

Anesthetic Management of a Pituitary Tumor Resection With Dexmedetomidine

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Dexmedetomidine (Precedex, Hospira, Lake Forest, Illinois), an alpha-2 agonist, mainly is used for sedating mechanically ventilated uncooperative patients in the intensive care setting. It also is being used by anesthesia providers for multiple purposes, including cardiothoracic surgeries, neurological surgeries, awake-fiberoptic intubations, and for patients with a high risk for airway obstruction.

This article reports the investigation of the off-label

use of dexmedetomidine as an anesthetic adjunct for a transsphenoidal pituitary tumor resection in an adult. The dexmedetomidine infusion not only provided the patient with added sedation but also decreased the need for narcotics and volatile agents while providing hemodynamic stability.

Keywords: Dexmedetomidine, neurosurgery, Precedex.

Dexmedetomidine (Precedex, Hospira, Lake Forest, Illinois) is an alpha-2 agonist. The receptors are located in the central nervous system (more specifically, the locus ceruleus and dorsal horn of the spinal cord), cerebral vessels, peripheral vasculature, and smooth muscle cells. Its sedation effect is very similar to that of clonidine, but the difference is in the receptor affinity. Clonidine has an alpha-2/alpha-1 ratio of 200:1, whereas the ratio for dexmedetomidine is 1,620:1. It acts by stimulating a negative feedback loop. It binds to the sympathetic postganglionic neurons' alpha-2 receptors presynaptically, stimulating a negative feedback loop and inhibiting the release of endogenous norepinephrine, owing to its sympatholytic effects. Dexmedetomidine also inhibits the outflow from the sympathetic nervous system by stimulating postsynaptic alpha-2 receptors located in the central nervous system.¹⁻³

Dexmedetomidine not only produces sedation but also provides respiratory and hemodynamic stability and reduces narcotic dependency and volatile agent requirements.⁴ Like any other drug, dexmedetomidine comes with limitations. Providers may notice bradycardia, xerostomia, hypotension, hypertension, fever, nausea, and vomiting.² Since its introduction in 1999, it has evolved as an anesthesia adjunct for a variety of procedures, including neurological surgery.^{5,6} This case study describes how dexmedetomidine can be used in adults undergoing transsphenoidal pituitary tumor resection.

Case Report

A 49-year-old man with a pituitary tumor underwent a resection of the tumor via the transsphenoidal approach. Preoperative signs and symptoms were headaches, dizziness, and facial bone growth secondary to acromegaly. His previous surgeries included colorectal resection of a

colon mass, colostomy takedown, and cervical discectomy, all without anesthesia complications. The patient's health history included arthritis in the lower back and both knees, type 2 diabetes mellitus (well-controlled with oral medication), obesity (body mass index of 36 kg/m²), and obstructive sleep apnea requiring continuous positive airway pressure at night. The patient's other body systems and laboratory values were unremarkable. A 12-lead electrocardiogram revealed sinus bradycardia (heart rate, 58/min). The patient was given an ASA physical status score of 2.

Before surgery, the patient received 2 mg of midazolam and 8 mg of dexamethasone. Once in the operating room, standard ASA monitors were put in place, and vital signs were taken. The patient's baseline heart rate, blood pressure, and oxygen saturation were 65/min, 120/70 mm Hg, and 97%, respectively. Just before induction, a bolus infusion of dexmedetomidine was initiated. Using a standard dexmedetomidine solution with a concentration of 4 µg/mL, a weight-based loading dose of 1 µg/kg was administered over 10 minutes. The patient weighed approximately 115 kg; therefore, 28 mL was given via intravenous infusion pump for 10 minutes.

Simultaneously, a standard induction proceeded. In a separate intravenous line, 100 µg of fentanyl, 100 mg of 2% lidocaine, 250 mg of propofol, and 50 mg of rocuronium were given. After a successful intubation using a GlideScope (Verathon Inc, Bothell, Washington) because of the increased potential for difficult airway secondary to the patient's acromegaly, the patient was mechanically ventilated with a fraction of inspired oxygen of 100%. Sevoflurane was the volatile gas of choice, and oxygen was set at 2 L/min. A bispectral index monitor was used to guide the anesthetic. Vital signs were taken every 5 minutes, and blood pressure was measured via automatic cuff. Hydrocortisone, 100 mg intravenously, was given

prophylactically for potential tumor-related decreases in cortisol secretion.

