

# Dexmedetomidine Does Not Increase the Incidence of Intracarotid Shunting in Patients Undergoing Awake Carotid Endarterectomy

Alex Bekker, MD, PhD\*

Mark Gold, MD\*

Raza Ahmed, MD\*

Jung Kim, MD\*

Caron Rockman, MD†

Glenn Jacobovitz, MD†

Thomas Riles, MD‡

Gene Fisch, PhD‡

Systemic administration of dexmedetomidine (DEX) decreases cerebral blood flow (CBF) via direct  $\alpha$ -2-mediated constriction of cerebral blood vessels and indirectly via its effect on the intrinsic neural pathway modulating vascular smooth muscle. Reduction in CBF without a concomitant decrease in cerebral metabolic rate has raised concerns that DEX may limit adequate cerebral oxygenation of brain tissue in patients with already compromised cerebral circulation (e.g., carotid endarterectomy [CEA]). In this study, we established the incidence of intraarterial shunting used as a sign of inadequate oxygen delivery in a consecutive series of 123 awake CEA performed in our institution using DEX as a primary sedative. Data were prospectively recorded in 151 patients who underwent CEA during the study period. Eighteen patients were sedated with midazolam and fentanyl (M/F) for medical or logistical reasons. Patients thought to be at risk of an intraoperative stroke were treated with a prophylactic intraarterial shunt. These patients, as well as those who required general anesthesia, were excluded from the final analysis. Five patients (4.3%) in the DEX group required intraarterial shunts. The incidence of shunting in patient undergoing awake CEA in our institution is 10% (historical control). No patients developed a stroke or other serious complications. It appears that the use of DEX as a primary sedative drug for CEA does not increase the incidence of intraarterial shunts.

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**W**e recently evaluated the effectiveness and safety of dexmedetomidine (DEX) for awake carotid endarterectomy (CEA) in a small randomized study (1). That study showed that patients sedated with DEX had a superior sedation profile and less postoperative hypertension than those in the control group. However, patients in the DEX group had a more frequent incidence of intraarterial shunting (19% vs 6%). Although the difference did not reach statistical significance, some authors have suggested not using DEX in patients undergoing CEA until further research establishes its safety in this patient population (2,3). The objective of this study was to establish the incidence of shunting in consecutive cases of awake CEA performed in our institution from May 2004 to January 2005 using DEX as a primary sedative.

## METHODS

The study was a prospective and observational investigation. After approval from the Institutional Board of Research Associates of the NY University Medical Center, 151 patients scheduled for CEA were included after giving written informed consent. Regional anesthesia is the preferred technique at our institution. General anesthesia (GA) was selected for patients with either a language barrier, a preference for GA, a recent stroke, or an inability to follow instructions. The operating surgeon (with input from both patient and anesthesiologist) determined which type of anesthetic to use for the individual patient before surgery.

All awake patients were evaluated for speech deficit (counting), contralateral arm strength (ability to squeeze a rubber toy), significant increase in agitation or confusion, or unresponsiveness before (to assess level of sedation) and after test clamping of the internal carotid artery. Patients who demonstrated signs of ischemia with test clamping of the internal carotid artery (aphasia, extremity weakness, loss of consciousness, confusion, or convulsion) were selectively treated with an intraarterial shunt intraoperatively. Patients thought to be at risk of an intraoperative stroke (i.e., patients with recent previous ipsilateral stroke or occlusion of the contralateral carotid artery) were treated with prophylactic intraarterial shunting. All patients who required a GA were also treated with an empirically placed intraarterial shunt.

From the Departments of \*Anesthesiology and †Surgery, New York University Medical Center, New York, New York; and ‡Department of Applied Sciences, Yeshiva University, New York, New York.

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Address correspondence and reprint requests to Alex Bekker MD, PhD, Associate Professor of Anesthesiology and Neurosurgery, Chief of Neuroanesthesia, 560 First Ave., New York, NY, 10016. Address e-mail to alex.bekker@med.nyu.edu.

