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Permalink
https://escholarship.org/uc/item/767225n8

Journal
Respiratory Care, 51(5)

ISSN
0020-1324

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Publication Date
2006-05-01

Peer reviewed
Use of Dexmedetomidine to Facilitate Extubation in Surgical Intensive-Care-Unit Patients Who Failed Previous Weaning Attempts Following Prolonged Mechanical Ventilation: A Pilot Study

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INTRODUCTION: Dexmedetomidine is a selective alpha-2 adrenergic receptor agonist that exhibits sedative, analgesic, anxiolytic, and sympatholytic effects without respiratory-drive depression. We prospectively evaluated the use of dexmedetomidine to facilitate the withdrawal of mechanical ventilation and extubation in 5 trauma/surgical intensive-care-unit patients who had failed previous weaning attempts due to agitation and hyperdynamic cardiopulmonary response. METHODS: Intravenous infusion of dexmedetomidine commenced at 0.5 or 0.7 μg/kg/h without a loading dose. Background sedation and analgesia with propofol, benzodiazepines, and opiates was discontinued or reduced as tolerated. Dexmedetomidine infusion was titrated between 0.2 and 0.7 μg/kg/h to maintain a stable cardiopulmonary response and modified Ramsay Sedation Score between 2 and 4. RESULTS: Following dexmedetomidine administration, propofol infusion was weaned and discontinued in 4 patients. In the fifth patient, benzodiazepine and opiate infusions were reduced. Ventilatory support in all patients could be weaned to continuous positive airway pressure of 5 cm H2O without agitation, hemodynamic instability, or respiratory decompensation. All patients were extubated while receiving dexmedetomidine infusion (mean dose of 0.32 ± 0.08 μg/kg/h). One patient required reintubation for upper-airway obstruction. CONCLUSION: Dexmedetomidine appears to maintain adequate sedation without hemodynamic instability or respiratory-drive depression, and thus may facilitate extubation in agitated difficult-to-wean patients; it therefore deserves further investigation toward this novel use. Key words: dexmedetomidine, ventilator weaning, extubation, sedation, agitation.
mechanical ventilation in patients who should otherwise tolerate unassisted breathing and extubation.

Dexmedetomidine hydrochloride (Precedex, Hospira, Lake Forest, Illinois) is an alpha-2 receptor agonist with both sedative and analgesic properties that reduce the sedation, anxiety, and analgesic requirements in the perioperative setting.9–12 In addition to its sedative effects, alpha-2 receptor stimulation in the central nervous system inhibits sympathetic activity13 and reduces plasma epinephrine and norepinephrine levels.14,15 Dexmedetomidine has been reported useful in attenuating hemodynamic stress secondary to hyperadrenergic over-reactivity16 and agitation associated with delirium.17 Because alpha-2 receptor stimulation does not cause respiratory depression,18,19 sedation with dexmedetomidine may facilitate the transition to unassisted breathing in agitated patients.

We evaluated the use of dexmedetomidine to facilitate the withdrawal of mechanical ventilation and extubation in 5 trauma/surgical ICU patients who failed weaning attempts due to agitation and hyperdynamic cardiopulmonary response.

Methods

Five patients in the surgical ICU were referred to the investigators by the critical care service. The study was approved by our institutional review board, and informed consent was obtained. Each patient was considered by the critical care service to be a suitable candidate for weaning from mechanical ventilation and extubation, based on the standardized institutional criteria. Each study patient had failed at least one trial of continuous positive airway pressure (CPAP), or had failed to tolerate low levels (5–10 cm H2O) of pressure support over several days because of respiratory and hemodynamic changes associated with agitation.

Dexmedetomidine infusion was started at 0.5 or 0.7 μg/kg/h. The infusion rate was calculated based on an average between the patient’s measured and predicted body weight, using a standard formula. After starting dexmedetomidine, background sedation (with lorazepam, midazolam, or propofol) and analgesia (with either fentanyl or hydromorphone) were titrated down or discontinued if possible. Dexmedetomidine dose was titrated according to the patient’s measured and predicted body weight. Dexmedetomidine dose was reduced by 28%, to 0.42 μg/kg/h.

