



Pharmacological management of acute confusional state in Latin America

Manejo farmacológico del Síndrome Confusional Agudo en América Latina

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Submitted: 30-03-2024 | Revised: 03-06-2024 | Accepted: 05-07-2024 | Published: 06-07-2024

ABSTRACT

Acute confusional syndrome (ACS) was described as an acute and fluctuating mental disorder, common in older adults hospitalised in Latin America. The pharmacological use of haloperidol and benzodiazepines in its treatment was analysed. Haloperidol was widely used due to its efficacy and low cost, although warnings were given about its adverse effects, such as extrapyramidal symptoms and arrhythmias. Benzodiazepines were reserved for cases of alcohol withdrawal due to their cognitive and respiratory risks. The importance of monitoring, prevention and staff training protocols was emphasised in order to improve the management of ACS in the region.

Keywords: haloperidol; benzodiazepines; delirium; hospitalization; monitoring

RESUMEN

El síndrome confundido agudo (SCA) se describió como un trastorno mental agudo y fluctuante, común en adultos mayores hospitalizados en América Latina. Se analizó el uso farmacológico de haloperidol y benzodiacepinas en su tratamiento. El haloperidol se utilizó ampliamente debido a su eficacia y bajo coste, aunque se advirtieron sobre sus efectos adversos, como síntomas extrapiramidales y arritmias. Las benzodiacepinas se reservaron para casos de abstinencia alcohólica debido a sus riesgos cognitivos y respiratorios. Se destacó la importancia de los protocolos de monitorización, prevención y formación del personal para mejorar la gestión del ACS en la región.

Palabras clave: haloperidol; benzodiacepinas; delirio; hospitalización; Monitorización

INTRODUCTION

Acute Confusional Syndrome (ACS), more commonly referred to in the international medical literature as delirium, is an acute neuropsychiatric syndrome characterized by disturbances in attention, awareness, and cognition that develop over a short period and tend to fluctuate throughout the day.(1,2) It is particularly frequent among hospitalized older adults, critically ill patients, individuals undergoing major surgical procedures, and patients with multiple chronic diseases. Unlike dementia, which usually follows a progressive course, delirium typically has an abrupt onset and is frequently associated with an identifiable underlying medical condition, exposure to medications, metabolic abnormalities, infection, surgery, pain, dehydration, or environmental factors.(3)

Delirium represents an important clinical problem because its presence is associated with unfavorable outcomes, including longer hospitalization, functional deterioration, institutionalization, cognitive decline, increased healthcare utilization, and mortality.(4) Despite its clinical relevance, the syndrome frequently remains underrecognized, particularly in its hypoactive form, in which patients may appear quiet, somnolent, withdrawn, or minimally responsive rather than agitated. This clinical heterogeneity makes systematic assessment and early identification fundamental components of patient management.(5)

The treatment of delirium is complex because the syndrome itself is usually a manifestation of another medical problem rather than an isolated disease. Consequently, identification and correction of precipitating causes constitute the central therapeutic objective. Pharmacological treatment occupies a more limited and specific role and should generally be considered when behavioral or perceptual disturbances produce severe distress, interfere with essential medical treatment, or create a risk of harm to the patient or other people.(6)

This distinction is especially important in older adults, who frequently have polypharmacy, cardiovascular disease, renal or hepatic impairment, neurodegenerative disorders, and increased susceptibility to adverse drug reactions. The decision to prescribe medication for delirium therefore requires careful assessment of the expected benefit, potential toxicity, underlying cause, clinical subtype, and characteristics of the individual patient.(7)

In Latin America, these principles must additionally be considered within heterogeneous healthcare systems. Differences in hospital infrastructure, availability of specialists, access to medications, monitoring capacity, professional training, and socioeconomic resources can influence how delirium is recognized and treated. The progressive aging of populations in Latin America and the growing burden of chronic neurological and cardiovascular diseases reinforce the importance of developing safe and context-appropriate approaches to delirium management.(8)

DEVELOPMENT

Pharmacological management should not replace the identification and treatment of the underlying cause of delirium. A patient presenting with acute confusion requires evaluation for potentially reversible precipitating factors such as infection, hypoxemia, dehydration, electrolyte abnormalities, hypoglycemia or hyperglycemia, organ failure, uncontrolled pain, urinary retention, constipation, sleep disruption, drug toxicity, medication withdrawal, and adverse pharmacological interactions.(9) In many cases, correction of these factors can improve delirium without the need for prolonged psychotropic treatment.

