that may occur with regular insulin administered by the subcutaneous route. Some patients are good candidates for insulin glargine, a long-acting analogue insulin given by the subcutaneous route. A typical patient who has been resuscitated from severe sepsis and achieved a degree of clinical stability may still be severely ill. The patient likely is receiving a constant source of calories by the enteral route and has required a significant amount of insulin, via either or both the IV and subcutaneous routes over the previous 24 hours. A fraction of this insulin requirement can be satisfied with once- or twice-daily administration of long-acting insulin. Feeding a patient with continuous enteral nutrition and using long-acting insulin for glycemic control is analogous to the use of total parenteral nutrition with insulin added to each day’s formula. Of course, enteral nutrition is preferable whenever possible. The use of long-acting insulin decreases or eliminates the need for IV insulin, helps the transition from IV therapy, and is more predictable than repeated subcutaneous doses of short-acting insulin. However, absorption of subcutaneous insulin in severely edematous or hemodynamically unstable patients is a concern, and the duration of action is not suitable for the clinically unstable patient.

“We must have effective data reporting tools in the ICU,” he said. “We cannot implement programs of intensive glycemic management without knowing this information. It’s like flying a plane without a control panel. The critical care community should no longer consider it reasonable or appropriate to provide critical care services without an ongoing assessment of clinical outcomes.”

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**Continuing Education Self-Assessment**

**Insulin Therapy in the ICU: The Role of Long-Acting Insulin**

13. Which of the following is true for instituting a tight glycemic control protocol in an intensive care unit?
   a. Directive protocols decreases independent decision making at the bedside.
   b. Knowing the culture of an intensive care unit is important when choosing between a directive or nondirective protocol.
   c. Usually, there is little resistance from staff to the idea.

14. Long-acting insulin:
   a. Decreases or eliminates the need for IV insulin.
   b. Shows little variation in onset and duration between patients.
   c. Has decreased subcutaneous absorption in patients on vasopressors.
   d. All of the above.

Pain in the ICU: How Should We Measure and Treat It?

Kathleen Puntillo, from the University of California, San Francisco, outlined the challenges and consequences associated with unrelieved pain, both physical and psychological. Pain is a physical stressor that the ICU team tries to relieve because it is the humane thing to do. One special area that the critical care community should focus on is iatrogenic pain, unintentional pain that results from diagnostic and therapeutic interventions. Iatrogenic pain is intrinsic to the ICU, as the pain scores for many of ICU procedures are very high. The American Association of Critical-Care Nurses’ (AACN) Thunder Project Study II found that turning was the most painful of the procedures studied (Puntillo et al. Am J Crit Care. 2001;10:238): “We need to keep looking at iatrogenic pain so we can minimize it as much as possible,” Dr. Puntillo suggested.


Not being capable of speech does not mean patients cannot communicate; many patients can self-report if they are provided the tools and opportunity. For example, ventilated patients can point to a numeric rating scale or a body diagram to show their caregivers where the pain is. For those who cannot self-report, a hierarchy of pain assessment practices should be considered. Pain behavior assessment tools include the Behavioral Pain Scale (BPS), Critical Care Pain Observation Tool (CCPOT) and the Thunder Project Study assessment tool.

Behavioral Pain Scale. The BPS was developed in France to consider non-noxious stimuli, such as compression stockings and central venous catheter (CVC) dressing, and noxious stimuli, such as endotracheal (ET) suctioning or turning, in nonverbal patients. BPS examined facial expressions, movement of the upper limbs (from no movement to permanent limb retraction) and compliance with a ventilator (Payen et al. Crit Care Med. 2001;29:2254).

In this study, one group was subjected to a non-noxious stimulus and the second group underwent a noxious stimulus. The noxious stimulus was repeated in a third group so researchers could look at repeated measures between group two and group three. In each of these paradigms and at times during the data collection period, two people were observing and scoring using BPS. Researchers concluded that the BPS tool was able to discriminate between pain and no pain in 30 patients and more than 300 observations.

