Patients in intensive care units (ICUs) are treated with many interventions (most notably endotracheal intubation and invasive mechanical ventilation) that are observed or perceived to be distressing. Pain is the most common memory patients have of their ICU stay. Agitation can precipitate accidental removal of endotracheal tubes or of intravascular catheters used for monitoring or administration of life-sustaining medications. Consequently, sedatives and analgesics are among the most commonly administered drugs in ICUs.

Early intensive care practice evolved from intraoperative anesthetic care at a time when mechanical ventilation was delivered by rudimentary machines that were not capable of synchronizing with patients’ respiratory efforts. As a result, deep sedation was commonly used until a patient was able to breathe without assistance. Developments over the past 30 years, including microprocessor-controlled ventilators that synchronize with patients’ own respiratory efforts and new, shorter-acting sedative and analgesic medications, have dramatically changed this approach. Equally important has been the recognition that pain, oversedation, and delirium are issues that if undetected and untreated are distressing to patients and associated with increased morbidity and mortality.

Just as the concept of the “triad of anesthesia” underscores the pharmacodynamic interactions among hypnotics, analgesics, and muscle relaxants and the recognition that the simultaneous administration of agents of each class permits the use of lower doses of drugs of all classes, the concept of the “ICU triad” recognizes that pain, agitation, and delirium — and therefore approaches to their management — are inextricably linked (Fig. 1). According to the principle that it is better to treat disease than to mask it, sedatives should be used only when pain and delirium have been addressed with the use of specific pharmacologic and nonpharmacologic strategies.

Pain, Analgesia, and Sedation in the ICU

Prospective studies confirm that the majority of patients who are treated in ICUs have pain, which makes the assessment of pain and provision of adequate analgesia essential components of ICU care. The short-term consequences of untreated pain include higher energy expenditure and immunomodulation. Longer-term, untreated pain increases the risk of post-traumatic stress disorder. Assessing whether a patient in the ICU is in pain may be difficult. The reference standard for the assessment of pain is self-reporting by the patient, but patients in the ICU may not be sufficiently interactive to give valid responses. Physiological indicators such as hypertension and tachycardia correlate poorly with more intuitively valid measures of pain, but pain scales such as the Behavioral Pain Scale and the Critical
Care Pain Observation Tool provide structured and repeatable assessments and are currently the best available methods for assessing pain.

A minority of ICU patients have an indication for continuous deep sedation, for reasons such as the treatment of intracranial hypertension, severe respiratory failure, refractory status epilepticus, and prevention of awareness in patients treated with neuromuscular blocking agents. This review will focus on the remaining overwhelming majority of patients undergoing mechanical ventilation for whom the use of sedatives and analgesics should be minimized, with the goal that they be calm, lucid, pain-free, interactive, and cooperative with their care.

Evidence from randomized, controlled trials consistently supports the use of the minimum possible level of sedation. In a landmark trial that compared routine daily interruption of sedative infusions with discretionary interruption by treating clinicians, patients whose sedation was routinely interrupted received less sedation overall and spent fewer days undergoing mechanical ventilation and fewer days in the ICU.

Although the trial was too small to assess differences in mortality or discharge destination, the observed reductions in the duration of mechanical ventilation and length of stay in the ICU were associated with a nonsignificant reduction in mortality and a nonsignificant increase in the proportion of pa-