Medication review is particularly important because hospitalized older adults are frequently exposed to multiple agents capable of contributing to delirium. Drugs with anticholinergic activity, sedative agents, opioids, corticosteroids, benzodiazepines, and combinations of centrally acting medications may alter cognition or precipitate behavioral changes in susceptible patients.(10) Consequently, pharmacological management involves not only deciding which medication to administer but also identifying medications that can be reduced, discontinued, or replaced when clinically appropriate.

Non-pharmacological strategies constitute an essential component of delirium treatment and should be implemented alongside correction of precipitating causes. Measures such as frequent orientation, maintenance of an appropriate sleep-wake cycle, adequate hydration and nutrition, early mobilization, pain control, provision of hearing aids or eyeglasses when needed, reduction of unnecessary environmental stimuli, and family involvement can help reduce factors that contribute to confusion.(11) Pharmacological therapy should therefore be understood as part of a broader therapeutic strategy rather than as the sole intervention.

Antipsychotics have traditionally occupied an important position in the symptomatic phar-

macological management of delirium, particularly when patients develop severe agitation, hallucinations, delusions, aggression, or behavior that compromises medical care. Haloperidol is one of the most extensively used agents for this purpose and remains available in many hospital settings because of its long clinical experience, multiple routes of administration, and relatively limited anticholinergic activity compared with some other psychotropic medications.(12)

However, current evidence does not support the indiscriminate use of haloperidol in every patient with delirium. Its principal role is the short-term control of severe symptoms in carefully selected patients rather than routine treatment of the underlying delirium itself.(13) Patients who are calm, cooperative, or presenting predominantly with hypoactive delirium generally do not require antipsychotic treatment solely because delirium has been diagnosed.

When haloperidol is considered necessary, conservative dosing is particularly important in older adults. The lowest effective dose should be used and treatment duration should be as short as clinically feasible.(13) Repeated evaluation is necessary to determine whether continued administration remains justified once agitation or severe behavioral symptoms have resolved.

The adverse-effect profile of haloperidol requires specific consideration. Extrapyramidal manifestations such as rigidity, tremor, akathisia, dystonia, and parkinsonism may occur, particularly with higher cumulative exposure. Cardiovascular effects are also clinically important because haloperidol can prolong ventricular repolarization and the QT interval, potentially increasing the risk of ventricular arrhythmias in susceptible individuals.(14)

Before and during treatment, clinicians should therefore evaluate relevant risk factors, including previous QT prolongation, cardiac disease, electrolyte abnormalities, concomitant QT-prolonging medications, and other circumstances that could increase arrhythmic risk. Electrocardiographic monitoring may be warranted according to the patient's clinical condition, medication exposure, route of administration, and institutional protocols.(14)

Particular caution is required in patients with Parkinson's disease or dementia with Lewy bodies because dopamine-blocking antipsychotics may aggravate motor manifestations or produce severe sensitivity reactions. In such situations, treatment must be individualized and alternatives may need to be considered when pharmacological control is unavoidable.(15)

Atypical antipsychotics, including quetiapine, olanzapine, and risperidone, have also been used for the symptomatic treatment of delirium. They are sometimes considered when haloperidol is poorly tolerated or when the patient's neurological characteristics make extensive dopamine blockade undesirable.(15) Nevertheless, these medications are not free from adverse effects and available evidence does not establish that routine administration of atypical antipsychotics resolves the underlying syndrome or consistently shortens its duration.

