THE JOURNAL OF FAMILY PRACTICE

Abdulraouf Ghandour, MD; Rola Saab, MD; David R. Mehr, MD, MS
Geriatric fellow (Dr. Ghandour), Family and Community Medicine (Drs. Saab and Mehr), University of Missouri-Columbia

Ghandour78@gmail.com

The authors reported no potential conflict of interest relevant to this article.

Detecting and treating delirium—key interventions you may be missing

Early identification of risk factors for delirium and routine use of screening are often overlooked—with dire effects. Here's what to look for and how to respond.

PRACTICE RECOMMENDATIONS

› *Nonpharmacologic interventions are the mainstay of treatment for delirium.* (B)

› *When medication is needed, atypical antipsychotics are as effective as typical antipsychotics for treating delirium in elderly patients, and have fewer side effects.* (B)

› *Benzodiazepines should be avoided in elderly patients with delirium that is not associated with alcohol withdrawal.* (A)

Strength of recommendation (SOR)

(A) Good-quality patient-oriented evidence
(B) Inconsistent or limited-quality patient-oriented evidence
(C) Consensus, usual practice, opinion, disease-oriented evidence, case series

CASE► Mr. D, a 75-year-old patient with a history of hypertension and congestive heart failure, sustained a femoral neck fracture and was admitted to the hospital for surgery. He underwent open reduction and internal fixation and was doing well postoperatively, until Day 2—when his primary care physician made morning rounds and noted that Mr. D was somnolent. The nurse on duty assured the physician that Mr. D was fine and "was awake and alert earlier," and attributed his somnolence to the oxycodone (10 mg) the patient was taking for pain. The physician ordered a reduction in dosage.

If Mr. D had been your patient, would you have considered other possible causes of his somnolence? Or do you think the physician's action was sufficient?

Derived from Latin, the word delirium literally means "off the [ploughed] track."[1] Dozens of terms have been used to describe delirium, with acute confusion state, organic brain syndrome, acute brain syndrome, and toxic psychosis among them.

Delirium has been reported to occur in 15% to 30% of patients on general medical units,[2] about 40% of postoperative patients, and up to 70% of terminally ill patients.[3] The true prevalence is hard to determine, as up to 66% of cases may be missed.[4]

Delirium is being diagnosed more frequently, however—a likely result of a growing geriatric population, increased longevity, and greater awareness of the condition. Each year, an estimated 2.3 million US residents are affected, leading to prolonged hospitalization; poor functional outcomes; the development or worsening of dementia; increased nursing home placement; and a significant burden for families and the US health care system.[5]

Delirium is also associated with an increase in mortality.[6,7] The mortality rate among hospitalized patients who de-

TABLE 1

Risk factors for delirium[8-14]

Advanced age
Alcohol use
Brain dysfunction (dementia, epilepsy)
Hypertension
Male sex
Malignancy
Medications (mainly anticholinergic)
Metabolic abnormalities:
- Na <130 or >150 mEq/L
- Glucose <60 or >300 mg/dL
- BUN/Cr ratio >20
Old age
Preoperative anemia
Preoperative metabolic abnormalities

BUN, blood urea nitrogen; Cr, creatinine; Na, sodium.

velop delirium is reported to be 18%, rising to an estimated 47% within the first 3 months after discharge.[6] Greater awareness of risk factors, rapid recognition of signs and symptoms of delirium, and early intervention—detailed in the text and tables that follow—will lead to better outcomes.

Assessing risk, evaluating mental status

In addition to advanced age, risk factors for delirium (**TABLE 1**)[8-14] include alcohol use, brain dysfunction, comorbidities, hypertension, malignancy, anticholinergic medications, anemia, metabolic abnormalities, and male sex. In patients who, like Mr. D, have numerous risk factors, early—and frequent—evaluation of mental status is needed. One way to do this is to treat mental status as a vital sign, to be included in the assessment of every elderly patient.[15]

The Confusion Assessment Method, a quick and easy-to-use delirium screening tool (**TABLE 2**), has a sensitivity of 94% to 100% and a specificity of 90% to 95%.[16,17] There are a number of other screening tools, including the widely used Mini-Mental State Exam (MMSE), as well as the Delirium Rating Scale, Delirium Symptom Interview, and Delirium Severity Scale.

