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Critical Care

Screening and Management of Delirium in Critically Ill Patients

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Delirium is highly prevalent in the critically ill population and has been associated with numerous negative outcomes including increased mortality. The presentation of a delirious patient in the intensive care unit (ICU) is characterized by a fluctuating cognitive status and inattention that varies dramatically among patients. Delirium can present in 3 different motoric subtypes: hyperactive, hypoactive, and mixed. Two tools, the Intensive Care Delirium Screening Checklist and Confusion Assessment ICU, are validated and recommended for the detection of delirium in critically ill patients. The identification of delirium in a critically ill patient should be facilitated using one of these tools. An intermediate form of delirium known as *subsyndromal delirium* also exists, although the significance of this syndrome is largely unknown. Another phenomenon known as *sedation-related delirium* has been recently described, although more research is needed to understand its significance. Patients in the ICU are exposed to many risk factors for developing delirium; controlling these risk factors is essential for preventing delirium development in critically ill patients. Nonpharmacologic interventions have been shown to prevent patients from developing delirium. Prevention is crucial because once delirium develops pharmacologic therapy is limited.

Delirium is highly prevalent in critically ill patients and has been reported to occur in over 80% of mechanically ventilated patients.[1-3] A host of negative outcomes have been associated with delirium including increased intensive care unit (ICU) mortality, increased inpatient mortality, increased ICU length of stay, increased inpatient length of stay, and long-term cognitive impairment.[2,4-8] Unfortunately, the pathophysiology of this syndrome is not well understood. Proposed mechanisms for pathogenesis include neuroinflammation and neurotransmitter imbalances.[9] The limited knowledge of delirium pathogenesis contributes to the difficulties encountered in managing this common, burdensome syndrome.

PRESENTATION

Patients with delirium present with an acute fluctuating cognitive status that is highlighted by inattention and an inability to form cohesive thoughts.[10] It is important to note that delirium and dementia are not the same: Delirium presents as an acute change in mental status, whereas dementia is a more chronic process.[11] Furthermore, a patient with dementia can go on to develop acute delirium.[11,12]

Delirium follows an unpredictable time course from patient to patient in the ICU. The majority of delirium events occur within the first few days of ICU admission; however, patients can also develop delirium at any point in the ICU stay.[13,14] Additionally, the fluctuating nature of delirium means that a patient may oscillate between different mental states at various points. For example, a patient may be delirious at one point in time, nondelirious 8 hours later, and then delirious again the next day. At the University of Pittsburgh Medical Center, we conducted a quality improvement project in 230 medical ICU patients that demonstrated that initial delirium occurred at various points of ICU stay, including over a week after ICU admission. Furthermore, 36.1% (13/36) of patients developed multiple episodes of delirium.[15] The course of delirium varies dramatically among

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patients in regard to both initial presentation and number of incidences.

Once delirium develops, it presents in 1 of 3 different motoric subtypes: hyperactive, hypoactive, and mixed.[16,17] Hyperactive delirium is characterized by agitation, restlessness, and hallucinations, whereas hypoactive delirium presents with lethargy and inability to concentrate. A mixed presentation involves elements of both hypoactive and hyperactive delirium. Hypoactive delirium occurs on a more frequent basis than either hyperactive or mixed delirium in critically ill patients; studies indicate that over 60% of delirious patients present exclusively in the hypoactive form.[18,19] The consequences associated with delirium appear to be consistent among all 3 types of presentation.

SCREENING

Delirium is difficult to recognize without the use of a diagnostic tool, especially when it presents with hypoactive symptoms such as lethargy.[20] Several tools for screening for delirium in the ICU are available. In the recent release of the pain, agitation, and delirium guidelines, 2 validated tools for screening of delirium are recommended: (1) Confusion Assessment Method for ICU patients (CAM-ICU) and (2) Intensive Care Delirium Screening Checklist (ICDSC).[21] Both tools were developed using the *Diagnostic and Statistical Manual of Mental Disorders* criteria and can be administered quickly by a bedside clinician. Although researchers attempted to ascertain whether the CAM-ICU or ICDSC is the superior screening tool, evidence is conflicting and both tools are widely utilized.[22-24] If patients in the ICU are going to be assessed for delirium, then either the CAM-ICU or ICDSC should be used.

