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Sedating critically ill patients

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Sedation has allowed doctors to perform procedures that might otherwise be unpleasant and terrifying, thereby deterring patients from accessing them. The ideal pharmacological therapy would provide safe analgesia, hypnosis and anxiolysis, with exemplary pharmacokinetic properties such as organ-independent elimination, predictable distribution and rapid titratability. These qualities would enable rapid recovery to 'street fitness' and even allow procedures to be performed outside traditional hospital settings.

Little evidence is available to suggest the superiority of one agent over another,[1] although synergistic combination therapies are frequently used. Commonly used agents include benzodiazepines, intravenous anaesthetic agents, opioids, neuroleptic agents and centrally acting alpha agonists. Doctors undertaking sedation require detailed knowledge of these agents and how they interact in the context of the patient's medical profile. Misguided use of sedation has resulted in morbidity and death.[2] With increasing sedation depth, patients' ability to maintain cardiovascular stability and independently maintain airway patency and ventilatory function may become impaired, and they may require critical interventions to avoid the possibility of 'lost airway'. Crucially, monitoring of vital signs needs to be delegated to appropriately skilled personnel who can undertake any medical intervention required[3] while the procedurist concentrates on the task at hand.

INTENSIVE CARE UNIT SEDATION

A lesser-known realm of sedation practices is that of intensive care unit (ICU) sedation, which is a highly specialised and demanding technique since these sedating drugs are used on some of the sickest patients with deranged physiology.

In neurocritical care, sedation is an indispensable therapeutic pillar in which injured brains are 'rested' to minimise brain metabolic activity and as a key therapeutic component for control of raised intracranial pressure.[4] In all ICUs, some critically ill patients are humanely sedated to improve experiences that are probably terrifying and noxious, including tracheal intubation, mechanical ventilation, invasive procedures such as line insertion or tissue sampling, and the necessary routine of orotracheal suctioning. This is advocated by the clinical practice guidelines for pain, agitation, delirium, immobility and sleep disruption.[5]

At another extreme, terminal or palliative sedation is sometimes practised in the ICU. The double-edged sword that is ICU sedation results in various central nervous system side effects such as delirium and agitation.[1] These are usually characterised by acute changes in motor and psychological activities, and frequently accompanied by a loss of control of action and disorganisation of thought. It may occur in isolation or be accompanied by other disorders such as severe anxiety and terror. The aetiology of delirium is multifactorial, ranging from the illness process, such as metabolic disorders, sepsis-associated encephalopathy and its associated treatment, to external factors such as noise, discomfort, pain, disorientation and sedation. Agitated and delirious ICU patients are a danger to themselves, as they risk dislodgement of lines and tubes, have increased metabolic requirements and subsequently have a greater risk of dementia and cognitive decline; their medical and nursing care may also be affected.[6] There is also an association with increased cost and length of stay in the ICU.[7] Needless to say, it is distressing for family and friends to witness a loved one in such a state and bound by restraints.

Assessment tools such as the Richmond Agitation and Sedation Scale and the Confusion Assessment Method for the Intensive Care Unit (CAM-ICU) are well validated and frequently used in many ICUs.[8] They allow repeated assessments over monitoring epochs. Familiarity with these tools has allowed for protocols to be written and studies to be designed to better understand the factors contributing to quality sedation and side effects such as delirium.

In this issue of the *Singapore Medical Journal*, Ng et al investigated sedation practices (i.e. sedation practices in intensive care evaluation [SPICE]) in Singapore public hospital ICUs to overcome the knowledge gap on this topic.[9] Data was compared with that from Malaysia and Australia/New Zealand (ANZ), since a uniform protocol, ANZ SPICE, was used.[10,11] The Singapore data showed lower proportions of ICU patients in the deep sedation range. CAM-ICU-positive delirium (at least one episode) was seen in 23.7% of their study cohort, far lower than the 44%–50.7% incidence in the other two SPICE studies.[9-11] At the risk of simplifying cause and effect, there was a higher frequency of benzodiazepine use in both the ANZ and Malaysian studies, while propofol and fentanyl were the most commonly used agents locally. Moreover, the local regimen's target was in the range of light sedation. Light sedation has been advantageous for reducing ventilation time when compared with deep sedation, as described by Treggiari et al.[12] Importantly, it also reduces subsequent post-traumatic stress four weeks after hospital discharge.

THE FUTURE OF SEDATION PRACTICES

The association between sedation and delirium/agitation has directed research towards finding drugs with better sedation profiles, using the best sedation regimen and better-defined,

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individualised sedation goals.[13] Creating or finding the best assessment regimens is also vitally important. These must be practical to be implemented across very heterogeneous ICU settings, as rightly evinced by Ng et al.[9]

Strategies to decrease overall exposure to sedation,[14] such as sedation hold/interruption, have failed to show benefit in terms of reducing the duration of mechanical ventilation or ICU stay, according to a study by the SLEAP Investigators and Canadian Critical Care Trials Group.[15] Current practices have moved away from continuous deep sedation, and with more suitable agents available, ICU patients will hopefully be at less risk of developing the morbidity associated with agitation and delirium.[7]

Protocolised ICU management[16] for analgesia, sedation and delirium, and early use of sedation algorithms and pathways that apply the concept of early goal-directed sedation, as reported by the recently completed SPICE III,[17] have also been shown to support clinical decision-making and improve clinical outcomes (e.g. subsyndromal delirium and mortality). Moreover, SPICE III demonstrated laudatory properties of the use of dexmedetomidine.[17] MIND-USA[18] (antipsychotics for delirium and sedation sparing effect) and MENDS II[19] (studying sedative choice in severe sepsis patients to best reduce delirium, improve survival and long-term brain function) are examples of studies that will continue to seek even better sedation for the critically ill. These ongoing studies will hopefully guide intensivists on their choice of sedating agents and adjuncts in order to achieve physiological endpoints with the least haemodynamic and mental perturbations.

The future of sedation is exciting. Picture the interplay of novel sedatives and the use of target-controlled infusion algorithms, which are informed by pharmacokinetic and pharmacodynamic principles. These will be integrated with the patient's physiological monitors, including depth of sedation monitoring. Such a system will react appropriately and automatically to clinical requirements while at all times keeping the patient safely sedated via feedback loops. Each component is currently being used in various aspects of clinical practice. However, a skilled human is still needed to orchestrate this complex task through the act of titration. Hence, more studies, such as the study by Ng et al,[9] are needed to focus interest and resources and to further develop cutting-edge sedation practices and technology in our local ICUs.

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