

Contents

Erratum	xiii
Preface	xv
Pratik Pandharipande and E. Wesley Ely	
Pharmacology of Commonly Used Analgesics and Sedatives in the ICU: Benzodiazepines, Propofol, and Opioids	431
John W. Devlin and Russel J. Roberts	
<p>Opioids, benzodiazepines, and propofol remain the mainstay by which to optimize patient comfort and facilitate mechanical ventilation in patients who are critically ill. Unfortunately none of these agents share all of the characteristics of the ideal sedative or analgesic agent: rapid onset, rapid recovery, a predictable dose response, a lack of drug accumulation, and no toxicity. To optimize care, critical care clinicians should be familiar with the many pharmacokinetic, pharmacodynamic, and pharmacogenetic variables that can affect the safety and efficacy of these sedatives and analgesics.</p>	
Pharmacology of Sedative-Analgesic Agents: Dexmedetomidine, Remifentanil, Ketamine, Volatile Anesthetics, and the Role of Peripheral Mu Antagonists	451
Oliver Panzer, Vivek Moitra, and Robert N. Sladen	
<p>In this article, the authors discuss the pharmacology of sedative-analgesic agents like dexmedetomidine, remifentanil, ketamine, and volatile anesthetics. Dexmedetomidine is a highly selective alpha-2 agonist that provides anxiolysis and cooperative sedation without respiratory depression. It has organ protective effects against ischemic and hypoxic injury, including cardioprotection, neuroprotection, and renoprotection. Remifentanil is an ultra-short-acting opioid that acts as a mu-receptor agonist. Ketamine is a nonbarbiturate phencyclidine derivative and provides analgesia and apparent anesthesia with relative hemodynamic stability. Volatile anesthetics such as isoflurane, sevoflurane, and desflurane are in daily use in the operating room in the delivery of general anesthesia. A major advantage of these halogenated ethers is their quick onset, quick offset, and ease of titration in rendering the patient unconscious, immobile, and amnestic.</p>	
Current Sedation Practices: Lessons Learned from International Surveys	471
Sangeeta Mehta, Iain McCullagh, and Lisa Burry	
<p>Patient outcomes are significantly influenced by the choice of sedative and analgesic agents, the presence of over- or undersedation, poor pain control, and delirium. Individualized sedation management using sedation assessment tools, sedation protocols, and daily sedative interruption can improve clinical outcomes. Despite the publication of randomized trials and numerous guidelines, the uptake of proven strategies into routine</p>	

practice can be slow. Surveys of clinicians' self-reported practice and prospective practice audits characterize sedation and analgesia practices and provide directions for education and future research. The objective of this review is to present the findings of surveys and practice audits, evaluating the management of sedation and analgesia in mechanically ventilated adults in the intensive care unit, and to summarize international critical care sedation practices.

Protocolized and Target-based Sedation and Analgesia in the ICU

489

Curtis N. Sessler and Sammy Pedram

Administering sedative and analgesic medications is a cornerstone of optimizing patient comfort and minimizing distress, yet may lead to unintended consequences including delayed recovery from critical illness and slower liberation from mechanical ventilation. The use of structured approaches to sedation management, including guidelines, protocols, and algorithms can promote evidence-based care, reduce variation in clinical practice, and systematically reduce the likelihood of excessive and/or prolonged sedation. Patient-focused sedation algorithms are multidisciplinary, including physician, nurse, and pharmacist development and implementation. Key components of sedation algorithms include identification of goals and specific targets, use of valid and reliable tools to assess analgesia, agitation, and sedation, and incorporation of logical medication selection. Sedation protocols generally focus on a) algorithms that incorporate treating sedation and analgesia based upon escalation, de-escalation, or changing medications according to specific targets, or b) daily interruption of sedative and opioid analgesic infusions. Many published sedation protocols have been tested in controlled clinical trials, often demonstrating benefit such as shorter duration of mechanical ventilation, reduced ICU length of stay, and/or superior sedation management compared to usual care. Implementation of sedation algorithms in ICUs is a challenging process for which sufficient resources must be allocated.

Sedation and Weaning from Mechanical Ventilation: Linking Spontaneous Awakening Trials and Spontaneous Breathing Trials to Improve Patient Outcomes

515

Michael H. Hooper and Timothy D. Girard

Liberation from mechanical ventilation is a vital treatment goal in the management of critically ill patients. The duration of mechanical ventilation is affected by strategies for ventilator weaning and sedation. The authors review literature on weaning from mechanical ventilation and delivery of sedation in critically ill patients, including current guidelines recommending the use of spontaneous breathing trials and spontaneous awakening trials. Implementation of these strategies in a wake-up-and-breathe protocol has demonstrated benefit over the use of spontaneous breathing trials alone.

