# **REVIEW ARTICLE**

# Not a Peep: Delirium in the Geriatric Patient

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# **Keywords:**

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Behavioral Medicine Delirium is a common acute geriatric syndrome with a fluctuating course that is characterized by inattention and cognitive changes that may not be attributed to dementia. Older patients, those with comorbidities or history of psychiatric illness as well as those with cognitive disorders or geriatric syndromes are at increased risk of developing delirium. Delirium is multifactorial and is often the first indicator of an acute illness in the geriatric patient. The work-up for delirium should include review of the patient's medications, evaluation for environmental factors as well as laboratory and radiologic studies. The mainstay for treating delirium is to identify and treat the underlying cause. Many treatment measures are also good preventive measures and include establishing normalcy for the patient by providing a care environment that is as similar to their home environment as possible and maintaining their daily schedule and regimen. Physical restraints should not be used and pharmacologic treatment should only be considered when there is concern about the patient's safety or the safety of others, non-pharmacologic treatments have already been utilized, and the underlying cause has been treated. Delirium has many long-term effects including distress, cognitive decline, loss of function, and increased morbidity and mortality. Patients with delirium also have longer hospital stays and there is increased economic cost.

#### INTRODUCTION

"She slept well all night, not a peep." These were the words of the nurse caring for my 89-year-old patient. Our geriatric medicine team was consulted by the orthopedics service for "medical management." I learned that the patient was an 89-year-old female who was admitted three days ago after a fall. Her fall resulted in an intertrochanteric hip fracture and she underwent open reduction internal fixation in the OR within 24 hours of admission. Her operative course went well, with no complications. Prior to being hospitalized, she was living in her own home alone and only required occasional assistance from her son with some instrumental activities of daily living including shopping and managing finances. She was a retired college professor who enjoyed spending her time volunteering as an usher at the theater. Her past medical history included osteoarthritis and she took acetaminophen on occasion to control her joint pains. According to her nurse, she was awake briefly in the recovery room but had been sleeping since. The patient's vital signs had been stable and her routine labs were unremarkable. On review of her hospital medications, I found that she had not received any medications in two days as the nurses were holding all medications due to her somnolence.

# **DELIRIUM DEFINED**

Would you recognize the above clinical case as delirium? Delirium is a common syndrome in the geriatric patient that is under-diagnosed and carries great risks including increased mortality. The word "delirium" is derived from three Latin roots, de which means

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"away from," lira which means "furrow in a field," and ium meaning "going off the ploughed track, a madness." According to the Diagnostic and Statistical Manual of Mental Disorders, fifth edition (DSM-5), delirium is defined as an acute syndrome characterized by inattention, cognitive changes that may not be attributed to dementia, acute onset (usually developing over hours to days) with fluctuation, and cause derived from a precipitating factor such as an underlying medical condition, intoxicating substance, adverse drug event, or multifactorial causes. The DSM-5 has not been widely studied yet, but the criteria for delirium appear less subjective than DSM-4. Non-detection rates of delirium using DSM-4 were reported to be 32%-67%.

Many words have been used to describe delirium. "Sundowning" is a term that is commonly used and describes the time period when delirium is most often detected, at night. Patients experiencing delirium tend to demonstrate signs of confusion most at night, after "sun down" when there is less structure or routine in their care setting and more negative stimulation¹ (such as the sounds of beeping alarms and hallway traffic in the hospital setting). Older patients are known to be more vulnerable to the syndrome.

# **Epidemiology**

Epidemiological studies of delirium most commonly include hospitalized older patients as opposed to patients in post-acute and community settings.<sup>4</sup> Studies of hospitalized older patients have reported the prevalence of delirium at admission as 14-24% and the incidence during hospitalization as 6-56%.<sup>4</sup> Rates in the intensive care unit have been reported as 70-87% and rates post-orthopedic surgery have been reported as 15-53%.<sup>4</sup> Furthermore, from the epidemiological studies conducted in long-term care and post-

acute settings, a rate of up to 60% has been reported.<sup>4</sup> Delirium is thought to occur in up to 83% of patients at the end of life.<sup>4</sup>

It is estimated that approximately 1.5 million older patients with delirium will present to the emergency department each year and emergency physicians fail to diagnose delirium 75% of the time that it is present.<sup>5</sup> This lack of recognition of delirium spans across all specialties with delirium being missed in up to 32-66% of cases.<sup>6</sup> Many factors influence a physician's ability to recognize delirium. Improving diagnosis of the syndrome may be achieved through physician education and care being taken by the osteopathic family physician to look closely for the syndrome.

