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Dexmedetomidine May Impair Cognitive Testing During Endovascular Embolization of Cerebral Arteriovenous Malformations: A Retrospective Case Report Series

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Summary

After the reported successful use of dexmedetomidine to sedate patients in the intensive care unit without respiratory depression, we began to use dexmedetomidine for interventional neuroradiologic procedures. We report on five patients who had dexmedetomidine administered for sedation during embolization of cerebral arteriovenous malformations. All patients were comfortably sedated and breathing spontaneously. However, although patients were awake and following simple commands 10 minutes after the discontinuation of the infusion of dexmedetomidine, they were nevertheless unable to undergo cognitive testing. They were still unable to undergo cognitive testing 45 minutes after the infusion was stopped. In contrast, 10 minutes after the discontinuation of the infusion of propofol, all patients were awake, alert, cooperative, and able to undergo cognitive testing without difficulty. In conclusion, on examination of five nonrandomly selected case records, we found that dexmedetomidine significantly prevented neurologic and cognitive testing.

Keywords

Dexmedetomidine; Interventional neuroradiology; Cerebral; Human

During certain types of neurosurgical and interventional neuroradiologic procedures, patients are examined using cognitive tests. When cognitive testing is required, the goals for the anesthesiologist are twofold: to achieve an adequate level of sedation and patient comfort with minimal respiratory depression during angiography and treatment, and to ensure that the patient will be awake, oriented, and cooperative during the time required to perform neuropsychologic testing. After the reported successful use of dexmedetomidine in sedating patients in the intensive care unit (1), we started to use dexmedetomidine for interventional neuroradiologic procedures such as embolization of cerebral arteriovenous malformations (AVMs) as well as for awake craniotomies. Both procedures require that patients be awakened during the procedure to perform cognitive testing. We therefore used dexmedetomidine with five patients

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having interventional neuroradiologic procedures. Although dexmedetomidine sedated patients without depressing respiration, we were unable to examine these patients using cognitive tests even after waiting for more than 45 minutes after the dexmedetomidine infusion was discontinued. The purpose of this communication is to alert others to problems associated with using dexmedetomidine when there is a need to perform cognitive testing.

METHODS

After Institutional Review Board exemption, the case records of five patients having elective superselective cerebral angiography and embolization of cerebral AVMs from January 2001 through April 2001 were retrospectively reviewed. No other criteria were used to select patients receiving dexmedetomidine. We studied the first five patients undergoing angiography and who were sedated with dexmedetomidine prior to testing with the Wada procedure and planned embolization.

These interventional neuroradiologic procedures consist of three parts: angiography, neuropsychologic testing as part of the Wada procedure, and embolization. Except for the period of neuropsychologic testing, all patients were sedated. We used the Ramsay sedation scale to establish the level of sedation achieved during the procedures (Table 1).

At our institution, we routinely perform superselective Wada testing in all patients with cerebral AVMs before embolization and/or surgery. This Wada procedure is tailored for each individual patient, based on the location of the AVM. Testing may include tests of language function (verbal fluency, comprehension, confrontational naming, repetition and reading), verbal memory, visual–spatial neglect, visual fields, speech clarity, sensation for primary sensory modalities and stereognosis, as well as limb strength, dexterity, and praxis (2). The procedure is performed as follows. During cerebral angiography, a microcatheter is navigated endovascularly into the feeding artery of the AVM. With the microcatheter in the selected artery, all sedative hypnotic medications are stopped, and the patient is awakened. Neurological and neuropsychological testing is performed to confirm baseline neurologic and cognitive functioning. Then amobarbital and lidocaine are injected into the feeding artery to mimic transiently the functional effects of the permanent therapeutic embolization of this feeder. The neurologic and neuropsychological testing is repeated within five minutes after injection, during which time the concentrations of amobarbital and lidocaine in the brain are expected to peak. The detection of any new deficits suggests that a permanent lesion in this region produced by glue embolization will result in a persistent neurologic deficit (3,4).

