Sedation, Analgesia and Muscle Relaxation in the Intensive Care Unit

Anjan Trikha 1, V Rewari 2

Summary

Sedation and analgesia is an essential part of therapy for critically ill patients as it provides comfort and minimizes pain suffering and anxiety. Effective sedation management is best achieved through interdisciplinary planning, knowledge of pharmacology of sedative drugs and the predisposing factors for various forms of distress including underlying medical illness, history of alcohol abuse and psychiatric illness. Frequent monitoring with validated tools helps in detecting and treating pain and agitation while avoiding excessive or prolonged sedation. Neuromuscular blocking agents are often used in an intensive care unit to facilitate mechanical ventilation. Monitoring of degree of neuromuscular blockade via periodic peripheral nerve stimulation is essential to prevent complications. The various modalities of sedation, analgesia and muscle relaxation are discussed in an attempt to provide for optimal care to a patient in the intensive care unit.

Key words Sedation, Analgesia, Neuromuscular blocking drugs, ICU, Muscle relaxation

Patients in the intensive care unit (ICU) are often uncomfortable because of anxiety, pain and presence of monitoring and various ventilation gadgets. This discomfort is best treated by continuous infusion of sedating agents and / or opioids. Critically ill patients may also require neuromuscular blockade to facilitate mechanical ventilation when sedation alone is inadequate in providing conditions for effective ventilation. However, all these medications can promote adverse consequences, including prolonged mechanical ventilation and duration of stay in ICU. An in depth knowledge about the application and monitoring of sedation, analgesia, and muscle relaxation in critically ill patients is of prime importance for an intensivist. In this review we attempt to discuss the various modalities of sedation, analgesia and muscle relaxation in the intensive care unit.

General principles

Effective sedation management is best achieved through interdisciplinary planning, knowledge of pharmacology of sedative drugs and practice. One needs to consider the possible predisposing and precipitating factors for various forms of distress, underlying medical illness, history of alcohol abuse and psychiatric illness. A commonly forgotten issue in an ICU is the routine medication that the patient had been taking at home.

The two major classes of medications used to promote comfort and tolerance of the ICU environment are the sedative-hypnotic agents (Table 1) and opioid analgesics (Table 2), which provide anxiolysis, sedation, amnesia, and analgesia to the patient. General considerations for medication selection include patients’ condition, co morbid illnesses, duration, onset, and offset of effect, adverse effects, costs and any recent history of opioid or benzodiazepine use. Most of these medications are administered by continuous IV infusions since absorption from the GI tract or following subcutaneous or IM injection is less reliable, in critically ill patients. Administration of medications via the transdermal or enteral route has a role in patients, who require long-term sedation and analgesia as this results
### Table 1 Sedative medication used in ICU

<table>
<thead>
<tr>
<th>Drug</th>
<th>Elimination</th>
<th>Onset Duration</th>
<th>Dosing (IV)</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lorazepam</td>
<td>Hepatic conjugation to inactive metabolite</td>
<td>5-20 minutes</td>
<td>BD: 2-4 mg MD: 1-10 mg/h</td>
<td>Inexpensive</td>
<td>Propylene glycol toxicity at high doses.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>6-8 hours</td>
<td></td>
<td>Long half-life</td>
<td></td>
</tr>
<tr>
<td>Midazolam</td>
<td>Cytochrome P450 Active metabolite excreted renally</td>
<td>5-10 minutes</td>
<td>BD: 1-5 mg MD: 1-10 mg/h</td>
<td>Shorter acting</td>
<td>Many drug interactions.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1-4 hours</td>
<td></td>
<td>Fast onset</td>
<td>Active metabolite accumulates in renal failure</td>
</tr>
<tr>
<td>Propofol</td>
<td>Conjugation</td>
<td>30-50 seconds</td>
<td>BD: 1-3 mg MD: 5-150 mcg/kg/min</td>
<td>Short acting</td>
<td>↓ BP, increase serum triglyceride, pancreatitis, propofol infusion syndrome</td>
</tr>
<tr>
<td></td>
<td></td>
<td>3-10 minutes</td>
<td></td>
<td></td>
<td>↓ BP, ↓ HR.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dexmedetomidine</td>
<td>Hepatic Cytochrome P450 and glucuronidation</td>
<td>Immediate 5-10 minutes</td>
<td>BD: 0.5-1 mcg/kg MD: 0.2-0.7 mcg/kg/h</td>
<td>Very short duration. No respiratory</td>
<td>Not approved for use more than 24 hours.</td>
</tr>
</tbody>
</table>

BD: Bolus dose, MD: Maintenance dose. HR: heart rate, BP: blood pressure. All doses are for adult patients, boluses need to be given slowly and doses may have to be decreased in patients with hepatic/liver failure.

