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EDITORIAL

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Volatile agents for ICU sedation?

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Sedation is a standard part of critical care and was unchallenged from 1960 to 2000. Classical sedation approaches are associated with significant post-traumatic stress traits [1]. Because of poor pharmacokinetics/pharmacodynamics and planning problems, patients in the intensive care unit (ICU) spend one-third of their duration of stay being ventilated after the resolution of the problem mandating intubation [2, 3]. The aim of sedation in the ICU is to make the patient calm and tolerant to the critical care therapies, in particular mechanical ventilation. Recently several approaches have proven beneficial for patient care and the healthcare system: prospective trials have shown that daily interruptions of sedation are associated with a decrease in length of ventilation and decrease in ICU stay [4]. If a spontaneous breathing trial is used in addition to daily sedation interruption, the 1-year survival is improved [5] without an increase in psychological consequences [6]. Recent data suggest that no sedation at all may be better [7]. This move has been made possible by the improvement in ventilator algorithms, which are increasingly flexible in dealing with variable patient efforts. Over the last 10 years, the pendulum has moved toward a decrease in sedation with proactive strategies [8]. In this frame, the quest for the ideal sedation agent is continuing. The ideal sedative agent should be fast acting, have a rapid onset, not be organ dependent in terms of degradation, not have metabolically active or toxic by-products, have little cardiovascular effects, and be cheap. Over the last 30 years, midazolam, propofol [9], and dexmedetomidine [10, 11] have been rolled out with the promise of being better than the previous generation of drugs.

Sedation management in the ICU is a complex process involving sedation level assessment, medication administration, and an overall strategy. These three components are essential for correct ICU sedation. No one will give norepinephrine in the ICU without measuring blood pressure and having a strategy and objectives for vasopressor use, i.e., norepinephrine up to 20 μg/min for a mean arterial pressure (MAP) of 65 mmHg. Why are we tolerating this "art" of sedation and analgesia in the ICU? There is confusion in the literature between sedation/hypnosis, analgesia, delirium management, and relaxation. This is shown by a recent meta-analysis regarding dexmedetomidine [12] pooling studies on dexmedetomidine used with sedation end points, morphine-sparing end points, and delirium end points. A hypnotic is a hypnotic, an analgesic is an analgesic, an antipsychotic is a drug used to treat delirium episodes [13], and a neuromuscular blocker is a relaxant medication. Although these classes of drugs have synergistic effects they cannot be used interchangeably.

Volatile anesthesia agents have been in use for 50 years in anesthesia but only marginally in the ICU [14, 15]. The first volatile agents were hepatotoxic and induced significant arrhythmias, which make then unsuitable for long-term ICU sedation. Sevoflurane is a very versatile inhalational anesthesia agent with interesting neuro- [16] and cardioprotective [17] properties. Its kinetic and marginal organ degradation make it interesting in the ICU setting. Its applicability depends on the ICU staff and their

Table 1

	Propofol	Dexmedetomidine	Sevoflurane
Advantages	Rapid onset, can be used for induction and as bolus for rapid control Does not need specialized equipment	No respiratory depression Co-analgesic properties Less delirium	No organ-dependent degradation Easy titration up and down Titration based on measured concentrations Shortest awakening/extubation times
Disadvantages	Significant administration of (nutritionally unhealthy) lipids Propofol infusion syndrome Context-sensitive pharmacokinetics	Insufficient potency for deep sedation Bradycardia, hypotension Rebound hypertension on withdrawal	Requires investment and training Malignant hyperthermia Cannot be used as a "bolus" for induction routinely
Approx. cost per 24 h	€44	€189	Anaconda, €65; vaporizer, €47

Costs based on 70 kg 80 μg/kg/min for propofol, 0.5 μg/kg/h for dexedetomidine, and 4 ml/h sevoflurane for an Anaconda (anesthetic conserving device) and 1% at 1 L/min fresh gas flow for vaporizer. Costs translated from Canadian prices

background: Anesthetists handle volatile agents daily in the operating room (OR), are familiar with the concepts of end tidal concentration and minimum alveolar concentration, and are prepared in the unlikely event of a malignant hyperthermia reaction. The paper by Capdevila et al. [18] in this issue of *Intensive Care Medicine* is welcome and shows the feasibility of sevoflurane anesthesia in uncomplicated ICU patients. The authors show that awakening and extubation times are much shorter with sevoflurane compared with those using midazolam or propofol. These awakening and extubation times almost compete with the sub-10-min anesthesia awakening times [19]. These encouraging preliminary data should be analyzed with caution because out of 438 intubated sedated patients admitted in their unit only 60 (14%) were randomized. ICU is traditionally associated with protracted recovery and very slow functional rehabilitation [20]. Sedation weaning is associated with a long time to extubation, a long time to get out of bed, and a long time to regain functional autonomy. Although the study by Capdevila et al. was not designed or powered to determine a difference in ICU length of stay or mortality, the predictability and quality of awakening makes the use of sevoflurane very interesting.

Adoption of volatile agent sedation in the ICU should be done with caution: There are very little data on it is administration over more than 24 h in various patient populations. We think that fluoride generation from sevoflurane is minimal and below toxic ranges, but longer administration in patients with impaired renal function may prove otherwise. Sevoflurane implementation in the ICU will require engineering upgrade of a significant part of the ICU for gas-scavenging infrastructure, and technical investments such as the filters, sevoflurane delivery pumps, and gas analyzer. This implementation will also require an important educational intervention directed at the physicians, nurses, and respiratory therapists. Knowledge about agents and malignant hyperthermia has to be maintained round the clock across all shifts and staff rotations.

ICU sedation has to move from the amorphous, catabolic, cachectic, amyotrophic ICU patient [21] to the proactive, tolerant, and participative patient [22, 23]. If a patient needs a procedure, e.g., tracheostomy, lines, dressing change, the patient needs to be deeply anesthetized. However, outside these periods he needs to be awake [24]. At all times perfect analgesia should be provided with potent opioids and a locoregional analgesia technique when feasible. In this context, sevoflurane certainly has a place in ICU sedation (Table 1); sevoflurane will not replace propofol, dexmedetomidine, or other hypnotic agents but it may be a very promising complement to allow predictable and fast awakening.

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