After starting treatment with dexmedetomidine, background sedation was reduced or discontinued while analgesic levels were either reduced or maintained at the baseline level. Propofol was discontinued in all patients within 30 min. All patients tolerated a spontaneous breathing trial with CPAP and were extubated after an average of 120 ± 43 min. One patient developed upper-airway obstruction and required reintubation after 45 min. The patients received dexmedetomidine infusion for an average of 211 ± 39 min. The mean initial dose of dexmedetomidine was 0.58 ± 0.11 μg/kg/h. At 1 hour the mean dose of dexmedetomidine was reduced by 28%, to 0.42 ± 0.18 μg/kg/h. During dexmedetomidine infusion, patients would open their eyes spontaneously or with mild stimulation, and they had an average Ramsay Sedation Score of 3.4, without signs of agitation. Patients were extubated on a mean dexmedetomidine dose of 0.32 ± 0.08 μg/kg/h and continued to receive dexmedetomidine infusion for an average of 91 ± 38 min following extubation.

Heart rate, mean arterial blood pressure, respiratory rate, oxygen saturation, pH, Paco2, and Paco2 at all time points were not different. A nonsignificant, transient increase in heart rate and mean arterial blood pressure occurred within 5 min of starting the dexmedetomidine infusion, but quickly subsided. Patients 1 and 4 required a 25-μg bolus of fen-
tanyl. Patient 3 required an increase in supplemental oxygen after extubation, which resolved within several hours. Patient 4 had 2 transient episodes of bradycardia, to a heart rate of 55 beats/min, which resolved after the dexmedetomidine dose was reduced by 0.1 μg/kg/h, following each event. Patient 4 also required a one-time 2-mg bolus of haloperidol at the end of the study.

**Discussion**

In this small, uncontrolled study of trauma/surgical ICU patients, the infusion of dexmedetomidine allowed downward titration of baseline sedation and successful extubation without the cardiopulmonary instability or signs of agitation that had been noted during prior weaning attempts.

Our study differed from previous reports in 2 respects. First, we did not use a loading dose, but rather began with the infusion rate of 0.5 or 0.7 μg/kg/h. This was done to assess whether a loading dose is necessary in the presence of other sedative agents and to avoid potential hypertension, reflex bradycardia, and hypotension, which is sometimes encountered during loading-dose administration.11,12 Effective analgesic-sparing sedation with minimal hemodynamic change has been reported without a loading dose prior to dexmedetomidine infusion,9 and with dose-infusion rates of 0.2 or 0.6 μg/kg/h.20 Second, our patients differed from previous reports in that three were recovering from traumatic brain injury, which is a cause of severe agitation. To our knowledge, use of dexmedetomidine to facilitate unassisted breathing and extubation in this subgroup of patients has not been previously reported.

A limitation of this small study is that it was an unblinded, single-arm trial and therefore subject to bias. In addition, the aerosolized lidocaine given to suppress cough reflexes introduced a confounding variable, as reduced airway reflexes may be the reason the patients could tolerate weaning of sedation without agitation and consequent cardiopulmonary stress response. Furthermore, the dosing method in this study used an average between the patient’s measured and predicted body weight, which may have resulted in under-dosing, as the recommended dose range is based on measured body weight.

The sedative, analgesic, and anxiolytic-sparing effects, and sympatholytic properties of dexmedetomidine occur with minimal respiratory-drive suppression.13,18,19 These characteristics may have important clinical implications in the sedation and care of critically ill ICU patients.