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A cervical plexus block was performed in all patients who underwent an awake CEA. The deep block was performed by three injections at C2, C3, and C4 using 1.5% mepivacaine with epinephrine 1:200,000 (15 mL total), as described previously (4). A superficial block was also performed, with a total of 15 mL of the same local anesthetic. Our intention was to use DEX for sedation in all patients undergoing an awake CEA. An initial loading dose of 0.5 mcg/kg was given over 15 min followed by an infusion of 0.1 to 0.5 mcg/kg/h. The five point Observer's Assessment of Alertness/Sedation Scale was used for assessing the patient level of sedation (1 = patient does not respond to mild prodding or shaking; 2 = patient responds only after mild prodding; 3 = patient responds to name only if called repeatedly, slurring speech; 4 = patient is sleepy, but responds to name readily, follows simple commands; 5 = responds to name, normal speech). The infusion rate was titrated to maintain a sedation level of 4 as measured by the Observer's Assessment of Alertness/Sedation Scale. The anesthesiologist was free to change the DEX infusion rate and administer midazolam, fentanyl, and/or propofol during placement of the cervical block and throughout the operation. If the patient complained of pain, incremental doses of fentanyl 25–50 mcg were administered (in addition to supplemental doses of a local anesthetic by the surgeon). Inadequate sedation was treated by increasing the rate of DEX infusion and, if there was no improvement, with boluses of midazolam 0.5 mg or propofol 10–30 mg. Dex infusion was stopped at the onset of wound closure. Eighteen patients could not be sedated with DEX for medical or logistical reasons. A commonly used drug combination of midazolam, fentanyl, and/or propofol (MF group) was used instead.

All patients were monitored using invasive and noninvasive arterial blood pressure (BP), heart rate (HR), pulse oxymetry, and 5-lead electrocardiogram. BP and HR were maintained within predetermined limits. Bradycardia was defined as HR <50 bpm, tachycardia as more than 20% increase above baseline (HR during preadmission testing). Atropine or ephedrine (when bradycardia was accompanied by a decrease in BP) was used to treat bradycardia. Tachycardia was treated by administering metoprolol. Systolic BP was maintained within 30% of the preadmission baseline values before and during cross-clamping of the internal carotid artery and within 110–160 mm Hg after restoration of carotid bloodflow. Phenylephrine, ephedrine, labetalol, hydralazine, and fluid boluses (in the Postanesthesia Care Unit only) were used as needed. This approach is consistent with common clinical practice.

We reported patients' demographics, incidence of shunting, and perioperative medications. Data were managed and analyzed by SPSS software (SPSS, Chicago, IL). Descriptive data were summarized as mean, median with ranges, and standard deviations as appropriate.

**Table 1.** Patient Characteristics and Perioperative Data

	Regional anesthesia with DEX, (N = 123)
Age, yrs (mean, sd)	73.1 ± 8.7
Sex (male:female)	84:39
Duration of anesthesia (min)	190.3 ± 47.4
PACU time (min)	219.8 ± 87.2
Medical history	
Coronary artery disease, (N, %)	54 (44)
Hypertension, (N, %)	96 (78)
Diabetes, (N, %)	30 (24)

DEX = dexmedetomidine; PACU = postanesthesia care unit.

## RESULTS

One-hundred-fifty-one CEAs were performed during a 12-mo period at the NY University Medical Center. Regional anesthesia was used in 141 patients (93.4%). Table 1 shows patient characteristics and perioperative data. We could not use DEX as a primary sedative in 18 patients for medical (two patients had a second degree heart block) or logistical reasons (some anesthesiologists were not familiar with DEX at the beginning of the study). Thus 123 patients were the study population. Two of these patients required conversion from cervical block to GA. One could not tolerate clamping. GA was induced before shunting. A second patient tolerated clamping well. GA was induced after completion of the endarterectomy. Both patients were counted in the regional anesthesia group.

There was no cardiac or other morbidity related to the operation. Five patients (4.3%) in the DEX group required intraarterial shunts because they could not tolerate test cross-clamping of the internal carotid artery. More specifically, one patient reported contralateral side weakness, one patient reported nausea and "not feeling well," and three patients had slurred speech and could not follow simple commands. Their symptoms resolved with shunt placement.

Most patients required supplementation with midazolam (85%) and fentanyl (74%) (Table 2). Only 15 (12%) patients required phenylephrine or ephedrine for BP support intraoperatively. One patient required treatment with atropine.

## DISCUSSION

Our data show that the use of DEX as a primary sedative does not increase the incidence of intraarterial shunts in patients undergoing an awake CEA (4.3%) as compared with historical control. A review of 3382 CEAs performed under regional anesthesia in our institution from 1962 to 1994 reported a 10% frequency of shunting for inadequate cerebral perfusion during test clamping of the internal carotid artery (5). Other investigators reported similar rates of shunting [5% (6), 8.6% (7), 12.4% (8)].

