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SPECIAL FEATURE

Assessment, Prevention, and Treatment of Delirium in the ICU

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Dr. McFeely reports no financial relationships relevant to this field of study.

The Society of Critical Care Medicine (SCCM) published a clinical practice guideline for the management of pain, agitation, and delirium in adult patients in the intensive care unit (ICU) as part of an overall program aimed at liberating patients from the ventilator (and from the ICU in general).[1] The purpose of this special feature will be to review the assessment, prevention, and treatment of delirium in ICU patients.

Delirium is a syndrome characterized by the acute onset of central nervous system dysfunction identified by the following four features: 1) a change or fluctuation in baseline mental status, 2) inattention, and either 3) disorganized thinking or 4) an altered level of consciousness. Delirium affects 60-80% of those on mechanical ventilation and a lesser number of ICU patients who are not ventilated. Delirium is an important predictor of negative outcomes in ICU patients. Even after adjusting for age, severity of illness, coma, and other relevant covariates, patients with delirium have a three-fold higher mortality rate at 6 and 12 months, have a longer hospital length of stay, and may develop long-term cognitive impairment resembling a dementia-like state.[2] Many studies have shown that ICU delirium cannot be accurately diagnosed unless a valid and reliable assessment tool is used. Yet the use of such tools is still limited in clinical practice, as is the use of a safe and effective strategy to ensure patient comfort while maintaining a light level of sedation.[3]

At least four risk factors have been associated with the development of delirium in the ICU:

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Table 1: CAM-ICU Diagnostic Criteria (Must have features 1 and 2, and either 3 or 4)
1. Patient's mental status is different than his/her baseline OR fluctuation in mental status in the previous 24 hrs identified based on an objective rating scale (such as RASS) or a previous delirium assessment
2. Inattention as evidenced by inability to identify letters or pictures when asked to do so
3. Altered level of consciousness (any RASS score other than 0)
4. Disorganized thinking evidenced by inability to answer questions

Table 2: Tips To Prevent the Development of Delirium
Repeated reorientation of patients
Minimization of unnecessary noise/stimuli
Cognitively stimulate patients multiple times daily
A non-pharmacologic sleep protocol
Use of a scheduled pain management protocol
Early mobilization
Regular assessment of the need for catheters and physical and chemical restraints
Use of eye glasses and magnifying lenses, hearing aids

pre-existing dementia, hypertension, alcoholism, and severity of illness. Other factors that may play a role include age, neurologic illness (such as coma), and use of medications (sedatives, antipsychotics, analgesics). Delirium develops rapidly in the ICU, often over hours to days, and is commonly reversible. There are three subtypes of delirium: hyperactive, hypoactive, and mixed. Most ICU patients have a mixed type.

ASSESSMENT

The most commonly recommended bedside tool for identifying delirium in the ICU is the Confusion Assessment Method for the Intensive Care Unit (CAM-ICU). The CAM-ICU tool is adapted for use at the bedside to identify the four diagnostic features of delirium. It has been shown to be a valid instrument in the ICU patient population, is easily and quickly applied at the bedside, and has good inter-rater reliability.[4]

The CAM-ICU tool consists of four tests (*see Table 1*). For the diagnosis of delirium to be made, the patient must have both elements 1 and 2 and at least element 3 or 4. The tool requires use of the Richmond Agitation-Sedation Scale (RASS), an objective measure of level of consciousness (LOC). Other LOC scales can be used and translated into the RASS for this purpose. This tool should be applied to all ICU patients at least once a shift, or as often as every 2 hours for a patient with fluctuating mental status. Patients deemed CAM-ICU positive are considered to have delirium.

PREVENTION

Delirium occurs at some point in most ICU patients. There are some actions that can be taken that will help minimize the likelihood of development of delirium and can help speed its resolution (*see Table 2*). Most of these are non-pharmacologic and involve environment of care. They include maintaining a normal sleep wake cycle and intellectual engagement between the patient and his/her family and care team.

