organization of background rhythm that correlates with its severity. It can be useful to differentiate organic etiologies from functional or psychiatric disorders in difficult-to-assess patients, to evaluate deteriorating mental status in patients with dementia and to identify occult seizures. Quantitative and spectral EEG can be useful but need further investigation¹⁰.

Delirium and Dementia

Delirium serves multiple roles: it is a marker of vulnerability, unmasks unrecognized dementia, mediates the effects of noxious insults and itself leads to permanent neuronal damage and dementia⁹.

Dementia is a chronic and progressive neurodegenerative condition, that evolves in months or years leading to deficits in the domains of cognition, decline in the functionality and with neuropsychiatric symptoms. It can be a delirium cause and its evolution may be enhanced by it^{1,8,9}.

In the clinical practice, sometimes it's difficult to distinguish between delirium and dementia^{1,4,7-11} and they may be

superimposed one another⁷⁻⁹. Both interfere with cognition, leading to its decline. Some authors refer that delirium and dementia share similarities in clinical and pathogenic features, leading to the idea that instead of being to separate clinical entities are two age-conditions linked by a common pathogenic mechanism^{1,6,8-10}. Literature shows that the presence of delirium in patients with dementia leads to bad prognosis and accelerate the trajectory of cognitive decline with patients not returning to their premorbid baseline once the acute delirium resolves^{8,9-11} leading to persistent and cognitive losses^{10,11}. It is an independent risk factor for dementia⁹. Dementia rises the risk of delirium in 2-5-fold¹⁰.

Prevention and Treatment

The treatment of delirium requires a multicomponent strategy aimed at both optimizing preventative measures in addition to pharmacologic management^{6,10-12}. It is preventable in about 30-40% of the cases⁹⁻¹¹. It is undetected in 33-66%¹³. The principal aims in the prevention and treatment of delirium is to identify the causes optimizing the environment to lessen confusion and associated distress^{8,10}. The patient safety is important, but also the active search for causes and symptom control¹⁰. There are better results when the family and the patient are involved in care, particularly for reorientation and prevention of self-harm^{10,12}. The major outcomes in the management of delirium is to focus on

treatments that enhance recovery, maximize functional status and improve clinical outcomes¹⁰.

Non-Pharmacological Measures

Due to delirium prevention, non-pharmacological strategies are the mainstay^{4,5,8,10,11}. Measures like automated medication review, education of the staff^{4,6,10,11,13} calendar or clock present in the room^{4,6} oral hygiene^{4,10} osteopathic manipulative treatment⁴ eviction of intramuscular administration and intravenous perfusions of drugs⁵, vision and hearing protocol^{6,10-12} hydration and nutrition^{6,8,10-12} removing Foley, nasogastric tubes and multiples intravenous lines^{6,12} sleep promotion^{8,10-12}, geriatric review^{10,11} managing pain, soothing music^{8,10-12} preventing skin breakdown¹⁰ early mobilization^{10,12} may be very useful. The health staff may evaluate the risk of falls, especially in the patients with hyperactive delirium and be sensible regarding to the use of restraints because its effect may be both harmful and beneficial^{11,12,16}. Most of these multicomponent interventions have good evidence in the hospital population but lack of evidence in the patients with dementia and delirium in the community⁸.

Pharmacological Approach

The pharmacological approach is reserved to patients with severe agitation^{10,12}. Targeted pharmacological approaches are usually

aimed at symptom reduction in the most severe cases but some studies point that they may have little impact altering the course of delirium and in some cases, may also aggravate the confusion⁸. The current on pharmacological agents are much more controversial and debatable⁵.

Antipsychotic medication, in low dose, is commonly used to treat patients with delirium. A review showed that all atypical antipsychotic medications demonstrate similar rates of efficacy, but haloperidol has lower rates of extrapyramidal adverse rates and no higher mortality^{4,5,6,11,12}. Another secondary effect is prolonged QT interval on the electrocardiogram^{6,11}. Dealing with that secondary effects, they may be reduced by lowering the dose or discontinuing the medication. The most acceptable initial dose for haloperidol is 2 mg orally, intramuscular or intravenous. It is possible to repeat every 15-20 minutes. The dose may be doubled if the agitation is very severe in the ICU. Regarding to the ward the dose is lower with 1 to 2 mg, with increasing of 0.25-0.5 mg every 4 hours according to the patient tolerance⁶. Other drugs may be used such as olanzapine 2,5 to 5 mg once per day, risperidone 0.5 mg orally twice per day, ziprasidone 2 mg to 5 mg intramuscular. They must be closely monitored and their use should be temporary and therefore must be reduced when symptoms are solved. There is no clear benefit for managing presumed delirium with these drugs unless severe behavioral or psychiatric symptoms are present. Terminal delirium is considered irreversible and its management involve palliative care and the use of drugs like

benzodiazepines, also useful in delirium due to alcohol and benzodiazepines withdrawal^{4,6,11,12}.

