The Evaluation and Management of the Acutely Agitated Elderly Patient

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Abstract

Delirium is an organic mental syndrome defined by a global disturbance in consciousness and cognition, which develops abruptly and often fluctuates over the course of the day. It is precipitated by medical illness, substance intoxication/withdrawal or medication effect.

Delirium is associated with significant morbidity and mortality, and is a leading presenting symptom of illness in the elderly. Elderly patients with altered mental status, including agitation, should be presumed to have delirium until proven otherwise. The clinical manifestations of delirium are highly variable. A mental status evaluation is crucial in the diagnosis of delirium.

Medical evaluation and stabilization should occur in parallel. Life-threatening etiologies including hypoxia, hypoglycemia and hypotension require immediate intervention. The differential diagnosis of etiologies of delirium is extensive. Patients with delirium need thorough evaluations to determine the underlying causes of the delirium. Pharmacological agents should be considered when agitated patient has the potential to harm themselves or others, or is impeding medical evaluation and management. Unfortunately, the evidence to guide pharmacologic management of acute agitation in the elderly is limited. Current pharmacologic options include the typical and atypical antipsychotic agents and the benzodiazepines. These therapeutic options are reviewed in detail.
Key Words: Delirium, geriatrics, agitation, antipsychotics, benzodiazepines.

Introduction

THE AGITATED ELDERLY PATIENT poses a unique clinical challenge. Delirium represents a leading presenting symptomatology in acutely ill elderly patients. Agitation in the elderly should be presumed to be a manifestation of delirium until proven otherwise. When mental status changes present as agitation, the clinician is faced with a particularly difficult and complex scenario. A potentially immediately life-threatening etiology must be searched for and addressed. If agitation is severe, it requires urgent intervention to reduce potential danger to both patient and staff. Managing the agitated geriatric patient requires a coordinated approach that allows the staff to gain control of the situation while facilitating the diagnostic work-up. This article will provide a framework to use when evaluating the agitated elderly patient, including a review of available pharmacologic treatment.

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Epidemiology

The population is becoming proportionately more elderly. The number of people over the age of 65 will double in the United States in the next 30 years (1). As the population ages, the elderly comprise a higher proportion of patients overall. This is especially true in the emergency department (ED). Persons age 65 and older account for 17.5 million ED visits in the U.S. annually and 15.4% of total ED visits (2). In a multicenter study, patients over age 65 accounted for 43% of hospital admissions from the ED (3).

The emergency department and acute hospital wards have the highest rates of patients presenting with delirium. Agitation in younger patients presenting to the ED are much more likely to be the result of substance abuse or underlying psychiatric disease (psychotic or mood disorder), than in the elderly population.

Delirium or mental status change is a leading presenting symptom for acutely ill elderly persons. In ED patients over 70 years old, it has been reported that up to 40% have an alteration in mental status, with approximately 25% diagnosed as having delirium (4). Levkoff et al. found that 24% of elderly patients from the community and 64% of those presenting from nursing homes were delirious upon hospital admission (5).

Delirium is a medical emergency requiring prompt evaluation and treatment. It is generally reversible if the underlying cause is discovered and addressed, and can be fatal if overlooked and untreated. Hospital mortality rates in patients with delirium ranges from 25–33%. Elderly patients who develop delirium during hospitalization have a 22–76% chance of dying during that hospitalization. Hospital mortality is very high in patients that develop delirium—it is as high as the mortality rate associated with acute myocardial infarction or sepsis (6–8).

Delirium: Definition and Diagnosis

Delirium is an organic mental syndrome defined by a global disturbance in consciousness and cognition. It is characterized by a global cognitive impairment due to a medical condition, which develops abruptly and often fluctuates over the course of the day (9). The underlying mechanism of delirium is poorly understood and its pathophysiology has not been well elucidated. Delirium is common among medically compromised patients and the elderly are highly vulnerable to its development.

