



The Assessment and Management of Hypoactive Delirium

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While serving as the on-call physician for a nursing home, you are contacted by the floor nurse about A.R., a 78-year-old woman who refused her medications and physical therapy. A.R. was transferred to the nursing home one week earlier for skilled rehabilitation after an elective and uneventful bio-prosthetic aortic valve replacement. Her medical history includes mild Alzheimer's dementia, bilateral cataracts, congestive heart failure, hyperlipidemia, hypertension, chronic renal insufficiency, osteoporosis, osteoarthritis, urinary incontinence, and multiple urinary tract infections. She has been widowed for five years, and lives in a house with her daughter. Medications include enteric-coated aspirin 81 mg daily, furosemide 40 mg twice daily, potassium chloride 20 mEq daily, atorvastatin 40 mg daily, lisinopril 2.5 mg daily, metoprolol XL 100 mg daily, alendronate 70 mg weekly, acetaminophen/hydrocodone (500/5) 1-2 tabs every 4-6 hr. as needed, ciprofloxacin 250 mg twice daily, zolpidem 5 mg at bedtime, and donepezil 5 mg at bedtime. Her appetite has been only fair since her arrival at the nursing home, and her last bowel movement was two days prior. A Foley catheter has been in place since her hospitalization. The nurse notes that A.R. is slightly more lethargic, a departure from one day earlier, when she cooperated with physical therapy and was pleasant to nurses. The nurse requests that you evaluate A.R.

Physical examination is unremarkable. A.R. answers all your questions appropriately, and scores a 26/30 on a Folstein Mini-Mental Examination—an identical score to one conducted prior to surgery. You order laboratory tests and consider the differential diagnosis for A.R.'s fatigue and noncompliance with medication.

IMPACT AND ETIOLOGY

This case illustrates the complexity of geriatrics care. On examination, A.R. appears to be at baseline; however, the floor nurse is adamant that A.R. appeared different earlier in the day. A differential diagnosis for A.R.'s fatigue and noncompliance with medications can be related to multiple possible etiologies, including the first sign of a severe systemic infection, a neurological insult, or merely an act of contrariness secondary to fatigue or depressed mood. As the clinician charged with evaluating A.R., it is imperative that you include in the differential diagnosis hypoactive delirium, a frequently missed subtype of delirium.

Delirium is a potentially life-threatening disorder, characterized by high morbidity and mortality, and is one of the most common reasons for hospital complications and rehospitalization following admission to a nursing home.¹ The **Confusion Assessment Method (CAM)** defines delirium as an acute, fluctuating change in mental status, with inattention plus disorganized thinking or altered levels of consciousness.² There are several subtypes,³ each classified on the basis of psychomotor activity:

1. **Hyperactive delirium**, a condition in which a patient demonstrates heightened arousal, with restlessness, agitation, hallucinations, and inappropriate behavior;
2. **Hypoactive delirium**, a condition in which a patient demonstrates lethargy, reduced motor activity, incoherent speech, and lack of interest; and
3. **Mixed delirium**, a combination of hyperactive and hypoactive signs and symptoms.

Table 1: Risk Factors for Delirium and Precipitating Insults

Predisposing Risk Factors	Precipitating Insults
Older age	Drugs: <ul style="list-style-type: none"> • Sedatives • Narcotics • Anticholinergics • Multiple drug use • Alcohol
Dementia or Cognitive Impairment	Primary Neurological injury: <ul style="list-style-type: none"> • Stroke • Intracranial bleeding • Meningitis
Visual or Hearing Impairment	Acute illness <ul style="list-style-type: none"> • Infection • Hypoxia • Shock • Dehydration • Fever • Iatrogenic complications
Functional Impairment/Immobility	Surgery (e.g. orthopedic, cardiac)
History of Delirium	Environmental Factors: <ul style="list-style-type: none"> • Physical restraint use • Use of catheters/invasive monitoring • Intensive care unit stay
Decreased oral intake (e.g. dehydration)	Pain
Polypharmacy	Prolonged sleep deprivation
Coexisting Medical Illness	Drug Withdrawal <ul style="list-style-type: none"> • Benzodiazepines • Alcohol

Adapted from: Inouye SK. Delirium in older persons. *N Engl J Med.* 2006;354:1157-65.