# Pathophysiology

Although the exact pathophysiology of delirium is still not well known, it is felt that delirium is most likely due to a functional as opposed to a structural lesion.<sup>4</sup> Electroencephalographic (EEG) findings have pointed towards functional derangements and decrease in cortical activity has been noted.<sup>4</sup> The current main hypotheses propose that delirium is the "final common pathway of many different pathogenic mechanisms, resulting from dysfunction of multiple brain regions and neurotransmitter systems."<sup>4</sup>

# Subtypes

There are three subtypes of delirium: hyperactive, hypoactive, and mixed. Patients with hyperactive delirium are most easily recognized. These patients are truly "hyperactive" demonstrating increased psychomotor activity and may appear restless, anxious, or agitated and may have behavioral disturbances that are combative. They may display loud or fast speech, swearing, singing, laughing, anger, wandering, or other increased activity. Patients with hyperactive delirium are often the ones that the nurse calls you about at night as their delirium is most easily recognized in the clinical setting. Hypoactive delirium is the "quiet delirium" that

# **TABLE 1:**Characteristics of Delirium Subtypes<sup>1,7,8</sup>

often goes unrecognized.<sup>7</sup> These patients have decreased psychomotor activity and may appear to be sleeping all the time or sedated, thought to be depressed, or possibly even lethargic.<sup>7</sup> They may appear to be staring blankly, have little conversation, or demonstrate slow speech.<sup>8</sup> These are often the patients that do not cause any disturbance at night and appear to be resting comfortably. Because they are "quiet," they often do not evoke clinical concern. Older patients tend to commonly experience hypoactive delirium.<sup>8</sup> The most commonly diagnosed subtype is mixed. It is composed of characteristics of both hyperactive and hypoactive delirium and thus has fluctuating levels of psychomotor activity.<sup>7</sup>

## **RISK FACTORS**

A small insult can precipitate delirium in a geriatric patient who has many risk factors. Some risk factors include:

## Age

Patients older than age 65 and of the male sex have increased risk for delirium.<sup>8</sup> This is especially true following procedures and in different care settings. For example, Allen and Frankel have reported that up to 50% of elderly patients suffer from delirium post-operatively.<sup>9</sup> Furthermore, patients who have undergone orthopedic procedures (as the patient in the above case) are more likely to develop delirium than patients who have undergone general surgery procedures.<sup>9</sup> It is estimated that 28% to 61% of geriatric patients with a hip fracture will experience delirium.<sup>8</sup> It is important for the osteopathic family physician to recognize older age alone as a known risk factor. It should also be noted that a patient's chronologic age may not correlate to their biologic age. Therefore, the patient's actual age as well as their overall medical condition and determination of their biologic age should be taken into account.

# Comorbidities and History of Psychiatric Illness

Patients with multiple acute or chronic medical conditions are more likely to suffer from delirium. The prevalence of older persons with delirium in the intensive care unit has been found to be 60% to 80% for those with mechanical ventilation and 20% to

Hyperactive	Hypoactive	Mixed
Increased psychomotor activity	Decreased psychomotor activity	Characteristics of both hyperactive and hypoactive
Restlessness / Anxious	Decreased alertness / Sleepy	Fluctuating levels of psychomotor activity
Loud or Fast Speech	Slow or little speech / Quiet	
Agitation / Combativeness / Anger	Unawareness / Staring blankly	
Laughing, Singing, Swearing	Apathy / Appear Depressed	
Hypervigilance	Lethargy	
Distractability		
Tangentiality		
Persistent thoughts		
Wandering		

50% for those without mechanical ventilation.<sup>8</sup> Brummel and Girard have referenced that the average medical ICU patient possesses eleven or more risk factors for delirium.<sup>10</sup> Patients with a history of alcoholism, use of intoxicating substances, and psychiatric illness are also more likely to be afflicted with delirium. Patients who reside in a long-term care setting are at a high risk of delirium as residents in long-term care tend to have more comorbidities and are more likely to have cognitive and physical impairments.<sup>8</sup>