---

**Figure 1. Causes and Interactions of Pain, Agitation, and Delirium.**

Drugs and other treatments for pain, agitation, and delirium form an "ICU triad" cognitive management analogous to the "triad of anesthesia," which highlights interactions among hypnotics, analgesics, and muscle relaxants to encourage balanced anesthesia. The "ICU triad" concept highlights that changing one element is unlikely to be as effective as a coordinated approach.
comes were either unaffected or improved. Adverse events, and long-term psychiatric out-
sedation did not increase the rate of short-term
comparison with deep sedation, the use of lighter
sedative, multicenter, longitudinal cohort study show-
benefit. Further support comes from a prospec-
tive, hospitalization context-specific and will depend on the popula-
tion in the total dose of sedative administered.
The conflicting findings also highlight that the
results of daily interruption of sedation may be
context-specific and will depend on the population
being studied, protocol adherence, and management of the control group. A random-
ized, controlled trial in which all patients under-
going mechanical ventilation received morphine
for the treatment of pain in an “analgesia first” approach compared a protocol of no sedation
with the routine use of sedation with daily inter-
ruption. Patients who were assigned to the
protocol of no sedation had shorter stays in the
ICU and the hospital and more days without
mechanical ventilation.
The consistent message from all these sedation-
interruption trials is that minimizing sedation
among patients in the ICU provides clinical
benefit. Further support comes from a prospective, multicenter, longitudinal cohort study show-
ing that the depth of sedation was independently associated with the duration of mechanical
ventilation, in-hospital mortality, and rates of
death within 180 days. In a randomized, con-
trolled trial, the use of lighter sedation resulted
in more ventilator-free and ICU-free days. In
comparison with deep sedation, the use of lighter
sedation did not increase the rate of short-term
adverse events, and long-term psychiatric out-
comes were either unaffected or improved.

**CHOICE OF SEDATIVE AGENT**

Despite at least 90 trials comparing sedative reg-
imens, in general, no sedative drug is clearly
superior to all others. Sedatives that are com-
monly used in the ICU are the benzodiazepines
midazolam and lorazepam (and to a lesser ex-
tent, diazepam), the short-acting intravenous an-
esthetic agent propofol, and dexmedetomidine. Remifentanil, an opioid, is also used as a sole
agent because of its sedative effects. Benzodiaz-
epines act through γ-aminobutyric acid type A (GABA<sub>A</sub>) receptors, as in part does propofol,
whereas dexmedetomidine is an α<sub>2</sub>-adrenoceptor
agonist, and remifentanil is a µ-opioid receptor
agonist (Table 1). Marked differences in prescribing
patterns among countries suggest that the
choice of agent is determined more by tradition
and familiarity than by evidence-based practice.

If minimizing the depth and duration of se-
dation is accepted as a desirable goal, then the
use of a short-acting agent with an effect that
can be rapidly adjusted such as propofol or remi-
fentanil should offer advantages over longer-
acting agents or agents with active metabolites.
As compared with benzodiazepines, propofol has
not been shown to reduce mortality but may
result in a reduction in the length of stay in the
ICU. Dexmedetomidine may also have advan-
tages over benzodiazepines, since it produces
analgesia, causes less respiratory depression, and
seemingly provides a qualitatively different type
of sedation in which patients are more interactive
and so potentially better able to communi-
cate their needs. As compared with lorazepam
and midazolam, dexmedetomidine resulted in less
delirium and a shorter duration of mechanical
ventilation but not reduced stays in the ICU or
hospital. When two short-acting and titrat-
able drugs such as propofol and dexmedetomi-
dine were compared, there was no significant
difference in the time spent at the target seda-
tion level and no difference in either the duration
of mechanical ventilation or ICU stay.

Remifentanil has a half-life of 3 to 4 minutes
that is independent of the infusion duration or
organ function. It has been investigated as a
sedative agent in ICUs predominantly among sur-
gical patients. It has been compared with mid-
azolam alone, midazolam with fentanyl, fentanyl
alone, and morphine. Although remifentanil
has been associated with a reduced duration of
mechanical ventilation and ICU stay in these
small trials, it has not yet been evaluated in a
large, heterogeneous population of critically ill
patients and is currently not a common choice in
most ICUs.
Table 1. Sedatives and Analgesics in Common Use in the ICU.*

