27 Practice Guidelines for the Treatment of Patients With Delirium

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SUMMARY OF RECOMMENDATIONS

In general, the treatment of delirium is broken down into three parts—psychiatric management, environmental and supportive interventions, and somatic interventions. In the broadest terms, the underlying cause of the delirium should be sought and treated if possible. Behavioral and environmental intervention should be optimized and instituted first. If necessary, to prevent patient distress or harm, pharmacological interventions should be instituted, the mainstay of which is haloperidol therapy.

DISEASE DEFINITION, EPIDEMIOLOGY, NATURAL HISTORY, AND DIFFERENTIAL DIAGNOSIS

Definition

Delirium is a disturbance of consciousness, attention, cognition, and perception that develops over a short period of time and tends to fluctuate

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during the course of the day. This usually represents a sudden and significant decline from a previous level of functioning and cannot be better accounted for by an evolving dementia. As *inattention* is a hallmark of delirium, cognitive function (for dementia evaluation) is difficult to assess clinically during periods of delirium.

Common Clinical Features

Common clinical features include dysarthria, dysnomia, dysgraphia, illusions, hallucinations, disturbances in sleep–wake cycles, and disturbances in emotion. Two subtypes of delirium are described based on changes in psychomotor activity. Agitation is seen in "hyperactive" delirium and lethargy is seen in "hypoactive" delirium. Additionally, a number of nonspecific neurological abnormalities such as tremor, myoclonos, asterixis, and reflex changes may be seen.

Prevalence

Delirium is found in 10–40% of all elderly, hospitalized patients, up to 51% of postoperative patients, and 80% of patients with terminal illnesses. Often, prodromal symptoms such as anxiety, restlessness, irritability, or sleep disturbances are seen 1–3 d before overt delirium. Episodes of delirium may last 1 wk to 2 mo with the typical episode resolving in 10–12 d. Longer courses and incomplete recovery characterize delirium in the elderly hospitalized patients. Indeed, delirium is a harbinger of poor long-term prognosis. Delirium in elderly, hospitalized patients has been associated with 22–76% chance of dying during the hospitalization and 25% death rate within 6 mo of discharge.

Differential Diagnosis

The most common differential diagnosis is whether the patient's clinical condition is owing to delirium alone, worsening of a pre-existing dementia alone, or a delirium superimposed on a pre-existing dementia. Careful history with a focus on temporal onset of symptoms and fluctuations during a 24-h period are helpful in clarifying the diagnosis. Patients with dementia usually do not have the fluctuations in consciousness that are seen in delirium.

Causes of Delirium

When delirium occurs as a result of a medical illness, careful and comprehensive assessment must be undertaken to determine its etiology. General medical conditions that commonly cause delirium are represented in Table 1.

Common causes of delirium include substances of abuse, prescription medications, and toxins (Table 2). Half-life of the drug/toxin is an important

Table 1
Underlying Conditions Commonly Associated With Delirium

Type	*Disorder*
Central nervous system disorder	Head trauma
	Seizures
	Postictal state
	Vascular disease (e.g., hypertensive encephalopathy)
	Degenerative disease
Metabolic disorder	Renal failure (e.g., uremia)
	Hepatic failure
	Anemia
	Hypoxia
	Hypoglycemia
	Thiamine deficiency
	Endocrinopathy
	Fluid or electrolyte imbalance
	Acid–base imbalance
Cardiopulmonary causes	Myocardial infarction
	Congestive heart failure
	Cardiac arrhythmia
	Shock
	Respiratory failure
Systemic illness	Substance intoxication or withdrawal
	Infection
	Neoplasm
	Severe trauma
	Sensory deprivation
	Temperature dysregulation
	Postoperative state

determinant of rapidity of onset and duration of delirium during exposure and withdrawal periods.

Due to multiple etiologies, fully 44% of elderly hospitalized patients have multiple causes of delirium.

USE OF FORMAL ASSESSMENT MEASURES

1. Several *screening* instruments are available to screen for dementia. These are mostly tailored for the usage of nurses.
2. Several formal *diagnostic* tools are available. For example, the confusion assessment method is utilized in many care settings.

Table 2
Substances That Cause Delirium Through Intoxication or Withdrawal

Category	*Substance*
Drugs of abuse	Alcohol
	Amphetamines
	Cannabis
	Cocaine
	Hallucinogens
	Inhalants
	Opioids
	Phencyclidine
	Sedatives
	Hypnotics
	Other
Medications	Anesthetics
	Analgesics
	Antiasthmatic agents
	Anticonvulsants
	Antihistamines
	Antihypertensive and cardiovascular
	Medications
	Antimicrobials
	Antiparkinsonian medications
	Corticosteroids
	Gastrointestinal medications
	Muscle relaxants
	Immunosuppressive agents
	Lithium and psychotropic medications with anticholinergic properties
Toxins	Anticholinesterase

3. Several instruments are available for rating *severity* of delirium. These are usually based on behavioral symptoms, confusion, and cognitive impairment.
4. No laboratory test is available with sufficient operating characteristics (sensitivity/specificity) to assist in the rule in or rule out of delirium.