**Table 1. Characteristics and Outcomes of Patients Treated With Dexmedetomidine for Failure to Tolerate Spontaneous Breathing Trial**

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age</th>
<th>Sex</th>
<th>Diagnosis</th>
<th>Weaning Started (days after intubation)</th>
<th>Weaning Days Before Dexmedetomidine Trial</th>
<th>Reasons for Failing Prior Weaning/SBT</th>
<th>Outcome of Dexmedetomidine Weaning/SBT</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>68</td>
<td>F</td>
<td>Motor vehicle accident, epidural hematoma, subdural hematoma, medical history of hypertension</td>
<td>0.5</td>
<td>4.0</td>
<td>Agitation, hypertension</td>
<td>Extubated, reintubated for upper-airway obstruction</td>
</tr>
<tr>
<td>2</td>
<td>29</td>
<td>M</td>
<td>Multiple gun-shot wounds to the abdomen</td>
<td>9.3</td>
<td>5.3</td>
<td>Agitation, hypertension, tachypnea</td>
<td>Extubated</td>
</tr>
<tr>
<td>3</td>
<td>32</td>
<td>M</td>
<td>Motor vehicle accident, diffuse axonal brain injury, pulmonary contusions</td>
<td>3.5</td>
<td>3.2</td>
<td>Agitation, hypertension, tachypnea</td>
<td>Extubated</td>
</tr>
<tr>
<td>4</td>
<td>61</td>
<td>F</td>
<td>Motor vehicle accident, subdural hematoma, acute respiratory failure, pneumonia</td>
<td>0.8</td>
<td>13.1</td>
<td>Agitation, hypertension, tachycardia, tachypnea</td>
<td>Extubated</td>
</tr>
<tr>
<td>5</td>
<td>38</td>
<td>M</td>
<td>Pancreatitis, pneumonia, ARDS</td>
<td>6.0</td>
<td>13.8</td>
<td>Agitation, hypertension, tachycardia, tachypnea</td>
<td>Extubated</td>
</tr>
</tbody>
</table>

SBT = spontaneous breathing trial
ARD S = acute respiratory distress syndrome
why our study patients could be extubated during dexmedetomidine infusion after failing previous attempts.

Current practice usually entails reducing or discontinuing sedation prior to extubation. Because of the lack of respiratory depression, use of dexmedetomidine allows continued sedation during the entire weaning process and the subsequent extubation and post-extubation period. Dexmedetomidine may inhibit the hemodynamic stress response during weaning from mechanical ventilation and may help eliminate emergence agitation when sedation is being tapered, and it therefore may help to facilitate earlier extubation in some patients.

Sedation with dexmedetomidine may also reduce or eliminate the need for continuous intravenous sedation with opiates and benzodiazepines in some patients. Continuous intravenous sedation with opiates and benzodiazepines are associated with prolonged duration of mechanical ventilation. Use of opiates and benzodiazepines is also a risk factor associated with the development of agitation and delirium. In adult ICU patients, sedative and analgesic withdrawal is also associated with prolonged stay and duration of mechanical ventilation. Dexmedetomidine has been reported to be useful in maintaining sedation and attenuating withdrawal symptoms while reducing opiate and benzodiazepine requirements without delaying weaning and extubation.

Although dexmedetomidine use for extended periods (up to 7 days) has been reported, it is approved by the Food-and-Drug-Administration only for use of < 24 hours duration in postoperative patients. Lack of addictive properties, cumulative effects, or clinical signs or symptoms of withdrawal make dexmedetomidine an attractive potential alternative to current ICU sedation regimens.

Conclusions

Infusion of dexmedetomidine without a loading dose appears to be adequate in maintaining sedation without hemodynamic instability or respiratory compromise and may facilitate weaning and extubation in trauma/surgical ICU patients who have failed previous attempts at weaning because of agitation and hyperdynamic cardiopulmonary response. Before dexmedetomidine can be recommended as a means to facilitate extubation under these circumstances, it must be tested and properly validated in prospective randomized controlled studies. Further investigation of long-term ICU sedation with dexmedetomidine is necessary to establish sedation guidelines and the safety profile of this promising new agent.

REFERENCES