<table>
<thead>
<tr>
<th>Drug (Brand Name)</th>
<th>Mechanism of Action</th>
<th>Typical Adult Dose</th>
<th>Pharmacokinetic Properties</th>
<th>Adverse Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Midazolam (Versed)</td>
<td>GABA&lt;sub&gt;A&lt;/sub&gt; agonist</td>
<td>Bolus, 1 to 5 mg; infusion, 1 to 5 mg/hr</td>
<td>Half-life, 3 to 11 hr; active metabolite accumulates with prolonged infusion; metabolized by hepatic oxidation, with renal excretion of active metabolite</td>
<td>Possibly a higher risk of delirium and tolerance with certain other sedatives</td>
</tr>
<tr>
<td>Lorazepam (Ativan)</td>
<td>GABA&lt;sub&gt;A&lt;/sub&gt; agonist</td>
<td>Bolus, 1 to 4 mg; infusion, 1 to 5 mg/hr</td>
<td>Slower onset (5 to 20 min) than that of midazolam or diazepam (2 to 5 min); half-life, 8 to 15 hr; metabolized by hepatic glucuronidation, with no active metabolites, so offset may be more predictable than that of midazolam in critical illness</td>
<td>Possibly a higher risk of delirium and tolerance with certain other sedatives</td>
</tr>
<tr>
<td>Diazepam (Valium; Diazemuls)</td>
<td>GABA&lt;sub&gt;A&lt;/sub&gt; agonist</td>
<td>Bolus, 1 to 5 mg</td>
<td>Half-life, 20 to 120 hr; metabolized by hepatic desmethylation and hydroxylation; active metabolite accumulates in renal failure</td>
<td>Poorly soluble in water, so prolonged peripheral intravenous infusion may cause phlebitis; possibly a higher risk of delirium and tolerance than certain other sedatives</td>
</tr>
<tr>
<td>Propofol (Diprivan)</td>
<td>GABA&lt;sub&gt;A&lt;/sub&gt; agonist, with other effects, including on glutamate and cannabinoid receptors</td>
<td>50 to 200 mg/hr or 1 to 3 mg/kg/hr</td>
<td>Half-life, 30 to 60 min after infusion; longer after prolonged infusion because of redistribution from fat stores; metabolized by hepatic glucuronidation and hydroxylation</td>
<td>Vasodilatation or negative inotropy causing hypotension or bradycardia; propofol infusion syndrome (lactic acidosis, arrhythmia, and cardiac arrest), mostly associated with prolonged infusion rates of &gt;4 to 5 mg/kg/hr; hypertriglyceridemia; pancreatitis</td>
</tr>
<tr>
<td>Dexmedetomidine (Precedex)</td>
<td>α&lt;sub&gt;2&lt;/sub&gt;-Agonist</td>
<td>0.2 to 1.5 μg/kg/hr</td>
<td>Half-life, 2 hr; does not accumulate with prolonged infusion; metabolized by hepatic glucuronidation and oxidation, with no active metabolites</td>
<td>Transient hypertension, then hypotension; bradycardia, dry mouth, nausea</td>
</tr>
<tr>
<td>Remifentanil (Ultiva)</td>
<td>μ-Opioid agonist (also with κ-opioid agonist effects)</td>
<td>0.5 to 2 μg/kg/min; loading dose of 0.4 to 0.8 μg/kg may be considered</td>
<td>Half-life, 3 to 4 min; does not accumulate with prolonged infusion; metabolized by plasma esterases and so is unaffected by organ function</td>
<td>Nausea, constipation, respiratory depression, bradycardia</td>
</tr>
<tr>
<td>Fentanyl (Sublimaze)</td>
<td>μ-Opioid agonist (also with κ-opioid agonist effects)</td>
<td>20 to 100 μg/hr; loading dose of 50 to 100 μg may be considered</td>
<td>Half-life, 1.5 to 6 hr; highly fat soluble, so rapid onset but accumulates with prolonged infusion; metabolized by hepatic oxidation; no active metabolites</td>
<td>Nausea, constipation, respiratory depression, skeletal-muscle rigidity with high bolus doses</td>
</tr>
<tr>
<td>Morphine (Roxanol; Duramorph)</td>
<td>μ-Opioid agonist (also with κ-opioid and δ-opioid agonist effects)</td>
<td>1 to 5 mg/hr; loading dose of 2 to 5 mg may be considered</td>
<td>Half-life, 3 to 7 hr; more water soluble, so slower onset than fentanyl with less accumulation; metabolized by hepatic glucuronidation to morphine-6-glucuronide (10%) (20 times as active as parent drug) and morphine-3-glucuronide (90%) (inactive as an analgesic but causes neuroexcitation, at least in animal models), both with renal excretion</td>
<td>Nausea, constipation, respiratory depression, histamine release and consequent vasodilatation and hypotension, itch</td>
</tr>
<tr>
<td>Hydromorphone (Dilaudid)</td>
<td>μ-Opioid agonist (also with κ-opioid and δ-opioid agonist effects)</td>
<td>0.5 to 2 mg/hr; loading dose of 0.4 to 1.5 mg may be considered</td>
<td>Half-life, 1.5 to 3.5 hr; 7 to 11 times as potent as morphine; metabolized by hepatic glucuronidation to hydromorphone-3-glucuronide, with effects similar to those of morphine-3-glucuronide</td>
<td>Nausea, constipation, respiratory depression</td>
</tr>
</tbody>
</table>