Hallmarks of delirium include disturbance in attention and memory impairment. Deficits in attention are characterized by ease of distractibility, with a reduced ability to focus, sustain or shift attention, resulting in difficulty in following commands. Patients may have trouble maintaining conversations, and conversations may be rambling or incoherent. Memory impairment usually involves recent memory; patients may be disoriented to time or place but only rarely to person. Perceptual disturbances that may occur include misinterpretations, illusions, or hallucinations. Often there are alterations in the patient's sleep/wake cycle. A fluctuating course is characteristic and lucid intervals may be misleading (Table 1).

The clinical manifestations of delirium are highly variable. Patients with delirium may present subtly or dramatically. If subtle, delirium may go unrecognized without formal mental status evaluation. Patients may present with psychomotor retardation with varying degrees of lethargy, withdrawal and somnolence. Alternatively, delirium may present dramatically with disruptive psychomotor agitation, emotional lability and hallucinations. In the elderly, delirium presents as agitation in less than one-third of cases (10).

TABLE 1
Key Features of Delirium

Altered level of consciousness ranging from stupor to agitation
Inattention, decreased ability to focus
Fluctuating course over hours or days
Often associated with sleep/wake cycle disturbance
Precipitated by medical illness, substance intoxication/withdrawal or medication effect
Leading presenting symptom of illness in the elderly
Life-threatening etiologies require immediate intervention
Underlying medical etiology must be determined and treated
Presume that altered mental status is delirium until proven otherwise

Dementia

Patients with dementia are at risk for the development of delirium. Additionally, behavioral disturbances, including agitation, are common among patients with dementia. Agitation in dementia may include aggression, combativeness, delusions or hallucinations. Agitation may develop either as part of the clinical course or as a response to a new illness. An etiology for the agitation in patients with dementia must be sought, as agitation can be precipitated by pain and acute illness. When confronted with a confused elderly patient in the ED or hospital ward, it may not be apparent if the confused state is acute, subacute or chronic. It may not be possible to immediately distinguish between delirium and dementia, or determine which patients are suffering from both.

Mental Status Evaluation

A mental status evaluation is crucial in the diagnosis of delirium. Disorientation to the environment begins with the inability to identify the date, progresses to day of week, time, month, and year, and eventually to place. Only in the most severe cases is the person unable to identify self. However, if the mental status exam is limited to orientation to person, place and time, subtle cases of delirium may be missed.

The Mini-Mental Status Examination (MMSE) is an easy and reliable test that can be administered at the bedside. The MMSE is used to test for cognition, which includes orientation, registration (storing new information so that is can be retrieved later), attention and calculation, recall, visual-spatial ability and language. A high score on the exam makes a cognitive deficit unlikely, however, a low score is nonspecific and not diagnostic of any specific disorder. For hospitalized patients it has a sensitivity of 87% and specificity of 82% in detecting organic brain syndrome. Note that the MMSE must be interpreted with care in delirium since the delirious patient has impairment with attention, which interferes with exam performance (11, 12).

The Confusion Assessment Method (CAM) has been developed as an easy to use, sensitive, specific, and reliable diagnostic tool for the rapid detection of delirium (13; Table 2). It has a sensitivity of 93–100% and specificity of 90–95% for the diagnosis of delirium. This tool has four key features (acute onset and fluctuating course, inattention, disorganized thinking, and altered level of consciousness) used for screening for delirium. The first two features and one of the last two must be present to make the diagnosis of delirium.

Differential Diagnosis and Assessment

The differential diagnosis of etiologies of delirium is extensive (Table 3). Delirium is caused by a medical condition, substance intoxication or withdrawal, or medication side effect. It is an occult manifestation of systemic illness. In delirium, the underlying etiology must be treated in order to attain resolution as soon as possible. Initially information may be lacking and the etiology of the delirium may not be readily apparent. It is important to remember that a potentially life-threatening situation exists and that prompt intervention can be life saving. Therapeutic interventions may be required even before a specific underlying etiology is identified. Medical evaluation and stabilization should occur in parallel. Examples of immediately life-threatening causes include hypoxia, hypoglycemia, hypotension, acute myocardial infarction, and sepsis.

Common causes of delirium include infections, insufficiency of any major organ, medication or substance use or withdrawal, electrolyte or metabolic derangements and dehydration.