### Table 2 Opioid analgesic medications used in ICU

<table>
<thead>
<tr>
<th>Drug</th>
<th>Elimination</th>
<th>Onset Duration</th>
<th>Dosing (IV)</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morphine</td>
<td>Conjugation; active Metabolite excreted by kidney</td>
<td>5-10 minutes</td>
<td>BD: 2-4 mg MD: 2-30 mg/h for ventilated patients</td>
<td>Cheap Good analgesic Euphoria</td>
<td>↓ BP, respiratory depression, active metabolite, accumulation in hepatic/renal failure</td>
</tr>
<tr>
<td>Hydromorphone</td>
<td>Hepatic</td>
<td>5-10 minutes</td>
<td>BD: 0.2-0.6 mg MD: 0.5-3 mg/h</td>
<td>May work if patients are tolerant to morphine/fentanyl</td>
<td>Respiratory depression, caution in non ventilated patient; highly addictive</td>
</tr>
<tr>
<td>Fentanyl</td>
<td>Cytochrome P450/3A4</td>
<td>30 – 60 seconds</td>
<td>BD: 25-50 mcg/kg/h for ventilated patients</td>
<td>Less hyotension than morphine</td>
<td>3A4 inhibitors may increase fentanyl; fever will increase patch fentanyl levels by 30%</td>
</tr>
<tr>
<td>Alfentanil</td>
<td>Hepatic Metabolites excreted By kidney</td>
<td>1 minute 30-60 min</td>
<td>BD: 50-75 mcg/kg MD: 0.5-3 mcg/kg/min</td>
<td>Very short-acting</td>
<td>↓ HR, ↓ BP, ↑ ICP</td>
</tr>
<tr>
<td>Sufentanil</td>
<td>Hepatic</td>
<td>1-3 minutes</td>
<td>BD: 1-2 mcg/kg MD: 8-50 mcg as needed</td>
<td></td>
<td>3A4 inhibitors may increase levels</td>
</tr>
<tr>
<td>Remifentanil</td>
<td>Tissue esterases</td>
<td>1-3 minutes 10-20 minutes</td>
<td>BD: 1 mcg/kg IV MD: 0.5-3 mcg/kg/min</td>
<td>No accumulation in hepatic or renal failure</td>
<td>↓ HR, ↓ BP, ↑ ICP</td>
</tr>
</tbody>
</table>

BD: bolus dosage, MD: maintenance dosage, HR: heart rate, BP: blood pressure, ICP: intracranial pressure. All doses are for adult patients, boluses need to be given slowly and doses may have to be decreased in patients with hepatic/liver failure.
Management of anxiety

Anxiety in the ICU can be managed using non pharmacologic or pharmacologic strategies. The role of non pharmacologic management is limited especially in critically ill patients but a few words of comfort spoken to critically ill patients during their sedation free period go a long way to allay anxiety. Benzodiazepines (diazepam, lorazepam, and midazolam) are the most widely used sedatives in the ICU. In our ICU midazolam is the most commonly used benzodiazepine, with diazepam reserved for patients with uncontrolled seizures. Benzodiazepines cause anxiolysis, amnesia, prevent awareness and may enhance the analgesic effects of opiates. Delayed emergence with midazolam has been attributed to accumulation of the parent compound in hepatic failure, or an active metabolite, α-hydroxymidazolam, which is cleared by the kidney and may lead to prolonged sedation in patients with renal insufficiency. Lorazepam is also a very useful drug for providing sedation in ICU, however prolonged high-dose administration of lorazepam can result in accumulation of the vehicle, propylene glycol, resulting in worsening renal function, metabolic acidosis, and altered mental status. There are relatively few randomized controlled trials in which lorazepam and midazolam are compared for long-term infusion. Two studies reported no significant difference in time to awakening. Barr et al reported significantly shorter emergence time and time to extubation for midazolam as compared to lorazepam in patients without significant co morbid conditions. Diazepam is less commonly used for continuous sedation in the ICU. It has a number of active metabolites especially desmethyldiazepam, which accumulate in the tissues and can lead to prolonged sedation. Diazepam is presently indicated as intravenous bolus to treat acute anxiety or agitation and orally for withdrawal syndromes.