In the hypoactive delirium drugs like benzodiazepines are not recommended⁴. Quetiapine is an alternative to haloperidol and is one of the drugs of election used for treating delirium in the ICU, acting in many receptors such as 5HTA1, 5HT2, D1, D2, α 1, α 2 and histamine H1 receptors². Cholinesterase inhibitors have shown no benefit in preventing the postoperative delirium. Other drugs like gabapentin, trazodone and dexmedetomidine are being investigated¹¹.

Because there is no certified scale to evaluate hypoactive delirium, the installation of antipsychotic drugs must be careful, because hyperactive delirium can turn into hypoactive, with poor outcomes¹⁰.

Delirium in Different Scenarios

Delirium in the post-operative: Dealing with the post-operative scenario its incidence ranges from 9% to 87% depending on the population and the degree of operative stress⁶, it can be present in the first two days after surgery¹¹ and it can be present until 1 year after the surgery¹⁰. In the hospital scenario, its overall prevalence is 15% to 50%, although may be higher specially in patients undergoing major surgical procedures^{8,9,11}.

Delirium outside the hospital: When talking in post-acute care (PAC) and long-term care (LTC), delirium is very frequent in the elder (18%)^{4,11}. Its development is more insidious and subtle in presentation, despite

systemic screening tools. LTC patients are 10 times more likely to have delirium than the ones that are not in LTC settings. Attention that the presence of residual sub-syndromal delirium at the time of hospital discharge also predicts adverse outcomes^{4,12}. The symptoms may persist weeks of months after its initial recognition^{4,5}.

Delirium in the ICU: Patients who develop delirium in the ICU are 2-4-fold increased risk of death both in and out of the hospital, those who develop delirium on general medical or geriatric wards are at 1,5-fold increased risk for death in the year following hospitalization and patients with delirium in the emergency department have approximately 70% increased risk of death during the first six months after the visit^{10,11}.

Emergency Department

On the presentation to the emergency department, delirium is present in 8-17% of all seniors and 40% of nursing home residents¹⁰.

Community: Delirium in the community is just 1% to 2%¹¹.

Prognosis

Delirium is consistently associated with an increased mortality rate across all nonsurgical patient populations, including general medical, geriatric, intensive care unit (ICU), stroke, dementia, nursing home and emergency department¹⁰. Patients with delirium have longer hospital stays and

longer 6-month survival than do patients without delirium^{2,7,8,10}.

If the treatment is successful in the ICU scenario, it may decrease morbidity, the number of sedative agents used, length of ventilator days and associated complications². Studies show a mortality of 40% with 1-2 days of delirium, which rose to 70% if delirium persisted for more than 5 days, in the ICU. The longer the delirium, higher is the mortality rate^{3,5,10,11}. When the delirium resolves, the prognosis improves³.

Complications Related to Delirium

At least 20% of the 12,5 million patients over 65 years of age hospitalized each year in the US experience complications during hospitalization because of delirium¹¹.

Delirium makes the hospital stay longer, increases immobility leading to delayed admission to rehabilitation programs, leads to autonomy persistent cognitive deficits, enhances health cost^{5-9,12} promotes harmful behaviors like falls, pulled lines or tubes, aspiration pneumonia and respiratory compromise^{6,9} decreases oral intake with dehydration and malnutrition and also increases the incidence of pressure ulcers, urinary tract infections, deep venous thrombosis and pulmonary emboli^{9,11}.

CONCLUSION

Nowadays it remains difficult the diagnosis of delirium because its many presentations. Consequently, it remains underdiagnosed and sub treated in the most different patient scenarios – ward, ICU, PLC, community.

The earlier it is diagnosed, less complications are linked to the patient, with substantial reduction in the its morbidity and mortality and with lower direct and indirect health costs. Non-pharmacological and pharmacological strategies are eligible, specially the first ones. Haloperidol is the most used drug, with a good safety profile.

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