ASSESSMENT AND TREATMENT

The treatment principles of delirium include psychiatric treatment, behavioral and environmental treatment, and somatic or pharmacological treatment.

Psychiatric treatment includes coordination of care with other clinicians, identifying causes and initiating immediate interventions, and treatment for reversible causes. The etiology of delirium is ascertained by careful history, physical examination, and evaluation of laboratory data. These are summarized in Table 3.

Table 3
Assessment of the Patient With Delirium

Domain	*Measure*
Physical status	History
	Physical and neurological examinations
	Review of vital signs and anesthesia record if postoperative
	Review of general medical records
	Careful review of medications and correlation with behavioral changes
Mental status	Interview
	Cognitive tests, for example, clock face, digit span, trail making tests
Basic laboratory tests—consider for all patients with delirium	Blood chemistry: electrolytes, glucose, calcium, albumin, blood urea nitrogen, creatinine, SGOT, SGPT, bilirubin, alkaline phosphatase, magnesium, PO_4
	Complete blood count
	Electrocardiogram
	Chest X-ray
	Measurement of arterial blood gases or oxygen saturation
	Urinalysis
Additional laboratory tests—ordered as indicated by clinical condition	Urine culture and sensitivity (C and S)
	Urine drug screen
	Blood tests, for example, venereal disease research laboratory, heavy metal screen, Vitamin B_{12} and folate levels, lupus erythematosus prep, antinuclear antibody, urinary porphyrins, ammonia, human immunodeficiency virus
	Blood cultures
	Measurement of serum levels of medications, for example, digoxin, theophylline, phenobarbital, and cyclosporine
	Lumbar puncture
	Brain computed tomography or magnetic resonance imaging

Initiate Interventions for Acute Conditions

As patients with delirium may have life-threatening medical illnesses, frequent monitoring of vital signs, fluid intake and output, and levels of oxygenation is essential *(1)*. The medication regimen should be carefully reviewed with unnecessary medications withdrawn and doses of necessary medications

Table 4
Examples of Reversible Causes of Delirium and Their Treatments

Condition	*Treatment*
Hypoglycemia or delirium of unknown etiology in which hypoglycemia	Tests of blood and urine for diagnosis Thiamine hydrochloride, 100 mg i.v. is suspected 50% glucose solution, 50 mL i.v.
Hypoxia or anoxia, for example, resulting from pneumonia, obstructive or restrictive pulmonary disease, cardiac disease, hypotension, severe anemia, or carbon monoxide poisoning	Immediate oxygen
Hyperthermia, for example, temperature	Rapid cooling
Above 40.5°C or 105°F Severe hypertension, for example, blood pressure of 260/150 mmHg, with papilledema	Prompt antihypertensive treatment
Alcohol or sedative withdrawal	Appropriate pharmacological intervention Thiamine, i.v. glucose, magnesium phosphate, and other B vitamins
Wernicke's encephalopathy	Thiamine hydrochloride, 100 mg i.v. thiamine daily, either intravenously
Anticholinergic delirium	In severe cases, physostigmine unless contraindicated

minimized. Medical disorders such as hypoglycemia, hypoxia, hyperthermia, hypertension, and substance-induced disorders should be rapidly corrected. Examples of reversible causes of delirium are found in Table 4.

Monitor and Ensure Safety

Suicidality, violence potential, fall risk, and wandering risk, inadvertent self-harm risk should all be assessed with appropriate measures taken to ensure safety. Use of restraints should be minimized as they may increase agitation and hence decrease safety.

Patients should also be monitored for hallucinations, delusions, aggressive behavior, agitation, affective liability, and sleep disturbances.

Environment and Supportive Intervention

There is some evidence that environmental interventions can reduce the severity of delirium and improve outcomes. Visual impairment, auditory impairment, and sensory overstimulation (such as an intensive care unit) and understimulation

should be assessed and, when possible, corrected. Reorientation efforts such as the introduction of clocks, calendars, and family pictures or other familiar household items can be beneficial. Family education about delirium and its cause cannot be overstressed. Constant reorientation to time and place and reassurance that the delirium is both reversible and temporary by caregivers and family alike is helpful.