It is essential that patients be sedated and comfortable for angiography and embolization (Ramsay 3–5) but be awake, oriented, and cooperative during neurologic and cognitive testing (Ramsay 2) (Table 1).

None of our patients had significant past medical problems besides those associated with the cerebral AVM. No patient received preoperative medication. In the interventional neuroradiology suite, the patients were monitored with noninvasive blood pressure, a pulse oximeter, and electrocardiogram. All cases were done under monitored anesthesia care; patients were breathing spontaneously and oxygen was delivered by nasal cannula. A femoral arterial line was placed by the neuroradiologist.

Five patients were sedated with dexmedetomidine (Table 2). Two patients received loading doses of 1 μg/kg and after that, infusions of 0.2–0.6 μg/kg/h were started, and the other three patients only received infusions from 0.2 to 0.7 μg/kg/h without loading doses (Table 2). Midazolam and fentanyl were administered at the beginning of the procedure.

RESULTS

The five patients who received dexmedetomidine were 36 ± 8 years of age and weighed 79 ± 12 kg (Table 2). All patients were sedated with fentanyl (160.0 ± 82.2 μg) and midazolam (2.8 ± 1.9 mg) at the beginning of the case.

Dexmedetomidine was then administered as a loading dose in two patients, and as a continuous infusion in these and the three other patients. The patients were comfortable, sedated, and breathing spontaneously (Ramsay 3–4). The average total dose of dexmedetomidine was 0.81 ± 0.53 μg/kg. Infusions were discontinued 10 minutes before neurologic testing was first attempted. Patients were awake and following simple commands to loud verbal stimulation, but were unable to perform more complex neurologic and cognitive testing even 60 minutes after the drug was stopped. Patient 1 was given naloxone (Narcan)(0.40 μg) and flumazenil (0.12 mg) approximately 10 minutes after the dexmedetomidine infusion was stopped. However, the patient was still unable to perform neurologic and cognitive testing. No neuropsychometric test was more affected than the others. In all cases, the procedure was canceled because neither a baseline examination nor an examination after an injection of amobarbital and lidocaine was possible.

DISCUSSION

Dexmedetomidine is a potent α2-adrenoreceptor agonist with sedative, analgesic (5,6), and anesthetic-sparing effects (7). It acts presynaptically to attenuate norepinephrine release and postsynaptically to inhibit sympathetic activity and decrease blood pressure and heart rate. Sedation and anxiolysis are thought to be mediated by the activation of postsynaptic α2-adrenoreceptors in the locus ceruleus, and analgesia via agonist activation of α2-adrenoreceptors in the spinal cord (1). One property of dexmedetomidine is that it preserves respiration and allows patients to be awakened from sedation by verbal stimulation (8). This may be caused in part by the pharmacology of dexmedetomidine. Dexmedetomidine is highly protein bound (93.7%). Although it has a terminal elimination of approximately two hours, it has a rapid distribution phase with a half-life of six minutes (1). Because of some of these properties, dexmedetomidine is indicated for use in patients in intensive care unit settings (9). Most recently, the use of dexmedetomidine has extended to operating rooms for a wide variety of cases that range from vascular cases to awake procedures where cognitive testing is indicated (10).

The ability to examine patients during intraoperative procedures for awake craniotomy and invasive neuroradiologic procedures is essential to decrease morbidity. The case report by Bekker et al. is particularly relevant to ours (10). In it they report on a patient having an “awake craniotomy” for removal of a brain neoplasm. Our report concerns patients that have endovascular embolization for treatment of AVMs. Treatment options for AVMs include endovascular embolization, surgical resection, radiosurgery, and combinations of all three. Despite advances in treatment techniques, treatment-related complications are still estimated to be as high as 16%, with a 7 to 10% rate of persistent procedure-induced neurologic deficits (11–13). To reduce these treatment-related complications, a Wada procedure is performed before definitive treatment to identify regions of functionally eloquent brain tissue in close proximity to the AVM, with the intention of preserving these regions during treatment and reducing procedural morbidity (3,4). During both types of procedures, awake craniotomy and endovascular embolization for treatment of AVMs, anesthesia requires an adequately sedated and comfortable (Ramsay 3–5) patient during part of the procedure, and an awake patient who is able to follow commands and perform neuropsychologic testing as part of the cognitive testing or Wada procedure (Ramsay 2).

