

AGITATION

Agitation, a heightened state of arousal and non-purposeful motor activity, represents the extreme of the arousal continuum. Its onset is usually quite abrupt, almost universally disruptive to patient care, and frightening to the patient and their family members.

Immediate Evaluation of Agitation

A rapid assessment should begin with ruling out any life-threatening situations. Many of these conditions (tension pneumothorax, occluded endotracheal tubes) can present with severe agitation and mental status changes and should be excluded first. Simultaneously, the patient should be protected from harming themselves through falls, self-extubation, and tube removal. Identifying and correcting less life-threatening issues should follow; ruling out ventilator dyssynchrony, bladder catheter occlusion, un-addressed pain, or pending bowel incontinence (especially in patients unable to communicate). Once such diagnoses have been excluded, appropriate management of agitation can proceed.

Pharmacological Management of Agitation

Haloperidol

Haloperidol is often utilized for the rapid control of the acutely and severely agitated patient. Initial dosing of 5 mg intravenously should be used and may be repeated every 10-15 minutes (usually with increasing dosages) until adequate control is achieved. If intravenous access is lost or unobtainable, intramuscular use is also successful but likely to take longer to achieve results. Its side effect profile, however, has historically limited the enthusiasm for its use (Table 4). Concomitant use of benzodiazepines or benztropine decreases extra-pyramidal symptoms (EPS) in the acutely agitated patient.

Atypical anti-psychotics

Atypical anti-psychotics have gained increased attention for use as alternative agents for management of acute agitation. In lower doses than that required for acute psychoses management, risperidone, ziprasidone, and olanzapine have been shown to be appropriate alternatives for treatment of acute agitation. Their safety profiles include lower incidence of EPS and better patient tolerance. As well, once agitation is under control, these agents can be changed to the enteral route for continued use until agitation has resolved.

However, these agents carry equal, if not higher, risk of arrhythmias. As such, they have failed to demonstrate a superior safety profile to haloperidol in managing the acutely agitated patient.

Table 4. Agents utilized for agitation and delirium

	<i>Initial dosing</i>	<i>Half-life</i>	<i>Renal Dosing</i>	<i>Hepatic Dosing</i>	<i>Adverse events/comments</i>
Haloperidol	2-5 mg IM/IV* ; double dose until effect achieved; use effective dose (?PO) scheduled q 6 h	21-24 hr	No adjustment	Caution with severe hepatic impairment	Neuroleptic malignant syndrome (NMS), akathisia, tardive dyskinesia, arrhythmias
Olanzapine	2.5-5 mg IM (or 5-10 mg PO/PT) q 2 hr prn; if effective, start 2.5-5 mg PO/PT qhs	21-50 hr	No adjustment	Caution with severe hepatic impairment	NMS, akathisia, tardive dyskinesia, severe hyperglycemia
Risperidone	0.5 mg-1 mg PO/PTq 6 hr prn, then use effective dose q 12 hr	20-36 hr	Half dose with CrCL<50; half dose and use qd with CrCL <10	Half dose and use qd with severe impairment	Available as dissolving tablet; NMS, akathisia, tardive dyskinesia
Quetiapine	25-50 mg PO/PT q 4-6 hr prn, then use effective dose q 12 hr	6-8 hr	No adjustment	Half dose and use qd with severe impairment	NMS, tardive dyskinesia, QTc prolongation, headache, severe hyperglycemia, hyperlipidemia
Ziprasidone	10-20 mg IM q2-4 prn or 20 mg PO/PT q 4-6 hr prn, then use effective dose q 12 hr	6-8 hr	Avoid IM use	No adjustment	NMS, tardive dyskinesia, QTc prolongation, headache, akathisia

*Not FDA approved for intravenous administration

DELIRIUM

Prevalence and Impact on Outcomes

Delirium is a global disturbance of consciousness characterized by fluctuating mental status, inattention, and disorganized thinking. Delirium has been historically dismissed as an expected complication of the hospitalized elderly patient, and its impact on outcomes thought to be negligible. However, recent studies have shown that delirium is significantly under-diagnosed, not limited to the elderly patient, and is associated with a 3-fold higher mortality. Additionally, patients with delirium have higher hospital costs and experience significant cognitive impairment long after discharge. We have recently demonstrated that delirium occurs in 80% of mechanically ventilated medical ICU patients and over 75% of mechanically ventilated patients in surgical ICUs. Surprisingly, we noted that the trauma ICU population, which is much younger than that of either medical or surgical ICU patients and less likely to have co-morbidities, has an almost 70% prevalence of delirium.