Somatic/Pharmacological Interventions

Antipsychotics have been the medication of choice in the treatment of delirium. Evidence for their efficacy has come from case reports and uncontrolled trials in comparison. There are no published randomized, double-blind, and placebo-controlled trials for drug treatment either for choice of drug or optimal dosing.

HALOPERIDOL

It is generally believed that haloperidol is the first drug choice for the treatment of delirium. It is a high-potent dopamine-blocking agent with few or no anticholinergic side effects, minimal cardiovascular side effects, and no active metabolites. It can be given orally, intramuscularly (i.m.) or intravenously (i.v.), which is an advantage in a patient unable or unwilling to take it orally. Generally, low starting doses of 0.25–0.5 mg of haldol every 4 has needed are suggested for the elderly patients and this can be titrated up to 1–2 mg every 2–4 h as needed. Higher doses of haloperidol, including continuous infusions, have been studied and can be safe and effective in selected patients.

OTHER ANTIPSYCHOTICS

Droperidol has a rapid onset of action and relatively short half-life. It is more likely to cause sedation and hypotension than haloperidol. It has been found to be an effective treatment for hospitalized patients with agitation, although not necessarily delirium.

There has been very little study of the newer antipsychotic medications (risperidone, olanzapine, and quetiapine) in the treatment of delirium. These agents, however, are increasingly being used for the treatment of delirium. Note because guideline was issued; the Food and Drug Administration (FDA) issued a warning that a typical antipsychotic drugs used to treat behavioral disorders in elderly patients with dementia have shown a higher death rate associated with their use compared with patients receiving a placebo. The FDA stated that in analyses of 17 placebo-controlled studies of four drugs in the atypical antipsychotic class, the rate of death for those elderly patients with dementia was about 1.6–1.7 times that of placebo. Over the course of these trials averaging about 10 wk in duration, the rate of death in drug-treated patients was about 4.5%, compared with a rate of about 2.6% in the placebo group. Whether this issue also applies to the traditional

antipsychotics is a matter of ongoing review (http://www.fda.gov/cder/drug/infopage/antipsychotics/default.htm, accessed 6/25/05).

Side Effects

Antipsychotics can increase the QTc interval and have been associated with *torsades de pointes* and ventricular fibrillation. A baseline electrocardiogram and cardiac monitoring is suggested for patients receiving high doses or intravenous dosing of haloperidol. All antipsychotics may be associated with sedation, anticholinergic effects, and α-adrenergic blockade effects causing hypotension. In addition, extrapyramidal side effects such as tardive dyskinesia and neuroleptic malignant syndrome can also occur. As with all pharmacological therapy, the risks and benefits of drug intervention should be weighed carefully.

OTHER PHARMACOLOGICAL TREATMENTS

Multiple other medications have been studied in the treatment of delirium, but are not recommended except in certain circumstances. Opioid analgesia may be indicated in the treatment of delirium in which pain is an aggravating factor.

Benzodiazepenes are recommended when withdrawal from benzodiazepines or alcohol is suspected. When used for nonwithdrawal-associated delirium, low-dose and short-acting benzodiazepines in combination with antipsychotics may increase efficacy and decrease side effects better than when either agent is used alone. As some patients may experience a worsening of delirium with benzodiazepines, antipsychotics, specifically haloperidol, remain the pharmacological treatment of choice. Cholinergic medications (cholinesterase inhibitors) have been used in a limited fashion to treat delirium.

Any patient with delirium who has a reason to be vitamin-B deficient (alcoholic, etc.) should be given multivitamin replacement. Electroconvulsive therapy has not been shown to be an effective treatment for delirium.

SPECIAL CONSIDERATIONS

The presence of delirium does not in itself mean that a patient is incompetent or lacks capacity to give informed consent.

CLINICAL FEATURES INFLUENCING TREATMENT

Comorbid Psychiatric Conditions

Treatment of comorbid psychiatric conditions such as dementia or depression should be minimized during episodes of delirium as medications to treat these conditions might exacerbate delirium.

Comorbid General Medical Conditions

AIDS/HIV

Approximately 30–40% of hospitalized AIDS patients develop delirium. AIDS patients may be more sensitive to extrapyamidal side effects from antipsychotics.

Liver Disease

When benzodiazeopines are required in the treatment of the delirious patient with liver disease, temazepam, oxazepam, or lorazepam should be used. These agents undergo glucuronidation and not p450 metabolism in the liver.

SOURCES

1. American Psychiatric Association Practice Guideline For the Treatment of Patients with Delirium (1999);(http://www.psych.org/psych_pract/treatg/pg/Practice%20Guidelines8904/Delirium.pdf accessed Oct. 14, 2005).