Table 2: Features of Delirium and Dementia

FEATURE	Delirium	Dementia
Onset	Acute	Usually insidious
Cognition	Fluctuating	Gradual decrement
Attention	Impaired	Often preserved
Consciousness	Altered	Usually intact
Behavioral changes	Present	Often present
Delusions	Common	Common
Hallucinations	Common (usually visual)	Occasional

Delirium is generally considered to be reversible, but recent studies suggest that delirium symptoms can remain for weeks to months following onset and specific treatment for the underlying cause.⁴ Delirium has been implicated as a risk for functional and cognitive decline, poor rehabilitation potential, and increased mortality.⁵ The prevalence of all forms of delirium in the community is believed to be 1-2%, a figure that increases to 14% for patients over 85.⁴ A study of skilled patients admitted to a nursing home following acute hospitalization noted a delirium prevalence of 16%.⁶

Despite its relatively high prevalence, delirium is frequently unrecognized, likely because of the fluctuating nature of symptoms and an overall insufficient appreciation of the significance of delirium by healthcare providers.⁷ The diagnosis is primarily clinical, requiring frequent observation by caregivers in cases where symptoms are less overt, such as the episode of hypoactive delirium described above.⁸ Elderly patients with hypoactive delirium tend to be difficult to arouse from sleep. Hallucinations (usually visual) may occur in both hypoactive and hyperactive delirium.

The etiology of delirium, including hypoactive delirium, is usually multifactorial. Table 1 highlights a list of predisposing risk factors and precipitating insults commonly implicated in delirium. In general, delirium occurs in the setting of a complex interplay of depressed functional reserve (secondary to predisposing factors) and precipitating insults.⁷ These interactions explain why some patients, particularly those with cognitive and functional impairments, become delirious with relatively minor insults, such as a urinary tract infection, while more robust individuals are unaffected. Furthermore, delirium may be the only presenting sign of a major, life-threatening illness, such as myocardial infarction or septicemia, with no other signs or symptoms.² The most powerful risk factor for delirium is underlying dementia; conversely, it is thought that delirium might precipitate dementia or permanently worsen preexisting dementia.⁷ Table 2 compares the often overlapping features of delirium and dementia.

ASSESSMENT AND INTERVENTION

The diagnostic approach to identified delirium requires careful utilization of clinical skills rather than specific diagnostic tests. Emphasis should be placed on defining and mitigating risk factors (if possible) and precipitating insults. (Table 2) Much of the diagnostic work-up involves a careful and thor-

ough history. It is helpful to interview family and friends, and to review medications with the pharmacist. Other important considerations include:

- **Previous Cognitive Status:** When delirium is considered as a diagnosis, it is first imperative to establish a baseline of cognitive and functional status prior to the onset of symptoms. Given that many symptoms and signs of delirium overlap with those of dementia, it is important to ascertain whether observed changes in mental status occurred acutely or have been chronically present.
- **Previous Functional Status:** There is an association of delirium with functional impairment, such as the inability to perform ADLs or vision/hearing impairment.
- **Medication Usage:** Since drugs are implicated in 12-39% of all cases of delirium, potentially high-risk medications should be discontinued or dose-reduced whenever possible.⁵ Herbal remedies, over-the-counter medications (including diphenhydramine contained in Tylenol PM and Advil PM), and illicit substances should also be considered in a medication review.
- **Co-morbid conditions:** Since delirium is frequently a symptom of commonly encountered medical conditions (including stroke, dementia, CHF, and chronic renal failure), a careful review of co-morbidities should be conducted.
- **Pain levels:** The presence of severe pain is associated with delirium.³
- **Alcohol and Drug Use:** Alcohol intoxication, alcohol withdrawal, and benzodiazepine withdrawal are frequently associated with delirium.⁵
- **Environmental Factors:** Restraint use, lack of environmental stimulation, and multiple procedures have been known to precipitate delirium.

