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# Sedation for the critically ill

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## Introduction

Pharmacological sedation is one of the basic therapeutic measures in intensive care. The aim is to protect patients from the numerous stressful and noxious stimuli as well as to provide anxiolysis, nocturnal sleep and sometimes amnesia. Sedation can be used to decrease sympathetic tone and oxygen consumption in critical conditions and indirectly stabilise haemodynamics. Additionally, sedation is necessary to treat agitation and motor activity, potentially harmful for the patient, and to facilitate invasive therapies such as mechanical ventilation or diagnostic procedures. Often sedatives are confused with analgesics, and, although both act synergistically, they actually treat different entities. Owing to the different severities of disease states, different sedative regimens and drugs or drug combinations are necessary to provide an adequate level of sedation. Moreover, changes in pharmacokinetics and pharmacodynamics (i.e. development of tolerance) during the disease course require continuous titration and adjustment of the sedation regimen. Oversedation can cause cardiorespiratory depression, decreased gastrointestinal motility, immunosuppression, unnecessary prolongation of mechanical ventilation and, thus, indirectly increase the risk of infection. Undersedation may result in hypertension, tachycardia, severe discomfort and (in patients with severe head injury) increased intracranial pressure. Thus, oversedation as well as undersedation entail significant risks which may contribute to increased morbidity and mortality. The use of older long-acting sedatives might be associated with increased costs due to prolonged weaning from mechanical ventilation or prolonged, unneeded care in the intensive care unit (ICU). New sedatives have a shorter half-life and might be easier to handle; however, these drugs are more expensive. The level of sedation thought to be optimal during critical care treatment and under mechanical ventilation has changed during the last few decades. About 20 years ago, patients had to be deeply sedated and even paralysed in order to be adapted to mechanical ventilation. Newer ventilatory modes are now partly controlled by the patient or mimic more physiological breathing patterns, and thus might permit only a slight sedation level. Some recently published studies are presented which investigated different aspects of sedation in the ICU setting.

### Kollef MH, Levy NT, Ahrens TS, Schaiff R, Prentice D, Sherman GTI (1998) The use of continuous i.v. sedation is associated with prolongation of mechanical ventilation. Chest 114: 541–548

This prospective observational study investigated the influence of administration strategy, i.e. continuous or bolus intravenous sedation, on the duration of mechanical ventilation. A total of 242 mechanically ventilated ICU patients were included. About 40% of the patients studied received continuous i.v. sedation, while 60% received either bolus administration of i.v. sedation or no i.v. sedation following intubation. The duration of mechanical ventilation as well as the length of intensive care and hospitalisation was significantly longer for patients receiving continuous i.v. sedation compared with patients not receiving continuous i.v. sedation. Mechanically ventilated patients receiving continuous i.v. sedation had lower arterial oxygentension/fractional inspired oxygen ratios and were more likely to suffer

from acute lung injury or the acute respiratory distress syndrome. Long-acting sedatives (lorazepam) and analgesics (fentanyl) were the two most common drugs prescribed for continuous i.v. sedation in this study.

**Barrientos-Vega R, Mar-Sanchez-Soria M, Morales-Garcia C, Robas-Gomez A, Cuena-Boy R, Ayensa-Rincon A (1997) Prolonged sedation of critically ill patients with midazolam or propofol: impact on weaning and costs. Crit Care Med 25: 33–40**

In Europe at present, midazolam and propofol are probably the most frequently used sedative drugs in the ICU. This randomised, prospective, clinical trial compared midazolam and propofol in regard to the effectiveness of sedation, the time required for weaning and the costs of long-term sedation. A total of 108 critically ill patients requiring mechanical ventilation for > 24 h were included in the study. Sedation was aimed at providing a sedation level of 4–5 on the Ramsay scale. Failure to achieve adequate sedation and outcome were no different between the two sedation regimens. For a similar duration of sedation, the cost of propofol was 2.5 times higher than that of midazolam. Duration of weaning from mechanical ventilation was significantly shorter in the propofol group than in the midazolam group, resulting, after all, in lower costs for overall treatment in the propofol group.

