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ONE MINUTE CONSULT
BRIEF ANSWERS TO SPECIFIC CLINICAL QUESTIONS

Q: How can I better recognize and manage delirium in my hospitalized patients?

A: The following 4 steps can help clinicians to better recognize delirium: (1) familiarize yourself with the 3 phenotypes of delirium (hyperactive, hypoactive, and mixed) that describe the associated motor activity in patients with delirium; (2) take into account the patient's baseline mental status, medical history, and timeline of symptom onset; (3) use a delirium assessment tool; and (4) consider ordering an electroencephalogram.

Managing delirium in the hospital begins with prevention. There are numerous nonpharmacologic, multicomponent interventions to consider that include having the family at the bedside (as much as possible) and minimizing unnecessary overnight care that interrupts sleep. While there is no medication currently approved by the US Food and Drug Administration for the management of delirium, antipsychotics have historically been used to treat delirium-related agitation in hyperactive and mixed subtypes. Dexmedetomidine is often used for agitation in the intensive care unit (ICU) setting. There also has been growing interest in the use of clonidine and guanfacine. However, adverse cardiovascular effects, including hypotension and bradycardia, can limit the use of alpha-2 agonists.

KNOW THE 3 PHENOTYPES (BECAUSE DELIRIUM IS OFTEN MISSED)

Delirium, also known as encephalopathy, has an acute onset and is characterized by a fluctuating disturbance in attention and cognition that is accompanied by reduced environmental awareness. As delirium is a direct consequence of an underlying insult, such as another medical condition, toxin or medication exposure, or substance intoxication and withdrawal (or from multiple etiologies), it is commonly encountered in the acute hospital setting.[1] Estimated incidence during hospitalization ranges from 11% to 14% on general medical services, 20% to 29% on geriatric services, and up to 82% in the ICU.[2] This carries important implications, as delirium has been associated with increased risk of functional impairment, cognitive impairment, and mortality.[3,4]

Although delirium is a clinical diagnosis, the identification of delirium can be difficult because the way it manifests can vary by phenotype. Diagnosis is further confounded by delirium's waxing and waning course. Given these challenges, it is estimated that up to 70% of patients with delirium go undiagnosed.[5] Therefore, familiarity with the nuances of how delirium can manifest is crucial in early identification and treatment. The 3 phenotypes of delirium are hyperactive, hypoactive, and mixed, which describe the associated observed motor activity (**Table 1**).[6]

- **Hyperactive** delirium is typically associated with agitated behaviors, such as hypervigilance, restlessness, hallucinations, thought disorganization, elevated or irritable mood, and increased or loud speech. Clinically, this can manifest with the patient removing lines or medical devices, attempting to get out of bed, and experiencing disrupted sleep-wake cycles.
- Patients with **hypoactive** delirium, in contrast, often present with apathy, lethargy, psychomotor slowing, staring, decreased alertness, and reduced engagement in care.
- The **mixed** phenotype shares features of both hyperactive and hypoactive delirium.[6]

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TABLE 1
Delirium subtypes and features

Delirium subtype	Features
Hyperactive	Agitation Hypervigilance Restlessness Hallucinations Thought disorganization Elevated or irritable mood Increased or loud speech
Hypoactive	Apathy Staring Lethargy Decreased alertness Psychomotor slowing Reduced engagement in care
Mixed	Features of hyperactive and hypoactive subtypes

Based on information from reference 6.

TOOLS FOR RECOGNIZING DELIRIUM

Delirium is a common cause for psychiatric and neurologic consultations because it can mimic not only primary psychiatric disorders, such as mood, anxiety, and psychotic disorders, but also neurocognitive disorders, strokes, and seizures.[7] Therefore, knowledge of a patient's baseline mental status, medical history (such as underlying health conditions, recent medication changes, or hospitalizations), and timeline of symptom onset is essential in accurately assessing for delirium.

There are multiple clinical instruments to assist with both screening for delirium and determining its severity, with the Confusion Assessment Method being among the most widely used.[3,8] The 4 A's Test has also gained in popularity in identifying delirium because it is accurate (sensitivity = 0.88, 95% confidence interval 0.80–0.93; specificity = 0.88, 95% confidence interval 0.82–0.92) and quick to administer and does not require special training to use.[8] In a 2019 systematic review by Jones et al,[9] the Confusion Assessment Method, Delirium Rating Scale, and Memorial Delirium Assessment Scale were the most commonly used instruments to assess delirium severity.

The electroencephalogram is an additional tool that can be used when assessing for delirium. However, it does not currently have utility in predicting additional details such as risk, phenotype, or underlying causes of delirium.[10] Generalized slowing is a common finding of delirium on electroencephalogram.

