

Delirium In the Elderly

Jeffrey M Burock, MD

DELIRIUM IS AN ACUTE ORGANIC MENTAL syndrome characterized by disturbance in level of consciousness, disorientation, attentional impairments, perceptual disturbances, cognitive impairments and occasionally severe behavioral problems. The term “delirium” is based on the Latin roots *de*, *lira*, and *ium*, which literally mean “a going off the ploughed track, a madness.” The term delirium has been known since 1 AD by the writer, Celsus, who described it in *De Medicina*. Nursing staff will often use the terms, “sundowning” or “ICU psychosis” to describe the acute mental status changes associated with delirium. Yet, neurologists prefer the term “encephalopathy”, which literally means “disease of the brain.” Regardless of the term used, delirium is not a benign condition and markedly extends hospital length of stay and increases the risk of further morbidity and mortality. *The Diagnostic and Statistical Manual of Mental Disorders, 5th Edition* (DSM-5) (due out in May 2013) will likely define delirium as a disturbance in level of awareness or attention (rather than consciousness as in the previous edition), marked by the acute or subacute onset of cognitive changes attributable to a general medical condition; and it tends to have a fluctuating course. DSM-5 will also likely add supportive features and subtypes, such as hypoactive, hyperactive, and mixed.¹

DEFINING THE PROBLEM AND EPIDEMIOLOGY

Delirium is one of the most common syndromes older patients develop and one that clinicians miss at the reported rate of 32% to 66%.² The prevalence of delirium upon admission to general medical units is between 10% and 31%, however most authorities place the estimate closer to 30% in the elderly population (65 years of age and older). In general, surgical patients have been found to have higher rates of delirium than medical patients, with coronary artery bypass graft patients having the highest risk of post-operative delirium (greater than 50% in five of 14 studies reviewed). The highest rates of delirium are found in the intensive care setting and in those with terminal illness, where rates of 80% or more have been

noted. Delirium is especially common in nursing homes after brief hospital admissions because the average length of duration of the delirium is 21 days, while the average hospital length of stay at most general medical hospitals is approximately five days. Therefore, many patients are being discharged to nursing homes while still delirious. In one study, 72% of 214 patients in nursing homes who were hospitalized for delirium still had delirium at the time of discharge back to the nursing home. The delirium persisted for 55% of the patients at one month and 25% at three months after discharge.³ The rates of delirium in patients who are ill and elderly, but cared for at home are much lower, than for those treated in the hospital.

The patients at the highest risk for delirium include older patients with severe dementia, who have multiple comorbidities.

PATHOGENESIS OF DELIRIUM

Delirium is a complex neuropsychiatric syndrome, often multifactorial in origin and likely affecting multiple domains of the central nervous system. The most widely accepted hypothesis involves the cholinergic neurotransmitter system, suggesting that deficiency may be one of the underlying factors causing delirium. It is well-known that anticholinergic drugs, such as atropine or diphenhydramine (Benedryl®) can elicit the symptoms of delirium in predisposed individuals. Other hypotheses include melatonin abnormalities, which would explain the term “sundowning”, in which behavioral symptoms emerge as light levels decline and melatonin levels spike during the evening. Neuronal damage is an alternative explanation, secondary either to oxidative stress or inflammation. A link between inflammation and neurotransmission has been proposed, with inflammation-induced perivascular edema

leading to hypoxia and subsequent reduced synthesis of acetylcholine.⁴

Electroencephalogram (EEG) is a sensitive but usually unnecessary test for the presence of delirium. EEG findings reveal a decrease in fast alpha frequencies and an increase in the slower theta rhythm. Unfortunately, this is a non-specific finding, but is telling of global brain dysfunction.