TABLE 2
Confusion Assessment Method (CAM) Diagnostic Tool

1. Acute onset and fluctuating course
2. Inattention, distractibility
3. Disorganized thinking, illogical or unclear ideas
4. Alteration in consciousness

The diagnosis of delirium requires the presence of both features 1 AND 2, plus EITHER feature 3 or 4.

Adapted with permission from Inouye S, van Dyck C, Alessi C, et al. Clarifying confusion: the confusion assessment method. Ann Intern Med 1990; 113:941 (13).

TABLE 3
Differential Diagnosis of Etiologies of Delirium

Hypoxemia
Hypercarbia
Hypoglycemia and hyperglycemia
Dehydration
Electrolyte disturbance (sodium, calcium, magnesium, phosphorus)
Infection (pneumonia, urinary tract)
Sepsis
Hypotension and hypoperfusion
CNS lesion, injury, infection (CVA, subdural hematoma, meningitis, encephalitis)
Endocrinopathies (thyroid, adrenal)
Acute abdominal pathology (diverticulitis, appendicitis, mesenteric ischemia, volvulus)
Renal failure
Hepatic failure
Cardiac disease (myocardial infarction, congestive heart failure, arrhythmia)

CNS = central nervous system; CVA = cerebrovascular accident.

History

A detailed medical history is important in elucidating the etiology of delirium. It is important to obtain information from as many sources as possible including the patient, emergency medical service providers, witnesses, family, caregivers and primary care providers. Information regarding the patient's baseline mental status and level of functioning should be ascertained. It is helpful to know if the patient has underlying dementia, if there has been an acute change and what underlying medical conditions exist. A very thorough review of medication use is important, as medications are very common precipitants of delirium in the elderly (14). The history should focus on causal factors related to the acute presentation such as history of trauma or fall, lack of oral intake, presence of systemic disease including metabolic and cardiopulmonary disorders, symptoms of infection, and substance use or withdrawal (15).

Physical Examination

Vital signs should be carefully reviewed and an accurate temperature and oxygen saturation measurement obtained. A bedside glucose determination is often considered the "fifth vital sign" and is particularly important in the evaluation of the agitated patient (16). A meticulous physical examination must be performed, including neurologic and mental status examination (see mental status evaluation above). The examination should search for evidence of medical or surgical causes for the patient's condition, including trauma, infections and focal neurologic deficits.

Diagnostic Testing

Delirium requires an extensive evaluation that is further directed by clinical suspicion and response to interventions (Table 4). Laboratory eval-

TABLE 4
Assessment of the Patient with Delirium

Vital signs including accurate temperature measurement
Physical examination with thorough neurologic exam
Oxygen saturation
Stat glucose
Chemistry including electrolytes, renal function, liver function panels
Urinalysis
Chest x-ray
Electrocardiogram
Dependent upon the clinical scenario consider: head CT, lumbar puncture, blood cultures, toxicology screening, thyroid function

uation usually includes a complete blood count, electrolytes, glucose, renal and hepatic testing. A urinalysis and chest x-ray should be obtained to rule out infection. An electrocardiogram is indicated to evaluate for myocardial ischemia and arrhythmia, and to assess for QTc prolongation. Additional tests including toxicologic screens, serum levels (alcohol, aspirin, acetaminophen), and thyroid function tests may be indicated if a cause is not found on initial evaluation. A history of falls, suspected trauma, and focal findings on physical exam are indications for early neuroimaging (17). Neuroimaging should also be considered if no etiology for the delirium is identified after an initial evaluation is completed (18). Examination of the cerebrospinal fluid is needed when meningitis or encephalitis are suspected.

Risk Factors, Supportive Care and Non-pharmacologic Interventions

Delirium is a multifactorial disorder. The elderly are particularly vulnerable to the development of delirium. It is of paramount importance to try to prevent delirium before it occurs. Implementation of preventive interventions has been demonstrated to substantially reduce the risk of delirium in older hospitalized patients (19–21). Patients should be provided with an optimum level of sensory stimulation. Environmental cues and family members should be available to help re-orient patients. Patients are particularly vulnerable to the development of delirium if they are sleep deprived, dehydrated, immobilized, or have vision or hearing impairments. Patients who require hearing aids or eyeglasses should have them available to prevent sensory deprivation. Excess noise should be avoided whenever possible and patients should be allowed to have uninterrupted sleep. Oral fluids should be encouraged and if oral fluids are contraindicated, intravenous hydration should be provided. Physical restraints should be avoided, since they may increase agitation and are associated with injury and death (22).