Propofol provides sedation and amnesia and has a rapid onset and short duration of sedation once discontinued. It remains a preferred choice for short term sedation in the ICU. Propofol infusion is associated with a number of adverse effects, such as hyper triglyceridemia, dose-dependent hypotension, and the propofol infusion syndrome. The pharmacokinetics of propofol in critically ill patients depends on various factors. Barr and his colleagues studied the pharmacology of propofol infusions in ICU patients and demonstrated that the offset of sedation varies considerably, being a function of depth of sedation, duration of the infusion, and patient size and body composition.

Various randomized controlled trials have compared propofol and midazolam infusion for sedation in the ICU. In a systematic review, it has been demonstrated that propofol leads to more effective sedation and shorter weaning time after short-term infusion but is associated with higher adverse event rates when compared to midazolam. In a meta-analysis, Ostermann and colleagues included 32 studies of sedation in the ICU. They found that propofol was at least as effective for sedation as was midazolam, and resulted in a shorter interval to extubation, but it was associated with increased risk for hypotension and higher cost. In contrast, Kress and coworkers found no difference in the duration of mechanical ventilation and length of stay in the ICU or hospital between midazolam and propofol in mechanically ventilated ICU patients. Hall and his colleagues published results of a multicenter trial conducted in four Canadian ICUs. They found that propofol sedation allowed for more rapid tracheal extubation than when midazolam sedation was used but this did not result in earlier ICU discharge. Comparative studies evaluating the ability of propofol sedation to accelerate ICU discharge have yielded contradictory results. The reason for this is not yet known and more randomized controlled multicenter trials are needed.

Dexmedetomidine is a selective alpha 2-adrenergic receptor agonist with a short half-life of approxi-
mately 2.3 hrs, and has sedative, analgesic, anxiolytic, and sympatholytic effects without causing respiratory depression. Dexmedetomidine efficacy as a short term sedative has been reported in postoperative ICU patients. It has also been shown to have analgesic sparing properties. Although dexmedetomidine is labeled in some countries only for sedation of less than 24 hours, the drug has not been extensively studied for long-term administration to critically ill patients. This drug is not available in India.

**Butyrophenones (Haloperidol)** can also be used for sedation of mechanically ventilated patients especially if they are agitated or are suffering from ICU psychosis. These drugs induce a state of tranquility and sense of detachment. The onset of action of intravenous haloperidol starts in 2–5 minutes. It is used in doses of 1–10 mg titrated to effect. It is not a reliable amnesic agent and does not appear to affect seizure activity. Haloperidol has an advantage over other sedative and analgesic drugs in that it does not have a significant effect on the ventilatory or hypoxic respiratory drive.

**Volatile sedation**

Isoflurane has successfully been used for sedation in ventilator-dependent ICU patients. Several studies have compared isoflurane with midazolam or with propofol and found adequate sedation with predictable and quick awakening, without reported tolerance or withdrawal symptoms. Initially, the lack of necessary equipment led to limited use of volatile anaesthetics as sedative agents in the ICU, but recently a device named AnaConDa® filter (Hudson RCI, Uppsland Växby, Sweden), has been introduced for this purpose. This device is connected between the patient and a normal ICU ventilator, and it maintains 90% of the volatile anaesthetic inside the patient, analogous to the action of a heat-moisture exchanger. Although volatile anaesthetics are not licensed for use for sedation in the ICU, volatile sedation in the ICU appears a promising alternative to intravenous sedatives for mechanically ventilated adult patients in the ICU, but more clinical studies are warranted.