Arriving at a delirium diagnosis

The clinical presentation of delirium is characterized by acute—and reversible—impairment of cognition, attention, orientation, and memory, and disruption of the normal sleep/wake cycle. The *Diagnostic and Statistical Manual of Mental Disorders* (DSM-IV-TR) criteria for a delirium diagnosis include all of the following:

- **disturbance of consciousness**, with a reduced ability to focus, sustain, or shift attention
- **change in cognition**, or a perceptual disturbance, that is not accounted for by a preexisting or developing dementia
- **rapid onset** of cognitive impairment, with fluctuation likely during the course of the day
- **evidence from the history, physical exam, or laboratory findings** that the disturbed consciousness is a direct physiological consequence of a general medical condition.[17]

There are 3 basic types of delirium, each associated with a different psychomotor disturbance.

1. **Hyperactive delirium—**the least common—is characterized by restlessness and agitation, and is therefore the easiest to diagnose.
2. **Hypoactive delirium** is characterized by psychomotor retardation and hypoalertness. It is often misdiagnosed as depression, and has the poorest prognosis.
3. **Mixed delirium**—the most common—is characterized by symptoms that fluctuate between hyper- and hypoactivity.[18]

CASE ▶ By lunchtime, Mr. D had awakened; however, he needed help with his meal. After eating, he slept for the rest of the day. At night, a nurse paged the resident to report that the patient's blood pressure was 82/60 mm Hg and his heart rate was 115. The physician ordered an intravenous fluid bolus, which corrected the patient's hypotension, but only temporarily.

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Treat mental status as a vital sign, to be included in the assessment of every elderly patient.

TABLE 2

Screening for delirium: The Confusion Assessment Method*[16,17]

Criteria	Evidence *Yes to questions 1, 2,* and *3 plus 4* or *5 (or both) suggests a delirium diagnosis*
1. Acute onset	Is there evidence of an acute change in mental status from the patient's baseline?
2. Fluctuating course	Did the abnormal behavior fluctuate during the day—ie, tend to come and go or increase and decrease in severity?
3. Inattention	Did the patient have difficulty focusing attention, eg, being easily distractible or having difficulty keeping track of what was being said?
PLUS	
4. Disorganized thinking	Was the patient's thinking disorganized or incoherent, such as rambling or irrelevant conversation, unclear or illogical flow of ideas, or unpredictable switching from subject to subject?
5. Altered level of consciousness	Would you rate the patient's level of consciousness as (any of the following): – Vigilant (hyperalert) – Lethargic (drowsy, easily aroused) – Stupor (difficult to arouse) – Coma (unarousable)

*CAM shortened version worksheet.

Adapted from: Inouye SK et al. Clarifying confusion: the Confusion Assessment Method. A new method for detection of delirium. *Ann Intern Med.* 1990;113:941-948; Inouye SK. *Confusion Assessment Method (CAM): Training Manual and Coding Guide*. Copyright 2003, Hospital Elder Life Program, LLC.

Brain imaging is not usually indicated for delirium, but may be used when the patient's condition continues to deteriorate while the underlying cause is unidentified.

The fluctuating nature of delirium—most notably, in patients' level of alertness—is helpful in establishing a diagnosis. The history and physical exam are the gold standard tools, both for diagnosing delirium and identifying the underlying cause (**TABLE 3**).[19,20] A review of the patient's medications should be a key component of the medical history, as drugs—particularly those with anticholinergic properties—are often associated with delirium. Environmental shifts, including hospitalization and a disruption of the normal sleep/wake cycle, endocrine disorders, infection, and nutritional deficiencies are also potential causes of delirium, among others.

If history and physical exam fail to identify the underlying cause, laboratory testing, including complete blood count, complete metabolic profile, and urinalysis, should be done. Brain imaging is usually not needed for individuals with symptoms of delirium, but computed tomography (CT) may be indicated if a patient's condition continues to deteriorate while the underlying cause remains unidentified.[21] Electroencephalography (EEG) may be used to confirm a delirium diagnosis that's uncertain, in a patient with underlying dementia, for instance. (In more than 16% of cases of delirium, the cause is unknown.[22])

The most common structural abnormalities found in patients with delirium are brain atrophy and increased white matter lesions, as well as basal ganglia lesions.[23] Single-photon emission CT (SPECT) shows a reduction of regional cerebral perfusion by 50%,[24] while EEG shows slowing of the posterior dominant rhythm and increased generalized slow-wave activity.[25]

Treating (or preventing) delirium: Start with these steps

Nonpharmacologic interventions are the mainstay of treatment for patients with delirium, and may also help to prevent the development of delirium in patients at risk. One key measure is to correct, or avoid, disruptions