# Cognitive Disorders / Geriatric Syndromes

Baseline cognitive disorders (such as mild cognitive disorder, dementia or history of memory impairment secondary to stroke) increase a patient's risk of delirium.<sup>3</sup> The risk of delirium also increases with the severity or stage of dementia.<sup>6</sup> Geriatric syndromes as a whole have been shown to be a predisposing factor for delirium. These include: dementia, immobility or decrease in function, sensory impairments including hearing loss and visual disturbances, malnutrition, depression, frailty and falls, polypharmacy, previous history of delirium, history of elder abuse, and pressure ulcers as well as others.<sup>7,8</sup>

# **CAUSES OF DELIRIUM**

Delirium is typically multifactorial and it may be impossible to isolate just one cause of delirium in a patient. Commonly, delirium is the first indicator of an underlying acute illness. Geriatric patients, especially, may demonstrate delirium prior to the development of vital sign changes such as fever, tachycardia, tachypnea or hypoxia. Some of the most common causes seen in the geriatric patient include:

# Infection

Infections are one of the most common causes of delirium. Of patients who develop delirium due to infection, urinary tract infections and pneumonia account for 34% to 43% of these cases. Assessing for infection should always be part of the diagnostic evaluation for delirium.

In the geriatric patient, delirium may be the first clinical indication of infection as vital sign changes and other clinical signs often present later in the clinical course. Some geriatricians consider delirium to be the sixth vital sign. In advocating that mental status should be the sixth vital sign, Flaherty et al. have argued that "the brain is as sensitive and vital an organ as the immune (temperature), cardiac (pulse, blood pressure), and respiratory systems (respiratory rate) for heralding that something is amiss." Furthermore, "each vital sign is nonspecific but an abnormal or changed value may signal something is wrong" and "in frail older patients with an infection, a change in mental status often occurs before a change in pulse, blood pressure, or respirations." In evaluation of the geriatric patient, it is most important for the osteopathic family physician to consider delirium as a sixth vital sign.

# External Devices, Environmental Factors, & Sleep

Any changes from the norm for a geriatric patient may contribute to delirium. When one thinks about the multiple changing factors that occur when a geriatric patient transitions from living at home to being hospitalized, it can be overwhelming just to think about. Imagine what this experience is like for a geriatric patient. The more transitions that occur, the more likely he/she is to develop delirium.

#### TABLE 2:

Risk Factors for Delirium<sup>7,8</sup>

Age greater than 65	Terminal illness
Male sex	Polypharmacy
Comorbidities	Immobility / functional decline
Alcoholism / substance abuse	Sensory impairments including hearing/vision loss
Depression and history of psychiatric illness	Malnutrition
History of chronic pain	Advanced illness / end-stage organ disease
Dementia and other cognitive disorders	Geriatric syndromes (including those not listed within this table)

## TABLE 3:

Medications Likely to Induce Delirium<sup>1,8,12</sup>

Class	Examples
Antibiotics	Quinolones, Macrolides, Linezolid, Antimalarials
Antidizziness, Vertigo	Scopolamine, Meclizine
Antihistamines	Diphenhydramine, Hydroxyzine
Antiemetics	Promethazine
CNS System / Psych	Benzodiazepines, Anticonvulsants, Sedatives, TCAs
Cardiovascular	Amiodarone, Digoxin, Diltiazem, Beta blockers, Clonidine
Gastrointestinal	Metoclopramide, Cimetidine, Ranitidine, Atropine
Pain / Anti-Inflammatory / Musculoskeletal	Corticosteroids, NSAIDs, Muscle Relaxants, Narcotics

It is estimated that the average ICU patient carries 11 or more risk factors for delirium. The setting of the intensive care unit alone also places them at risk as it is far from the norm of their daily life. Often, these patients are in isolation and everyone that enters their room is not easily recognizable to them due to all the protective clothing that must be worn by healthcare team members and visitors. There are many "tethers" on the intensive care patient. These may include a bladder catheter, telemetry monitor, continuous pulse oximetry, perhaps endotracheal tube, gastric tube, routine blood pressure monitor, etc. All of these may cause overstimulation and contribute to delirium. Lack of sleep appears to be

a major factor in the development of delirium in the ICU. Several studies have found the correlation of lack of sleep to delirium and it has been found that the average amount of sleep in ICU patients is approximately 1 hour and 51 minutes in a 24-hour time period.<sup>1</sup>