* GABA<sub>A</sub> denotes γ-aminobutyric acid type A.
The New England Journal of Medicine

Prevention and Treatment of Delirium

The Diagnostic and Statistical Manual of Mental Disorders, 4th edition (DSM-IV), lists four domains of delirium: disturbance of consciousness, change in cognition, development over a short period, and fluctuation. Delirium is defined by the National Institutes of Health as “sudden severe confusion and rapid changes in brain function that occur with physical or mental illness.” The most common feature of delirium, thought by many to be its cardinal sign, is inattention. Delirium is a nonspecific but generally reversible manifestation of acute illness that appears to have many causes, including recovery from a sedated or oversedated state.

The pathophysiology of delirium that is associated with critical illness remains largely uncharacterized and may vary depending on the cause. The increased risk associated with the use of GABA 

agonists and anticholinergic drugs led to the suggestion that the GABAergic and cholinergic neurotransmitter systems play a contributory role. In particular, central cholinergic deficiency may be a final common pathway. Alternative hypotheses include excess dopaminergic activity and direct neurotoxic effects of inflammatory cytokines. Currently, these hypotheses are unproven, making pharmacologic management strategies largely empirical.

Studies using magnetic resonance imaging have shown a positive association between the duration of delirium in the ICU and both cerebral atrophy and cerebral white-matter disruption. These preliminary investigations indicate either that delirium in the ICU gives rise to alterations in brain structure or that the presence of such cerebral atrophy and white-matter disruption renders patients more susceptible to delirium.

Regardless of the cause and the underlying pathophysiology, delirium is now recognized as a frequent and serious event in critically ill patients. There is no diagnostic blood, electrophysiologic, or imaging test for delirium, which therefore remains a clinical diagnosis. Estimates for the incidence of delirium in the ICU range from 16% to 89%, with the reported incidence affected both by the characteristics of the population being studied and by the diagnostic criteria used. Risk factors that have been identified include an advanced age and the presence of more than one condition associated with coma, followed by treatment with sedative medications, a neurologic diagnosis, and increased severity of illness. A diagnosis of delirium is associated with increased mortality (estimated as a 10% increase in the relative risk of death for each day of delirium) and decreased long-term cognitive function.

