

Technique

Dexmedetomidine in awake craniotomy: a technical note

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Abstract

Background: Resection of lesions in eloquent areas of the brain are sometimes best done with the patient awake. An awake patient provides neurological feedback as the lesion is resected. This increases the chances of a complete resection without leaving a patient neurologically devastated. Unfortunately, this procedure is not always well tolerated by the patient.

Methods: We performed a case series of awake craniotomies using a dexmedetomidine infusion.

Results: All 17 patients included in our study tolerated the procedure well with no major complications.

Conclusions: The addition of dexmedetomidine to our technique improves safety and comfort for patients undergoing awake craniotomy.

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Keywords: Awake craniotomy; Cortical mapping; Dexmedetomidine

1. Introduction

Resection of lesions in eloquent areas of the brain represents a clinical challenge for surgeons and anesthesiologists. Many of these lesions are best resected while the patient is awake. An awake patient provides instant neurological feedback as a lesion is resected. This increases the chances of a complete resection without leaving a neurologically devastated patient. Unfortunately this procedure is not always well tolerated by the patient. Lack of cooperation, pain, and airway obstruction are major impediments to awake procedures.

Sedation during awake craniotomy has traditionally been provided using a combination of opioid and droperidol (neuroleptanalgesia) [12]. More recently, propofol has proved popular and is used by several authors [8–10]. The airway is generally unsecured, but the use of an endotracheal tube [7] or laryngeal mask airway (LMA) [3,4] during the period in which testing is not required has been described. Although few major problems were reported in large-scale surveys of anesthesia for awake craniotomies [1],

concerns have been raised regarding the degree of patient cooperation, patient drowsiness, pain, and intraoperative seizures. In addition, the sedatives and narcotics used to decrease patient discomfort may impair ventilation. The ideal anesthetic for this procedure should provide anxiolysis, sedation, and pain relief without impairing ventilation.

Dexmedetomidine is a new highly selective α_2 -agonist with sedative, analgesic, and anesthetic-sparing effects [6]. It does not suppress ventilation. The primary action of α_2 -adrenoreceptor agonist is the inhibition of norepinephrine release that causes attenuation of excitation in the central nervous system. Small-dose infusion of this drug in healthy volunteers provided sedation that could be easily reversed with verbal stimulation [6]. In this report, we describe the use of dexmedetomidine in patients requiring intraoperative functional testing. We believe the addition of dexmedetomidine to our anesthetic regimen adds significantly to patient comfort and safety.

2. Materials and methods

Seventeen patients scheduled for excision of epileptogenic focus or tumor resection and requiring intraoperative cortical mapping were evaluated. Table 1 shows patients'

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Table 1
Demographic and clinical characteristics of patients

Characteristics	Mean \pm SD	Range
Age (y)	35.8 \pm 17.4	12-74
Sex (women/men)	6/11	
Weight (kg)	72 \pm 12	46-95
Length of anesthesia (min)	480.2 \pm 89.4	370-685
Awake time (min)	128.5 \pm 34.1	85-195

demographics and clinical characteristics. Only patients capable of understanding and following instructions were included. The neuropsychologist prepared these patients by practicing the neurology examination they would undergo during surgery. The surgeon and anesthesiologist reinforced this preparation. It was explained that the most painful episodes occur during the initial and final parts of the procedure. We stressed that the patient would be asleep during these phases of the operation and awake for intraoperative testing only. It was emphasized that the anesthesiologist would be at bedside throughout the procedure and would administer analgesics and sedatives as required. We feel that the preoperative preparation was crucial to success.

We used an asleep-awake-asleep technique with an LMA [2,4]. Patients were not premedicated. An intravenous line was established, and standard monitors were placed. Ondansetron (4 mg), dexamethasone (10 mg), and metoclopramide (10 mg) were given before induction of anesthesia to prevent nausea and/or vomiting. After denitrogenation with 100% O₂, anesthesia was induced with propofol and fentanyl. An LMA was placed and the patient was allowed to breathe spontaneously. Anesthesia was maintained with N₂O, O₂, and sevoflurane. In some cases, a low-dose remifentanyl infusion was added. Radial A-line, Foley catheter, and bispectral electroencephalogram index monitor were placed after induction of anesthesia. The surgeon or anesthesiologist performed a scalp block with bupivacaine (0.25%, 30 mL).