During the case reported by Bekker, they were also unable to wake up their patient for meaningful cognitive testing even at the lowest concentration recommended by the manufacturer (0.2 μg/kg/h) (10). They had to reduce the infused concentration by half to 0.1 μg/kg/h to perform cognitive testing. One concern of theirs was that coadministration of sevoflurane, midazolam, fentanyl, or propofol could lead to enhancement of the sedative effects of dexmedetomidine (10).

Our case series looks at the cognitive effects of dexmedetomidine in five patients having endovascular embolization of AVMs. These patients were unable to perform complex neuropsychological tests 45 minutes after discontinuation of the infusion, whereas our experience with patients sedated with propofol has been that they are easily awakened 10 minutes after discontinuation of the infusion with no impairment of cognitive testing. Dexmedetomidine was administered within the recommended dosage range of the manufacturer. Although we cannot rule out that other medications enhanced the sedative effects of dexmedetomidine, we think that there was little interaction with other sedative medications. Fentanyl and midazolam were administered at the beginning of the case in some patients, but no patient received more than 100 μg of fentanyl and 2 mg of midazolam (other than patient 1).

Our results are consistent with earlier studies performed in healthy volunteers (8), in which patients treated with dexmedetomidine were easily awakened to perform testing but their cognitive performance was impaired up to one hour after the end of the infusion. There is now evidence that dexmedetomidine affects complex cortical processing. A recent case report of the effect of dexmedetomidine on somatosensory evoked potentials in two patients having cervicooccipital fusion showed that dexmedetomidine affected the latter cortical peaks but not the earlier potentials (14). It may be that this electrophysiologic finding is the equivalent of the cognitive impairment described in this report. Nevertheless, the cause of this cognitive impairment is still uncertain. One possibility is that impairment of cognitive performance may be caused by significant concentrations of dexmedetomidine in cerebrospinal fluid (15). Dexmedetomidine enters the cerebrospinal fluid reaching 4 ± 1% of the plasma concentration (15). Surprisingly, the dexmedetomidine concentration peaked in the cerebrospinal fluid 2 to 10 minutes after the end of the infusion, and remained elevated up to 45 minutes (15).

In conclusion, dexmedetomidine has recently been added to the array of drugs used for sedating perioperative patients in the intensive care unit. However, on examination of five nonrandomly selected case records, we found that dexmedetomidine for sedation significantly prevented neurologic and cognitive testing at concentrations recommended by the manufacturer.

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References

1. Precedex: Redefining Sedation, a Clinical Monograph. Chicago: Abbott Laboratories; 2001.
2. Wada J. Intracarotid injection of sodium amytal for the lateralization of cerebral speech dominance: experimental and clinical observations. J Neurosurg 1960;17:266–82.
3. Rauch RA, Vinuela F, Dion J, et al. Preembolization functional evaluation in brain arteriovenous malformations: the ability of superselective Amytal test to predict neurologic dysfunction before embolization. AJNR Am J Neuroradiol 1992;13:309–14. [PubMed: 1595467]

4. Rauch RA, Vinuela F, Dion J, et al. Preembolization functional evaluation in brain arteriovenous malformations: the superselective Amytal test. AJNR Am J Neuroradiol 1992;13:303–8. [PubMed: 1595466]

5. Bloor BC, Ward DS, Belleville JP, Maze M. Effects of intravenous dexmedetomidine in humans. II. Hemodynamic changes. Anesthesiology 1992;77:1134–42. [PubMed: 1361311]

