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REVIEW

Do sedation and analgesia contribute to long-term cognitive dysfunction in critical care survivors?

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Abstract Deep sedation during stay in the Intensive Care Unit (ICU) may have deleterious effects upon the clinical and cognitive outcomes of critically ill patients undergoing mechanical ventilation. Over the last decade a vast body of literature has been generated regarding different sedation strategies, with the aim of reducing the levels of sedation in critically ill patients. There has also been a growing interest in acute brain dysfunction, or delirium, in the ICU. However, the effect of sedation during ICU stay upon long-term cognitive deficits in ICU survivors remains unclear. Strategies for reducing sedation levels in the ICU do not seem to be associated with worse cognitive and psychological status among ICU survivors. Sedation strategy and management efforts therefore should seek to secure the best possible state in the mechanically ventilated patient and lower the prevalence of delirium, in order to prevent long-term cognitive alterations.

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¿Contribuye la sedación y la analgesia a la disfunción cognitiva en supervivientes de una enfermedad crítica?

Resumen La sedación profunda durante la estancia en una Unidad de Cuidados Intensivos (UCI) puede afectar negativamente al estado clínico y cognitivo de los pacientes críticos sometidos a ventilación mecánica. En la última década ha aparecido gran cantidad de literatura sobre diferentes estrategias dirigidas a reducir los niveles de sedación en el paciente crítico. Además, ha aumentado el interés sobre la disfunción cerebral aguda o delirium. Sin embargo, el efecto de la sedación sobre los déficits cognitivos a largo plazo continúa siendo poco conocido. Las estrategias centradas en reducir los niveles de sedación en UCI no parecen estar asociadas con un peor estado cognitivo y psicológico de los supervivientes. Por lo tanto, las estrategias de manejo de la sedación en UCI deberían focalizarse en mejorar el estado del paciente ventilado, así como en disminuir el delirium, con el fin de prevenir las alteraciones cognitivas a largo plazo.

Introduction

Sedative and analgesic agents are widely used by physicians to treat pain, stress and discomfort in critically ill patients admitted to Intensive Care Units (ICUs). During the late 1990s, ICUs worldwide developed a culture of very deep and prolonged sedation and paralysis, especially in patients requiring vital support techniques such as mechanical ventilation (MV).

However, sedation may also have deleterious effects. Several negative short- and long-term outcomes have been associated with increased levels of sedation in medical and surgical ICU patients undergoing MV. The administration of sedative agents may produce respiratory depression, hemodynamic instability or metabolic acidosis, and can prolong mechanical ventilation and ICU stay and increase the likelihood of the development of delirium.[1,2]

Over the last decade there has been an increasing interest in the study of acute brain dysfunction, or delirium, in ICU patients.[3–5] This growth can be attributed to the impact of delirium on clinical outcomes in critically ill patients on MV, including increased mortality,[6,7] prolongation of MV and hospital stay,[8] higher costs of care,[9] and long-term cognitive impairment.[10] Various sedative agents have been identified as likely predictors of the development of delirium in mechanically ventilated ICU patients, suggesting a link between sedation and critical illness-associated brain dysfunction.[11–13] However, outside the context of delirium, the contribution of sedation to long-term brain dysfunction in critically ill patients has not been discussed or comprehensively evaluated.[14] Therefore, the aim of this review is to explore the role of sedative dosing strategy in the development of neurocognitive dysfunction after ICU stay.

Clinical outcomes and sedation strategy

The current trend in patients undergoing mechanical ventilation in the ICU is to moderate the depth of sedation. This procedure has been promoted by clinical trials that have indicated the need for lower levels of sedation in critical care and have implemented a variety of strategies including daily sedation interruption, goal-directed sedation, or even no sedation at all.[15]

The daily sedation interruption strategy

Daily sedation interruption is defined as a short-term suspension, holding, discontinuation, or cessation of intravenous sedation or (in some cases) analgesic medication.[16] The first clinical trial using this sedation strategy[16] concluded that daily interruption of the infusion of sedative drugs was a safe and practical strategy to treat ICU patients undergoing MV which also improved clinical outcomes, decreasing the duration of MV and shortening ICU stay. To test whether lower sedation doses in ICU patients might affect the long-term psychological status of ICU survivors, a small sample of the study cohort was monitored for psychological symptoms[17]; at six months, no significant differences between groups were observed for anxiety, depression and functionality. However, patients in the intervention group had a lower Impact of Event Score ($p = 0.02$), suggesting that the daily sedation interruption strategy was beneficial rather than harmful and reduced symptoms of post-traumatic stress disorder.

Since that study, several trials have explored the effect of daily sedation interruption on clinical outcomes in ICU patients.[18] Daily spontaneous awakening trials seem to reduce time in coma, ICU and hospital length of stay, sedation and to increase time off MV, and the 1-year survival rates.[19,20] Although other authors did not find significant improvements in different clinical and psychological outcomes,[21–23] daily sedation interruption has been recommended by the Society of Critical Care Medicine guidelines in order to achieve light levels of sedation in mechanically ventilated ICU patients.[11]

The goal-directed sedation strategy

The impact of deep sedation during the first 48 hurs of ICU admission on the short- and long-term clinical outcomes was