The 2002 Society of Critical Care Medicine (SCCM) guidelines recommend lorazepam as the preferred sedative drug for ICU patients who require prolonged therapy, whereas midazolam was recommended only for short-term (<48 h) sedation because of concerns for unpredictable awakening observed after prolonged infusion. Midazolam or diazepam should be used for rapid sedation of acutely agitated patients. Propofol is the preferred sedative when rapid awakening (e.g., for neurologic assessment or extubation) is important. Midazolam is recommended for short-term use only, as it produces unpredictable awakening and time to extubation when infusions continue longer than 48–72 hours. The titration of the sedative dose to a defined endpoint is recommended with systematic tapering of the dose or daily interruption with reiteration to minimize prolonged sedative effects. Triglyceride concentrations should be monitored after two days of propofol infusion and total caloric intake from lipids should be included in the nutrition support prescription.

**Assessment of sedation**

Sedation in a critically ill patient is most often assessed using standard subjective scales which can be easily understood and applied by the nursing staff. However in certain situations such as neuromuscular blockade and deep sedation these scales can not be applied and the objective tools for assessment of sedation need to be used. A number of sedation scales have been developed for use in ICU. The following scales have been tested for inter rater reliability in multiple patient populations at multiple hospitals. Ramsay Scale, Riker Sedation–Agitation Scale (SAS), Motor Activity Assessment Scale (MAAS), The Observers Assessment of Alertness/Sedation (OAA/S), and Richmond Agitation Sedation Scale (RASS). For paediatric patients the Comfort Scale has been advocated. It has been shown that using such scales results in precise dosing, reduced sedative and analgesic drug use, shorter duration of mechanical vent-
tilation, and a decreased incidence of oversedation. RASS has also been validated against bi spectral index and a good correlation has been reported.

Objective testing of the level of sedation may be helpful during very deep sedation or when therapeutic neuromuscular blockade is being used. The assessment of brain activity can be performed using EEG signals processed by proprietary algorithms such as with the bispectral index, patient state index, cerebral state index, Narcotrend index, entropy, and auditory evoked potentials. In spite of the advantages of these modalities, they are rarely used in ICU.

**Daily interruption of sedation**

Continuous infusions have been linked to prolonged sedation and longer length of ICU stay. Protocols that provide daily interruption of sedation are often employed to avoid excessive and prolonged effects. Kress and his colleagues demonstrated that daily interruption of continuous sedation decreased the length of time patients spend on the ventilator and in the ICU. This also diminished the number of diagnostic tests performed to evaluate why a patient was not waking up once sedatives had been discontinued. There have been concerns regarding the psychiatric impact of repeated abrupt awakening on critically ill patients, however it has been demonstrated that there is no increase in symptoms of post traumatic stress disorders in such patients.

The 2002 SCCM guidelines recommend that a sedation goal or endpoint should be established and regularly redefined for each patient. Regular assessment and response to therapy should be systematically documented. The use of a validated sedation assessment scale (SAS, MAAS) is recommended.

**Management of Analgesia**

Pain in ICU patients can occur from factors, such as preexisting diseases, invasive procedures, presence of monitoring and therapeutic devices, routine nursing care and prolonged immobility.

**Pain evaluation**

In patients who are unable to communicate evaluation of pain is difficult and one has to rely on objective signs that are either physiological or behavioral (heart rate, blood pressure, breathing pattern, diaphoresis, body posturing, guarding etc). Assessment of pain is less reliable and less valid when inferred through observation of patient behaviors. Visual Analogue Scale (VAS) and Numerical Rating Scale (NRS) are the two most commonly used measurement scales for pain in conscious patients. It has been shown in a study that NRS may be preferable to VAS in critically ill patients. Multidimensional tools, such as the McGill Pain Questionnaire and the Wisconsin Brief Pain Questionnaire, have been shown to be impractical for the ICU environment. A Critical Care Pain Tool (CCPT) has been formulated to address this issue and has shown promise. The components of CCPT are based on recognition of common behaviors, such as facial grimacing, restless body movement, rigid limbs, and patient/ventilator asynchrony observed during painful procedures and validated against self-report.

According to the 2002 SCCM guidelines pain assessment and response to therapy should be performed regularly by using a scale appropriate to the patient population and systematically documented. Use of the NRS is recommended to assess pain. Patients who cannot communicate should be assessed through subjective observation of pain-related behaviors and physiological indicators and the change in these parameters following analgesic therapy should be noted.