The BPS tool needs further psychometric evaluation, however; two validation studies showed differences in reliability scores. Investigators in Morocco compared pain scores on the BPS when patients were at rest and when they underwent one of two noxious stimuli: ET suctioning or IV insertion (Aissaoui et al. Sleep Med. 2005;10:1470). In the second follow-up validation study, which was done in Australia, researchers also chose to compare non-noxious and noxious procedures (Young et al. Intensive Crit Care Nurs. 2006;22:32). Both of these studies showed some increase in content and construct validity of the BPS, but reliability is inconclusive because both studies showed differences in reliability scores. “The BPS tool is a great start,” Dr. Puntillo said. “With some modifications, it might be a very useful instrument for our nonverbal patients.”

Critical Care Pain Observation Tool. The CCPOT, developed and tested in Canada during observations of cardiac surgery patients, was used at three different times immediately after surgery: at rest, during repositioning, and after repositioning (Gelinas et al. Anesth Analg. 2006;11:420). Facial expressions, body movements, muscular tension, and ventilator compliance were evaluated to assess pain behaviors. The study showed that in the unconscious state, in the conscious intubated state and in the conscious extubated state, pain scores on the CCPOT increased during the supposedly noxious procedure. The inter-rated reliability for the CCPOT scale is moderate to high, the criterion validity is strong, and the scale has some discriminate validity. “I think it is causing a great deal of interest in critical care units, and I think it shows great promise, although it is still undergoing improvements,” Dr. Puntillo commented.

Thunder Project Study. The Thunder Project Study (TPS), sponsored by the AACN, studied behavioral responses to procedural pain in almost 6,000 adult patients across the country. The 30-item scale was divided into facial behaviors, verbal behaviors, and body movement behaviors, which were studied prior to and during procedures (Puntillo et al. Crit Care Med. 2004;32:599). The study found an increase in frequency of behaviors from pre-procedure to procedure times. However, that did not answer all of the researchers’ questions, as they wanted to know if those behaviors were related to pain. Researchers divided the patients into two groups: those who did and did not report pain during the procedure. The subjects who reported pain during a procedure had more frequent behaviors than those who did not report pain (see Figure 1). “I think we have to be very cautious in saying the more behaviors we see in a patient, the more pain they are experiencing,” Dr. Puntillo stressed. “With that said, we did find that in this study, patients with versus patients without procedural pain were 10 times more likely to have verbal responses, four times more likely to have increased body movement responses and three times more likely to have increased facial responses.”
Another study by these investigators focused on patients who were weaned off of the ventilator and in the ICU. It was also associated with fewer days on the ventilator and fewer days in the ICU. Dr. Kress pointed to earlier studies that first identified prolonged delirium and its management as an issue of concern. In 1998, a study published in CHEST suggested that continuous intravenous sedation led to longer time on the ventilator (Kollef et al. CHEST. 1998;114:541). The next year, a study in Critical Care Medicine suggested using a protocolized sedation algorithm that called for frequent reassessment of the patient. In that study, reassessment was done every 4 hours (Brook et al. Crit Care Med. 1999;27:2609). “We took it a step further,” Dr. Kress said. “We thought that a simpler approach would be to let the patient wake up every day. That was associated with shortened time on the ventilator and in the ICU. It was also associated with fewer drugs being used.” As more data came forward, the team also found that benzodiazepines may carry a burden for the patient in the long and short term (Kress et al. Crit Care Med. 2002;35:365).

In addition, a group in France conducted a before-and-after trial using the Adaptation to the Intensive Care Unit (ATICE) sedation scale. The group targeted an end point and used frequent reassessments much like Brook et al; in this case, the ATICE score was the targeted end point. “So this was a moving target,” Dr. Kress said. “You don’t just lock into one setting and stay there. You wouldn’t lock into one setting on a vasoactive drug regimen. You’re asking yourself, ‘Do I need this much norepinephrine, do I need this much epinephrine or dopamine, etc.? ’ Researchers then wondered if they could help avoid the common complications of critical illness, such as ventilator-associated pneumonia, venous thromboembolism and bacteremia, by waking patients every day, said Dr. Kress. With a daily sedative interruption, further research found that only half of the 7 common ICU complications occurred in the daily sedative interruption group compared to the control group. Scheweick et al. Crit Care Med. 2004;32:1272). However, Dr. Kress noted that this may have been because these patients spent fewer days on the ventilator and fewer days in the ICU.