The use of unnecessary medications should be avoided and required therapeutic agents should be selected with the most favorable side effect profile possible (14). However, pain is an important precipitant of delirium and it is important to provide adequate analgesia to patients suffering from pain (23–25).

Pharmacologic Management

Pharmacologic management is necessary in more severe cases of agitation in which patients are a danger to themselves or others, or are impeding medical evaluation and care. The ideal agent for undifferentiated acutely agitated geriatric patients would be effective with a rapid onset of action and would be safe with minimal side effects. Pharmacologic therapy in the elderly is complicated by altered concomitant age-related disorders and altered pharmacokinetics and pharmacodynamics. The elderly are more susceptible to drug toxicity in part due to decreased renal and hepatic function, as well as confounding polypharmacy. In general, drugs should be administered in the lowest effective dose.

Unfortunately, there is little evidence in the literature to guide the pharmacologic treatment of acute agitation in the elderly population. Most studies of the emergent sedation of acutely agitated patients are in a younger patient population and typically include substance abusers and patients with underlying psychiatric disturbances (e.g., psychotic or mood disorders), often without other concomitant medical problems. There are several studies that evaluate the long-term management of chronic agitation but not acute agitation in the demented elderly.

Pharmacologic options include the benzodiazepines and the typical and atypical antipsychotics agents. These options are discussed in the following sections. For rapid sedation of an acutely psychotic patient the intravenous (IV) route is preferred. In situations where establishing an IV is difficult or hazardous because of the patients agitation, the intramuscular (IM) route may be necessary. In general, oral sedation has little role in the uncooperative acutely agitated patient in an emergency setting. However, an oral agent may be considered if symptoms of agitation are not severe and may be considered prior to the escalation of symptoms.

Typical (First-Generation) Antipsychotics

Typical or conventional antipsychotics block dopamine D-2 receptors in the brain. The mechanism

by which they reduce agitation has not been elucidated, even though they are used extensively for this purpose. Typical antipsychotics are grouped into high, mid and low potency agents. High-potency typical antipsychotics include the butyrophenones (haloperidol) and droperidol. Low-potency typical antipsychotics include the phenothiazines (chlorpromazine), and thioridazine. Typical antipsychotics are associated with extrapyramidal symptoms (including rigidity, dystonia, bradykinesia, tremor, akathisia, and tardive dyskinesia) and anticholinergic side effects (including dry mouth, urinary retention and decreased cognitive function). Caution should be used in treating patients suffering from Parkinson's disease with typical antipsychotics because of the significant risk of worsening of the extrapyramidal features of the disease. A rare side effect of antipsychotic medication is the neuroleptic malignant syndrome, which is manifested by high fever, rigidity, mental status changes and autonomic instability. Patients on long-term antipsychotic therapy are at cumulative risk for the development of tardive dyskinesia, which is characterized by involuntary choreoathetoid movements. Low-potency antipsychotics are associated with a high incidence of anticholinergic side effects that can worsen cognitive function. They are much more sedating due to their antihistaminergic effects, and their alpha-adrenergic blocking effects may lower blood pressure. The side effect profile of the low-potency agents renders them inappropriate for use in the elderly.

Haloperidol is commonly used for the treatment of agitation because of its lower incidence of respiratory depression, hypotension and anticholinergic effects. Haloperidol is not Food and Drug Administration (FDA) approved for IV use, although it is commonly administered by this route and thought to be safe. Numerous studies have demonstrated its efficacy in treating aggression; however, most of these studies were of younger patients with a known psychiatric disorder (26). In 1999, the American Psychiatric Association published a practice guideline that recommended haloperidol as a drug of choice for managing the patient with delirium (27). Although there is substantial evidence of haloperidol's efficacy and safety in controlling acute agitation, published studies have included few if any elderly patients. In a study by Clinton et al., haloperidol was demonstrated to be safe and effective for the sedation of disruptive ED patients in a study in which the mean patient age was only 33 years (28). In a randomized, double-blind study of hospitalized AIDS patients with delirium, either haloperidol or chlorpromazine was found superior to lorazepam in controlling symptoms (29).