TREATMENT

Once a patient is identified as having delirium, initiation of a management protocol is appropriate (*see Tables 3 and 4*). Many non-pharmacologic interventions can both prevent and treat delirium. Pharmacologic therapy remains controversial. There are no data indicating the use of haloperidol reduces the duration of delirium in ICU patients. Atypical antipsychotics may reduce delirium duration.[5] Development of torsades is always a concern. No

Table 3: Treatment of Delirium (CAM-ICU Positive) Patients
1. Consider differential diagnosis (sepsis, medications, CHF, etc).
2. Consider removing drugs that promote delirium (metoclopramide, H2 blockers, promethazine, diphenhydramine, steroids, etc)
3. Begin non-pharmacologic protocol (*See Table 4*)
4. If patient is agitated (RASS +2 to +4), assess and treat pain if present. If not, use minimum (non-benzodiazepine) sedative needed for comfort. Consider typical or atypical antipsychotics.
5. If patient is calm (RASS 0 to +1), assure pain control. Consider typical or atypical antipsychotics.
6. If patient is sedate (RASS -1 to -3), reassess sedation goal or perform spontaneous awakening trial.

Table 4: Non-Pharmacological Protocol
Orientation Provide visual and hearing aids Encourage communication and reorient patient repetitively Have familiar objects from patient's home in the room Attempt consistency in nursing staff Allow television during day with daily news Non-verbal music .
Environment Sleep hygiene: Lights off at night, on during day. Sleep aids (zolpidem, mirtazipine) Control excess noise (staff, equipment, visitors) at night Ambulate or mobilize patient early and often
Clinical parameters Maintain systolic blood pressure > 90 mmHg Maintain oxygen saturations > 90% Treat underlying metabolic derangements and infections

recommendations were made in the most recent guidelines for use of any class of antipsychotics to treat delirium. Dexmedetomidine is preferred over benzodiazepines as a sedative for treatment of non-alcohol or benzodiazepine withdrawal delirium. It is also preferred over benzodiazepines for ventilated patients with delirium.[6,7]

Ultimately, identification and treatment of delirium is part of the overall goal of early liberation from the ventilator and the ICU in general. Incorporating the preventive measures listed here and routine use of a validated assessment tool such as CAM-ICU will minimize development of delirium, as well as allow early initiation of pharmacologic and non-pharmacologic treatments when it does occur. Vanderbilt University has developed an excellent website (icudelirium.org) that provides resources and educational materials for delirium assessment. There you will find a training manual, worksheets, pocket cards for bedside providers, and patient education materials, as well as information on the other elements of the liberation bundle. More information on delirium and additional free tools to facilitate implementation of the guidelines in your facility can be found at iculiberation.org. ■

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ABSTRACT & COMMENTARY

Does Functional Ability Prior to an ICU Admission Influence Outcomes in Older Adults?

By Linda Chlan, PhD, RN, FAAN

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Dr. Chlan reports no financial relationships relevant to this field of study.

SYNOPSIS: Admission to an ICU results in functional decline and increased mortality in older adults, particularly in those severely disabled prior to critical illness or injury.

SOURCE: Ferrante L, et al. Functional trajectories among older persons before and after critical illness. *JAMA Intern Med* 2015 February 9 [Epub ahead of print].

The impact of an older person's functional status prior to experiencing hospitalization for a critical illness is difficult to determine. Given that ICU admission is generally an unplanned event, obtaining prospective evaluations of function prior to a critical illness or injury is almost impossible. Most evidence to date has utilized proxy reports for a patient's functional status to determine what, if any, pre-ICU disability may have on an older adult's outcomes after hospitalization for a critical illness or injury.

The study by Ferrante and colleagues had the opportunity to access a rich longitudinal dataset containing 754 community-dwelling persons age 70 years and older in the New Haven, CT, area. Participants in the parent study had no disabilities initially and had in-home assessments at 18-month intervals for a total of 162 months, followed by monthly telephone interviews through December 31, 2012. In total, participants were followed for 15 years. These monthly interviews queried participants for impairments in 13 disabilities including basic, instrumental, and mobility activities. Medicare claims data were used to determine if any of the participants experienced an ICU admission. If so, ICU data were then obtained for length of ICU stay, receipt of mechanical ventilation, diagnosis of shock, specific ICU service (medical, surgical, neurological, cardiac), and discharge diagnosis. Modeling techniques were used to determine participants' functional trajectory in the year before and year after ICU admission. A number of important clinical covariates (age, sex, education, race, chronic conditions, mechanical ventilation, ICU length of stay, cognitive impairment, etc.) were then modeled to determine the trajectory of participants during the post-ICU period, including 30-day and 1-year mortality.