The dexmedetomidine infusion was started shortly after induction. We used approximately 50% of the loading dose recommended by the manufacturer (0.5 vs 1 μ g/kg). Reducing the loading dose likely decreases the incidence of hypotension and oversedation associated with dexmedetomidine, yet still provides adequate sedation. The dexmedetomidine package insert recommends a maintenance infusion of 0.2 to 0.7 μ g/kg per hour. We start at the low end of this range and only increase if the patient reports discomfort. Our surgeon does not pin these patients, reasoning that they will be more comfortable and cooperative without it. Advances in frameless stereotactic devices allow for patient movement and make this option possible.

General anesthesia was maintained during scalp incision, bone flap removal, and dural opening. We use the bispectral electroencephalogram index monitor to guide administration of sevoflurane with a target range of 50 to 60. When the surgeon had an adequate exposure, all anesthetics were

stopped except for dexmedetomidine. The patient emerged from anesthesia and the LMA was removed. Cortical mapping and neurology testing were performed while surgical resection took place. The dexmedetomidine infusion was titrated to patient comfort and sedation level. Narcotics were added if a patient complained of pain.

After the surgeon finished the resection, anesthesia was reinduced with propofol and the LMA reinserted. The surgical closure was done under general anesthesia with the patient once again breathing spontaneously. At the end of the surgery, all anesthetics were stopped including dexmedetomidine, allowing the patient to emerge from anesthesia.

3. Results and discussion

Table 2 lists perioperative medications used in our series. The infusion rate of dexmedetomidine during the awake portion of the procedures was 0.1 to 0.4 μ g/kg per hour. Sixteen of 17 patients required supplemental doses of fentanyl for bone flap removal and dural opening. Only 5 patients, however, were treated with fentanyl during the awake portion of the procedure. Remifentanyl was used in the last 8 patients, which allowed us to reduce the amount of fentanyl required. Elevated blood pressure (systolic arterial pressure > 130 mm Hg) was treated with labetalol (3 patients) and hydralazine (1 patient). Hypotension (systolic arterial pressure < 90) was treated with phenylephrine (2 patients) or fluid bolus (1 patient). No episodes of bradycardia or tachycardia were encountered.

Intraoperative problems are compared with the series of Archer et al [1] in Table 3. We did have 2 episodes of agitation that were managed with reassurance alone. Three patients complained of headache. This was treated either with boluses of fentanyl (25 to 50 μ g) or an increase in the remifentanyl infusion rate (0.01 μ g/kg per minute increments). Bolus fentanyl did produce oversedation on 2 occasions. One patient required naloxone 40 μ g to reverse sedation. One patient had a subclinical seizure that did not require treatment.

Overall, the surgeon was pleased with the surgical results and the anesthetic technique. In informal postoperative questioning, the patients we studied also reported a high degree of satisfaction with the anesthetic care. Our technique

Table 2
Intraoperative medications

Medications	Number of patients	Dose
Dexmedetomidine (μ g)	17	118.4 \pm 44.4 (42-210)
Fentanyl (total, μ g)	16	190.6 \pm 97.8 (75-450)
Fentanyl while awake (μ g)	5	59.0 \pm 30.1 (20-100)
Propofol (total, mg)	17	329.4 \pm 101.5 (190-520)
Midazolam (mg)	6	1.7 \pm 0.5
Remifentanyl (μ g)	8	0.68 \pm 0.67 (0.1 -2.1)
Normal Saline (mL)	17	2358 \pm 1038
Albumin 20% (mL)	3	100

Table 3
Summary of intraoperative problems (compared with the study of Archer et al)