The efficacy and safety of haloperidol in the management of chronic behavioral symptoms in the demented elderly has been evaluated. A Cochrane Systematic Review of five randomized, placebo-controlled trials showed that demented subjects receiving haloperidol exhibited no significant improvement in overall agitation scores when compared to those treated with a placebo, but did find that aggression, one subtype of agitation, decreased in the haloperidol group when compared to controls (30). Unfortunately, in these studies outcomes were measured no earlier than 3 weeks after initiation of treatment. Patients receiving haloperidol reported more adverse reactions but there was no significant difference in the dropout rate from the studies between haloperidol-treated subjects and placebo controls.

Droperidol is more potent and more sedating, and has a more rapid onset and a shorter half-life than haloperidol. IM droperidol has been demonstrated to have more rapid onset and greater efficacy than IM haloperidol alone for patients with acute psychosis (31, 32). Droperidol has been used effectively for the rapid tranquilization of acutely agitated and violent patients in the ED (33). A retrospective review of its use and safety in 2,500 emergency department patients, including 141 patients over the age of 66, found that despite its widespread use, complications were extremely rare (34). In 2001, the FDA required a boxed warning for droperidol because of reports of death associated with QTc prolongation and development of torsades de pointes. There is controversy in the literature regarding the boxed warning issued to droperidol, given the decades of successful clinical use (35, 36). There is evidence to suggest that haldol is also associated with QTc prolongation and torsades de pointes (37–39).

Atypical (Second-Generation) Antipsychotics

Atypical antipsychotics act at both serotonin and dopamine receptors, and have been approved by the FDA for the treatment of schizophrenia. However, they have not been approved for the treatment of behavioral disorders in patients with dementia. In recent years numerous agents have been developed, with the anticipation of an improved side effect profile compared with typical or first-generation antipsychotics. Atypicals have been marketed as having safety profile with fewer side effects of akathisia, parkinsonism, tardive dyskinesia, sedation, peripheral and central anticholinergic effects, postural hypotension and cardiac conduction defects. A recent FDA advisory with a mandatory boxed warning on manufacturers

labeling calls this into question (40, 41). The FDA determined that the treatment of behavioral disorders in elderly patients with dementia with atypical (second generation) antipsychotic medications is associated with increased mortality. Analyses of 17 placebo-controlled studies with enrollment of 5,106 patients receiving four different drugs (olanzapine, aripiprazole, risperidone, and quetiapine) had a death rate 1.6–1.7 times higher than with placebo. Therefore, the FDA concluded that the effect is probably related to the common pharmacologic effects of all atypical antipsychotic medications, including those that have not been studied in the dementia population. Over the course of these trials, averaging 10 weeks in duration, the death rate in the treated groups were 4.5% compared to the rate of 2.6% in the placebo groups. Varied causes of death, most were either cardiovascular or infectious (e.g., congestive heart failure, sudden death, pneumonia). However, the FDA has considered adding a similar warning to the labeling for typical antipsychotic medications because the limited data suggest a similar increase in mortality for these drugs. Additionally, the recently published Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE), which compared the effectiveness of atypical antipsychotic agents with that of older agents in patients with chronic schizophrenia, also sheds doubt on the advantage of atypical agents over typical antipsychotics (42). This study found no statistically significant difference in efficacy or the incidence of extrapyramidal side effects.

Despite the FDA warnings, there is significant literature to support the use of these agents in the management of agitation in dementia. Just prior to the FDA warning bulletin, *The Expert Consensus Guideline Series. Treatment of Dementia and Its Behavioral Disturbances* recommended the use of atypical antipsychotics over conventional antipsychotics (43).

