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*"I would have everie man write what he knowes and no more."—Montaigne*

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# Editorial I

## Sedating patients undergoing mechanical ventilation in the intensive care unit—winds of change?

The majority of mechanically ventilated patients in the intensive care unit (ICU) require sedation to reduce anxiety, encourage sleep and to increase tolerance to tracheal tubes and the ventilator. Sedative and analgesic drugs are amongst the most commonly prescribed medications in the ICU.[1] The choice of agent and the way in which they are used varies widely between and within ICUs. In a survey of 164 ICUs in the US,[2] 18 different sedative agents were used, the commonest of which were the opiates and benzodiazepines. A more recent study[3] revealed substantial differences in the clinical use of drugs for sedation and analgesia in the western European countries surveyed.

These differences in clinical practice can have an important impact on patient outcome and cost of care: excessively deep sedation will prolong ventilator dependence and length of stay in the ICU, which can be avoided by careful monitoring and interruption of sedative infusions.[4 5] But failure to provide appropriate sedation and analgesia may add to the well-recognised psychological burden of critical illness for patients,[6 7] and indirectly for relatives. The appropriate use of sedative drugs is an important process measure of quality of care.[8] But to tread the fine line between adequate comfort and avoidance of excessive sedation demands both the use of clinically relevant sedation scales,[9 10] and the availability of more 'responsive' sedative agents. The volatile anaesthetic agents offer considerable potential in this respect.

In this issue of the journal, Meiser and colleagues[11] report the use of the inhalation anaesthetic desflurane and compare it with propofol for postoperative sedation in the ICU. Inhalation anaesthetic agents have been used for sedation for many years. Sir Humphry Davy first suggested that nitrous oxide inhalation could be used to provide analgesia and sedation during surgical operations more than 200 years ago. In the 1960s, using nitrous oxide in a technique called 'relative analgesia', Langa[12] demonstrated that by increasing inspired concentrations of nitrous oxide, an increasing depth of sedation could be achieved. Guedel certainly described the first stage of surgical anaesthesia[13] in terms of deepening levels of sedation. Therefore, in sub-anaesthetic concentrations, inhalation anaesthetics can be used to achieve easily modifiable levels of sedation, which may allow contact with family and attendants while facilitating cooperation with therapeutic interventions. Until recently, the most promising agent in this respect was isoflurane. With its low blood solubility and minimal metabolism, isoflurane, when compared with midazolam,[14 15] and propofol,[16] was shown to provide safe and effective sedation in mechanically ventilated patients with a range of severity of illness. However, despite its advantages, isoflurane has not gained acceptance as a sedative in the ICU, probably because of the lack of convenient equipment for administering and scavenging it, and unresolved concern about potential fluoride ion nephrotoxicity with prolonged administration.

Inhalation agents may be advantageous when used for sedation of mechanically ventilated patients in the ICU for many reasons. Inhalation is a dependable route of drug administration and elimination. Drugs administered via this route generally have a rapid onset of action and the recovery period is short. I.V. sedatives have a flatter dose–response curve than do the inhalation anaesthetics, and the range of blood concentrations and their consequent effects is greater. The steeper dose–response curve with inhalation anaesthetics indicates a more consistent time to the onset of sedation and less variability in the doses required. In clinical practice, this would facilitate easy adjustment of dose to the desired sedative effect.

Many critically ill patients have impaired hepatic and/or renal function. I.V. sedatives that depend on liver metabolism or renal excretion for elimination all have cumulative or prolonged effects. In contrast, recovery from inhalation agents that are administered and excreted through the lungs is both rapid and predictable. Any adverse effects arising from an overdose of an inhalation sedative can be reversed rapidly by reducing the inspired concentration. Inhalation anaesthetics are also useful in facilitating treatment procedures in the ICU, such as bronchoscopy, insertion of chest drains and invasive monitoring procedures. The desired level of sedation can be titrated rapidly, ranging from a light level to that approaching a general anaesthetic. It is also

easy to appreciate how inhalation sedatives have specific benefits in those patients requiring repeated neurological assessments.

Some of these advantages of inhalation sedation are described in the study by Meiser and colleagues.[11] When desflurane was used to sedate patients requiring mechanical ventilation for up to 22 h after surgery, recovery was significantly faster from desflurane sedation than from propofol sedation. Patients were also extubated sooner, with superior cognitive function, after desflurane sedation. In addition, recovery from sedation was more predictable. In contrast, recovery times from propofol sedation showed far greater variability and in some instances were several times longer.

This study has demonstrated the prerequisites for the successful application of inhalation techniques in the ICU. Appropriate gas scavenging systems with a sufficient turnover of ambient air are required in units where inhalation anaesthetics are used. The medical and nursing staff prescribing and providing inhalation sedation must be trained appropriately. There has been a recent convergence in the facilities offered by ventilators used in the operating theatres and the ICU. It is now possible to deliver accurate concentrations of inhalation anaesthetic agents in ventilators with suitable ventilatory functions for use in the ICU.

In 1998, Michalopoulos and colleagues[17] showed that a change in anaesthetic practice and postoperative sedation reduced the length of stay in the ICU and hospital following coronary artery bypass surgery. The readily controllable dose-related level of sedation and the rapid recovery from inhalation agents are particularly advantageous in post-operative patients who require a period of intensive care and stabilization before tracheal extubation. It remains to be seen whether the shorter and more predictable recovery from desflurane sedation can be translated into other benefits, such as earlier patient mobilization and discharge, and more efficient resource utilization. Meiser and colleagues[11] have calculated the pure drug costs for sedating patients with desflurane or propofol, and demonstrated cost savings with desflurane. Whilst this is encouraging information, presentation of pure drug costs *per se* is inadequate. Moreover, drug acquisition costs vary from hospital to hospital and from country to country. Further economic evaluation is clearly warranted to encompass a complete evaluation of the components of costs and effects in a clinical context.[18 19]

The issues surrounding the practice of sedation for postoperative patients for a period of stabilization before tracheal extubation are, of course, very different from those involved in providing long-term sedation in critically ill patients. To date, no randomized controlled trial examining the safety and efficacy of inhalation agents for long-term sedation of patients with multiple organ failure has been published.

In 1992, the American Society of Critical Care Medicine Task Force[20] developed practice parameters for sedation in the ICU. The level of published evidence available to the Task Force at that time was limited, and the practice parameters were drawn largely from expert opinion and clinical experience. The lack of scientific data has possibly hampered the wide acceptance of these practice guidelines. In a national survey of the use of sedating and muscle relaxants in American ICUs, Rhoney and Murry[21] found that most ICUs did not use any sedation protocol and did not follow the Society's recommendations in sedation practice. Similarly, when a modified version of these guidelines was introduced into a medical ICU,[22] the investigators found that the overall adherence to these guidelines occurred in only 23% of patients. More well designed studies are needed to examine the safety and cost-effectiveness of the different agents for sedating different categories of patients in the ICU. Such information will go some way towards helping physicians make appropriate decisions for better patient care in the ICU.

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