Many physicians are not addressing analgesia adequately, commented Dr. Kress. A study published in Critical Care Medicine looked at 30 patients who received midazolam or midazolam plus an analgesic (Richman et al. Crit Care Med. 2006;34:1935). Researchers used a protocol for sedation and found they could achieve their sedation target (using the Ramsay Sedation Scale) with the analgesic agent fentanyl. An additional benefit included less ventilator dysynchrony without hypventilation, hypotension or coma. “A combined multidrug approach using sedatives and analgesics is an important standard,” Dr. Kress said.

Many questions remain with these management approaches. Is there a price to pay with turning off the sedation? What about psychological outcomes? Data suggest that patients whose memories of ICU experiences are not factual, but delusional, do worse. They are more likely to develop anxiety and post-traumatic stress disorder than those who remember factual events accurately. (Ely et al. Crit Care Med. 2001;29:573).

Dr. Kress and his colleagues studied the long-term psychological effects of daily wakenings. After a year, researchers followed up with patients and found that only two-thirds of the patients remembered being in the ICU and not a single person remembered the daily wakening. Also, no one in this group reported post-traumatic stress disorder, whereas about one-third of the control patients did (Am J Respir Crit Care Med. 2003;168:1457).

Managing Different Patient Populations

Patients with coronary risk factors who are critically ill present a new set of challenges. Myocardial ischemia can occur during spontaneous breathing trials. Dr. Kress and colleagues studied 74 patients with established coronary risk factors and looked for myocardial ischemia using a Holter assessment. All patients underwent a daily sedative interruption. Researchers found that about one-third of the patients had found ischemia, and the daily wakenings did not seem to be the inciting event (Crit Care Med. 2007;35:365). “So the patient who is sedated and mechanically ventilated is experiencing ischemia just as often as the patient who is not sedated,” concluded Dr. Kress.

Two back-to-back papers in Critical Care Medicine suggested that patients who have lung injury do not have lung injury. Patients with acute lung injury do not have different sedation needs with low versus high tidal volume strategies (Cheng et al. Crit Care Med. 2005;33:363; Kahn et al. Crit Care Med. 2005;33:776). This suggests that the type of strategy used for patients – low tidal volume, for example – does not necessarily mandate a more aggressive sedative regimen. Still, another group of researchers thought that permissive hyperventilation may require a more aggressive sedative (Vinayak et al. Crit Care Med. 2006;34:1668). The only thing they found was that clinicians tended to use more propofol when using permissive hyperventilation strategies. Apart from that, there were no differences among the different strategies used to manage patient sedation. In 2005, a nonrandomized study reported that an unconventional drug, haloperidol, was associated with a significant benefit with regard to outcomes, including survival (Muirhead et al. Crit Care Med. 2005;33:226).

What is New in Delirium Management?

Delirium can be viewed as the clinical manifestation of the brain’s organ dysfunction. In multiple organ dysfunction syndrome, delirium provides evidence of brain dysfunction. Studies show that delirium is an incredibly common problem, developed by 50% to 80% of ventilated, severely ill patients and 20% to 50% of other ICU patients (Ely et al. JAMA. 2001;286:2703).

Studies reveal that delirium is associated with a higher mor-
tality rate after adjusting for severity of illness. It also is associated with longer hospital stays and much higher healthcare costs, explained Wes Ely, MD, from Vanderbilt University Medical Center. “It appears that there is a relationship between experiencing delirium while in the ICU and the likelihood of long-term neuropsychological deficit. For every additional day spent in the ICU, it appears there is a 29% to 33% increased risk of neuropsychological deficit,” he said.

