

## PRESIDENT'S MESSAGE

### Dexmedetomidine and Hextend: Their Role in Trauma Care

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Anesthesia now seems so safe that sometimes one may wonder how to further improve our patients' perioperative care. Perhaps we fine-tune existing strategies, such as adding the volatile agent sevoflurane, which improved acceptance of inhalation induction, decreased hemodynamic perturbations, and markedly impacted care of pediatric patients. Nonetheless, this may be just a reinvention of the same old wheel. When I first began practicing anesthesiology, I often imagined characteristics of an ideal perioperative drug. Ideally it would offer an easily arousable sedation, provide pain relief while not depressing respiratory drive, and have relatively mild hemodynamic effects. At a meeting in the spring of 2000 I found out that just such a drug, dexmedetomidine, a specific  $\alpha_2$ -adrenergic agonist that induces a sleep-like state, was soon to be introduced to the United States market. I quickly envisioned the utility of dexmedetomidine and, as chief of anesthesiology at my hospital, requested that dexmedetomidine be added to the formulary as soon as possible. Initially, I was interested in its potential for bariatric surgery patients, patients at significant risk for airway obstruction, atelectasis, and hypoxemia, but quickly realized its vast potential to augmenting perioperative pain control while maintaining respiratory drive with a predictable hemodynamic effect.

Over the intervening years, I have expanded my use of dexmedetomidine to include nearly all patient categories, ranging from same-day surgery to congenital cardiac surgery patients, and of course critically ill and injured trauma patients. Unfortunately, when the Food and Drug Administration approved the use of dexmedetomidine (Precedex, Hospira Inc., Lake Forest, Illinois) in 1999, it was for the limited indication of sedation for initially intubated and mechanically ventilated adult patients in intensive care units and limited to a 24-hour infusion. This relatively narrow indication limited use of dexmedetomidine in some medical centers, while in many other facilities, its off-label utilization grew as experience and comfort with dexmedetomidine expanded and clinicians realized the utility of this new class of medications.

This issue of *TraumaCare* contains three articles by clinicians with substantial experience with and interest in the use of dexmedetomidine in a variety of clinical settings. Their reports cover not only the approved uses of this powerful and selective sedative but also the extensions of its use into scenarios in which short-term blunting of physical responses is beneficial, as is the ability to arouse the patient by verbal stimuli. The issue concludes with a

review of another innovation in trauma anesthesia practice—the use of Hextend during trauma surgery.

Opening the issue is an extensive systems-based literature review, compiled by Joseph D. Tobias, MD, from the University of Missouri. Dr. Tobias discusses the preoperative, perioperative, and postoperative scenarios in which dexmedetomidine is, could be, and is not effective. Following a brief overview of the drug's pharmacokinetics, the article continues with a comprehensive discourse on the end-organ effects and clinical applications of dexmedetomidine. Cardiovascular and hemodynamic effects are described, as are effects on the sympathetic and central nervous systems. The passage on respiratory effects includes summaries of studies of drug combinations, emphasizing the need for careful monitoring of the respiratory function of patients receiving dexmedetomidine. It should be kept in mind that the amount of narcotics typically required to achieve comfort in the setting of dexmedetomidine is generally cut in half. Thus, if this is not accounted for, one may effectively give a patient a narcotic overdose, thereby blunting the respiratory drive.

Tobias introduces interesting thoughts regarding the anticonvulsant/proconvulsant effects of dexmedetomidine in brain-injured patients and the mechanism of action for the drug's neuroprotective effect. It is clear that dexmedetomidine offers distinct advantages for the control of shivering and opioid-induced muscle rigidity, again of particular importance in the trauma patient, particularly in head-injured patients in whom some degree of hypothermia may be desired for cerebral protection.

Other issues of importance in the intensive care unit include gastrointestinal motility, adrenocortical function, and inflammatory response. Tobias provides an illuminating review of dexmedetomidine's influence on these aspects of postoperative care and how, in contrast to other commonly used sedation medications, dexmedetomidine either supports or at least does not depress anabolic activities in the critically ill.

In clinical applications, Tobias notes that dexmedetomidine has been used as a premedication, as an intraoperative infusion, by intraoperative bolus dosing, and for postoperative sedation in intubated and nonintubated patients. The drug has been used in patients undergoing gynecologic procedures, hand surgery, and craniotomy. In balanced anesthetic technique, dexmedetomidine can decrease anesthetic requirements and improve intraoperative stability. It also may find a role as part of monitored anesthesia care with a regional anesthetic technique. Its postoperative analgesic effects are well established, and it may serve as a useful adjunct to epidural analgesia or patient-controlled analgesia (PCA). In my practice with bariatric surgery patients receiving postoperative dexmedetomidine infusions, I noted, as have others, a nearly halved utilization of PCA narcotic doses over the first 24 postoperative hours.

Several studies have documented the successful use of dexmedetomidine to prevent emergence agitation and delirium following general anesthesia with sevoflurane or desflurane. In addition, dexmedetomidine seems to decrease the incidence of coughing on emergence from anesthesia.

Although dexmedetomidine is effective for sedation during nonpainful procedures such as computed tomography and radiation

therapy (especially useful for calming children undergoing such procedures), it is not sufficient, when used alone, for painful invasive procedures such as gastroduodenoscopy unless extremely high doses (between 10 and 20 times the standard sedating doses) such as those used by Ramsey to provide a general anesthesia are given to the patient, as noted in Tobias' article. Unfortunately, such large doses result in excessive and prolonged sedation, making dexmedetomidine difficult to consider using as a full general anesthetic agent in the outpatient setting.