Of the participants in the parent study, 291 (38.6%) were admitted to an ICU. A majority of those patients were female (58%), non-Hispanic whites (88.7%) with a mean age of 83.7 years. Most patients were admitted to a medical or general ICU, followed by surgical or cardiothoracic, neurosurgical ICU, or burn. Functional trajectories were identified as minimal disability (20.8%), mild-to-moderate disability (28.1%), and severe disability (51.1%). A full 53.4% of the participants had functional decline or experienced early death after ICU admission. For those older patients with minimal disability prior to ICU admission, approximately 25% developed serious disability or early death after hospitalization in the ICU. Of participants with mild-to moderate disability, 39.5% developed serious disability and 25% early death. Lastly, a full one-third of those participants admitted to a critical care unit with severe pre-ICU disability experienced early death. Approximately 24% of the participants died in the ICU. Overall, the 30-day mortality rate was 21%, most significantly influenced by the receipt of mechanical ventilation, diagnosis of shock, and cognitive impairment. Whereas pre-ICU functional trajectory was not significantly associated with 30-day mortality, mild-moderate and severe pre-ICU functional trajectories were associated with more than double and triple the risk of death within 1 year of ICU admission compared to minimal disability. Overall 1-year mortality was 43%, and it was also influenced by ICU length of stay, receipt of mechanical ventilation, and diagnosis of shock.

■ COMMENTARY

The study by Ferrante and colleagues reports the influence of functional status prior to ICU admission on outcomes in older adults. The effect of pre-

ICU functional trajectories is independent of and comparable to use of mechanical ventilation and diagnosis of shock on 1-year mortality outcomes in older adults. Even those older adults with minimal or mild disability 1 year prior to a critical illness or injury experienced declines in functional status and increased mortality after ICU admission. Unfortunately, those older adults with greater functional status impairment in the year prior to ICU admission had worse outcomes with higher 30-day and 1-year mortality rates.

This study was unique in that functional status was obtained prospectively in a cohort of older adults followed over a number of years, overcoming many limitations of previous investigations in the area of post-ICU outcomes that relied solely on proxy reports of functional status. As older adults are living longer, they may be at risk for admission to a critical care unit. Investigations are urgently needed to design and test innovative interventions to prevent further decline in functional abilities, particularly in those patients with lengthy ICU stays and receipt of mechanical ventilatory support. Efforts are needed to ensure older adults can maintain their functional abilities and not decline after a critical illness or injury, which has significant implications for ICU care processes. ■

ABSTRACT & COMMENTARY

Neuromuscular Blockade and Successful Endotracheal Intubation

By Samuel Nadler, MD, PhD

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Dr. Nadler reports no relationships relevant to this field of study.

SYNOPSIS: In this single-center observational study, the use of neuromuscular blockade during intubation improved first attempt success.

SOURCE: Mosier JM, et al. Neuromuscular blockade improves first attempt success for intubation in the intensive care unit: A propensity matched analysis. *Ann Am Thorac Soc* 2015 Feb 26 [Epub ahead of print].

Previous studies have shown the utility of neuromuscular blocking agents (NMBA) for endotracheal intubation in the operating room and emergency department. However, airway management in the ICU often involves unplanned, emergent intubations under suboptimal conditions. This study asked whether NMBAs improved first attempt success (FAS) of intubations in the ICU. Additionally, these authors asked whether succinylcholine or rocuronium improved first attempt success and the effects of NMBA on intubations using video laryngoscopy.