Once the bolus infusion of dexmedetomidine was given (over 10 minutes), a weight-based maintenance dose was started. It should be noted that Hospira recommends a dose range of 0.2 to 0.7 $\mu\text{g}/\text{kg}$ per hour.² However, for this patient, the highest recommended dose of 0.7 $\mu\text{g}/\text{kg}$ per hour, or 21 mL/h, was initiated for blood pressure control, keeping in mind the possibility of reflexive bradycardia and/or bradycardia due to the ability of dexmedetomidine to decrease sympathetic outflow from the central nervous system. At lower plasma concentrations, the sympatholytic effects dominate to produce a reduction of blood pressure, whereas at much higher doses, the vasoconstrictive effects dominate to produce an elevation in blood pressure.^{3,7} Vasoconstriction occurs via, oddly enough, presynaptic blockade of alpha-2 adrenergic receptors that can increase the release of norepinephrine.⁸ It should be noted that there is a wide margin of safety with dexmedetomidine.

The procedure lasted approximately 1 hour and 45 minutes. The sevoflurane end-tidal value was never higher than 1.1%, and the bispectral index monitor reading stayed in the low 30s throughout the case. The electrocardiogram revealed sinus bradycardia with a heart rate between 50 and 60/min, except at induction, when it was recorded at 65/min for the first 5 minutes. The heart rate did not increase substantially with direct laryngoscopy for 2 probable reasons: (1) The patient was well-narcotized/sedated by the synergistic effects of midazolam, fentanyl, propofol, and dexmedetomidine. (2) Dexmedetomidine has the ability to cause bradycardia, as indicated earlier. The blood pressure consistently remained stable, and systolic pressures were between 95 and 110 mm Hg. The temperature was normal throughout the case, and end-tidal carbon dioxide was maintained at a range between 29% and 38%. A single dose of 50 μg of intravenous fentanyl was given approximately 1 hour after the initial induction dose.

With the procedure coming to an end, 30 minutes before extubation, the dexmedetomidine infusion was decreased from 21 mL/h to 12 mL/h (0.4 $\mu\text{g}/\text{kg}$ per hour). A reversal dose containing 5 mg of neostigmine and 0.6 mg of glycopyrrolate and a prophylactic antiemetic dose of 4 mg of ondansetron also were given at this time. In 10 to 12 minutes, the patient began spontaneously breathing. At the end of surgery, sevoflurane was shut off, with an end-tidal sevoflurane concentration of 1.0%, and oxygen was increased to 10 L/min. The patient's heart rate remained at 48 to 50/min, and his blood pressure increased from 100/47 to 120/55 mm Hg during a 10-minute span. In 10 to 12 minutes after sevoflurane was shut down, the patient opened his eyes on command and had spontaneous tidal volumes greater than 500 mL. The patient gave an overall impression of

contentment. The endotracheal tube was removed, and the patient maintained the airway and spontaneous breathing. His heart rate and blood pressure at this time were 48/min and 120/55 mm Hg, respectively. Fluid calculations were as follows: urine output, 250 mL; estimated blood loss, 200 mL; and infused lactated Ringer's solution, 1,300 mL.

With the dexmedetomidine still continuously infusing at 0.4 $\mu\text{g}/\text{kg}$ per hour, the patient was moved to his hospital bed and transported to the postanesthesia care unit for further observation. On arrival to the unit, the patient's vital signs were as follows: blood pressure, 120/67 mm Hg; heart rate, 56/min; respiratory rate, 9/min; temperature, 97.7°F; and oxygen saturation, 96%. The patient indicated a pain score of 1 of 10. For the case, 288 μg of dexmedetomidine was given. The infusion was discontinued shortly thereafter. The drug's elimination half-life of 2 hours helped carry analgesia well into the postoperative period.^{2,9}

Discussion

Studies have reported that dexmedetomidine can have various advantageous effects. Those useful for neurosurgery are intraoperative hemodynamic stability, including during intubation and extubation, and no increase in intracranial pressure.¹⁰ If used correctly, it can allow for faster awakening and, thus, an earlier neurological examination by decreasing necessary volatile agent and opioid doses.^{7,11} Tanskanen et al⁶ studied the effects of dexmedetomidine on hemodynamic stability during intracranial tumor surgery in 54 patients. The study concluded that with dexmedetomidine, there was a decreased response to noxious stimuli, intubation, and extubation, thus yielding greater hemodynamic stability compared with placebo.⁶

Dexmedetomidine helps maintain hemodynamic stability by falsely exciting the negative feedback loop of norepinephrine by stimulating alpha-2 receptors and presynaptically decreasing the peripheral release of norepinephrine. In turn, it decreases available norepinephrine postsynaptically, which lessens possible sympathetic surges. Centrally, it stimulates alpha-2 receptors, postsynaptically causing inhibitory action on the sympathetic nervous system. As alluded to earlier, alpha-2 adrenergic stimulation presynaptically can increase the release of norepinephrine.⁸ Therefore, during the loading phase when the dexmedetomidine plasma concentration is dramatically increased, one might see hypotension, hypertension, tachycardia, and bradycardia (via sympatholytic or reflexive mechanisms).^{2,4} It is imperative—and safer—to allow the bolus to infuse via intravenous infusion pump during the allotted 10 minutes.

