Dexmedetomedine versus Standard Sedatives in Weaning from Mechanical Ventilation

Thesis

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By

Ayman Elsaid Ahmed Abdellatif

M.B., B. Ch. & M.Sc.

Under Supervision of

Prof. Dr. Nabila Mohamed Fahmy
Professor of Anesthesiology & Intensive Care Medicine
Faculty of Medicine – Ain Shams University

Prof. Dr. Hatem Said Abdel Hamid
Professor of Anesthesiology & Intensive Care Medicine
Faculty of Medicine – Ain Shams University

Dr. Amal Hamed Rabie
Lecturer of Anesthesiology & Intensive Care Medicine
Faculty of Medicine – Ain Shams University

Dr. Hany Maher Salib
Lecturer of Anesthesiology & Intensive Care Medicine
Faculty of Medicine Ain Shams University

Faculty of Medicine
Ain Shams University
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Ayman Elsaid Ahmed Abdellatif

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List of Abbreviations

Abbrev.	Full term
ICUs	: Intensive care units
VAP	: Ventilator-associated pneumonia
SAS	: Sedation Agitation Scale
EEG	: Electroencephalogram
RASS	: Richmond Agitation Sedation Scale
BIS	: Bispectral Index
AER	: Auditory evoked responses
CNS	: Central nervous system
IL	: Interleukin
FDA	: Food and Drug Administration
cAMP	: Cyclic AMP
VLPO	: Ventrolateral preoptic nucleus
GABA	: Gama-aminobutyric acid
TMN	: Tuberomamillary nucleus
AVP	: Action of vasopressin
BZD	: Benzodiazepines
BzR	: Benzodiazepine receptors
CBF	: Cerebral blood flow
$CMRO_2$	: Cerebral metabolic rate
NMDA	: *N*-methyl-D-aspartate
ICP	: Intracranial pressure

CPP : Cerebral perfusion pressure

ACTH : Adrenocorticotropic hormone

ICU : Intensive care unit

MV : Minute ventilation

MVV : Maximum voluntary ventilation

VC : Vital capacity

VT : Tidal volume

RSBI : Rapid shallow breathing index

SBT : Spontaneous breathing trial

SBP : Systolic blood pressure

SIMV : Synchronized intermittent mandatory ventilation

MAP : Mean arterial blood pressure

CPOT : Critical care Pain Observation Tool

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Abstract

Background: Sedation in the intensive care unit Patients is assumed to reduce discomfort from care interventions, increase tolerance of mechanical ventilation, prevent accidental removal of instrumentation, and reduce metabolic demands during cardiovascular and respiratory instability. **Aim of the Work:** The aim of the work is to evaluate the use of dexmedetomedine as a sedative to facilitate weaning from mechanical ventilation and extubation, so decrease the incidence of reintubation, ventilator complications and decrease the ICU cost and stay. **Patients and Methods:** This was a controlled randomized prospective clinical trial carried out in Ain-Shams University Hospitals. After approval of institutional ethical committee, the study included 90 adult postoperative patients and requiring postoperative mechanical ventilation in the surgical ICU for maximum duration of 48 hours postoperatively. **Results:** As regard to time to extubation, results of the current study showed a highly statistically significant difference between three groups regarding time to extubation (hr) when p-value was < 0.001. **Conclusion:** dexmedetomidine has clinically relevant benefits compared to midazolam and propofol in facilitating extubation because of its shorter time to extubation, more hemodynamic stability, easy arousability and lack of respiratory depression; hence, it can be used as an effective, and safe sedative agent to facilitate extubation in ICUs and decreasing ICU length of stay.

Key words: dexmedetomedine, standard sedatives, mechanical ventilation, weaning

Introduction

Pain, agitation and delirium commonly occur in critically ill patients, with potential consequences that necessitate treatment with analgesic, sedative and antipsychotic medications. Over the last 15 years, considerable evidence has accumulated demonstrating that both choice of agent and how we use these drugs can significantly impact clinically relevant patient outcomes. This, in turn, has influenced recent pain, agitation and delirium guidelines ***(Barr et al., 2013).***

Patients requiring mechanical ventilation are typically having significant anxiety and pain ***(Hughes et al., 2012)***. These patients require sedation to tolerate the tracheal tube and the ventilator, to suppress cough, to prevent respiratory fighting during intensive care procedures and to prevent psychological complications associated with pain and anxiety. An ideal sedative agent should allow for rapid modification of the sedation level by titration of doses, no depressant effects on the cardiovascular or respiratory systems, cheap, have short duration without cumulative effects, and allow rapid recovery of effective spontaneous respiration after stopping the infusion ***(Devlin and Roberts, 2011).***

The pharmacologic control of analgesia and sedation is nearly a routine in everyday practice in intensive care units (ICUs) worldwide, especially in the management of symptoms of mechanically ventilated patients ***(Barr et al., 2013).***

Sedative medications are often provided for comfort in mechanically ventilated patient but have been associated with harm, including occurrence of delirium, ventilator-associated pneumonia (VAP), and prolonged mechanical ventilation ***(Jackson et al., 2010).***

The process of weaning from mechanical ventilation is central to the management of critically ill patients. It is a very complex and difficult task. Attention should be paid to wean off the ventilator as quickly as possible after the conditions that warranted placing the patient on the ventilator begin to resolve and stabilize ***(MacIntyre et al., 2001).*** Delayed or unnecessarily prolonged weaning increases length of intensive care unit (ICU) stay, health-care cost, decreases the ICU bed availability and adversely affects patient outcome ***(Kress et al., 2000)***.

Dexmedetomidine is a selective alpha-2-adrenoceptor agonist. It exerts both sedative and analgesic effects via mechanisms different from other sedatives such as midazolam and propofol, and provides sedation characterized by prompt response to stimuli with no respiratory depression ***(Hsu et al., 2004).*** Therefore does not interfere with weaning from mechanical ventilation. Because of this characteristic, infusions of dexmedetomidine can be continued after extubation without the risk of respiratory failure, a complication that can occur with propofol, lorazepam, and midazolam ***(Sessler and Varney, 2009).***

Aim of the Work

The aim of the work is to evaluate the use of dexmedetomedine as a sedative to facilitate weaning from mechanical ventilation and extubation, so decrease the incidence of reintubation, ventilator complications and decrease the ICU cost and stay.

Sedation in ICU

Multisystem adverse effects of sleep deprivation have been reported. Use of sedation is important to help achieve the right balance between sleep and wakefulness; the correct balance is essential for incorporating physical activity and patients' cooperation in the plan of care. Other goals of adequate sedation include optimizing safety for patients and caregivers, facilitating mechanical ventilation, reducing anxiety and delirium, inducing sleep, and, ultimately, providing comfort and safety ***(Murthy, 2007).***

Continuous chemical sedation in the intensive care unit (ICU) is commonly used to control respiratory rate and anxiety and thus promote sleep and ultimately optimize care ***(Pandharipande et al., 2007).***

Sedative medications are commonly prescribed within the ICU environment primarily for the treatment of agitation and anxiety, which themselves may be caused by many different conditions (eg, dyspnea, delirium, mechanical ventilation, lack of sleep, and untreated pain). The appropriate use of sedatives can facilitate patient care and contribute to patient safety; however, their use is associated with both short- and long-term negative patient outcomes, including prolonged mechanical ventilation and cognitive dysfunction. It is important, therefore, to define the indication for sedation, as this may affect the