Altering Intensive Care Sedation Paradigms to Improve Patient Outcomes

527

Richard R. Riker and Gilles L. Fraser

Providing sedation and comfort for intensive care patients has evolved in the last few years. New approaches to improving outcomes for intensive care unit (ICU) patients include providing analgesia before adding sedation and recognizing dangerous adverse effects associated with sedative

medications, such as prolonged effects of midazolam, propylene glycol toxicity with lorazepam, propofol infusion syndrome, the delirigenic effects of benzodiazepines and propofol, and bradycardia with dexmedetomidine. There are now reliable and valid ways to monitor pain and delirium in ICU patients. Dexmedetomidine reduces the incidence of delirium, reduces the duration of mechanical ventilation, and appears to be cost effective.

Sedation and Sleep Disturbances in the ICU

539

Gerald L. Weinhouse and Paula L. Watson

The need for compassionate care of the critically ill often compels clinicians to treat these patients with pharmacologic sedation. Although patients may appear to be asleep under the influence of these sedating medications, the relationship between sleep and sedation is complex and not fully understood. These medications exert their effects at different points along the central nervous system's natural sleep pathway, leading to similarities and differences between the two states. This relationship is important because critically ill patients sleep poorly and this phenomenon has been linked to poor intensive care unit outcomes. Therefore, greater awareness of the effects of these medications on sleep may lead to sedation protocols that further improve outcomes. This article reviews the relationship between sedation and sleep from physiologic and clinical perspectives.

Sedation & Immunomodulation

551

Robert D. Sanders, Tracy Hussell, and Mervyn Maze

The management of critically ill patients necessitates the use of sedatives and analgesics to provide patient comfort and cooperation. These drugs exert profound effects on all organ systems, not only the central nervous system, and this article describes the immunologic effects of the commonly used critical care sedatives: propofol, the benzodiazepines, opioids, and α_2 -adrenoceptor agonists. Benzodiazepines, opioids, and possibly even propofol worsen outcome in animal models of infection, whereas preliminary evidence suggests that the α_2 -adrenoceptor agonist, dexmedetomidine, may improve outcomes in the setting of infection. Given the burden of sepsis and secondary infections in critical care, choice of sedation may need to be carefully considered to preserve immune responses in critically ill patients.

Pharmacoeconomics of Sedation in the ICU

571

Joseph F. Dasta and Sandra Kane-Gill

Despite considerable information on the pharmacotherapy of sedation in the ICU, there is little published on the pharmacoeconomics of sedation in patients who are critically ill. The purpose of this article is to discuss the various components that contribute to the cost of treating the agitated ICU patient and to critically review the articles published since 2000 that evaluated costs and cost-effectiveness in ICU patients receiving drugs for agitation and/or pain. Clinicians should look beyond the acquisition cost of a sedative and include the effect of sedatives on the cost of care when selecting the most appropriate sedative.

Delirium Prevention and Treatment

585

Yoanna Skrobik

Delirium occurs in 35% to 80% of critically ill hospitalized patients. Little is known of delirium prevention and treatment in the critical care setting. Trials emphasizing early mobilization suggest that this nonpharmacologic approach is associated with improved outcome as well as “delirium days”. Titration and reduction of opiate analgesics and sedatives may improve subsyndromal delirium rates. All critical care caregivers should rigorously screen for alcohol abuse, apply alcohol withdrawal scales in alcoholic patients, and titrate sedative drugs. No nonpharmacologic approach or drug has been shown to be beneficial once delirium is established. Considering the importance and the consequences of delirium in the critical care setting, addiction studies are urgently needed.

Delirium: An Emerging Frontier in the Management of Critically Ill Children

593

Heidi A.B. Smith, D. Catherine Fuchs, Pratik P. Pandharipande,
Frederick E. Barr, and E. Wesley Ely

The objectives of this article are (1) to introduce pediatric delirium and provide understanding of acute brain dysfunction with its classification and clinical presentations (2) to understand how delirium is diagnosed and discuss current modes of delirium diagnosis in the critically ill adult population and translation to pediatrics (3) to understand the prevalence and prognostic significance of delirium in the adult and pediatric critically ill population (4) to discuss the pathophysiology of delirium as currently understood, and (5) to provide general management guidelines for delirium.

Cognitive Functioning, Mental Health, and Quality of Life in the ICU Survivors: An Overview

615

James C. Jackson, Nathaniel Mitchell, and Ramona O. Hopkins

Critical illness can and often does lead to significant cognitive impairment and to the development of psychological disorders. These conditions are persistent and, although they improve with time, often fail to completely abate. Although the functional correlates of cognitive and psychological morbidity (depression, anxiety, and posttraumatic stress disorder) have been studied, they may include poor quality of life, inability to return to work or to work at previously established levels, and inability to function effectively in emotional and interpersonal domains. The potential etiologies of cognitive impairment and psychological morbidity in ICU survivors are particularly poorly understood and may vary widely across patients. Potential contributors may include the potentially toxic effects of sedatives and narcotics, delirium, hypoxia, glucose dysregulation, metabolic derangements, and inflammation. Patients with preexisting vulnerabilities, including predisposing genetic factors, and frail elderly populations may be at particular risk for emergence of acceleration of conditions such as mild cognitive impairment.