

## Introduction

# Analgesia and sedation in the intensive care unit: an overview of the issues

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## Abstract

Analgesic and sedative medications are widely used in intensive care units to achieve patient comfort and tolerance of the intensive care unit environment, and to eliminate pain, anxiety, delirium and other forms of distress. Surveys and prospective cohort studies have revealed wide variability in medication selection, monitoring using sedation scales, and implementation of structured treatment algorithms among practitioners in different countries and regions of the world. Successful management of analgesia and sedation incorporates a patient-based approach that includes detection and management of predisposing and causative factors, including delirium; monitoring using analgesia and sedation scales and other instruments; proper medication selection, with an emphasis on analgesia-based drugs; and incorporation of structured strategies that have been demonstrated to reduce likelihood of excessive or prolonged sedation.

All clinicians who provide care to critically ill patients face many daily management challenges, including ensuring patient comfort and tolerance of the intensive care unit (ICU) environment, while avoiding complications related to therapy. This seemingly straightforward task of safely maintaining patient comfort in fact requires an appreciation of the many factors that may influence the patient's state of comfort or distress and the inter-relationship with ICU-related processes.

Pain is the root cause of distress experienced by many ICU patients [1-4], but anxiety, dyspnea, delirium, sleep deprivation, and other factors can contribute and are often additive or synergistic [5-8]. The predisposing and causative conditions that provoke these components of distress range widely, and include underlying medical conditions (such as arthritis or chronic pain syndrome) and acute medical or surgical illness, as well as many 'routine' aspects of critical care such as mechanical ventilation, indwelling tubes and catheters, iatrogenic illness, medication side effects, nursing

interventions such as turning and suctioning, and excessive ICU noise and light [9]. Thus, improving the patient's tolerance of these common issues that contribute to a state of relative discomfort or outright distress is important [9-13].

Analgesia and sedation management has routinely been employed in ICU patients for many years, particularly among those receiving mechanical ventilation [14]. Surveys of ICU practitioners indicate continued widespread use and provide insight into the diversity of approaches, including the relative frequency with which specific medications are utilized and variability in monitoring, protocol use, and other clinical practice parameters [15-25]. An international cohort study of mechanically ventilated adults conducted in 1998 [26] (48% from Europe, 24% from Latin America, and 28% from North America) provides an instructive global composite of clinical practice. Only 68% of patients received an analgesic or sedative drug at some time during mechanical ventilation, with a median of 3 days of use. At least one analgesic or sedative drug was used on 58% of days of ventilatory support, including benzodiazepines in 69%, propofol in 21%, and opioids in 63% of sedation days. Heterogeneity in clinical practice for different regions of the world was demonstrated, with use of analgesic and sedative drugs being most common in Europe and least common in Latin America. Soliman and colleagues [19] found considerable variability among European countries regarding use of sedatives (midazolam and propofol were used most widely) and analgesic medications (morphine and fentanyl were most often utilized). A recent observational study conducted in 44 ICUs in France [25] indicates slightly greater use of opioids (90%) as compared with sedatives (72%), a transition to sufentanil and fentanyl as preferred analgesics, and continued under-use of monitoring, with only about 40% receiving sedation or analgesia assessments.

ICU = intensive care unit.

The use of a sedation scale and sedation guidelines also varies widely among countries [19]. Surveys and observational studies indicate that no more than one-half of practitioners, when queried during the late 1990s through to 2004, reported routine use of a sedation scale [16,19-25]. Whether these published findings accurately reflect current practice in 2008 is speculative, however, because the most recently reported survey period is 2004 [25]. It is likely that the publication of the Society of Critical Care Medicine's clinical practice guidelines for the management of sedation and analgesia [27], as well as clinical trials that reported improved outcomes with algorithm-based approaches to sedation management [28-32], have raised clinician awareness and led to more structured management.