This was a single-center, prospective, observational study of 664 consecutive intubations in a major academic referral center from Jan 1, 2012 to June 30, 2014. Using this cohort, NMBAs significantly improved FAS (80.9%, 401/496) as compared with intubations performed without NMBA (69.6%, 117/168; $P = 0.003$) with an odds ratio (OR) of 1.84 (95% CI, 1.24-2.74). In patients intubated with video laryngoscopy specifically, NMBA also led to a higher FAS (84.6%, 334/394 vs 69.1%, 103/149; $P < 0.001$). There were no significant differences in age, gender, individual difficult airway characteristics, or reasons for intubation between these two groups, but the patients intubated without NMBA had a higher median number of difficult airway characteristics, higher use of ketamine as an induction agent, and tended to be intubated by a physician with a higher level of training. There was no difference in complication rates between those intubated with and without NMBA, and there was no difference in outcomes in patients intubated with rocuronium vs succinylcholine.

As this was an observational study, the authors developed a propensity score to address potential clinical confounders in their analysis. This score was generated using variables that might influence clinicians' use of NMBA such as the presence of difficult airway conditions, emesis, trauma, airway edema, obesity, etc. The score was then used to generate 5000 data sets of cases of failed first attempts matched with successful controls with

similar propensity scores, and conditional logistic regression was used to analyze the outcomes. Using these data, NMBA led to a greater FAS with an odds ratio of 2.37 (95% CI, 1.36-4.88) in the logistic regression model and a propensity score-adjusted odds ratio of 2.22 (95% CI, 1.32-3.75).

■ COMMENTARY

The authors address a clinical question that has not previously been well studied, the utility of NMBA in endotracheal intubations in the ICU. However, this was an observational study and subject to bias. Although the patient demographics seem closely matched and the propensity score is used to reduce this bias, other variables than those in the propensity score could influence outcomes. For example, in the NMBA group, many more patients were given etomidate (83.3%) than in the control group (34.5%). The use of ketamine and propofol was far lower in the NMBA group (8.9% vs 39.3% and 5.0% vs 11.3%, respectively). Thus, these conclusions must be interpreted with caution.

Other variables not in the primary analysis may have equal or greater effects on FAS than the choice of using NMBA. In this study, video laryngoscopy improved FAS rates with an unadjusted OR of 1.87 to 2.58 compared with direct laryngoscopy, depending on the device. The level of training also had a significant influence with attending level providers having an OR = 8 of first attempt success compared with PGY-1s (95% CI: 0.97-65.82).\

Overall, this study provides preliminary evidence that neuromuscular blockade agents improve first attempt success rates both with direct laryngoscopy and video laryngoscopy, although these findings should be replicated in a randomized, prospective study. ■

ABSTRACT & COMMENTARY

Corticosteroids in Severe Community-Acquired Pneumonia: The Controversy Continues

By Kathryn Radigan, MD, MSc

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Dr. Radigan reports no financial relationships relevant to this field of study.

SYNOPSIS: Treating patients with severe community-acquired pneumonia and high inflammatory mediators with methylprednisolone may decrease the number of treatment failures.

SOURCE: Torres A, et al. Effect of corticosteroids on treatment failure among hospitalized patients with severe community-acquired pneumonia and high inflammatory response: A randomized clinical trial. *JAMA* 2015;313:677-686.

Treatment failure in hospitalized patients with severe community-acquired pneumonia (CAP) is associated with an excessive inflammatory response and worse outcomes. Torres and colleagues sought to determine the effect of corticosteroids in patients with severe CAP and a significant inflammatory response. In this multicenter, randomized, double-blind, placebo-controlled trial, 120 severe CAP patients with C-reactive protein (CRP) levels > 150 mg/L were randomized to receive either an IV methylprednisolone bolus of 0.5 mg/kg every 12 hours or placebo. Treatment began within 36 hours of hospital admission and lasted for 5 days. Severe CAP was defined as two out of the three minor criteria independently associated with severity including PaO_2/FiO_2 < 250, multilobar involvement, and systolic blood pressure < 90 mmHg, or one out of two major criteria, including a requirement for mechanical ventilation or septic shock.[1] Risk class V for the Pneumonia Severity Index was also considered severe CAP.[2] The primary outcome was early or late treatment failure. Early treatment failure was defined as the development of shock, need for mechanical ventilation not present at baseline, or death within 72 hours of treatment. Late treatment failure was defined as radiographic progression, persistence of

severe respiratory failure, development of shock, need for invasive mechanical ventilation not present at baseline, or death between 72 hours and 120 hours after treatment.