Assessment of Delirium

The Confusion Assessment Method for the ICU (CAM-ICU) tool is a valid and extremely reliable tool, taking an average of 60 seconds to perform. The CAM-ICU is comprised of four features: acute change or fluctuation in mental status (Feature 1), inattention (Feature 2), disorganized thinking (Feature 3) or an altered level of consciousness (Feature 4) (Figure 3). In patients who are medically, traumatically, or pharmacologically comatose (RASS of -4 or -5), CAM-ICU is not assessed due to lack of any response to verbal stimulation. In patients with RASS scores of -3 or higher, CAM-ICU should be utilized. To be diagnosed as delirious, the patient should have a

RASS score of -3 or higher, with an acute change or fluctuation in mental status (feature 1), accompanied by inattention (feature 2) and either disorganized thinking (feature 3) or an altered level of consciousness (feature 4).

Risk Factors for the Development of Delirium

Sleep deprivation, hypoxia, sensory impairment, as well as exposure to numerous medications (sedatives, analgesics, anti-cholinergics, anti-histamines, anti-arrhythmics, and steroids) have all been implicated as risk factors for delirium. In a recent study of surgical and trauma patient, we identified only two risk factors for developing delirium. Midazolam was associated with a 3 fold higher risk of developing delirium. This is consistent with data from our MICU study in which lorazepam was an independent risk factor. In addition, fentanyl demonstrated an increased risk for development of delirium, while morphine appeared to have a protective effect. This “protective effect,” however, needs to be considered in the context that fentanyl is often (inappropriately?) used as a sedative, while morphine is exclusive used as an analgesic.

Prevention of Delirium

Avoiding high risk medications, preserving sleep hygiene, and treating symptoms with appropriately targeted medications (i.e.-opiates for pain, benzodiazepines for anxiety, anti-histamines for pruritus, not for sleep) are the foundations upon which one can hope to prevent delirium. Preserving or re-establishing the patient’s senses (eye glasses and hearing aids) and providing sufficient daytime cognitive stimulation (through staff and family interactions) may help to prevent development of delirium or at least shorten its duration and reduce symptom severity.

Treatment of Delirium

Initial management

Initial treatment is aimed at reversing and or treating any underlying medical conditions suspected of contributing to its development (Figure 4). After evaluating potential metabolic or infectious sources, all efforts should be made to remove “deliriogenic” medications. These include benzodiazepines, anti-histamines, anti-cholinergics (specifically diphenhydramine), and corticosteroids. Instituting daily interruption of sedatives and analgesics, and using these agents within a strict protocol, has both been shown to improve patients’ outcomes. Next, interventions focusing on environmental control, cognitive re-orientation, and “normalization” of clinical parameters should be implemented. Environmental control entails re-establishing sleep hygiene, through control of excessive noise and staff disturbances at night and ensuring lights are on in the daytime and off at night. Sleep agents may be added to assist with sleep onset, depth, and duration. Increasing daytime communication with family and friends, increasing physical activity, and ensuring replacement of eye glasses and hearing aids is vital to achieving re-orientation of the delirious patient.

Pharmacological intervention

Haloperidol: Haloperidol is the agent most often used at our institution as it has few anti-cholinergic effects, few active metabolites, and mild sedating side effects. It is available in oral and intramuscular forms, but we typically use it intravenously (although not FDA approved) because of its rapid onset and control of agitation.

Atypical anti-psychotics: In patients with enteral access, risperidone, olanzapine, quetiapine, and ziprasidone are available and have been used at our institution. These

medications, however, often require titration to higher doses and increased frequency, but are associated (as with haloperidol) with arrhythmias, including QTc prolongation and Torsades de pointes. Use of these medications has, in our experience, been associated with better tolerance of treatment and fairly quick return to the patient's baseline mental status. Improved sensorium and resolution of delirium symptoms appear to coincide with the re-establishment of the sleep-wake cycle. Unless delirium is felt to be the result of sedative or alcohol withdrawal, benzodiazepine monotherapy should be avoided.