# Meds, Meds, Meds Until Proven Otherwise

Medications should be considered to be a cause of delirium in the geriatric patient until proven otherwise. As the number of medications in a patient's regimen increases, so does the risk for delirium. The highest incidence of medication-induced delirium is noted in patients taking more than three medications. Medications with anticholinergic properties are the most notable for precipitating delirium in the geriatric patient. These include diphenhydramine, promethazine, hydroxyzine, meclizine, amitriptyline among others. Some medications, such as benzodiazepines can contribute to delirium in patients but also have a protective effect in others. It is important to review the patient's medication list daily to investigate for any medications that may be causing delirium or place the patient at risk. Some medications are more obvious than others.

Other causes include inadequate pain control, dehydration, metabolic abnormalities (such as hepatic or renal failure, electrolyte disturbances, hypo/hyperglycemia), cerebrovascular accident, acute myocardial infarction, seizure, subdural/epidural hematoma, meningitis or encephalitis, hypoxia/respiratory failure, hypotension, hypoperfusion, congestive heart failure, trauma, shock, constipation, and urinary retention.<sup>7,8</sup> The osteopathic family physician must keep all systems in mind as well as medications and environmental factors.

# **ASSESSMENT & DIAGNOSIS**

Assessment for delirium should begin on initial evaluation in the emergency department and ongoing assessment should occur regularly as signs of delirium may fluctuate throughout day and night.<sup>2</sup> Several tools exist to assess for delirium, but the Confusion Assessment Method (CAM) is the most widely embraced by healthcare providers.<sup>7</sup> The CAM has 4 features:<sup>7</sup>

- 1. Acute mental status change and fluctuating course
- 2. Inattention
- 3. Disorganized thinking
- 4. Altered level of consciousness

In order to meet criteria for the diagnosis of delirium, a patient must have features 1 and 2 and either feature 3 or 4.7 The CAM has been found to have sensitivity of 94%-100% and specificity of 90%-95% in screening hospitalized patients.<sup>13</sup>

Geriatric patients with delirium should be admitted to the hospital for further investigation as geriatric patients who are discharged from the emergency department have higher death rates than patients without delirium. The diagnostic evaluation should be focused on finding the underlying cause. In addition to taking a complete history (including medications and any medication changes, history of drug/alcohol use) and performing a thorough physical examination (including neurological), the evaluation of the geriatric patient with delirium includes laboratory and perhaps radiologic studies. Table 4 summarizes these studies that should be considered. Clinical judgment must be used to determine studies that are appropriate for each patient.

#### TABLE 4:

Laboratory & Radiologic Studies-Evaluating the Geriatric Patient with Delirium<sup>7,8</sup>

Laboratory	Radiologic / Other
Complete blood count	12-lead electrocardiogram
Comprehensive metabolic panel (electrolytes, glucose, BUN/Creatinine, LFTs)	Chest radiograph
Ammonia	CT of the head
Urinalysis / urine culture	Electroencephalography (if seizure expected or delirium is unclear)
Cardiac biomarkers	
Lumbar puncture	
Blood cultures	
Thyroid-stimulating hormone	
Vitamin B12 & Folate levels	
Urine drug screen	
Arterial blood gas	
Rapid plasma reagin	

# TREATMENT & PREVENTION

Many of the treatment measures for delirium are also good preventive measures. When a hospitalized geriatric patient becomes delirious, the patient benefits from efforts to maintain a regular schedule and create surroundings that are as close to their home life as possible. This includes insuring that the patient is out of bed for meals unless contraindicated, establishing early mobility, occupational and physical therapy, setting a day/night and wake/sleep schedule with positive cognitive stimulation during the day (including turning on the lights, opening the blinds so that sunlight is in the room, and avoiding daytime naps) and limited interruptions to allow for restful sleep at night, surrounding the patient with familiar items from home and encouraging family and friends to visit regularly.<sup>12</sup> If a patient wears hearing aids or glasses at home, he/ she should be wearing them in the hospital (even in the ICU). Interruptions at night should be limited and noise kept to a minimum when the patient is sleeping. As physicians, we should avoid ordering frequent checks of vital signs, procedures, lab draws, and radiologic studies (especially at night) unless absolutely needed for patient safety.8 Regular medications should be given during daytime hours when possible.