TABLE 3

A DELIRIUM mnemonic to get to the heart of the problem[19,20]

Cause	Comment
Drugs	*Drug classes:* Anesthesia, anticholinergics, anticonvulsants, antiemetics, antihistamines, antihypertensives, antimicrobials, antipsychotics, benzodiazepines, corticosteroids, hypnotics, H2 blockers, muscle relaxants, NSAIDs, opioids, SSRIs, tricyclic antidepressants *Drugs:* digoxin, levodopa, lithium, theophylline *OTCs:* henbane, Jimson weed, mandrake, *Atropa belladonna* extract
Environmental	Change of environment, sensory deprivation, sleep deprivation
Endocrine	Hyperparathyroidism, hyper-/hypothyroidism
Low perfusion	MI, pulmonary embolism, CVA
Infection	Pneumonia, sepsis, systemic infection, UTI
Retention	Fecal impaction, urinary retention
Intoxication	Alcohol, illegal drugs/drug overdose
Undernutrition	Malnutrition, thiamin deficiency, vitamin B12 deficiency
Metabolic	Acid-base disturbances, fluid and electrolyte abnormalities, hepatic or uremic encephalopathy, hypercarbia, hyper-/hypoglycemia, hyperosmolality, hypoxia
Subdural	History of falls

CVA, cerebrovascular accident; MI, myocardial infarction; NSAIDs, nonsteroidal anti-inflammatory drugs; OTCs, over-the-counter agents; SSRIs, selective serotonin reuptake inhibitors; UTI, urinary tract infection.

in the patient's normal sleep/wake cycle—eg, restoring circadian rhythm by avoiding, to the extent possible, awakening the patient at night for medication or vital signs. Preventing sensory deprivation, by ensuring that the patient's eyeglasses and hearing aid are nearby and that there is a clock and calendar nearby and adequate light, is also helpful. Other key interventions (**TABLE 4**)[26-28] include:

- limiting medications associated with delirium (and eliminating any nonessential medication)
- improving nutrition and ambulation
- correcting electrolyte and fluid disturbances
- treating infection
- involving family members in patient care
- ensuring that patients receive adequate pain management
- avoiding transfers (if the patient is hospitalized) and trying to secure a single room.

Several studies have evaluated the effectiveness of nonpharmacologic interventions in preventing or lowering the incidence of delirium. A large multicomponent delirium prevention study of patients >70 years on general medical units focused on managing risk factors. The interventions studied included (1) avoidance of sensory deprivation, (2) early mobilization, (3) treating dehydration, (4) implementing noise reduction strategies and sleep enhancement programs, and (5) avoiding the use of sleep medications. These interventions proved to be effective not only in lowering the incidence of delirium, but in shortening the duration of delirium in affected patients (NNT=20).[27]

One study found that proactively using a geriatric consultation model (ie, implementing standardized protocols for the management of 6 risk factors) for elderly hospitalized patients led to a reduction in the incidence of delirium by more than a third.[26] Admission to

One study revealed that hospitalization on a geriatric unit was associated with a lower incidence of delirium compared with being on a general medical unit.

TABLE 4

Helpful interventions in the hospital or at home[26-28]

- Avoid sensory deprivation (provide hearing aids, eyeglasses, clock, calendar, adequate light)
- Avoid patient transfers; consider using private rooms
- Be especially vigilant in monitoring for postoperative complications/infection
- Eliminate nonessential medications
- Get patients out of bed as soon as possible
- Ensure that nurses identify patients at risk and use delirium screening tools
- Institute measures, as needed, to prevent fecal impaction and urinary retention
- Institute more frequent checks to ensure adequate oxygen delivery
- Involve family and caregivers in patient care
- Prevent or provide early treatment of dehydration
- Provide adequate nutrition
- Provide adequate pain management (with scheduled pain management protocol)
- Reduce noise
- Seek early geriatric or geropsychiatric consult
- Take steps to restore normal sleep/wake cycle (eg, avoid nighttime disturbances for medications or vital signs, whenever possible)

It's important to avoid disrupting patients' normal sleep/wake cycle as much as possible.

a specialized geriatric unit is associated with a lower incidence of delirium compared with being hospitalized on a general medical unit.[29]

Reducing the incidence of postoperative delirium. Bright light therapy (a light intensity of 5000 lux with a distance from the light source of 100 cm), implemented postoperatively, may play a role in reducing the incidence of delirium, research suggests.[30] Music may be helpful, as well. An RCT involving patients (>65 years) undergoing elective knee or hip surgery found that those who listened to classical music postoperatively had a lower incidence of delirium.[31] Similarly, playing music in nursing homes has been shown to decrease aggressive behavior and agitation.[32]

