

Dexmedetomidine Facilitates the Withdrawal of Ventilatory Support in Palliative Care

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WITHDRAWAL of ventilatory support in the setting of a terminal illness presents the challenge to the physician of maintaining the comfort of the patient and optimizing sedation and analgesia for the time that the patient has remaining to be with his or her family and friends. Opiates and benzodiazepines are most commonly used for terminal palliation, but this combination of medications has the disadvantage of depressing ventilatory drive and airway reflexes to the degree that it may hasten the patient's death. This problem has been discussed in medical and legal literature invoking the medieval theological concept of the "rule of double effect" to assist physicians who are faced with the need to make the distinction between euthanasia and appropriate symptom relief in the terminally ill.^{1,2} Dexmedetomidine (Abbott Laboratories, Abbott Park, IL), with its highly selective α_2 agonism, provides physicians with another pharmacologic treatment option that addresses many of the possible sources of end-of life distress,³ with less of a problem with the double effect. We report on the care of a patient where provision of palliative care and withdrawal of ventilatory support was optimized by the use of a dexmedetomidine infusion.

Case Report

A 97-yr-old woman presented to the emergency department with an acute abdomen and peritoneal free air. Before her illness and admission, she was alert and oriented but was dependent on her daughters, with whom she lived, for assistance with all activities of daily living. She had a preoperative history of severe aortic stenosis, a remote myocardial infarction, hypertension, and glaucoma.

The patient underwent an emergency laparotomy for an anterior wall gastric ulcer that was repaired by omental patch. She remained intubated, ventilated, and sedated postoperatively because of hemodynamic instability and oliguria. Her postoperative electrocardiogram and troponin indicated a new lateral wall non-ST elevation myocardial infarction. She was evaluated by a cardiologist and was not a candidate for a revascularization procedure. Postoperative analgesia was provided with a fentanyl infusion ranging from 50 to 150 $\mu\text{g}/\text{h}$. The patient

did not follow any commands and, at the lower range of the fentanyl infusion, resisted nursing care with surprising strength.

During the next 72 h, the patient manifested cardiogenic and septic shock, a new onset of atrial fibrillation, acute renal failure, and thrombocytopenia. She failed to wean from ventilatory support because of hypercarbic respiratory failure.

The patient's predicted mortality from her multiple organ dysfunction and APACHE II scores was greater than 65%. Based on this prognosis and a discussion with her family regarding the patient's previously expressed wishes, it was decided to abandon curative treatments. An accurate assessment of the patient's neurologic status and potential ability to communicate with her family were confounded by the presence of the endotracheal tube and fentanyl infusion. To facilitate the possibility of communication between the patient and her family and the provision of care outside the intensive care unit, the critical care and palliative care physicians believed that the optimal form of withdrawal of ventilatory support would be extubation rather than a terminal wean. There were no obvious indicators that would predictably result in a distressing primary airway problem after extubation, *e.g.*, excessive airway secretions or prolonged intubation with expected laryngeal edema and stridor. Although the patient's predicted mortality was high, the care team was not certain that withdrawal of ventilatory support would lead to her immediate death.

Dexmedetomidine was chosen as the sedative and analgesic agent to facilitate extubation. A dexmedetomidine infusion was started with a 20- μg loading dose (0.5 $\mu\text{g}/\text{kg}$ with patient weight of 43 kg) over 10 min with a continuing infusion at 20 $\mu\text{g}/\text{h}$ (0.5 $\mu\text{g} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$). The fentanyl infusion (50 $\mu\text{g}/\text{h}$) was turned off at that time. The patient had required a phenylephrine infusion at a rate of 25 $\mu\text{g}/\text{min}$ to maintain a mean arterial pressure of 65 mmHg. Twenty minutes after the dexmedetomidine infusion was initiated, the phenylephrine infusion was increased to 50 $\mu\text{g}/\text{min}$. The dexmedetomidine infusion was continued for 7 h before extubation to allow the family to gather at the bedside; throughout that time, the patient seemed to be in no distress. After extubation, the patient was not verbally communicative, but assessment of respiratory rate, heart rate, and the absence of diaphoresis and agitated movement suggested no new source of distress. She did not require any airway support for obstruction. After 2 h, both infusions were discontinued, again without the appearance of any signs of distress. She was transferred from the surgical intensive care unit. In keeping with the palliative approach, analysis of arterial blood gases was not performed, but clinical examination continued to suggest no evidence of air hunger or obstructive respiratory distress. The patient died in a private room with her family in attendance 2 h after her transfer.