Olanzapine have been shown to be effective in the treatment of chronic agitation in the elderly patient. Most studies have focused on the management of behavioral disturbances in nursing home patients over the course of days to weeks and not on the treatment of acute agitation (44–46). There is some data to support the use of olanzapine in the management of acute agitation in the elderly. IM olanzapine was compared to haloperidol and lorazepam in the treatment of acute agitation in the ED for patients with schizophrenia and bipolar disorders (>18 years of age) and dementia (>55 years of age) (47). In the dementia group agitation was significantly reduced by olanzapine (2.5 mg) when compared with placebo, with no more sedation than lorazepam (1 mg). Olanzapine was not compared to haloperidol in the dementia group. Meehan et al. (48) compared the efficacy and safety of rapid-acting IM olanzapine in treating agitation associated with Alzheimer's disease and vascular dementia. In this double-blind study, 272 acutely agitated patients were randomized to treatment with olanzapine (dosages of 2.5 and 5.0 mg), lorazepam (1.0 mg), or placebo. At 2 hours, both olanzapine (2.5 and 5 mg) and lorazepam showed superiority over placebo in terms of reduced agitation. At 24 hours both olanzapine groups maintained superiority over placebo; lorazepam did not. There were no significant differences in sedation, adverse events, extrapyramidal symptoms, QT interval, or vital signs among all groups. Currently data supporting the use of olanzapine for acute agitation in the elderly are limited.

Ziprasidone is available in an IM formulation. In double-blind, randomized study in a younger population (79 subjects, age 20–62 years of age), ziprasidone was shown to be effective in reducing acute agitation associated with psychosis, with an excellent side effect profile (49). A retrospective study of the safety of IM ziprasidone in agitated elderly patients admitted to a neuropsychiatric service found no significant differences in QTc intervals of treated patients (50). A case series of 5 patients with Parkinson's disease demonstrated no deterioration of motor function or other relevant side effects in patients treated with IM ziprasidone for acute agitation (51). Data are limited to support or refute the use of ziprasidone for acutely agitated elderly patients.

Risperidone has been extensively studied for the management of psychosis and behavioral disturbances in patients with dementia. The only currently available parenteral formulation is an extended-acting, slow-release formulation that is dosed bi-weekly and therefore not suitable for use in acute agitation. However, there is an available rapidly dissolving oral tablet. A number of studies have demonstrated its efficacy and safety for the longer-term management of agitation in the elderly (52–54). There is one study suggesting the efficacy of risperidone in controlling the agitation of delirium over several days (55). In this retrospective review, 41 subjects received risperidone and 36 received haloperidol, with both agents demonstrating effectiveness. However, the use of risperidone to immediately control acute agitation has not been studied.

Benzodiazepines

Benzodiazepines potentiate the effect of gamma amino butyric acid (GABA) by binding to GABA receptors in the brain. Benzodiazepines are effective and commonly used to sedate violent and severely agitated younger patients. In younger patients benzodiazepines produce a rapid decrease in agitation with minimal side effects. However, they are respiratory

depressants and respiratory status must be closely monitored after administration. There are few data in the literature regarding the use of benzodiazepines for the control of acute agitation in the elderly.

Diazepam has no role in the treatment of the elderly because of its prolonged half-life and active metabolites. Midazolam has the fastest onset of action and the shortest duration of effect.

In a study by Nobay et al. in younger patients (mean age 40.7), IM midazolam had significantly shorter onset of action and shorter duration of effect than both IM haloperidol and IM lorazepam (56). In a study by Martel et al. of acute undifferentiated agitation in patients with a mean age of 37 years (range 19–68), 5 mg of IM midazolam achieved adequate sedation more rapidly than 5 mg of droperidol or 20 mg of ziprasidone (57). Respiratory depression requiring supplemental oxygen administration was a frequent adverse effect.

Intramuscular lorazepam has been widely studied for sedation of the agitated young patient in the ED (56–59). However, only one randomized, controlled trial investigated its use in the delirious elderly patient (48). In this study, lorazepam was more effective than placebo in reducing agitation and was well tolerated. The risk of respiratory depression was not specifically assessed.

There are many recommendations in the literature advising against the use of benzodiazepines in the elderly. Elderly demented patients with chronic agitation treated with benzodiazepines are at an increased risk of falls, sedation and cognitive impairment (60–62). However, these adverse effects are probably not relevant to the acute temporary management of an agitated patient.