Intraoperative problem	This study (N = 17), n (%)	Archer et al (N = 354), %
Hypertension	4 (24)	Not applicable
Hypotension	3 (18)	Not applicable
Respiratory depression	0	Not applicable
Hypoxemia	0	Not applicable
Oversedation	2 (12)	3
Agitation	2 (12)	Not applicable
Seizure	1 (6)	16
Nausea	1 (6)	8
Change to general anesthesia	0	2
Local anesthetic toxicity	0	2
“Tight” brain	0	1.4

allows the patient to be deeply anesthetized during maximal surgical stimulus, yet they are awake, comfortable, and able to respond during cortical mapping. We were able to achieve this result with no episodes of airway obstruction or hypoxemia. None of our patients required conversion to general anesthesia and only one experienced transient nausea. Intraoperative transition to the awake phase of the procedure was remarkably smooth with minimal coughing and little disorientation. Awake patients were generally calm. Part of our success was undoubtedly due to patient selection. We would not suggest this technique for morbidly obese patients, those with active gastroesophageal reflux disease, or other conditions that would preclude LMA placement.

4. Conclusion

We were able to perform anesthesia for awake craniotomies with a high degree of safety and few side effects. One of the primary concerns of an anesthesiologist is airway management, and we believe that the addition of dexmedetomidine makes airway obstruction and hypoxemia less likely. The anesthetic sparing effect of dexmedetomidine [5] allows us to use lower doses of other anesthetics. This facilitates rapid emergence and greater control of anesthetic depth. Our patients tolerated the procedure well and appeared comfortable. A similar conclusion was reached by Venn and Grounds [11], who compared sedation with dexmedetomidine and propofol in intubated patients. The dexmedetomidine patients appeared calm and cooperative and later described their intensive care unit stay as pleasant.

Our surgeon reported good operating conditions and no brain swelling. This might be related to a decreased cerebral blood flow associated with dexmedetomidine [13]. We believe that dexmedetomidine makes awake craniotomies safer and more comfortable, and perhaps, improves operating conditions.

References

[1] Archer DP, McKenna JM, Morin L. Conscious-sedation analgesia during craniotomy for intractable epilepsy: a review of 354 consecutive cases. *Can J Anaesth* 1988;35:338–44.

- [2] Ard J, Doyle W, Bekker A. Awake craniotomy with dexmedetomidine in pediatric patients. *J Neurosurg Anesth* 2003;15(3):263–6.
- [3] Audu P, Cooper H. Craniotomy performed with LMA. *J Neurosurg Anesth* 2000;12(2):112–3.
- [4] Bekker A, Kaufman B, Samir S, et al. The use of dexmedetomidine for awake craniotomy. *Anesth Analg* 2001;92:1251–3.
- [5] Fragen RJ, Fitzgerald PC. Effect of dexmedetomidine on the minimum alveolar concentration of sevoflurane in adults 55–70 years. *J Clin Anesth* 1999;11:466–70.
- [6] Hall J, Uhrich T. Sedative, amnestic, and analgesic properties of small-dose dexmedetomidine infusions. *Anesth Analg* 2000;90:699–705.
- [7] Hunke K, Van de Wiele B. Asleep-awake-asleep anesthetic technique for intraoperative language mapping. *Neurosurgery* 1998;42(6):1312–6.
- [8] Meyer F, Bates LM. Awake craniotomy for aggressive resection of primary gliomas located in eloquent brain. *Mayo Clinic Proc* 2001;76(7):677–87.
- [9] Silbergeld DL, Mueller WM, Colley PS, Ojemann GA, Lettich E. Use of propofol for awake craniotomies: technical note. *Surg Neurol* 1992;38:271–2.
- [10] Tobias J, Jimenez D. Anesthetic management during awake craniotomy in a 12-year-old boy. *Paediatr Anaesth* 1997;7:341–4.
- [11] Venn RM, Grounds RN. Comparison between dexmedetomidine and propofol for sedation in the intensive care unit: patient and clinician perspectives. *Br J Anaesth* 2001;87:684–90.
- [12] Welling E, Donegon J. Neuroleptanalgesia using alfentanil for awake craniotomy. *Anesth Analg* 1989;68:57–60.
- [13] Zornow MH, Maze M, Dyck JB, Shafer SL. Dexmedetomidine decreases cerebral blood flow velocity in humans. *J Cereb Blood Flow Metab* 1993;13:350–3.