**Table 2.** Perioperative Drug Requirement

Drug	Intraoperative requirements		Postoperative requirements	
	Patients treated (#, %) N = 123	Dose administered, median (range)	Patients treated (#, %) N = 123	Dose administered, median (range)
Fentanyl (mcg)	91 (74)	75 (25–225)		
Midazolam (mg)	104 (85)	1.5 (1–4)		
Propofol (mg)	1 (1)	70		
Fluid bolus (mL)	n/a	n/a	11 (9)	250 (250–500)
Phenylephrine (mcg)	10 (8)	250 (50–1200)	16 (13)	100 (50–600)
Ephedrine (mg)	5 (4)	7.5 (5–50)	0 (0)	
Labetalol (mg)	29 (23)	20 (5–50)	16 (13)	10 (5–40)
Hydralazine (mg)	21 (17)	7.5 (5–25)	26 (21)	10 (5–20)
Nitroglycerine (mcg)	2 (1)	50 (25–100)	3 (2)	100 (50–200)
Metoprolol (mg)	7 (6)	5 (2–10)	7 (6)	5 (1–5)
Atropine (mg)	1 (1)	0.2	0 (0)	
DEX (mcg)	123 (100)	74 (28–158)	n/a	

DEX = dexmedetomidine; n/a = not available.

The conclusion of the study contradicts results of our previous smaller investigation, which suggested that sedation with DEX may lead to an increased number of shunts (6% in the control group vs 19% in the DEX group,  $P = 0.16$ ). The objective of that controlled randomized study was to evaluate the efficacy (an ability to achieve and maintain the desired sedation level), hemodynamic stability, and the side effects of DEX-based sedation in patients undergoing CEA. That study was not powered to detect a difference in the incidence of a particular complication. In the correspondence that followed, we pointed out that sample size was inadequate to make far-reaching conclusions (9). A small sample size, a low incidence of the event, as well as random sampling error led to the erroneous suggestion.

DEX increases cerebral vascular resistance via  $\alpha$ -2 mediated vascular smooth muscle constriction (direct effect) as well as via stimulation of intrinsic neural pathways innervating cerebral vasculature (indirect effect) (10,11). Measurements of regional and global CBF using transcranial Doppler ultrasonography and positron emission tomography in healthy volunteers demonstrated that DEX reduces CBF by approximately 30% at a clinically relevant concentration with the preservation of CO<sub>2</sub> reactivity and cerebral autoregulation (12,13). Several authors have raised concerns that DEX may reduce CBF without decreasing cerebral metabolic rate for oxygen (CMRO<sub>2</sub>), potentially limiting adequate cerebral oxygenation of brain tissue at risk for ischemic injury (13,14). Despite the large reduction in CBF with an unaltered CMRO<sub>2</sub>, there was no evidence of global cerebral ischemia in dogs (15). The CMRO<sub>2</sub> effect of DEX administration has not been investigated in humans.

The incidence of intraarterial shunting, which is similar to our historical controls and the published literature, suggests that there is no gross clinical consequence of CBF reduction associated with DEX; however, we can not exclude that DEX administration may lead to an

exacerbation of cognitive impairment associated with CEA (16). We did not perform tests of cognitive function postoperatively because the current study was not designed to address these concerns. Hence, the significance of the cerebral vasoconstriction in patients treated with DEX should be further investigated.

Perioperative hemodynamic instability is common in patients undergoing CEA. Both hypertension and hypotension may increase a risk of complications (8). A recent randomized study of 56 patients demonstrated that DEX is associated with less intraoperative and postoperative hypertension when compared with midazolam/fentanyl sedation (17). There were no significant differences in the numbers of patients requiring intraoperative treatment for hypotension (DEX 52% vs 31% M/F group). We reported similar findings (DEX 29% vs M/F 16%) (1). Twelve percent of patients required treatment for hypotension in the current study. The difference is probably explained by the more rigid hemodynamic management in the setting of a controlled randomized study. One patient only required treatment with atropine for bradycardia. Hence, we believe that hypotension and bradycardia associated with DEX are clinically inconsequential, because vasoactive drugs are often used during CEA.

We conclude that DEX provides a sedation profile that does not impede neurological evaluation or cause hemodynamic instability. Contrary to our previous results in a smaller study, the use of DEX as a primary sedative drug for CEA does not increase the incidence of intraarterial shunting.

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