When medication is needed, proceed with caution

None of the medications currently used to treat delirium are approved by the US Food and Drug Administration for this indication, and many of them have substantial side effects. Nonetheless, palliative or symptomatic treatment requires some form of sedation for agitated patients with delirium. Thus, it is necessary to strike a balance in order to manage the symptoms of delirium and avoid potential side effects (primarily, sedation). Overly sedating patients can confuse the clinical picture of delirium and make it difficult to differentiate between ongoing delirium and medication side effects. Medication should be started at a low, but frequent, dose to achieve an effective therapeutic level, after which a lower maintenance dose can be used until the cause of delirium is resolved.

Antipsychotics are the cornerstone of drug treatment

Haloperidol has traditionally been used to treat delirium[33] and has proven effectiveness. However, it is associated with increased risk of extrapyramidal manifestations compared with atypical antipsychotics.

Atypical antipsychotics (olanzapine, risperidone, quetiapine) are increasingly being used to treat delirium because they have fewer extrapyramidal side effects.[34] With the exception of olanzapine (available in intramuscular and oral disintegrating form), atypical antipsychotics are available only in oral form, which may limit their usefulness as a treatment for agitated, delirious patients.

Risperidone (at a dose ranging from 0.25

to 1 mg/d) and olanzapine (1.25 to 2.5 mg/d) have shown similar efficacy to haloperidol (0.75 to 1.5 mg/d) in both the prevention and treatment of delirium, but with fewer extrapyramidal side effects.[35-39] Quetiapine, a second-generation antipsychotic, is widely used to treat inpatient delirium, although there are no large RCTs comparing it with placebo. One pilot study and another open-label trial found the drug to be beneficial for patients with delirium, with fewer extrapyramidal side effects than haloperidol.[40,41]

Do a risk-benefit analysis. The use of antipsychotics in elderly patients with delirium has been associated with increased morbidity and mortality. The incidence of stroke and death were higher for community-dwelling patients (NNH=100) and patients in long-term care (N=67) who received typical or atypical antipsychotics for 6 months compared with that of patients who did not receive any antipsychotics.[42,43] Thus, a risk-benefit analysis should be done before prescribing antipsychotics for elderly patients. Both typical and atypical antipsychotics carry black box warnings of increased mortality rates in the elderly.

Other drugs for delirium? More research is needed

Cholinesterase inhibitors. Procholinergic agents would be expected to be helpful in treating delirium, as cholinergic deficiency has been implicated as a predisposing factor for delirium and medications with anticholinergic effects have been shown to induce delirium. However, several studies of cholinesterase inhibitors have not found this to be the case.[44-47]

Benzodiazepines. There is no evidence to support the use of benzodiazepines in the treatment of delirium, except when the delirium is related to alcohol withdrawal.[48] When indicated, the use of a short-acting benzodiazepine such as lorazepam is preferred for elderly patients (vs long-acting agents like diazepam) because of its shorter half-life and better side effect profile.[2] Drowsiness, ataxia, and disinhibition are common side effects of benzodiazepines.

Gabapentin. A pilot study conducted to assess the efficacy of gabapentin (900 mg/d) for the prevention of postoperative delirium found a significantly lower incidence of delirium among patients who received gabapentin compared with placebo. This may be associated with gabapentin's opioid-sparing effect.[49] Larger studies are needed to recommend for or against the use of gabapentin in patients receiving opiates.

Further study of the pathophysiology of delirium is needed, as well, to increase our ability to prevent and treat it.

CASE ▶ After receiving the IV fluid bolus, Mr. D became increasingly short of breath and required more oxygen to keep his oxygen saturation in the 90s. Labs were ordered during morning rounds, and the patient was found to have urosepsis. He was admitted to the ICU in septic shock, and was intubated and died several days later.

In retrospect, it was determined that Mr. D had developed hypoactive delirium brought on by the infection—and that his somnolence on the second postoperative day was not a sign of overmedication. Had this been recognized early on through the use of an appropriate screening tool, the outcome would likely have been more favorable. JFP

CORRESPONDENCE
Abdulraouf Ghandour, MD, Green Meadows Clinic University Physicians, 3217 Providence Road, Columbia, MO 65203; Ghandour78@gmail.com

There is no evidence to support the use of benzodiazepines in the treatment of delirium, except when the delirium is related to alcohol withdrawal.

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