There are two distinct forms of delirium, hypoactive and agitated (or hyperactive). When individual patients intermittently have both forms, it is termed mixed delirium. The hypoactive form is characterized by inattention, disordered thinking, and a decreased level of consciousness without agitation. Pure agitated delirium affects less than 2% of patients with delirium in the ICU. Patients with hypoactive delirium are the least likely to survive, but those who do survive may have better long-term function than those with agitated or mixed delirium. Separating the effects of delirium status from those of illness severity with respect to the risk of death is difficult, since patients with more serious illnesses are at increased risk for both delirium and death. Association studies typically adjust for illness severity on admission to the ICU rather than at the time that delirium is diagnosed. Although the association between delirium and a worse outcome is clear, a causal relationship has not been established. Currently, the evidence that specific treatment of delirium may improve outcomes is tenuous.

Assessment and Monitoring of Sedation and Delirium

Although ICU practice is characterized by close monitoring of carefully administered care, surveys that have been conducted in various countries have shown that the depth of sedation frequently goes unmonitored. This finding is surprising and unacceptable, since evidence suggests that the routine monitoring of sedation may improve patients’ outcomes.

Sedation Scales

Of the sedation scales described, the Riker Sedation–Agitation Scale and the Richmond Agitation–Sedation Scale are the most commonly reported, but in head-to-head comparison,
neither is demonstrably superior\textsuperscript{39} (Table 2). For the majority of patients undergoing mechanical ventilation in an ICU, an appropriate target is a score of 3 to 4 on the Riker Sedation–Agitation Scale (which ranges from 1 to 7, with scores of <4 indicating deeper sedation, a score of 4 indicating an appearance of calm and cooperativeness, and scores of ≥5 indicating increasing agitation) or a score of −2 to 0 on the Richmond Agitation–Sedation Scale (which ranges from −5 to +4, with more negative scores indicating deeper sedation and more positive scores indicating increasing agitation, and with 0 representing the appearance of calm and normal alertness).

**IDENTIFYING DELIRIUM**

In routine practice, ICU staff members typically do not diagnose delirium in almost three quarters of their patients who have the condition, whereas active screening by research nurses identified delirium in up to 64% of patients who were considered to be delirious by a psychiatrist, a geriatrician, or a neurologist.\textsuperscript{40} Scales with respect to delirium in the ICU apply the four DSM-IV domains defining delirium in general medical and psychiatric patients to those in the ICU whose severity of illness can rapidly fluctuate, who receive multiple analgesics and sedatives, and who are unable to speak owing to endotracheal intubation. Two scales are in common use, the Confusion Assessment Method for the ICU (CAM-ICU)\textsuperscript{41} and the Intensive Care Delirium Screening Checklist (ICDSC)\textsuperscript{29} (Table 3). The CAM-ICU reports a dichotomous assessment at a single time point, whereas the ICDSC lists signs that can be observed over a period of time. Although such

<table>
<thead>
<tr>
<th>Table 2. Sedation Scales for Patients in the ICU.</th>
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</thead>
<tbody>
<tr>
<td><strong>Scale and Scoring Method</strong></td>
</tr>
<tr>
<td><strong>Riker Sedation–Agitation Scale (SAS)</strong>\textsuperscript{*}</td>
</tr>
<tr>
<td>Dangerous agitation (score of 7)</td>
</tr>
<tr>
<td>Very agitated (score of 6)</td>
</tr>
<tr>
<td>Agitated (score of 5)</td>
</tr>
<tr>
<td>Calm and cooperative (score of 4)</td>
</tr>
<tr>
<td>Sedated (score of 3)</td>
</tr>
<tr>
<td>Very sedated (score of 2)</td>
</tr>
<tr>
<td>Cannot be aroused (score of 1)</td>
</tr>
<tr>
<td><strong>Richmond Agitation–Sedation Scale (RASS)</strong>\textsuperscript{†}</td>
</tr>
<tr>
<td>Combative (score of 4)</td>
</tr>
<tr>
<td>Very agitated (score of 3)</td>
</tr>
<tr>
<td>Agitated (score of 2)</td>
</tr>
<tr>
<td>Restless (score of 1)</td>
</tr>
<tr>
<td>Alert and calm (score of 0)</td>
</tr>
<tr>
<td>Drowsy (score of −1)</td>
</tr>
<tr>
<td>Light sedation (score of −2)</td>
</tr>
<tr>
<td>Moderate sedation (score of −3)</td>
</tr>
<tr>
<td>Deep sedation (score of −4)</td>
</tr>
<tr>
<td>Cannot be aroused (score of −5)</td>
</tr>
</tbody>
</table>