The absence of a universal pharmacological solution highlights an important principle: suppression of visible agitation should not be confused with successful treatment of delirium. Sedation may make a patient appear behaviorally improved while the underlying infection, metabolic disorder, drug toxicity, hypoxia, or other precipitating condition remains unresolved.(16) Clinical success should therefore be evaluated in terms of correction of causes, recovery of attention and cognition, functional status, safety, and overall clinical evolution rather than solely by reduction of disruptive behavior.

Benzodiazepines occupy a different position in the pharmacological management of delirium. Agents such as lorazepam can be appropriate when delirium is related to alcohol withdrawal or withdrawal from sedative-hypnotic drugs.(17) In these circumstances, benzodiazepines address an important component of the underlying pathophysiological mechanism and can be essential to prevent complications associated with severe withdrawal.

Outside these specific situations, routine benzodiazepine administration for delirium is generally discouraged. Benzodiazepines can produce excessive sedation, respiratory depression, impaired balance, falls, and deterioration of cognitive function, particularly among frail older adults.(17) They may also make subsequent neurological assessment more difficult because medication-induced sedation can obscure changes in consciousness and cognition.

This does not mean that benzodiazepines have no role outside withdrawal syndromes. Their use may be justified in selected circumstances, including particular palliative-care situations or when other therapeutic options are inappropriate. Nevertheless, such decisions should be individualized, with explicit consideration of therapeutic objectives and potential adverse consequences.(18)

The intensive care unit constitutes another important clinical context. Delirium in critically ill patients can arise from severe illness, mechanical ventilation, sedation, infection, organ dysfunction, sleep disruption, immobilization, and numerous medications. In this setting, pharmacological decisions may differ from those made on conventional medical wards, and sedative strategies

must be integrated with ventilatory status, hemodynamic condition, pain management, and the possibility of reducing unnecessary sedation.(18)

Dexmedetomidine has attracted interest in critical care because of its sedative profile and its potential usefulness in selected mechanically ventilated patients. Nevertheless, its indication cannot simply be extrapolated to every patient with delirium, and its use requires appropriate monitoring because clinically important cardiovascular effects, including bradycardia and hypotension, can occur.(18)

An additional challenge is polypharmacy. Older adults admitted to Latin American hospitals frequently have multiple chronic disorders and may receive numerous medications simultaneously. The addition of an antipsychotic or sedative can generate drug interactions and increase cumulative adverse effects.(10,19) A structured medication reconciliation process is therefore fundamental when acute cognitive changes appear.

The pharmacological approach should also distinguish among hyperactive, hypoactive, and mixed presentations of delirium. Hyperactive delirium is characterized by agitation, restlessness, emotional lability, hallucinations, or aggressive behavior and is more likely to attract immediate clinical attention. Hypoactive delirium, by contrast, can manifest as lethargy, reduced spontaneous movement, diminished interaction, and somnolence.(5) Because these patients are not disruptive, the condition can be overlooked or incorrectly interpreted as depression, fatigue, or progression of dementia.

This distinction has therapeutic implications. A patient with hypoactive delirium should not automatically receive stimulating or antipsychotic medication. Treatment should instead focus on identifying the underlying precipitating factors, restoring physiological stability, minimizing unnecessary psychoactive drugs, and implementing supportive measures.(16)

In Latin America, the implementation of these principles is influenced by substantial differences in healthcare resources. Large tertiary hospitals in major cities may have geriatricians, neurologists, psychiatrists, intensivists, pharmacists, continuous cardiac monitoring, and access to several pharmacological alternatives. Smaller hospitals and healthcare facilities may operate with a more restricted formulary and limited availability of specialized personnel or diagnostic monitoring.(8,19)

Cost and availability may partly explain the continued frequent use of traditional drugs such as haloperidol in many settings. However, low acquisition cost alone should not determine therapeutic selection. The complete clinical cost includes adverse events, additional monitoring, falls, cardiovascular complications, prolonged hospitalization, and the consequences of inappropriate sedation.(19) Rational pharmacotherapy therefore requires balancing accessibility with efficacy, safety, and patient-specific characteristics.