HOW TO OPTIMIZE MANAGEMENT OF DELIRIUM

Nonpharmacologic approaches

Delirium management starts with prevention. In the ICU setting, this is best achieved through the ABCDEF bundle (assess, prevent, and manage pain; both spontaneous awakening and breathing trials; choice of analgesia and sedation; delirium assessment, prevention, and management; early mobility and exercise; family engagement and empowerment), which has been associated with a lower likelihood of delirium in a large, prospective, multicenter cohort study.[11]

There is also moderate-quality evidence supporting the use of nonpharmacologic, multicomponent interventions (colloquially known as "delirium precautions") in non-ICU hospital settings, as found in a 2021 Cochrane Review.[12] This review found that the interventions are likely effective in lowering the incidence of delirium in these settings by about 43%, and there is potential for their role in decreasing hospital length of stay.[12] There was less evidence to support these interventions in reducing delirium severity. In terms of interventions, the evidence appears strongest for reorientation, cognitive stimulation, and sleep hygiene in reducing delirium. There is less evidence for attending to nutrition, hydration, oxygenation, and bowel and bladder care; however, these interventions carry low risk. Additional techniques to reduce delirium include having family members at the bedside as much as possible, providing sensory aides (glasses, hearing aids), maintaining mobility, and minimizing unnecessary overnight care to promote uninterrupted sleep.

It is also important to minimize the use of restraints. While restraints can prevent a patient from harming themselves or others, early mobility (rather than restraint) prevents deconditioning and decreases days spent in delirium.[13] When restraints are needed, the healthcare team should use the least restrictive restraint for the shortest amount of time in an effort to prevent adverse outcomes.

Overall, these "precautions" represent low-risk, potentially high-benefit strategies to decrease the risk of delirium during hospitalization.

Pharmacologic approaches

The mainstay of delirium treatment has been to recognize and manage the underlying cause of the delirium. While the symptoms of delirium, such as agitation, hallucinations, or sleep-wake cycle disturbances, may require pharmacologic intervention, the current literature supports the use of pharmacotherapy as a means of symptom management rather than as a disease-

modifying treatment.[14] The challenges have been the limited evidence for pharmacotherapy-based treatment across delirium subtypes and the fact that no medication is approved by the US Food and Drug Administration for management of delirium.

Antipsychotics have been used for years in the treatment of delirium-related agitation in both hyperactive and mixed subtypes. Unfortunately, antipsychotics have limited evidence to support reductions in either severity or length of delirium.[14] Haloperidol, one of the more frequently studied antipsychotics in this population, has been shown to reduce agitation and improve outcomes in some, but not all, studies. Atypical (second-generation) antipsychotics, particularly risperidone, olanzapine, and quetiapine, also have been shown to improve agitation, but their antihistaminergic, antiadrenergic, and anticholinergic properties raise concerns over increased sedation, hypotension, and potential worsening of confusion.[14] When used, antipsychotics should be prescribed at the lowest effective dose and discontinued once delirium has resolved.

Dexmedetomidine, a commonly used intravenous alpha-2 agonist for agitation in the ICU setting, has been shown to decrease time on mechanical ventilation, length of ICU stay, and potentially length of delirium when compared with antipsychotics.[14] There has also been growing interest in both clonidine and guanfacine for delirium management, given that they have a similar mechanism of action to dexmedetomidine.[14,15] Guanfacine has been found to be beneficial, but clonidine remains controversial. Use of alpha-2 agonists can be limited because of adverse cardiovascular effects, including hypotension and bradycardia. A small retrospective study (N = 46) found that valproic acid may also reduce agitation and possibly length of delirium in critical care patients.[16] Although primarily studied in ICU populations, guanfacine, clonidine, and valproic acid may also be considered for use in patients on general medical floors given the various routes of administration.

For hypoactive delirium, there is currently limited evidence to support the use of medications, including antipsychotics and stimulants.[7]

Outside of agitation, the regulation of the circadian rhythm is an important component of delirium management. While melatonin is often prescribed to help restore disrupted sleep-wake cycles in patients with delirium, the evidence for its role in reducing (and even preventing) delirium incidence remains mixed.[14,17,18]

THE BOTTOM LINE

Delirium evaluation and management remain challenging, given delirium's multiple etiologies and varying manifestations across motor phenotypes, as well as the limited evidence for pharmacologic interventions. This highlights the importance of nonpharmacologic interventions in reducing the risk of delirium. By familiarizing themselves with common precipitants, mimickers, and considerations for workup, clinicians can implement nonpharmacologic strategies for prevention, better identify patients who are experiencing delirium, and optimize symptom management.

DISCLOSURES

The authors report no relevant financial relationships which, in the context of their contributions, could be perceived as a potential conflict of interest.

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