Delirium in the Intensive Care Unit: Medications as Risk Factors

Earnest Alexander, PharmD, replies:

Delirium is a clinical syndrome characterized by a disturbance in consciousness, attention, cognition, and perception. It may develop over a period of hours to days and is the most common clinical neuropsychiatric condition, occurring in 26% to 44% of hospital admissions. An alarmingly high incidence of up to 80% has been reported in critically ill patients. Delirium is associated with prolonged mechanical ventilation, self-extubations, and the need for reintubation, which have led to increased hospital stay, mechanical ventilator days, and mortality risk. This negative impact on outcomes and potential reversibility of the condition in up to 50% of cases, makes understanding risk factors for ICU delirium extremely important.

Predisposing and Precipitating Risk Factors

Delirium, especially in older patients, is usually multifactorial in origin. The risk factors for ICU delirium can be divided into 2 basic categories: predisposing factors (host factors) and precipitating factors. Predisposing factors are present before the patient is admitted to the ICU, therefore making them difficult to alter. Some examples are older age (incidence of 0.4% in those >18 years old, 1.1% of those over age 55, and 13.6% in those over 85 years) or history of hypertension, smoking, or alcoholism. Conversely, precipitating factors occur during the ICU stay. These factors may be secondary to the patient’s acute illness or may be iatrogenic in nature, including severity of illness, metabolic disturbances (eg, abnormal sodium, calcium, and blood urea nitrogen levels), acute infection, hypoxemia, surgery, anemia, acidosis, and hypotension. In addition to these factors, there are some commonly used ICU medications that are considered precipitating risk factors for ICU delirium.

Fortunately, precipitating risk factors are considered potentially modifiable. Strategies may be focused on either prevention or treatment of ICU delirium. Because of this unique opportunity to affect patient care, it is critical that the bedside nurse be aware of both types of risk factors and strategies to minimize ICU delirium. This brief review will focus on commonly used ICU medications as precipitating risk factors for ICU delirium.

Medications

It is reported that medications alone may account for 12% to 39% of all cases of delirium. The Table outlines some commonly used medications associated with delirium. Some of these medications include, but are not limited to, opioids (eg, fentanyl, morphine), anxiolytics (eg, benzodiazepines), antidepressants (eg, tricyclic antidepressants), and corticosteroids. Data supporting a role of sedatives and analgesics as risk factors for ICU delirium are accumulating rapidly. These agents represent the leading precipitating risk factors for ICU delirium. Benzodiazepines (eg, lorazepam) and narcotics (eg, morphine and meperidine) have a proven association in both medical and

Q What medications commonly used in the intensive care unit (ICU) would predispose the patients to delirium? Are there any drug interactions that we should be paying attention to?
surgical ICU settings. Opioid use has been associated with delirium in several large prospective studies in hospitalized patients. Some data suggest that the risk of opioid-induced delirium is dose related, occurring with dose increases of fentanyl. Additional studies are warranted to identify the exact dosing thresholds and amount of dose increase and/or duration of therapy linked to delirium.

Benzodiazepines are commonly used sedatives within the ICU and have also been implicated as the cause of paradoxical hostility, aggressiveness, confusion, and agitation. This relatively infrequent response to therapy is thought to be due to anticholinergic activity. There is a well documented relationship for anticholinergic medications with muscarinic receptor affinity. Interestingly, there are a number of agents aside from benzodiazepines (more than 600 medications) identified with anticholinergic effects. Anticholinergic-induced delirium is characteristically associated with agitated behavior and visual hallucinations. The lack of these symptoms in many delirious patients has led to some debate over whether anticholinergic activity is solely responsible for delirium.

There are a number of agents with a potential association with delirium. Much of the data are limited to case reports and case series, with relatively few randomized controlled studies in these patients. Over the past few decades, the bulk of medication-induced delirium cases have been published in the setting of palliative care. In the past 10 years, a number of studies have provided data specific to the ICU. These data in critically ill patients have been invaluable tools in evaluating precipitating risk factors, especially medications, in the development of ICU delirium.

**Conclusion**

Identifying the relationship between medications and delirium continues to be a challenge for clinicians and researchers. The Confusion Assessment Method-ICU...
(CAM-ICU) is a useful tool for bedside assessment of cognitive function and diagnosis of delirium on admission and throughout ICU stay. Medication administration must precede the onset of symptoms (usually hours to days). As signs of delirium occur, withdrawal of the offending agent(s) must be considered. Upon withdrawal of the medication, a return to baseline cognitive function should occur. If withdrawal is not possible, then decreasing the dosages of these potential culprits to the lowest possible dosages is warranted. Additionally, any other clinical conditions that may be contributing to the delirium (e.g., hypoxemia, anemia, infection) must be managed as well. The bedside nurse is in a front-line position to manage and more importantly prevent delirium before it negatively affects patient outcomes.

References

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