Alleviation of pain in an ICU setting should involve both pharmacological and non pharmacological measures. Simple interventions including attention to proper positioning of patients, stabilization of fractures, and elimination of irritating physical stimulation (e.g., proper positioning of ventilator tubing to avoid traction on the endotracheal tube) are important to maintain...
patient comfort and decrease pain, however non pharmaco-
logical methods alone can only help to decrease
the need for analgesics.

Opioids

Opioids are the most important medications for
managing pain in ICU. The advantage of opioids is
that they have minimal hemodynamic effects in
euvolemic patients. All opioids have essentially similar
side-effects and include respiratory depression, muscle
rigidity, hypotension, delayed gastrointestinal transit,
nausea, choledochoduodenal sphincter spasm, pruri-
tus, and urinary retention. Opioids used for analgesia in
ICU are displayed in Table-2. Surveys and surveillance
studies indicates the widespread use of fentanyl and
morphine, although sufentanil is popular in Europe.

Morphine is the most common opioid used in
the ICU because of its low cost, superb analgesic effic-
cacy, and euphoric effects. Fentanyl is the agent of
choice for patients with renal insufficiency, or
haemodynamic instability. Pethidine has an active
metabolite that causes neuroexcitation and may inter-
act with antidepressants so it is not recommended for
repetitive use. Remifentanil, unlike many other
opioids, which are non-specific, is selective for the μ
receptors that mediate pain. It has quick onset and short
duration of action even after infusion of long duration.
Therefore, analgesia-based sedation with remifentanil
has been introduced as an option in ICU patients.
Muellejans and colleagues compared the efficacy and
safety of remifentanil and fentanyl in post surgical ICU
patients. Both agents were effective in achieving the
targeted sedation level and recovery was rapid, with-
out any apparent difference between agents. In con-
trast, in their comparison of a remifentanil- based ver-
sus a morphine-based regimen under similar conditions,
Dahaba and coworkers found that the mean duration
of mechanical ventilation and extubation times were sig-
nificantly shorter in the remifentanil group. In critically
ill patients requiring prolonged mechanical ventilation
for up to 10 days, Breen and colleagues compared
remifentanil versus midazolam-based sedation regimen
to which fentanyl or morphine was added for analge-
sia. The remifentanil- based sedation regimen was as-
sociated with significantly reduced duration of mechani-
cal ventilation by more than 2 days. Similar result was
reported by Baker and his colleague. In addition,
remifentanil does not exert significantly prolonged clin-
ic effects when it is administered to ICU patients with
renal failure. Based on these studies, it can be con-
cluded that remifentanil is effective for providing both
analgesia and sedation in critically ill patients, even those
suffering from multiple organ failure. It has been shown
that when sedative infusions are given in combination
with analgesic infusions a reduced dose of both the
medications can be used and is effective with better
results than when they were used alone. The terms “co–
sedation” or analgosedation” have been used for such
regimens. Studies from Europe have demonstrated
shorter duration of mechanical ventilation with an anal-
gesic based versus sedative based protocol.

Non opioids can also be used as analgesics in
such settings. Ketamine, has analgesic properties at sub
anaesthetic doses that usually do not cause airway com-
promise or ventilatory depression. As a result, ketamine
is used in the ICU for specific painful procedures, par-
ticularly burn dressing changes. NSAIDs in an ICU
are best utilized as part of a multimodal analgesic regi-
men in post surgery patients. Acetaminophen’s role
in critical care is limited to relieving mild pain or dis-
comfort, such as that associated with prolonged bed
rest or use as an antipyretic.

The 2002 SCCM guidelines recommend that
a therapeutic plan and goal of analgesia should be es-

tablished for each patient and communicated to all
caregivers to ensure consistent analgesic therapy. If in-
travenous doses of an opioid analgesic are required,
fentanyl, hydromorphone, and morphine are the rec-

commended agents. Scheduled opioid doses or a con-
tinuous infusion is preferred over an “as needed” regi-
men to ensure consistent analgesia. Fentanyl is preferred
for a rapid onset of analgesia in acutely distressed pa-

tients. Fentanyl or hydromorphone are preferred for
patients with haemodynamic instability or renal insuffi-
Epidural analgesia in ICU

Often post surgical patients are shifted to the ICU for elective ventilation with epidural infusions. These patients ideally need both sedatives and analgesics for pain relief as well as for mechanical ventilation. There are no specific guidelines on these sub groups of patients. A meta-analysis of more than 5,000 surgical patients has shown that postoperative epidural analgesia reduces time to extubation, ICU stay and improves forced vital capacity. Epidural analgesia has been shown to benefit ICU patients after cardiac surgery, thoracic trauma and acute pancreatitis. However, whether sepsis, is an absolute contraindication for the use of epidural analgesia is still a matter of debate. Further research is therefore required to define the role of epidural analgesia in this high-risk group.