Commentary

Dexmedetomidine is a highly specific α_2 -agonist that has recently been approved by the Food and Drug Administration for use as a sedative for intubated patients in the intensive care unit. It is to be administered as a continuous intravenous infusion for a maximum of 24 hours. In this case series, the authors use dexmedetomidine as the major sedative/hypnotic throughout the entire asleep-awake-asleep paradigm for awake resection of cerebral pathology.

This is not the first presentation of the use of dexmedetomidine as an intraoperative sedative agent. It allows patients to lie comfortably sedated in the operating room while responding readily to verbal command. However, this drug is not without problems. Although it does not depress respiration, it can produce respiratory obstruction by relaxation of the pharyngeal muscle tone. Respiration is reestablished when a slight jaw thrust is applied. The authors were successful in using an LMA to support the airway during the asleep portions of the protocol when the patients were also receiving inhalational anesthesia. Dexmedetomidine can also produce significant hypotension and bradycardia if the loading bolus is administered too quickly. Because dexmedetomidine acts primarily centrally, by reducing sympathetic tone, peripheral α_1 - and β -receptors are available for activation if needed to counteract the side effects of hypotension and bradycardia.

I am surprised that it has taken so long for dexmedetomidine to be approved by the Food and Drug Administration. I first became aware of this class of sedation in the late 1980s

to early 1990s when both dexmedetomidine and clonidine (a less pure α_2 -agonist with α_1 -agonist properties) were shown to decrease anesthesia requirements by 40% to 90% [1,3-5]. It is amazing to me that dexmedetomidine was not aggressively pursued as an anesthetic adjuvant to decrease the amount of anesthetic drugs administered for surgery, thereby decreasing their side effects. Of potential interest to neurosurgeons is the laboratory work showing dexmedetomidine to be a cerebral protectant, improving neurological outcome after incomplete ischemia in a rat model [2].

I am happy that dexmedetomidine is moving into the operating room with such good results as described in this report. I am sure that careful patient selection and preparation contributed to the excellent results the authors describe. The authors are to be congratulated for an interesting and useful report of the use of this new drug.

References

- [1] Aantaa R, Kanto J, Scheinin M, Kallio A, Scheinin H. Dexmedetomidine and alpha-2-adrenoceptor agonist, reduces anesthetic requirements for patients undergoing gynecologic surgery. *Anesthesiology* 1990; 73:230-5.
- [2] Hoffman WE, Kochs E, Werner C, Thomas C, Albrecht RP. Dexmedetomidine improves neurologic from incomplete ischemia in the rat. *Anesthesiology* 1991;75:328-32.
- [3] Savalo MK, MacIver MB, Doze VA, Kendig JJ, Maze M. The alpha-2-adrenoreceptor agonist dexmedetomidine increases the apparent potency of the volatile anesthetic isoflurane in rats in vivo and in hippocampal slice in vitro. *Brain Res* 1991;548:23-8.
- [4] Segal IS, Vickery RG, Walton JK, Doze VA, Maze M. Dexmedetomidine diminishes halothane anesthetic requirements in rats through a postsynaptic alpha-2-adrenergic receptor. *Anesthesiology* 1988;69: 818-23.
- [5] Thornton C, Lucas MA, Newton DEF, Dore JJ, Jones RM. Effects of dexmedetomidine on isoflurane requirements in healthy volunteers. 1: Pharmacodynamic and pharmacokinetic interactions. *Br J Anaesth* 1999;83:373-80.

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Outsourcing. By promoting medical services alongside tourist destinations, Thailand and Malaysia attracted more than 600,000 patients in 2003. Surgery brokers are springing up in UK and Australia to arrange private treatment in Asia for patients stuck on waiting lists. The practice is in its infancy in Canada. Patients from Calgary applaud the excellent service in India. Dr. Sunil Patel, President of the Canadian Medical Association, says that some Asian hospitals offer treatment better than that available in North America. And “doctors are starting to learn that patients suffering long waits suffer irreparable harm.” After waiting six months for hip or knee replacements, patients’ joints “stiffen like strips of leather left out in the sun,” said Dr. Michael Dunbar, a Halifax orthopedic surgeon (H. Sokoloff, *National Post*).

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