Previous studies have shown that dexmedetomidine can dramatically reduce end-tidal concentrations of volatile anesthetics. A study by Fragen and Fitzgerald¹²

indicated that dexmedetomidine reduces the amount of sevoflurane necessary to effectively and safely anesthetize humans by 17%.¹² Thornton et al¹³ randomly placed subjects in a control group, a low-dexmedetomidine-plasma-concentration group, or a high-dexmedetomidine-plasma-concentration group. The volunteers were given isoflurane by mask until a response to tetanic stimuli was elicited. Isoflurane end-tidal percentages were quartered and halved in the low- and high- concentration dexmedetomidine groups, respectively.¹³

The present case report shows a 50% reduction of sevoflurane from its minimum alveolar concentration value of 2.0 to 2.2. Although narcotics and paralytics were used as well, the amounts given were not remarkable. The combined synergistic effect of these drugs could not, alone, account for the 50% reduction of sevoflurane. Dexmedetomidine stimulates the locus ceruleus, inducing sleep as close to natural as possible while providing hypnosis and anxiolysis.³ It does not produce amnesia, a common misconception among anesthesia providers.

Dexmedetomidine also decreases the need for narcotics.¹¹ Stimulation of alpha-2 receptors, located in the dorsal horn of the spinal cord, inhibits the release of substance P. Therefore, it diminishes transmission of pain action potentials.¹⁴ The patient in the present case report required a minuscule dose of fentanyl (0.78 µg/kg). Furthermore, once in the postanesthesia care unit, the patient did not require immediate relief of pain. Although it has analgesic properties, dexmedetomidine does not act on receptors of the medulla oblongata or respiratory center, which would result in respiratory depression.³ Thus, a patient's airway, such as in this case, is not compromised or subject to obstruction.

It is important to reiterate the patient's history of obstructive sleep apnea, acromegaly, and body mass index of 36 kg/m². According to the National Heart, Lung, and Blood Institute, a body mass index of greater than 30 kg/m² is considered significantly obese and increases the risk of collapse of soft air tissue.¹⁵ Once in the postanesthesia care unit, the patient was alert, comfortable, and without respiratory issues and did not need continuous positive airway pressure. Tufanogullari et al⁹ studied laparoscopic bariatric surgeries using dexmedetomidine. While patients benefited from minimal opioid consumption intraoperatively and minimal respiratory depression postoperatively, the dexmedetomidine group had longer postanesthesia recovery times, possibly due to the drug's long elimination half-life.⁹ This is something to consider if an anesthesia provider is planning to use it in an outpatient or surgical center setting.

The maintenance infusion was started at the highest dose within the given drug guidelines and was not titrated until halved at the end of the procedure, simply because the patient exhibited adequate hemodynamic stability throughout the case. Currently in the United

States, dexmedetomidine has been approved by the US Food and Drug Administration for short-term sedation in the critical care setting. Off-label use has increased during the past 5 years as a result of its proven benefits and minimal side effects. However, its off-label use is not guided by the Food and Drug Administration.

Summary

The advantages of dexmedetomidine and the various anesthetic procedures it can be used for make this drug dynamic. Specifically, this neurological case demonstrates how useful it can be to anesthesia providers and patients. This patient's acromegaly raised concern for a potentially difficult airway owing to an extended intubation and an increase in noxious stimuli. The neurological procedure also required hemodynamic stability and a prompt post-procedure neurological examination. The patient also was at high risk for postoperative respiratory obstruction.

The patient received minimal narcotics and required lower amounts of volatile agents, while at the same time remained in hemodynamically stable condition. On awakening, there was little fluctuation in blood pressure and heart rate, and the patient's history of obstructive sleep apnea and need for narcotics were not factors in recovery.

Dexmedetomidine, like any drug, has pitfalls. First-tier side effects include bradycardia, hypertension, hypotension, and nausea. It should only be used when the anesthesia provider has a strong understanding of its side effects and its ability to potentiate opioids, sedatives, and anesthetics. This case report gives anesthesia providers a sense of what dexmedetomidine can do in the anesthesia arena.

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