Discussion

All of the different methods of withdrawal of ventilatory support share the common goal of avoiding patient distress during the process. Although there are authors who strongly advocate one practice as optimal for the withdrawal of ventilatory support,⁴ the variety of presentations and symptom combinations that must be addressed in planning the withdrawal of ventilatory support suggest that a variety of plans should be considered

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by the physicians caring for these patients. The methods can be broadly considered within the categories of terminal extubation and terminal weaning. Terminal extubation entails the rapid cessation of mechanical ventilation and removal of the endotracheal tube, followed by the administration of humidified air or oxygen.⁴ Terminal weaning is a stepwise reduction of ventilatory support, leaving the artificial airway in place during the withdrawal of ventilation.⁴⁻⁷ The choice of a method should be based on the patient's level of consciousness, the volume of airway secretions, the likelihood that the patient may be able to communicate if extubation is undertaken, the degree of pulmonary compromise, and the possibility that extubation may result in primary airway distress, *i.e.*, stridor or complete obstruction. The central principle overarching these factors in the decision-making process is their impact on patient comfort. Secondary considerations include the perceptions and sensibilities of family and friends and the policies governing the provision of types of palliative support at various locations within the institution.

The mainstay for symptom relief during the withdrawal of ventilatory support is an opiate medication supplemented with a benzodiazepine. There is evidence supporting the contention that opiate-based sedation for symptom relief does not hasten the process of death,^{8,9} but this is likely due to awareness among physicians and nurses of the problem addressed by the rule of double effect. This rule specifies that an action with two possible effects, one good and one bad, is morally permitted if the action (1) is not in itself immoral; (2) is undertaken only with the intention of achieving the possible good effect, without intending the possible bad effect, even though it may be foreseen; (3) does not bring about the possible good effect by means of the possible bad effect; and (4) is undertaken for a proportionately grave reason.² The rule as applied to the use of sedatives and analgesics in palliative care is that the undesired and unintended but foreseeable effect of hastening the end of the patient's life may be tolerated when the primary intention is to provide comfort to the patient. Surveys of practice and attitudes indicate that physicians have concerns about hastening death in the setting of withdrawing life-supporting treatments,¹⁰⁻¹³ whereas surveys of critical care nurses report their impression that some physicians are reluctant to use sedation in palliative critical care for fear of hastening death.^{14,15} The opiate and benzodiazepine combination frequently results in depression of airway reflexes to the extent that the option of extubation for withdrawal of ventilatory support may seem to be less desirable because of the likelihood of immediate airway obstruction. Despite careful titration, patients are frequently somnolent or unresponsive with this combination of medications, limiting the opportunity for communication with family and friends during the time of their last contact with one another.

Dexmedetomidine has been used in the setting of sedation for intractable distress of the dying,³ but we believe that this is the first case report of its use to facilitate the withdrawal of ventilatory support in palliative care. In this case, dexmedetomidine sedation was chosen for reasons that were specific to our patient's comorbidities, in addition to its attributes that are generalizable to other patients requiring sedation for the withdrawal of ventilatory support. Specifically, in light of severe aortic stenosis and recent myocardial infarction, we wanted to avoid tachycardia during extubation; dexmedetomidine usually causes bradycardia. In general, dexmedetomidine can provide sedation, anxiolysis, and analgesia in dose ranges that do not suppress the respiratory drive and reflexes;¹⁶⁻¹⁸ our patient had previously failed to wean while on a fentanyl infusion because of hypercarbic respiratory failure. Dexmedetomidine sedation is also less likely to result in airway obstruction than an opiate and benzodiazepine technique. Although it was not manifest in our patient, the quality of sedation provided by dexmedetomidine may be an improvement over an opiate and benzodiazepine combination in that it is more likely to allow the patient to communicate and interact when aroused.^{3,19}

Dexmedetomidine does not reliably produce amnesia at the usual sedative dose, and its analgesic effect may have a ceiling;²⁰ therefore, its use as a single sedative and analgesic agent should be carefully considered in the context of the many possible sources of severe distress in palliative care patients. Its cost, which is substantially more than that of opiates and benzodiazepines, would suggest that it remain a carefully chosen adjunct in palliative care, particularly to be considered in the context of withdrawal of ventilatory support and in sedation for intractable distress of the dying.

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