Physical restraints are not recommended for managing delirium or for use in patients at risk of delirium. In fact, the use of physical restraints increases the risk of a patient developing delirium and also have been found to increase the severity of delirium. <sup>14</sup> Oftentimes, physicians order physical restraints because they believe that this will prevent injury from falls. This is a misconception as studies have demonstrated an increased fall rate with the use of physical restraints. <sup>14</sup>

Before considering pharmacologic treatment for delirium, the above interventions should be taken and the underlying cause should be treated.<sup>7</sup> The patient should be evaluated for pain. Sometimes, patients with hypoactive delirium and/or those with cognitive decline are unable to voice their pain. A regular regimen for pain control often results in resolution of their delirium. If delirium persists after the underlying medical condition has been treated and environmental interventions have been taken, pharmacologic management may be needed. In general, benzodiazepines should be avoided as they are known to not only cause but also exacerbate delirium. The American Psychiatry Association advises only using benzodiazepines in the setting of alcohol and benzodiazepine withdrawal, not as monotherapy in delirious patients.<sup>7</sup> Instead, antipsychotic medications are recommended. Haloperidol is known as the "agent of choice" but as with all antipsychotics, must be prescribed with caution and attention paid to possible adverse effects such as extrapyramidal effects, prolonged corrected QT interval/torsades de pointes, among others.8 Haloperidol should be avoided if a patient has underlying parkinsonism, withdrawal syndrome, hepatic insufficiency, or neuroleptic malignant syndrome.8 Osteopathic family physicians should consult the U.S. Food and Drug Administration boxed warnings for medications prior to prescribing them for delirium and also evaluate risks/ benefits to the patient and discuss this openly with the patient when possible and the family/health care surrogate. Pharmacologic treatment for delirium should be the last option chosen in treatment and used only when there is concern about the patient's safety or that of others.8

# LONG-TERM EFFECTS: DISTRESS, COST, & DEATH

Only 14% of patients with delirium have returned to their baseline level of cognitive functioning at discharge.<sup>1</sup> Many times, this results in the need for placement in long-term care as opposed to discharge to home. Delirium is a strong prognostic indicator and is associated with increased morbidity and mortality.<sup>7,9</sup> Post-operative delirium is linked to increased morbidity as well as a 1 year mortality of 40%.9 Han and colleagues found that delirium in geriatric patients in the emergency room is an independent predictor of increased 6-month mortality.<sup>5</sup> Patients with delirium also stay hospitalized for an average of 5-10 days longer than patients who have the same medical problems but have not had delirium.<sup>1</sup> The economic cost for care is also increased. On average, patients in the ICU with delirium have health care costs that are 31% higher than patients with the same medical problems but without delirium. The national burden of delirium on the health care system is somewhere between \$32 billion to \$152 billion per year. Grover and Shah studied distress due to delirium and found that the overall experience of delirium distresses the patient and the majority of patients studied reported at least a moderate level of distress post-delirium.15

# THE FUTURE

"Not a peep" as described in the introductory case should raise concern for hypoactive delirium. For this post-operative patient, treatment involved a scheduled regimen of pain medication and nursing staff was educated about the clinical signs of hypoactive delirium and the importance to not hold the patient's doses unless

there were signs of respiratory depression, bradycardia, hypotension, or other clinical concern. Nursing staff was asked to contact the geriatric medicine team to evaluate the patient if there was any concern about giving the patient's scheduled pain medication. With the patient receiving her scheduled regimen of pain medication, she slowly returned to her normal cognition. With time, she only required pain medication prn and was subsequently discharged to sub-acute rehab.

Although a large amount of research has been conducted on delirium and much is understood, there remain many opportunities for investigation as the causes of delirium are multifactorial and the treatments (pharmacologic and non-pharmacologic) are numerous. Continuity of care is very beneficial to the patient with delirium and thus there is a great role for the osteopathic family physician to affect outcomes. The approach to treating delirium must involve educating the healthcare team and be multidisciplinary with the osteopathic family physician serving as the team leader.

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