Once a careful history is taken, the initial diagnostic workup for delirium should include serial administration of the **mini-mental state examination (MMSE)** or Mini-Cog to assess for cognitive impairment, if the patient is able to cooperate. Although neither test should be used exclusively to diagnose delirium, changes in scoring over time may be clinically useful. The CAM or DSM-IV criteria³ may also be used to establish a formal diagnosis of delirium. The sensitivity and specificity of the CAM are 94-100% and 90-95%, respectively, but similar data are not available for the DSM-IV criteria.⁹

In addition to a thorough physical examination, targeted laboratory studies should be ordered to uncover the etiology of delirium, including a complete blood count (CBC), chemistries (including calcium), BUN/creatinine, as well as urinalysis and urine culture. Other potentially useful studies might include liver function tests, serum albumin, vitamin B12 level, ammonia level, TSH, urine toxicology screen, blood culture, chest x-ray, pulse oximetry, arterial blood gas, lumbar puncture, EKG, and EEG. Head CT does not need to be performed unless there is an antecedent history of trauma or neurological deficit on physical examination, or unless no etiology of delirium can be identified.²

Once diagnosed, the management of delirium need not always include pharmacologic agents. Most agents which modify symptoms of delirium prolong the condition. Interventions should be targeted at the underlying etiology of delirium. Non-pharmacologic interventions might include posting a calendar in the hospital room, the presence of family members or a hired companion, provision of sensory aids (e.g., hearing aids and glasses), communication aids such as dry-erase boards, relaxing music, and uninterrupted sleep facilitated by minimizing medication administration overnight. Placement in a noisy area (e.g. near the nurses' station) or with another delirious patient should be avoided if possible. Physical restraints should be avoided except for severe agitation when the patient poses a danger to self, and they should be used for the shortest possible time with frequent re-evaluation.

If pharmacologic management becomes necessary, reasonable choices include haloperidol 0.5 to 1 mg IV or IM twice daily as needed, quetiapine 12.5 mg orally twice daily as needed, or trazodone 25 to 50 mg orally at bedtime. Since the anti-dopaminergic activity of haloperidol frequently causes extrapyramidal problems, with worsened gait being the most problematic, the total daily dose of haloperidol should not exceed 2 to 3 mg. Benzodiazepines and other hypnotics should be avoided in elderly patients except in cases of alcohol or benzodiazepine withdrawal.¹⁰ Once the diagnosis of delirium is established, the clinician should monitor the patient, since symptoms typically wax and wane and may persist beyond hospital or nursing home discharge for weeks to months.

RESOLUTION

Evaluation of A.R. revealed several possible precipitants of hypoactive delirium. Mild contraction alkalosis and borderline hyponatremia thought secondary to her diuretic were identified. The Foley catheter was removed, and her nightly zolpidem was held. She was treated for a urinary tract infection. The furosemide dosage was reduced by half. The patient's daughter was encouraged to spend more time with her mother and to bring in pictures from home. For the next 24 hours, A.R.'s symptoms continued to wax and wane. At 48 hours post-diagnosis, A.R. was noted to have returned to baseline, and two weeks later she was discharged home to complete physical therapy.

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Disclosure of Financial Interests

The authors have no financial interests to disclose.

8SOW-RI-GERIATRICS -102007

THE ANALYSES UPON WHICH THIS PUBLICATION IS BASED were performed under Contract Number 500-02-RI02, funded by the Centers for Medicare & Medicaid Services, an agency of the U.S. Department of Health and Human Services. The content of this publication does not necessarily reflect the views or policies of the Department of Health and Human Services, nor does mention of trade names, commercial products, or organizations imply endorsement by the U.S. Government. The author assumes full responsibility for the accuracy and completeness of the ideas presented.

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