Tobias concludes the article with sections on the best known uses of dexmedetomidine: during mechanical ventilation and for the management of withdrawal symptoms. In numerous studies, dexmedetomidine has decreased the need for narcotics (i.e., morphine); however, other investigators have found no advantage offered by dexmedetomidine over those associated with propofol. For the management of withdrawal from opioids, benzodiazepines, and alcohol, dexmedetomidine has the advantages of a relatively short half-life and titratability. Reports on the administration of dexmedetomidine to mechanically ventilated children are beginning to emerge, cautiously documenting promising results. In my clinical experience, a majority of the pediatric congenital heart surgery patients I care for receive dexmedetomidine for postoperative sedation in our cardiac intensive care unit with a safe and satisfactory sedation.

In the second article, Rafi Avitsian, MD, Mariel Manlazaz, MD, and John Doyle, MD, PhD, from the Cleveland Clinic, describe the benefits conveyed to patients and practitioners in trauma scenarios requiring awake intubation. These authors compare dexmedetomidine with other  $\alpha_2$ -receptors that have been used in clinical practice for decades. The unique features of dexmedetomidine include its shorter half-life, which allows titration as an intravenous infusion; its insignificant effect on respiratory function and gas exchange; and its ability to effect sedation yet preserve the ability to arouse the patient. This latter characteristic is particularly useful during awake intubation of patients with potential cervical instability. Patients brought to a resuscitation unit following traumatic injury, particularly injuries of the head and neck, are understandably anxious, and thus can be uncooperative with airway-management procedures. Administration of dexmedetomidine allows the physician to achieve a desired level of sedation for awake intubation and to retain the ability to arouse the patient through verbal stimulation so that neurologic status can be monitored. In my own clinical practice, I have been using dexmedetomidine for awake fiberoptic intubations since shortly after I first gained access to the medication. I find that a convenient way to facilitate these fiberoptic intubations is to initiate an infusion of 1 mcg/kg/hr of dexmedetomidine and at the same time administer a nebulized lidocaine and Pontocaine treatment to augment topicalization of the airway. In the roughly ten minutes it takes for the nebulizer treatment, the patient will typically be comfortably sedated with the dexmedetomidine and ready for their awake intubation. In the rare circumstances when the patient still appears to need a bit more sedation, I may consider small doses (0.5-1 mcg/kg) of fentanyl and/or midazolam (0.1-0.2 mg/kg), dosed in increments until an acceptable degree of sedation is obtained.

The third article on dexmedetomidine, written by Mohanad Shukry, MD, from the Oklahoma University College of Medicine, and myself, focuses on the use of this drug to mitigate the agitation and confusion that accompany withdrawal from alcohol,

dexmedetomidine is as effective as diazepam in easing withdrawal from alcohol. Extrapolation to alcohol-dependent humans awaits further study. Dexmedetomidine has proven effective in treating several withdrawal symptoms in patients addicted to cocaine, narcotics, and benzodiazepines and in intensive care unit patients who received dexmedetomidine during hospital procedures. The value of dexmedetomidine in the management of withdrawal symptoms in children and teenagers has been documented in recent case reports. We also review reports of the use of dexmedetomidine in children undergoing tonsillectomy and other surgical procedures. Although the pharmacokinetics and pharmacodynamics of dexmedetomidine are not completely understood, the drug seems to hold great promise when administered properly, under close clinical scrutiny, for the prevention and treatment of postprocedural agitation in adults and children. At this author's institution, the pharmacy now offers premixed syringes of dexmedetomidine (10 mL with 4 mcg/mL) for use as both a component in a balanced anesthetic and in preventing postanesthesia agitation and delirium. Dexmedetomidine is also used as a rescue drug in the care of these pediatric patients exhibiting such postanesthesia agitation. In both these settings, when used as bolus doses, the drug is most commonly delivered in 0.25-0.5 mcg/kg doses. When bolus doses of more than 0.5 mcg/kg are used, the initial  $\alpha_1$ -agonist effect predominates for the first 5 minutes or so after induction, causing an increase in blood pressure and a decrease in heart rate, which in some patients may be undesirable.

The fourth article reviews the intraoperative use of Hextend, a colloid delivered in a balanced salt solution, and another compound that is a relatively new component for trauma care. Hextend may be simply thought of as a hetastarch in a lactated Ringer's solution. This contrasts to the older Hespan, effectively a hetastarch in 0.9% normal saline. Hespan is accepted to induce coagulopathies when delivered to patients in volumes above 1.5-2 liters. Hextend does not appear, in vivo, to precipitate coagulopathies even in doses up to 5 liters. Based on a retrospective review, Drs. Karl Wagner, Ramachandra Avula, and Charles E. Smith, from MetroHealth Medical Center in Cleveland, compare outcomes in two groups of patients who underwent surgery during the first day after admission to a trauma center. Despite the patients in the study receiving Hextend being sicker than those receiving crystalloid infusions when assessed by injury severity scores, there was no difference in morbidity or mortality in the Hextend group. While we await a prospective, randomized, double-blind study on the use of Hextend in the perioperative care of the trauma patients, this article provides us a measure of comfort in using Hextend, in the same fashion as the SAFE (saline vs. albumin) trial established that it is not harmful to use albumin in the critically ill.

In closing, this issue of the journal offers a view of two innovations in trauma care. Dexmedetomidine is, for all practical purposes, a new class of medication, perhaps offering some ideal characteristics for use in the trauma setting: easily arousable sedation and pain control along with a predictable hemodynamic response without significant respiratory depression. Hextend offers a colloid with a balanced salt solution that appears to have no significant deleterious effects, and may perhaps offer an efficient means for volume expansion in the critically injured trauma patient. This author's hope is that the readers of this journal edition will be stimulated to further investigation themselves, and perhaps by pursuing quality research, provide answers to some of the questions elicited by these articles.