\textsuperscript{*} Data are from Riker et al.\textsuperscript{37}

\textsuperscript{†} Data are from Sessler et al.\textsuperscript{38}
scales are essential in objectively diagnosing delirium for research purposes, it is not clear that the use of these scales is more sensitive than unstructured assessments made by trained bedside nurses who are prompted to look for delirium. Some studies have shown a high sensitivity when such assessments are performed by bedside nurses, whereas other studies have shown conflicting results. Used alone (without an accompanying sedation scale), none of the published scales distinguish hyperactive from hypoactive delirium, and none of the published scales quantify the relative importance of individual elements of the scales despite recognition that specific treatments may shorten the duration of some elements and prolong the duration of others. All the scales dichotomize delirium as being either present or absent, although it would seem to be intuitive that delirium has different degrees of severity. The CAM-ICU and ICDSC are currently the two accepted methods for identifying a condition that otherwise frequently goes undiagnosed.

### Table 3. Scoring Systems for the Diagnosis of Delirium in Critically Ill Patients

<table>
<thead>
<tr>
<th>System, Scoring Method, and Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Confusion Assessment Method for the ICU (CAM-ICU)†</td>
</tr>
<tr>
<td>Scoring is positive or negative according to the presence or absence of criteria listed</td>
</tr>
<tr>
<td>Patient must be sufficiently awake (RASS score, −3 or more) for assessment according to the following criteria:</td>
</tr>
<tr>
<td>An acute change from mental status at baseline or fluctuating mental status during the past 24 hr (must be true to be positive)</td>
</tr>
<tr>
<td>More than 2 errors on a 10-point test of attention to voice or pictures (must be true to be positive)</td>
</tr>
<tr>
<td>If the RASS is not 0 and the above two criteria are positive, the patient is delirious</td>
</tr>
<tr>
<td>If the RASS is 0 and the above two criteria are positive, test for disorganized thinking using 4 yes/no questions and a 2-step command; &gt;1 error means the patient is delirious; ≤1 error excludes delirium</td>
</tr>
</tbody>
</table>

| Intensive Care Delirium Screening Checklist (ICDSC)‡ |
| A score of ≥4 is positive for delirium (with scores of 1 to 3 termed “subsyndromal delirium”) |
| Patient must show at least a response to mild or moderate stimulation. Then score 1 point for each of the following features, as assessed in the manner thought appropriate by the clinician: |
| Anything other than “normal wakefulness” |
| Inattention |
| Disorientation |
| Hallucination |
| Psychomotor agitation |
| Inappropriate speech or mood |
| Disturbance in sleep or wake cycle |
| Fluctuation in symptoms |

* RASS denotes Richmond Agitation–Sedation Scale.
† Data are from Ely et al.
‡ Data are from Bergeron et al.

### Prevention and Treatment of Delirium

**Prevention**

There is some evidence that delirium can be prevented. Outside the ICU, repeated reorientation, noise reduction, cognitive stimulation, vision and hearing aids, adequate hydration, and early mobilization can reduce the incidence of delirium in hospitalized patients. Haloperidol prophylaxis in patients undergoing hip surgery reduced the severity and duration of delirium. Among patients in the ICU, the duration of delirium was cut in half with early mobilization during interruptions in sedation.