6. Belleville JP, Ward DS, Bloor BC, et al. Effects of intravenous dexmedetomidine in humans. I. Sedation, ventilation, and metabolic rate. Anesthesiology 1992;77:1125–33. [PubMed: 1361310]

7. Aho M, Lehtinen AM, Erkola O, et al. The effect of intravenously administered dexmedetomidine on perioperative hemodynamics and isoflurane requirements in patients undergoing abdominal hysterectomy. Anesthesiology 1991;74:997–1002. [PubMed: 1675042]

8. Hall JE, Uhrich TD, Barney JA, et al. Sedative, amnestic, and analgesic properties of small-dose dexmedetomidine infusions. Anesth Analg 2000;90:699–705. [PubMed: 10702460]

9. Venn RM, Hell J, Michael Grounds R. Respiratory effects of dexmedetomidine in the surgical patient requiring intensive care. Crit Care 2000;4:302–8. [PubMed: 11056756]

10. Bekker AY, Kaufman B, Samir H, et al. The use of dexmedetomidine infusion for awake craniotomy. Anesth Analg 2001;92:1251–3. [PubMed: 11323355]

11. Gobin YP, Laurent A, Merienne L, et al. Treatment of brain arteriovenous malformations by embolization and radiosurgery. J Neurosurg 1996;85:19–28. [PubMed: 8683274]

12. Mast H, Koennecke HC, Meisel J, et al. Therapy of cerebral arteriovenous malformations. Nervenarzt 1998;69:287–95. [PubMed: 9606678]

13. Vinuela F, Dion JE, Duckwiler G, et al. Combined endovascular embolization and surgery in the management of cerebral arteriovenous malformations: experience with 101 cases. J Neurosurg 1991;75:856–64. [PubMed: 1941114]

14. Bloom M, Beric A, Bekker A. Dexmedetomidine infusion and somatosensory evoked potentials. J Neurosurg Anesthesiol 2001;13:320–2. [PubMed: 11733664]

15. Talke P, Richardson CA, Scheinin M, et al. Postoperative pharmacokinetics and sympatholytic effects of dexmedetomidine. Anesth Analg 1997;85:1136–42. [PubMed: 9356115]

TABLE 1

Ramsay sedation scale

Score	Symptoms/signs
1	Subject anxious, agitated, or restless
2	Subject cooperative, oriented, and tranquil
3	Subject responds to commands
4	Subject asleep but with brisk response to light glabellar tap or loud auditory stimulus
5	Subject asleep, sluggish response to light glabellar tap or loud auditory stimulus
6	Subject asleep, no response

TABLE 2

Sedative administration for embolization of arteriovenous malformations

			Dexmedetomidine						
Patient No.	**Age (y)**	**Weight (kg)**	**Total dose (μg/kg)**	**Rate (μg·kg^{-1}·h^{-1})**	**Loading Dose (μg)**	**Midazolam (mg)**	**Fentanyl (μg)**	**Total time of infusion (min)**	**Total waiting time (min)**
1	33	99.8	1.34	0.2–0.7		6	300	105	70
2	46	70.8	0.1	0.2–0.5		3	100	120	60
3	38	74.8	0.76	0.2–0.6	70	1	150	120	80
4	36	77	1.03	0.2–1.0		2	150	90	60
5	25	75		0.2–0.6	75	2	100	60	75
Mean	36	79	0.81		72	2.8	160.0	97.5	69.0
SD	8	12	0.53		4	1.9	82.2	28.7	8.9

Total dose = total amount of dexmedetomidine administered as a loading dose and an infusion.

Total time of infusion (min) = time from the beginning of the dexmedetomidine infusion until we attempted to awaken the patient for cognitive testing.

Total waiting time (min) = total amount of time from the end of the dexmedetomidine infusion until the final attempt to test the patient. No patients became testable.

Midazolam and fentanyl were administered before the loading dose or infusion of dexmedetomidine. Therefore, the time between these medications and our attempt to awaken the patients was at least the total time of infusion.