Treatment failure was less common in patients treated with methylprednisolone (8 patients, 13%) compared with the placebo group (18 patients, 31%) (P = 0.02). Although treatment with corticosteroids in patients with severe CAP reduced the risk of treatment failure (OR, 0.34; 95% CI, 0.14-0.87; P = 0.02), there was no difference in in-hospital mortality in the methylprednisolone group (six patients [10%] vs nine patients [15%] in the placebo group; P = 0.37). Eleven patients (18%) in the methylprednisolone group and seven patients (12%) in the placebo group experienced hyperglycemia (P = 0.34). There were no additional adverse reactions in the methylprednisolone group.

■ COMMENTARY

In developed countries, community-acquired pneumonia is the leading cause of death from infection and the sixth most common cause of mortality.[3] Severe CAP is often associated with a profound increase of inflammatory cytokines that often correlates with outcome. Although the upregulation of cytokines helps to eliminate infection, an excessive inflammatory response may be detrimental to other organ systems. Attenuating this response may be beneficial for improved patient outcomes.

Corticosteroids are one of the most potent inflammatory inhibitors. The idea for attenuating the inflammatory response in CAP is an old one, with the first randomized control trial (RCT) being published in 1972.[4] These investigators concluded there may be some benefit to steroid use in CAP (e.g., relieve fever) but cautioned that more robust trials were needed. Almost 50 years and a number of RCTs later, we have failed to make substantial progress. Torres and colleagues concluded that the use of methylprednisolone compared with placebo decreased treatment failure with less radiographic progression. This suggests that the benefit of corticosteroids may result from a controlled inflammatory response preventing ARDS or an attenuated reaction to endotoxin-like products released by the death of bacteria during antibiotic treatment. The decreased numbers of treatment failures were observed without a significant benefit on length of stay or mortality. Unfortunately, this study had significant limitations including an eight-year recruitment period, less statistical power than predicted, and no assessment of adrenal function was performed. Again, the investigators recommended their study be replicated prior to general use.

Unfortunately, it is not clear how far we have come since 1972 when the first trial of steroids for use in pneumonia was published. Ut is fair to say that the use of corticosteroids for regular use in severe CAP is not favored until further trials are completed. Torres and his colleagues suggest there is a trial already underway. Hopefully, this trial will be able to recruit adequate patients within a shorter time frame. One may question how many trials must be done before we decide that at best, steroids have a marginal, if any, benefit. For the time being, the controversy continues. ■

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CME QUESTIONS

1. What percentage of ventilated patients develop delirium?

a. Less than 10%

b. 10-20%

c. 20-30%

d. 40-50%

e. 60-80%

2. Which of the following statements is *true* concerning the older adults participating in this longitudinal cohort study?

a. Most of the participants were severely disabled in the 5 years prior to admission to the ICU.

b. The participants with the most cognitive impairment had the lowest rates of post-ICU disability.

c. A greater number of those hospitalized for a critical illness or injury were women.

d. A majority of those older adults hospitalized in the ICU had significant and severe disability the year prior to their critical illness or injury.

3. Mosier et al studied the success rate of intubations with and without neuromuscular blockade and concluded:

a. neuromuscular blockade decreased the success rate of intubation.

b. neuromuscular blockade increased the rate of success with direct laryngoscopy only.

c. neuromuscular blockade increased the rate of success with both direct laryngoscopy and video laryngoscopy.

d. neuromuscular blockade had no effect on the success rate of intubation.

e. neuromuscular blockade significantly affected the grade of laryngoscopic view.

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Upon completion of this educational activity, participants should be able to:

- identify the particular clinical, legal, or scientific issues related to critical care;
- describe how those issues affect physicians, nurses, health care workers, hospitals, or the health care industry; and
- cite solutions to the problems associated with those issues.

[IN FUTURE ISSUES]

Community-acquired Pneumonia