The contents of this supplement to *Critical Care* highlight key principles and new developments in the management of analgesia and sedation in the ICU setting. Successful management of patient comfort and tolerance of the ICU environment incorporates recognition and management of predisposing and causative factors, use of nonpharmacologic measures to reduce discomfort and distress, and use of analgesic and sedative medications to control pain and anxiety. Although pain and anxiety are widely recognized as important underlying conditions and targets for therapy, there is increasing evidence that delirium is common and associated with worse outcomes in mechanically ventilated ICU patients [33]. In their review (included in this supplement), Girard and coworkers [34] address basic concepts of as well as novel approaches to detection and management of delirium. An important component of addressing causative factors such as pain, as well as assessing the response to therapy and avoidance of over-sedation, is a structured approach to monitoring [35]. The available tools, rationale, and use of pain assessment tools, sedation scales, agitation scales, and technology-based brain monitoring are reviewed as part of this supplement by Sessler and colleagues [36].

It is important to keep in mind the considerable variability among patients with respect to the most important issues and optimal choices in pharmacologic management, based on such factors as age and organ dysfunction. There is emerging evidence that genetic variability exists for relative susceptibility to opioids [37] and probably for other important drug classes [38]. In addition, the patient's condition typically changes over the course of ICU hospitalization, as do the targets for analgesia and sedation. For example, although low-tidal volume ventilation is not associated with increased sedation needs [39], use of unique ventilatory strategies such as high frequency oscillatory ventilation may require deep sedation until improvement occurs [40]. Thus, utilizing a patient-focused approach to analgesia and sedation with frequent re-evaluation and adjustment is important to achieving optimal outcomes.

The final three papers included in this supplement address various aspects of comprehensive analgesia and sedation

management. Gommers and Bakker [41] provide a comprehensive review of the analgesic and sedative drugs that are currently utilized, comparing pharmacologic characteristics as well as advances in the use of individual agents and their limitations.

Although it is well accepted that analgesics play a central role in modern analgesia and sedation concepts [32,42], continuous infusions of conventional opioids can lead to accumulation and prolonged drug effects, thereby potentially increasing the time on the ventilator, the length of ICU stay, and the probability of acquiring ventilator-associated pneumonia [43]. Remifentanyl, a short-acting opioid that is metabolized by unspecific blood and tissue esterases independent of the duration of infusion or organ insufficiency, was shown in recent clinical research to have a rapid and predictable offset of effect, potentially allowing for a reduction in weaning and extubation times and better differentiation between over-sedation and brain dysfunction [44]. Wilhelm and Kreuer [45], in this supplement, provide an overview of the role of short-acting opioids in ICU analgesia and sedation.

Other major advances in analgesia and sedation management have been achieved through optimizing the use of newer and older medications through novel treatment strategies, which have been demonstrated in prospective trials to improve outcomes such as duration of mechanical ventilation. Several key concepts underlie these strategies. Many newer approaches emphasize titrating medications to achieve targets while avoiding over-sedation [46]. Others focus on providing defined periods during which medications are discontinued in order to achieve a period of relative alertness, thus reducing the likelihood of drug accumulation and providing additional opportunities for ventilator weaning [28,29,31]. It is now appreciated that the interplay between various underlying factors is important for effective management. This recognition has led to comprehensive approaches that emphasize structured detection and quantification of pain, agitation and patient-ventilator interactions, and measurement of the depth of sedation [1,30]. In their review (included in this supplement), Schweikert and Kress [47] address important published analgesia and sedation management algorithms, with particular emphasis on daily interruption of sedation as an effective tool for avoiding excessive sedation.

Although considerable attention is given to initiation and maintenance of effective sedative therapy, de-escalation and discontinuation of therapy is an area of increasing focus. There is a need to consider alternatives to parenteral therapy, such as enteral therapy [48], for long-term or de-escalation of therapy. Withdrawal syndromes from opioids and sedatives may occur during the recovery phase of critical care illness [49], but the prevalence and timing of their development are unclear [50]. Finally, the long-term effects of analgesic and sedative drug management on neuropsychological function remain to be defined [51-53].

It is clear that analgesic and sedative drug therapy in ICU patients is evolving rapidly, with newer medications and novel management strategies. The goals of providing patient comfort and tolerance of the ICU environment while avoiding excessive or prolonged sedation remain central to supportive care of the critically ill patient. Effective, structured approaches to sedation can pay important dividends, such as more precise control of analgesia and sedation, shorter time on mechanical ventilation, fewer complications, and faster discharge from the ICU. Many challenges remain that will be addressed by future research and innovative thinking.

### Competing interests

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