RISK FACTORS FOR DELIRIUM

Delirium is often the initial manifestation of an underlying acute medical illness and may be present before signs such as fever, tachypnea, tachycardia, or hypoxia. The patients at the highest risk for delirium include older patients with severe dementia, who have multiple comorbidities. In these highly vulnerable patients, a medication such as an opioid narcotic may induce delirium. Older patients are more likely to have multiple vulnerability factors, therefore, they are disproportionately more susceptible to becoming delirious compared with younger patients. Dementia is probably the most consistently observed independent vulnerability factor for delirium across different clinical settings.⁵ Marcantonio and colleagues identified seven predictors that could be used preoperatively to stratify an individual patient's risk of delirium. These factors include age greater than 70 years, self-reported alcohol abuse, poor cognitive status, poor functional status, abnormalities of serum sodium, potassium, or glucose, non-cardiac thoracic surgery, or abdominal aneurysm surgery.⁶ Lower education, by reducing cognitive reserve, increases delirium risk, and when present, is of longer duration. Sensory impairments, especially visual loss, also greatly increases the risk of delirium in a vulnerable population.

Medications, especially polypharmacy, are a well-known cause of delirium in the elderly. Medications with anticholinergic properties, benzodiazepines, and narcotics are notorious for precipitating and exacerbating delirium. Medications with anticholinergic properties are more frequently associated with delirium than any other drug class; moreover, there are over 600 medications known to have these properties on the market. One-third of all of the elderly use over-the-counter sleep aids, most

of them antihistamines with anticholinergic properties. Delirium with mania may occur in patients exposed to parenteral steroids and occasionally even oral steroid doses.

At this point, there are no known genetic markers for predisposition to delirium. Although one study showed higher rates with those patients with apolipoprotein E4, this was confounded by the high rate of Alzheimer's dementia in this population. Another study on this gene showed no effect on the rate of delirium.

INTERVENTIONS TO PREVENT DELIRIUM

Multidisciplinary strategies have been implemented at many hospitals in order to prevent delirium and mitigate its duration. These strategies rely upon nursing care and the environment of care rather than additional pharmacotherapy. Patient safety is a high priority given the propensity for delirious patients to fall, aspirate, and develop pressure ulcers. At our institution, The Miriam Hospital, restraints are almost never used with the delirious elderly patient. In the case of delirium tremens, most studies indicate an increased mortality in those patients who required restraints during the admission. Instead, we have chosen to specially train certified nursing aids in a skill set that allows them to be both sitters and clinicians adept at handling delirious patients. They are usually assigned to one individual patient and can help mitigate falls, aspiration and skin breakdown. They provide frequent reorientation, access to sunlight, and they help optimize sensory losses that may be contributing to confusion. Urinary catheters are removed as soon as possible and the patients mobilize early in their stay. Delirium tool kits are also implemented when the delirious patient is found tugging at lines or medically necessary tubing. When these non-pharmacologic methods are unsuccessful, the team usually will obtain consultation from our geriatric psychiatry advanced practice nurse and/or the psychiatry consultation-liaison service. In fact, at our institution, approximately one-third of the psychiatry consultation-liaison consults are for evaluation and management of the delirious patient.

There have been some recent studies that have looked at preemptive use of antipsychotics to prevent delirium in highly vulnerable patients. At least one randomized, controlled trial addressed the issue of

prophylactic haloperidol. In at-risk patients aged greater than 70 years, oral haloperidol 0.5mg twice a day was administered up to 72 hours preoperatively until the third post-operative day. The study found that prophylactic haloperidol use did not alter the incidence of post-operative delirium (15.1%) compared to placebo (16.5%).⁷ Other studies on prophylactic haloperidol, in patients undergoing elective hip surgery, have showed a decrease in delirium duration and hospital length of stay but no difference in incidence of delirium.⁸ Studies on risperidone and olanzapine were also conducted and seem to point toward decreased incidence of post-operative delirium, however, antipsychotic prophylaxis is generally not utilized at this point due to potential drug-induced side effects and lack of solid data.