The CAM-ICU was first validated in 2001 and returns a dichotomous value of either delirious or not delirious.[1] It was translated into a flowsheet that has been utilized to easily assess for delirium.[25] Screening with the CAM-ICU is often conducted on a once- or twice-daily basis.[1,26]

The ICDSC screens for delirium on 8 different domains, 4 of which screen for hypoactive delirium and 4 for hyperactive delirium. It was also validated in 2001 and yields an ordinal score that can classify patients into the domains of nondelirious (ICDSC = 0-3) or delirious (ICDSC = ≥4).[27] The ICDSC has been studied in use up to 4 times daily.[28]

SUBSYNDROMAL DELIRIUM

An intermediary state between delirium and lack of delirium known as *subsyndromal delirium* is described in critically ill patients. Patients with subsyndromal delirium are reported to have worse clinical outcomes for ICU and inpatient length of stay and long-term cognitive impairment relative to patients with no symptoms of delirium.[29] Subsyndromal delirium is common in ICU patients; one study reported a prevalence approaching 90% in patients who did not have full delirium.[5] It is unknown whether subsyndromal delirium is a transitive state that is predictive of the imminent development of full delirium. At the University of Pennsylvania Medical Center, we found the prevalence of subsyndromal delirium to be common in patients who did and did not go on to develop full delirium (47.2% of delirious patients vs 42.7% of nondelirious patients).[15] In regard to screening, the CAM-ICU does not easily recognize subsyndromal delirium due to its dichotomous nature; the ICDSC more easily recognizes subsyndromal delirium, with a score of 1 to 3 being indicative of this syndrome.[29] Despite the potential negative outcomes, the significance and management of subsyndromal delirium are still unclear.

SEDATION-RELATED DELIRIUM

Recently, a phenomenon known as *sedation-associated delirium* has been described in critically ill patients.[30] Sedation-related delirium is a type of delirium that rapidly ceases once sedation is removed from a patient and it is not associated with the negative outcomes of traditional or persistent delirium. The study describing sedation-related delirium screened for delirium using the CAM-ICU. The CAM-ICU may not be as specific in sedated patients and may falsely identify nondelirious patients as delirious. The ICDSC may be better suited for delirium screening in sedated patients.[31] Until more research is conducted, including a study describing sedation-related delirium using the ICDSC, the significance of sedation-related delirium remains controversial.

RISK FACTORS

Several risk factors render a critically ill patient more susceptible to developing delirium. Some of these risk factors are nonmodifiable and include higher severity of illness upon ICU admission, sepsis, preexisting dementia, older age, and history of smoking.[4,11,13,14,23] Several other risk factors can be modified, and limiting these risk factors is crucial to prevent delirium from developing in patients. One of the most controversial risk factors is administration of benzodiazepines. Although many studies have

shown that benzodiazepine administration does not increase risk of delirium, there are also ample data to suggest the contrary.[5,6,14,26] The pain, agitation, and delirium guidelines state that benzodiazepine use may be a risk factor for delirium development.[10] It is prudent to avoid administering benzodiazepines as first-line sedatives or in excessively high doses to critically ill patients due to the potential delirious effects of these medications. Administering dexmedetomidine as a sedative agent has shown promise in regard to reducing the duration of delirium in critically ill patients.[32,33] Oversedation has been associated with an increased incidence of delirium.[4] Conflicting data also exist regarding the role of opioid exposure in delirium development; it seems that morphine sulfate likely is associated with delirium development.[5,14] Other risk factors that have been associated with development of delirium include hypertension, chronic obstructive pulmonary disease, hypoalbuminemia, and elevated bilirubin levels.[14,34] Many ICU patients unfortunately possess many of these factors at once and as a result are at especially high risk for developing delirium.

MANAGEMENT

Prevention

In addition to controlling risk factors, nonpharmacologic therapy has been shown to be beneficial for preventing development of delirium in patients. Early mobility protocols have been shown to be quite effective in preventing the development of delirium.[35] Other interventions that have been shown to be valuable for delirium prevention include reorientation strategies, visual and hearing aids, sleep protocols, and nursing education.[36-38]

Treatment

Once delirium is recognized and diagnosed, what is to be done to treat these patients? Unfortunately, the evidence for efficacy of pharmacotherapy is limited. Haloperidol lactate is the historical drug of choice for delirium, especially the hyperactive subtype, most likely due to its calming effects and ability to be administered parenterally; however it has not been shown to reduce the course of delirium in patients.[39] Atypical antipsychotics such as olanzapine and quetiapine fumarate have been shown to reduce the duration of delirium and are commonly used in delirious patients, although the data are limited.[40,41] All of the antipsychotic medications carry a risk for adverse events, particularly QTc prolongation.[28,40,41] Consideration should be given to limiting the number of agents with pharmacokinetic and pharmacodynamic properties that may yield QT prolongation in patients.[42] Realistically, the best method to manage delirium is to prevent it from occurring. This requires careful management of the risk factors mentioned previously and utilization of nonpharmacologic interventions.

CONCLUSION

Delirium is an extremely common syndrome in critically ill patients and is associated with many extremely negative outcomes. It can present at any time during a patient's ICU stay and in a variety of different manners. Both the CAM-ICU and ICDSC are validated for detecting delirium in critically ill patients. Practitioners should seek to actively prevent delirium before it occurs via modification of risk factors and nonpharmacologic protocols; once delirium develops in patients, pharmacotherapy options are limited. Delirium is a prominent issue in the care of critically ill patients, and all inpatient pharmacists should have an understanding of this syndrome in order to provide optimal patient care.

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