Neuromuscular blockade

Neuromuscular blocking drugs (NMBD) are occasionally used to facilitate mechanical ventilation in patients in ICU (Fig 1). It has been proposed that all modalities to improve clinical situation must be tried before using NMBD. The most common indications for long-term administration of NMBD include facilitation of mechanical ventilation, control of ICP, ablation of muscle spasms associated with tetanus, decreasing oxygen consumption, acute respiratory distress syndrome, acute lung injury and after cardiac arrest. Due to the difficulty in oxygenating such patients, unique modes of mechanical ventilation are often used, e.g., inverse ratio, high frequency, or prone-position ventilation when neuromuscular blockade becomes necessary. The muscle relaxants that are used in an ICU are atracurium, panceuronium, vecuronium, rocuronium, and cisatracurium (Table 3). Pancuronium is inexpensive and has been widely used in the ICU. Because of their unique metabolism, atracurium and cisatracurium are the preferred muscle relaxants for patients with liver of renal disease.

Table 3 Neuromuscular blocking drugs used in ICU

<table>
<thead>
<tr>
<th>Drug</th>
<th>Structural class</th>
<th>Dosing (IV)</th>
<th>Elimination</th>
<th>Duration</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pancuronium</td>
<td>Aminosteroid</td>
<td>BD: 0.1 mg/kg</td>
<td>Hepatic: 30%-40%</td>
<td>40 – 60 min</td>
<td>Sympathomimetic, Caution in patients with CVS problems, Effect prolonged in renal failure, liver diseases, elderly, Effect enhanced with repeated dosing.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>MD: 0.03-0.1 mg/kg/ hour</td>
<td>Renal: 40%-60% Biliary: 10%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vecuronium</td>
<td>Aminosteroid</td>
<td>BD: 0.1 mg/kg</td>
<td>Hepatic: 35%-45%</td>
<td>25 – 40 min</td>
<td>Minimal CVS effects, Prolonged effect in liver dysfunction</td>
</tr>
<tr>
<td></td>
<td></td>
<td>MD: 0.05-0.1 mg/kg/ hour</td>
<td>Renal: 15%-25% Biliary: 40%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rocuronium</td>
<td>Aminosteroid</td>
<td>BD: 0.5 mg/kg</td>
<td>Hepatic: 30 – 35%</td>
<td>25 – 30 min</td>
<td>Anaphylaxis – a concern, Minimal CVS effects</td>
</tr>
<tr>
<td></td>
<td></td>
<td>MD: 0.2-0.5 mg/kg/hr</td>
<td>Renal: 50% Biliary: 40%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Atracurium</td>
<td>Benzylisoquinolinium</td>
<td>BD: 0.5 mg/kg</td>
<td>Hofmann elimination (produces the metabolite laudanosine), plasma ester hydrolysis</td>
<td>20-40 min</td>
<td>Histamine release – dose and rate-related, Laudanosine – seizure potential, Ideal in renal and hepatic failure</td>
</tr>
<tr>
<td>Cisatracurium</td>
<td>Benzyliso-quinolinium</td>
<td>BD: 0.20 mg/kg, MD: 0.03-0.2 mg/kg/hr</td>
<td>Hofmann elimination</td>
<td>20 – 35min</td>
<td>Ideal in renal and hepatic failure</td>
</tr>
</tbody>
</table>
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Fig 1 Flow diagram for using neuromuscular blocking agents in ICU

Note: Monitor degree of blockade – clinical and train of four, (1 – 2 twitches are ideal), reassess every 12 – 24 hours for need for continuation of neuromuscular blocking drugs.

Monitoring neuromuscular blockade.