**Hall RI, MacLaren C, Smith MS, McIntyre AJ, Allen CT, Murphy JT, Sullivan J, Wood J, Ali I, Kinley E (1997) Light versus heavy sedation after cardiac surgery: myocardial ischemia and the stress response. Anesth Analg 85: 971–978**

Deep levels of sedation have been advocated to reduce stress response and thus, myocardial ischaemia after coronary artery bypass graft (CABG) surgery. In this prospective randomised study, 50 patients received either slight or deep sedation with a continuous propofol infusion. The aim of the study was to investigate the influence of depth of sedation after uncomplicated CABG surgery on the development of postoperative myocardial ischaemia. Analgesia was provided with low-dose sufentanil infusion and additional i.v. morphine. Myocardial ischaemia (detected by electrocardiography) occurred more often in the group with deep sedation. There was no difference in biochemical stress response parameters, myocardial infarction rate and outcome between the two sedation regimen.

**Rathgeber J, Schorn B, Falk V, Kazmaier S, Spiegel T, Burchardi H (1997) The influence of controlled mandatory ventilation (CMV), intermittent mandatory ventilation (IMV) and biphasic intermittent positive airway pressure (BIPAP) on duration of intubation and consumption of analgesics and sedatives. A prospective analysis in 596 patients following adult cardiac surgery. Eur J Anaesthesiol 14: 576–582**

This prospective observational study compared the use of sedatives and analgesics under different ventilatory modes in patients after CABG surgery with an uneventful postoperative course. The patients were ventilated either with assist/controlled mandatory ventilation (CMV), synchronised intermittent mandatory ventilation (SIMV) or biphasic positive airway pressure ventilation (BIPAP). During CMV the patient could only change the rate of the mandatory machine breaths, during SIMV spontaneous breathing was possible between each mandatory machine breath, and unrestricted spontaneous breathing was possible during BIPAP. Analgesics (pethidine or piritramide) and sedatives (midazolam) were prescribed on an "as-needed" basis. The mean cumulative midazolam dose was significantly higher in the CMV group than in the SIMV group and in the BIPAP group, which also had a significantly lower analgesic requirement. Duration of intubation was significantly shorter in the BIPAP group compared to the CMV and SIMV groups.

## Discussion

Continuous administration of sedative drugs via an infusion pump is commonly advocated because high peak plasma concentrations by bolus doses and low drug concentrations occurring before the administration of the next dose are avoided. Kollef et al.'s study demonstrated that continuous administration of sedative drugs is associated with prolongation of mechanical ventilation. However, one might surmise from their data that the group with continuous i.v. sedation included per se more severely ill patients than the control group and, thus, the long sedation period might be desired rather than accidental. Unfortunately, neither an algorithm or guideline for the sedation regimen (e.g. desired sedation level) nor the selection of the chosen drugs was described, and no data were given about the duration of weaning from mechanical ventilation. Moreover, in this study drugs with long duration of action (lorazepam and fentanyl) were used for continuous i.v. sedation. Continuous administration of short-acting drugs such as propofol avoids unwarranted delay between discontinuation of the sedative infusion and regaining consciousness, as demonstrated by Barrientos-Vega et al. Although in the study of Barrientos-Vega et al. the patients were deeply sedated (Ramsay 4–5) for a mean duration of 140 h, the first T-piece trial was performed only 4 h after stopping the propofol infusion. The advantage of the shorter weaning time compensated for the higher drug cost of propofol (which could even be expected to

decrease because the patent protection for propofol has ended). Thus, it is not continuous i. v. sedation but rather the choice of long-acting sedatives which is associated with prolongation of mechanical ventilation.

There appears to be a close relationship between the invasiveness of the critical care therapy and the depth of sedation necessary to protect the patient from discomfort and stress. During mechanical ventilation and after major surgery, particularly after cardiac surgery, deep sedation is thought to reduce the stress response and, thus, decrease morbidity. However, Hall and co-workers demonstrated that light sedation (i. e. Ramsay 2: patient cooperative, oriented, tranquil) did not result in an increased stress response compared to deep sedation. In contrast to controlled mechanical ventilation, new ventilatory modes permit patients to maintain their own control over the breathing pattern. Consequently, the need for deep sedation to adapt the patient to the machine (to prevent "fighting the ventilator") is reduced by the use of new ventilatory modes. Rathgeber et al. have shown that this approach can reduce the duration of intubation. However, it must be stressed that sufficient analgesia is a precondition for this concept. The advantage of this strategy seems obvious: reduction of unnecessary ICU stay and, consequently, a decrease in costs. Negative effects of oversedation are avoided and the neurological state can be assessed much more appropriately. Moreover, by being awake, these patients can communicate with their family, friends and the ICU staff. They stay human. Deep sedation with a comatose and virtually anaesthetised patient in the ICU must be restricted to only a few indications.