There is a body of evidence regarding safety and efficacy information of benzodiazepines in elderly patients undergoing conscious sedation for elective procedures or receiving them as pre-anesthetic adjuncts. Randomized trials do not reveal a significant risk of post-sedation cognitive impairment in elderly patients receiving intravenous midazolam for conscious sedation (63, 64). Clinical trials have identified a risk of hypoxia and respiratory depression with IV administration of midazolam when given alone to the elderly (65). This risk may be higher in the elderly than in younger patients (66). There may be an increased risk of hypoxia in patients with underlying respiratory disease, such as chronic obstructive pulmonary disease, as well.

There is little data to support concerns of potential behavioral disinhibition or paradoxical agitation in response to benzodiazepine administration in the elderly. The literature is generally limited to case series (67, 68), and there is no strong evidence that the elderly are at any increased risk of this adverse effect.

There are several clinical scenarios in which benzodiazepines offer an advantage over antipsychotics. Benzodiazepines are the treatment of choice for delirium related to alcohol or benzodiazepine withdrawal (27). Benzodiazepines are particularly effective in agitated patients with sympathomimetic toxidromes, such as in cocaine and phencyclidine intoxication (33). Since benzodiazepines are not associated with extrapyramidal symptoms, they are not contraindicated in patients with Parkinson's disease. Benzodiazepines may be the preferred sedative in situations where raising the seizure threshold is important.

Combination Therapy

The combination of an antipsychotic and a benzodiazepine is often used for the rapid tranquilization of acutely agitated, violent younger patients. A study of haloperidol and lorazepam in patients with an average age of only 34.2 years demonstrated that the combination of the two was more effective than either drug alone (59). However, the American Psychiatric Association's Practice Guideline for the treatment of delirium cited combination therapy with a typical antipsychotic and a benzodiazepine as potentially beneficial in that it allows for the use of a lower dose of each medication and thus lowers the risk of each drug's side effects (27). The treatment of elderly agitated patients with a combination drug therapy has not been studied. In general it is thought to be best to minimize the number of medications when treating geriatric patients.

Summary

The hallmarks of delirium include global cognitive impairment, relatively rapid onset of symptoms, and a fluctuating clinical course over a period of hours to days. The elderly are particularly susceptible to delirium. Delirium is associated with significant morbidity and mortality. Elderly patients with acute mental status changes including agitation should be assumed to be suffering from an acute medical illness until proven otherwise. More subtle cases of delirium may not be recognized if an accurate mental status examination is not performed. Delirium is a medical emergency due to the multiple possible serious underlying medical causes. There is a need to provide immediate interventions for urgent medical conditions. Medical evaluation and stabilization should occur in parallel. Virtually any medical condition can precipitate the development of delirium. Patients with delirium need thorough

TABLE 5
Summary of the Initial Evaluation and Management of the Agitated Elderly Patient

Provide immediate interventions for urgent medical conditions
Assume the etiology of the agitation is delirium
Assess for underlying etiology or exacerbating factors and manage appropriately
Review history of present illness, medical history and medication profile
Provide optimal environmental and supportive interventions
Pharmacological agents should be considered when the patient has the potential to harm themselves or others, or is impeding medical evaluation and management
Pharmacolo]ents must be used in age-adjusted doses

work-ups to evaluate for the underlying cause of the delirium.

Rapid sedation is necessary if the patient is a danger to self or others, or if the agitation is impeding medical evaluation and management. Unfortunately, the evidence to guide pharmacologic management of acute agitation in the elderly is limited. Current pharmacologic options include the typical and atypical antipsychotic agents and the benzodiazepines. There are FDA boxed warnings of increased mortality for the use of droperidol and the atypical antipsychotics, rendering their use problematic. Haloperidol appears to be generally safe and effective and causes less respiratory depression than the benzodiazepines. However, the benzodiazepines may be preferable in particular clinical scenarios. It is important to remember to reduce dosing in elderly patients as they have altered pharmacodynamics and pharmacokinetics (Table 5).

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