MANAGEMENT OF DELIRIUM INCLUDING BEHAVIORAL PROBLEMS

The single most effective treatment of delirium is to diagnose and treat the underlying cause. At this point, there are no FDA-approved medications for the treatment of delirium. The most commonly used drug for behavioral problems in delirium remains haloperidol. Haloperidol (Haldol®) is a commonly used antipsychotic and has been shown to improve delirium severity. Intravenous haloperidol should be administered cautiously in light of the black box warning regarding possible QT prolongation and subsequent torsades de points. There have been few studies on the newer atypical antipsychotics such as quetiapine (Seroquel®), risperidone (Risperdal®), olanzapine (Zyprexa®), and aripiprazole (Abilify®), however they are often used in the medical setting due to health provider fears over the black box warning on haloperidol. Until solid clinical studies are performed on these medications, there are few if any benefits over the traditional use of haloperidol in this setting. At least one caveat exists, that patients with parkinsonian disorders, and especially dementia with Lewy bodies, avoid haloperidol due to the possibility of irreversible motor damage. In these cases, quetiapine would be a safer option for treatment of the behavioral symptoms associated with delirium.

One randomized trial attempted to compare the efficacy of antipsychotic medications and lorazepam (Ativan®) in delirious patients, but was prematurely

terminated because the lorazepam arm showed a higher prevalence of treatment-limiting side effects such as oversedation, disinhibition, ataxia, and increased confusion.⁹ The typical antipsychotics studied, including haloperidol and chlorpromazine (Thorazine®), were found to be effective in controlling behavioral symptoms in these delirious patients. However, in the case of delirium tremens from alcohol or benzodiazepine withdrawal, lorazepam still remains the medication of choice.

REFERENCES

1. Meagher D, Trzepacz PT. Phenomenological distinctions needed in DSM-5: delirium, subsyndromal delirium, and dementias. *J Neuropsychiatry Clin Neurosci*. 2007; 19(4): 468–70.
2. Inouye SK. Delirium in hospitalized older patients: recognition and risk factors. *J Geriatr Psychiatry Neurol*. 1998;11: 118–25.
3. Kelly KG, Zisselman M, Cuttillo-Schmitter T, et al. Severity and course of delirium in medically hospitalized nursing facility residents. *Am J Geriatr Psychiatry*. 2001;9: 72–7.
4. Hala M. Pathophysiology of post-operative delirium: systemic inflammation as a response to surgical trauma causes diffuse microcirculatory impairment. *Med Hypotheses*. 2007;68(1): 194–6.
5. Inouye SK, Viscoli CM, Horwitz RJ, et al. A predictive model for delirium in hospitalized elderly medical patients based on admission characteristics. *Ann Intern Med*. 1993; 119(6): 474–81.
6. Marcantonio ER, Goldman L, Mangione CM, et al. A clinical prediction rule for delirium after elective noncardiac surgery. *JAMA*. 1994;271: 134–9.
7. Schrader SL, et al. Adjunctive haloperidol prophylaxis reduces postoperative delirium severity and duration in at-risk elderly patients. *Neurologist*. 2008;14(2):134–7.
8. Kalisvartt KJ, et al. Haloperidol prophylaxis for elderly hip surgery patients at risk for delirium; a randomized placebo-controlled study. *J Am Geriatr Soc*. 2005;53(10): 1658–66.
9. Breitbart W, Marotta R, Platt MM, et al. A double-blind trial of haloperidol, chlorpromazine, and lorazepam in the treatment of delirium in hospitalized AIDS patients. *Am J Psychiatry*. 1996;153(2):231–7.

Jeffrey M Burock, MD, is a Clinical Assistant Professor, Department of Psychiatry and Human Behavior, at the Warren Alpert Medical School of Brown University, and is a Division Director in the Department of Psychiatry at The Miriam Hospital.

Disclosure of Financial Interest

The author and/or his spouse/significant other have no financial interests to disclose.

CORRESPONDENCE

Jeffrey M. Burock, MD
phone: 401-793-4300
e-mail: JBurock1@lifespan.org