The best way to monitor muscle relaxant drug effect in the ICU is not clear. There have been studies that have tried to ascertain the best method of monitoring the depth of neuromuscular blockade in critically ill patients. A prospective, randomized, single-blinded trial of 77 patients in a medical ICU who were administered vecuronium based on either clinical parameters or train of four (TOF) monitoring, with a goal of one of four twitches. The latter resulted in a significantly lower NMBD dosages as well as a faster time to recovery of neuromuscular function and spontaneous ventilation⁶⁹. Another study sought to compare the depth of blockade induced by atracurium either by “best clinical assessment” or TOF monitoring. Analysis of the 36 medical ICU patients in this prospective, nonrandomized trial revealed no difference in the total dose, mean dose, or the mean time to clinical recovery⁷⁰. An additional study examining the results of the implementation of a protocol using a peripheral nerve stimulator to monitor the level of blockade in patients receiving a variety of
NMBD found a reduction in the incidence of persistent neuromuscular weakness. Although TOF monitoring may result in the use of lower doses of NMBD and faster recovery from neuromuscular blockade inpatients in the ICU, clinical evaluation may be equally effective.

The choice of the number of twitches necessary for “optimal” blockade is influenced by the patient’s overall condition and level of sedation. The choice of the “best” nerve for monitoring may be influenced by site accessibility, risk of false positives, considerations for the effect of stimulation on patient visitors, and whether faint twitches should be included in the assessment of blockade.

**Adverse effects of neuromuscular blocking agents**

Literature is replete with reports of an association between use of muscle relaxants in critically ill patients and muscle weakness. Usage of these medications has been associated with longer duration of mechanical ventilation, weaning time and stay in ICU. However, it is important to realize that there are many causes other than use of NMBD (due to accumulation of metabolites) of muscle weakness in critically ill patients in an ICU (Table - 4). Prolonged weakness due to NMBD is best avoided by limiting the dose and duration of NMBD administration, particularly in high-risk settings such as renal or hepatic failure, and by frequently monitoring the drug effect.

**Table 4 Common causes of muscular weakness in ICU.**

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Prolonged recovery from NMBD (due to the drug / metabolite / drug interaction).</td>
</tr>
<tr>
<td>2.</td>
<td>Electrolyte imbalances (hypomagnesemia, hypophosphatemia, hypokalemia).</td>
</tr>
<tr>
<td>3.</td>
<td>Disuse atrophy.</td>
</tr>
<tr>
<td>4.</td>
<td>Steroid myopathy.</td>
</tr>
<tr>
<td>5.</td>
<td>Critical illness polyneuropathy.</td>
</tr>
<tr>
<td>6.</td>
<td>Myasthenia gravis, Guillain-Barre syndrome</td>
</tr>
<tr>
<td>7.</td>
<td>Muscular dystrophy</td>
</tr>
<tr>
<td>8.</td>
<td>HIV-related myopathy</td>
</tr>
</tbody>
</table>

The 2002 SCCM clinical practice guidelines for sustained neuromuscular blockade in the adult critically-ill patient recommend - optimize sedatives and analgesics prior to initiation and monitor and adjust accordingly during course. In case tachyphylaxis develops it is advisable to switch to another neuromuscular blocker (taking into consideration the patient’s organ function) if paralysis is still necessary.

In conclusion, not only sedation and analgesia are essential for patients in ICU but optimizing their doses and following protocols are important. Neuromuscular blockade is a essential modality for an intensivist but needs careful administration and monitoring. Volatile anaesthetics and dexmedetomidine could be the important drugs in this regard for the future.

**References**


Anjan Trikha et al. Sedation analgesia in the ICU

is easier to manage and is more cost-effective. Crit Care Med 1999;27:1461-1465.


Anjan Trikha et al. Sedation analgesia in the ICU


OBITUARY

Indian Society of Anesthesiologists (Delhi Branch) deeply mourns the sad demise of Dr. Punnoose, Sr. Cardiac Anesthesiologist, Ex. Head of the Deprt. Of Anesthesiology & Intensive Care at All India Institute of Medical Sciences. He was an eminent teacher, guide and mentor to many of us. His demise has created an irreparable loss.

ISA (Delhi Branch) prays to the Almighty to grant eternal peace to the departed soul. Our heartfelt condolences to the bereaved family.

ISA (Delhi Branch)