Training of healthcare professionals is another critical element. Nurses, general practitioners, emergency physicians, internists, geriatricians, intensivists, and pharmacists all participate in the detection and management of delirium. Failure to recognize its fluctuating characteristics or to differentiate delirium from dementia, psychiatric disease, or medication-induced sedation can delay appropriate intervention.(5,20)

Standardized institutional protocols could improve management by establishing procedures for screening, etiological investigation, medication review, non-pharmacological interventions, indications for antipsychotic use, dosing precautions, ECG assessment when appropriate, benzodiazepine restrictions, and criteria for treatment discontinuation. Such protocols are especially relevant in environments where specialist consultation is not continuously available.(20)

The Latin American context also requires attention to equity. Older adults receiving care in resource-limited institutions should not be exposed to unnecessarily higher pharmacological risk simply because diagnostic alternatives or specialized services are unavailable. Strategies adapted to local resources can prioritize interventions with high clinical value, including early recognition, medication reconciliation, correction of reversible causes, basic laboratory assessment, adequate hydration, orientation, mobilization, rational use of psychotropic agents, and clear referral criteria.(8,20)

Future research in the region should evaluate not only which medications are used but also how, why, and in which patients they are administered. Studies comparing prescribing patterns, dosing, duration of treatment, adverse events, monitoring practices, and clinical outcomes among Latin American countries could identify important variations in practice. Regional evidence would also help determine whether international recommendations can be implemented directly or require adaptation to different healthcare environments.

FINAL CONSIDERATIONS

Acute Confusional Syndrome or delirium is a complex clinical syndrome whose management cannot be reduced to the administration of a specific psychotropic medication. The first therapeutic objective is to identify and correct its underlying causes while simultaneously implementing supportive and non-pharmacological interventions. Pharmacological therapy should be reserved for clearly defined clinical situations and periodically reassessed.(6,9)

Haloperidol continues to have a role in the short-term management of severe agitation, psychotic symptoms, or behavior that compromises patient safety or essential treatment. Nevertheless, its use requires careful patient selection, conservative dosing, limited duration, and attention to extrapyramidal and cardiovascular adverse effects.(12-14) It should not be interpreted as a universal treatment for every patient diagnosed with delirium.

Benzodiazepines have a more restricted indication and are particularly important in delirium associated with alcohol or sedative withdrawal. Routine administration in other forms of delirium may cause excessive sedation and cognitive and respiratory complications and should therefore be avoided unless a specific clinical indication exists.(17,18)

Other pharmacological alternatives, including atypical antipsychotics and selected sedative agents used in critical care, may be appropriate in particular circumstances, but none eliminates the need for etiological assessment and comprehensive patient management. The choice of medication should be individualized according to the clinical presentation, comorbidities, concurrent medications, cardiovascular and neurological risk, monitoring capacity, and therapeutic objectives.

For Latin America, improving the management of delirium requires more than expanding access to medications. It requires systematic screening, professional education, medication safety programs, standardized institutional protocols, access to appropriate monitoring, and research capable of describing regional prescribing patterns and outcomes.(19,20) These strategies are particularly important as population aging increases the number of vulnerable older adults treated in hospitals and other healthcare facilities.

Ultimately, rational pharmacological management of delirium in Latin America should seek to use the minimum necessary medication for the shortest appropriate period while prioritizing identification of reversible causes and protection of patient safety. A standardized but adaptable approach, supported by clinical evidence and adjusted to available resources, could reduce unnecessary pharmacological exposure, improve recognition of the syndrome, and contribute to safer and more equitable care for older and critically ill patients throughout the region.(20)

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FUNDING

None.

CONFLICT OF INTEREST

None.

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