



## Newer Medication May Offer Advantages Over Agents Often Used For Sedation In ICU

Providing sedation for patient comfort is an important part of bedside care for nearly every patient in the intensive care unit (ICU). For decades, the type of drugs known as  $\gamma$ -aminobutyric acid (GABA) receptor agonists (including propofol and benzodiazepines such as midazolam) have been the most commonly administered sedative drugs for ICU patients worldwide, according to background information in the article. Despite well-known hazards associated with prolonged use of GABA agonists, few investigations of ICU sedation have compared these agents to other drug classes. Preliminary research has indicated that dexmedetomidine, an  $\alpha_2$  agonist type of drug, may have advantages.

Richard R. Riker, M.D., of the University of Vermont College of Medicine and Maine Medical Center, Portland, Maine, and colleagues examined whether sedation using dexmedetomidine, compared with the standard GABA agonist midazolam, would result in improved outcomes for 375 critically ill ICU patients who were expected to require mechanical ventilation for more than 24 hours. The patients were randomized to receive either dexmedetomidine or midazolam until extubation (removal of the breathing tube inserted into the trachea) or 30 days. The trial was conducted in 68 centers in five countries between March 2005 and August 2007.

Targeting a light level of sedation and incorporating a daily arousal assessment for every patient, the authors found that there was no difference between the drugs in the percentage of time within the target sedation range. There was about a 23 percent difference in the rate of delirium; the prevalence of delirium was 54 percent (132/244) in dexmedetomidine-treated patients vs. 76.6 percent (93/122) in midazolam-treated patients. Despite the shorter duration of study drug treatment, the number of delirium-free days was greater for patients treated with dexmedetomidine (2.5 days vs. 1.7 days).

More patients treated with dexmedetomidine had study drug stopped because the patient was extubated (59 percent vs. 45 percent), with estimated median (midpoint) time to extubation 1.9 days shorter for dexmedetomidine-treated patients (3.7 days vs. 5.6 days).

Dexmedetomidine-treated patients were more likely to develop bradycardia (abnormally slow heartbeat; 42.2 percent vs. 18.9 percent), with a nonsignificant increase in the proportion requiring treatment, but had a lower likelihood of tachycardia (abnormally rapid heartbeat; 25.4 percent vs. 44.3 percent) or hypertension requiring treatment (18.9 percent vs. 29.5 percent).

"To our knowledge, this is the first study to show that even when the elements of best sedation practice (including daily arousal, a consistent light-to-moderate sedation level, and delirium monitoring) are used for all patients, the choice of dexmedetomidine as the foundation for patient sedation further improves these important outcomes," the authors write. "Dexmedetomidine appears to be the first drug to both reduce the development of delirium and to improve the resolution of delirium if it develops in the ICU."

"In addition to the medication administration protocol and incorporation of best sedation practices, the choice of medication used to provide sedation for ICU patients is a fundamental component of efforts to deliver safe and effective care. Although it did not increase the time within target sedation range, dexmedetomidine appears to provide several advantages for prolonged ICU sedation compared with the GABA-agonist midazolam."

Editorial: A New Era for Sedation in ICU Patients

This study provides important information regarding the sedation of critically ill patients, writes Hannah Wunsch, M.D., M.Sc., of Columbia University, New York, and John P. Kress, M.D., of the University of Chicago, in an accompanying editorial.

"The study by Riker et al failed to demonstrate that dexmedetomidine was superior to benzodiazepines for

ensuring light sedation. However, the reduced prevalence of delirium is an important secondary outcome that both highlights the problems of traditional benzodiazepines and provides encouraging data regarding the potential benefits of dexmedetomidine. With the demonstration of the safety of dexmedetomidine at higher doses and for longer periods, clinicians now have a widened choice of sedatives and should always consider not only the need for sedation but also the possible clinical implications of the choice of sedative."

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