**Monitoring Delirium**

Dr. Ely suggested several methods for monitoring delirium, including the Intensive Care Delirium Screening Checklist (ICDSC), the Nechama Scale and the Confusion Assessment Method for the Intensive Care Unit (CAM-ICU). “The diagnosis of delirium is anchored by the presence of inattention or the lack of ability to pay attention,” Dr. Ely commented (Meagher et al. Br J Psychiatry. 2007;190:135). Dr. Ely offered a few techniques for detecting inattention. The healthcare practitioner can ask the patient to squeeze his or her hand each time the letter “X” is heard while the practitioner spells the phrase “save a heart.” For those who cannot move, the care practitio

Dr. Ely cautioned physicians not to disregard the causes of delirium, including sedatives. While it is difficult to ascertain whether a specific drug is causing the patient’s delirium, there are certain categories that appear closely associated with transitions to delirium, most importantly benzodiazepines. “I believe that we do things in the ICU that cause delirium. Patients are exposed to delirogenic drugs, prolonged immobilization, and disrupted sleep/wake cycles,” he explained. “Just because delirium was caused by heavy doses of benzodiazepines, doesn’t mean that the delirium is not contributing to the overall morbidity of the patient. When our patients lack the ability to pay attention, we need to reconsider whether or not the drug is still indicated.”

Dr. Ely recommended developing a protocolized approach to help prevent this brain dysfunction, even though most supporting data are from non-ICU settings (Meagher et al. N Engl J Med. 1999;340:600; Marcantonio et al. J Am Geriatr Soc. 2001;49:516; Milisen et al. J Int Med. 2005;52:79). Congestive heart failure and infections such as sepsis tend to be the most common diagnoses that lead to delirium in the ICU, and these conditions must be treated aggressively. Dr. Ely also suggested correcting metabolic disturbances such as hyponatremia and maintaining oxygen saturation. “Frequently reorientate the patient,” he said. “Use goal-directed sedation and analgesia. Stop the ventilator daily and perform a spontaneous breathing trial. In the intervention arm, the patients received targeted sedation and mandated daily awakening along with a spontaneous awakening trial followed with a spontaneous breathing trial. The intervention group experienced 3 more ventilator-free days and was extubated successfully 2 days earlier than the control group. The intervention group also was discharged from both the ICU and the hospital 4 days earlier than the control group. “Although we weren’t powered to show a difference in mortality, we actually saw a trend toward a reduction in mortality that improved survival from 34% to 28%, and coma went down by one day,” Dr. Ely said. Researchers were not able to bring delirium down.

“We may find that this actually contributes as much to reducing mortality as do FDA-approved drugs for severe sepsis,” concluded Dr. Ely.

Dr. Ely noted that for each day spent in the ICU for fulminant pulmonary disease, there are 2 days spent during the weaning period.

**The Role of Dexmedetomidine**

The Maximizing Efficacy of Targeted Sedation and Reducing Neurological Dysfunction (MENDS) Trial was the first double-blind, placebo-controlled study to show a reduction in delirium with dexmedetomidine, an alpha-2 agonist, compared with lorazepam, a gammabutyric acid (GABA) agonist (Pandharipande et al. Manuscript in preparation). When compared with the lorazepam group, the dexmedetomidine treatment group had better readiness. or daily awakenings. Use goal-directed sedation/analgesia and/or daily awakenings. **Continuing Education Self-Assessment**

**Sedation and Delirium: Current Concepts in 2007**

15. How common is delirium in ventilated, severely ill patients in the intensive care unit?
   a. Very few ventilated patients will experience it.
   b. 30% to 50% of the population will experience it.
   c. 50% to 80% of the population will experience it.
   d. All of the above.

16. Daily awakenings:
   a. Do not seem to incite ischemia in patients with coronary risk factors.
   b. Improved or eliminated post-traumatic stress syndrome in patients in one study.
   c. Helped patients in one study to be taken off ventilators sooner and discharged earlier than patients who were not awakened.
   d. All of the above.

Complete the post-test at www.sccm.org/2007conreview. **Prevention of ICU Delirium**

- Consider developing a protocolized approach, though most data are from non-ICU settings.
- Treat underlying infection and congestive heart failure.
- Correct metabolic disturbances and hypoxemia.
- Ask nurses and family to reorientate the patient frequently.
- Use goal-directed sedation/analgesia and/or daily awakenings.
- Stop the ventilator each day to test readiness.
- Apply early mobilization and physical therapy.
- Optimize sleep patterns.