Pharmacologic studies of delirium prevention include trials comparing one sedative–analgesic regimen with another and studies of antipsychotic drugs administered with the specific intent of preventing delirium. Four placebo-controlled trials have evaluated pharmacologic prophylaxis of delirium; low-dose haloperidol and low-dose risperidone both reduced the incidence of delirium, as did a single low dose of ketamine during the induction of anesthesia. However, these trials were conducted among patients undergoing elective surgical procedures, and it is not clear whether their results can be extrapolated to the general ICU population. In contrast, the cholinesterase inhibitor rivastigmine was ineffective in preventing delirium.

Sedation with dexmedetomidine rather than benzodiazepines appears to reduce the incidence of delirium in the ICU. In a multicenter, randomized trial predominantly involving medical patients in the ICU, the administration of dexmedetomidine or midazolam resulted in similar proportions of time within the target range of −2 to +1 on the Richmond Agitation–Sedation Scale among patients, but those assigned to receive dexmedetomidine had a reduced risk of delirium and spent less time undergoing mechanical ventilation. As compared with a lorazepam infusion, sedation with dexmedetomidine
resulted in more time at the target level of sedation and longer survival without delirium or coma.20 In a multicenter European trial, patients were randomly assigned to continue treatment with their current sedative (midazolam or propofol) or to switch to sedation with up to 1.4 μg of dexmedetomidine per kilogram of body weight per hour.20 There were no between-group differences in the proportion of time at the target level of sedation. The rates of the composite end point of agitation, anxiety, or delirium were lower with dexmedetomidine than with propofol, but the rates with dexmedetomidine were equivalent to those with midazolam. When delirium was assessed with the use of the CAM-ICU 48 hours after sedation was discontinued, there were no significant differences among the groups.
TREATMENT

There is very little evidence to guide the management of established delirium, and most existing trials were categorized by the investigators as pilot studies. Only one small placebo-controlled trial supports the efficacy of a drug treatment for established delirium in patients in the ICU. In a study of 36 patients who were randomly assigned to treatment with quetiapine or placebo, delirium resolved faster in patients who received quetiapine. The use of quetiapine also increased the number of patients who were discharged to their own home or to rehabilitation.53 A study of 103 patients who were randomly assigned to receive regular haloperidol, ziprasidone, or placebo showed no significant differences in the number of days that patients survived without delirium or coma.54 The single study comparing haloperidol with an atypical antipsychotic (olanzapine) showed equivalent efficacy.55 None of these trials distinguished between hyperactive and hypoactive delirium.

In a pilot study comparing dexmedetomidine with haloperidol in patients with hyperactive delirium, dexmedetomidine was associated with a shorter time to extubation and shorter length of stay in the ICU.56 This finding is supported by a randomized trial of dexmedetomidine versus midazolam in which patients with delirium at the time of enrollment had a more rapid resolution of delirium if they were assigned to receive dexmedetomidine than if they were assigned to receive midazolam.57 However, definitive evidence supporting the use of dexmedetomidine for the treatment of delirium is not currently available.

Quality Improvement Techniques

Frameworks that facilitate the aforementioned approaches have been developed. These include the “pain, agitation, and delirium” (PAD) guidelines44 and the “spontaneous awakening and breathing coordination, attention to the choice of sedation, delirium monitoring, and early mobility and exercise” (ABCDE) bundle.56 These guidelines emphasize improving team communication in the ICU, standardizing care processes, and prioritizing methods to lighten sedation and facilitate early mobilization and extubation. Each guideline recognizes the conceptual evolution from spontaneous-breathing trials and interruption of sedation to a comprehensive approach to monitoring and managing pain, agitation, and delirium.

CONCLUSIONS

Accumulating evidence suggests that the management of sedation and delirium can have an important effect on the outcomes of patients who are treated in ICUs. Currently available data suggest that the best outcomes are achieved with the use of a protocol in which the depth of sedation and the presence of pain and delirium are routinely monitored, pain is treated promptly and effectively, the administration of sedatives is kept to the minimum necessary for the comfort and safety of the patient, and early mobilization is achieved whenever possible (Fig. 2).

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