Dexmedetomidine Effects on Brain Tissue Oxygenation Measured by Frequency Domain Near Infrared Spectroscopy

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Citation

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Abstract

Dexmedetomidine (DEX) is a selective alpha2-adrenergic agonist that produces cerebral vasoconstriction. We used frequency domain near infrared spectroscopy (FD-NIRS) to study brain oxygenation during DEX intravenous bolus injection. Oxyhemoglobin (OHb), deoxyhemoglobin (HHb), brain oxygen saturation (SO2) and total hemoglobin (tHb) were acquired on the frontal right and left side in 4 neurosurgery patients without cerebral pathology. Measurements were performed using a portable brain oxymeter, Oxiplex TS (ISS, Champaign, IL). Dexmedetomidine 0.2 mcg/kg was given to attenuate hypertension during the initial stages of desflurane anesthesia. During DEX administration, regional cerebral OHb decreased from 17.7 ± 6.9 Mol/L to 16.1 ± 6.3 Mol/L ($p < 0.05$) and SO2 from 61 ± 12 % to 58 ± 12 % ($p < 0.05$). HHb did not change from 10.5 ± 2.8 Mol to 10.5 ± 2.7 Mol/L. Recovery of brain oxygenation to pre-DEX levels occurred within 5 minutes. After administration of DEX, a small but consistent decrease in OHb was observed, probably mediated by a local vasoconstrictor effect. Brain oxygenation decreased transiently with DEX treatment without an increase in HHb production.

INTRODUCTION

Dexmedetomidine (DEX) is a selective alpha$_2$-adrenergic agonist with sedative and analgesic effects [1,2]. DEX enhances anesthesia produced by other anesthetic drugs and decreases blood pressure by stimulating central alpha2 and imidazoline receptors [3,4]. The use of DEX in neuroanesthesia generate a reduction in the sympathetic tone and a decrease in peripheral noradrenaline release reducing hypertensive responses to neurosurgical patient stimulation during catheterization and head pin holder application. However, initially direct activation of cerebral $_{2b}$ receptors produces local vasoconstriction effect that leads to a transient increase in arterial blood pressure and a decrease in cerebral blood flow [5,6].

A common problem during neurosurgical procedures is the interference of anesthetic drug during intraoperative action potential recording. DEX has been used as an elective anesthetic drug in awake craniotomy during resection of brain lesions in eloquent areas in order to decrease anesthetic use without attenuating neuronal function [7]. Procedures performed with intraoperative feedback from the patient reduced the morbidity associated with surgical treatment of critical brain areas. A rapid restoration in the level of consciousness in the postoperative period without respiratory depression and significant cognitive impairment has popularized the use of this drug in intensive care units [2].

In previous studies, a neuroprotective mechanism has been described with the use of DEX [8], that may be related to a reduction in the release of catecholamine during cerebral hypoxic-ischemia [9]. However, this may conflict with other reports that DEX produces direct cerebral vasoconstriction and may decrease brain oxygen delivery[10].

Quantitative brain tissue oxygenation monitoring has been established in animals using frequency domain near infrared spectrometry method (FD-NIRS) [11], and more recently in clinical studies [12]. As opposed to continuous wave methods of brain tissue oxygenation monitoring, FD-NIRS utilizes spatially resolved frequency domain information to measure absolute absorption and scattering of near infra-red light and calculate absolute concentrations of oxyhemoglobin (OHb) and deoxyhemoglobin (HHb) in brain tissue.

The purpose of this investigation was to determine if brain oxygenation decreased during the initial period of DEX

bolus treatment in relation to cerebral vasoconstriction.

METHODS

Clinical protocol: Four patients who underwent neurosurgery were enrolled on this initial study. Surgeries included spinal cord or peripheral nerve procedures. Institutional review approval from the University of Illinois at Chicago was obtained for this study. Written informed consent was obtained from all subjects prior to participation in this study. Subjects ranged in age from 29 to 59 years.

Two probes were placed on the right and left side of forehead at one centimeter above the eyebrows and 2 centimeters from the midline. This position avoided false readings related to the frontal sinus. The patients were initially spontaneously breathing room air and subsequently supported by mask of O2 at 100%. Anesthesia was induced with 1 mcg/kg fentanyl and 2 mg/kg propofol, and after intubation was maintained with 4% end-tidal desflurane in a 30% oxygen 70% nitrogen gas mixture. After 5 minutes of desflurane anesthesia, if intraoperative hypertension was present (mean pressure > 100 mmHg), DEX 0.2 mcg/kg was given as a bolus over 2 minutes. Regional brain tissue oxygenation was recorded every 2 seconds from the awake state until 20 minutes after DEX treatment.

Instrumentation: The Oxiplex TS (ISS Inc., Champaign, IL) is a FD-NIRS oximeter with multidistance light sources to monitor OHb, HHb, brain oxygen saturation (SbO2) and total hemoglobin (tHb) concentrations. The light sources used in the Oxiplex are modulated at a frequency of 110 MHz. The detected light source intensity has 3 elements, a constant (DC) component, a alternating (AC) component, and a phase component[$_{11}$]. The oximeter determines the absorption coefficient and the scattering coefficient of the tissue by measuring how the AC, DC, and phase change as a function of distance between the light source and the sensor.

We employed optical probes inserted in soft and flexible polyurethane. Each laser diode of the oximeter was coupled to an optical fiber (400 m in a core diameter) that provided light to the tissue. Each fiber emitted light at wavelengths 690 or 830 nm. The four source-detector distances of the probe ranged from 1.98 to 4.08 cm. The optical probes were calibrated using a phantom of known optical properties comparable to the optical properties of the brain tissue prior to measurements on the subject. The probes were placed bilaterally on the forehead 2 cm above the eyebrow and 1 cm lateral from the midline and was shielded from outside light and data were collected every 2 seconds.

Other data, including Response Entropy of the electroencephalogram, and end-tidal desflurane concentration were collected by computer from a Datex-Ohmeda anesthetic monitor (General Electric, Madison, WI) every 10 seconds. Non-invasive mean blood pressure was measured every 2 minutes.

Statistical analysis: The data, including OHb, HHb, SO2, and tHb were collected by the near infrared brain oxymeter using a software package provided with the instrument. The records were transferred for statistical analysis and plotted (Sigmastat, Sigmaplot). Bilateral measurements were averaged for each measurement and these data were analyzed. Repeated measures analysis of variance compared changes at one and five minutes after DEX compared to baseline anesthetized and post-hoc Tukey tests were used to compare changes with a $p < 0.05$ chosen for statistical significance.

RESULTS

The average age of the patients was 38 + 13 years. An example of the change in OHb and HHb with DEX injection is shown in figure 1. OHb decreased transiently after DEX with no change in HHb. Baseline bilateral frontal measurements of the four subjects showed similar changes as the example (Table 1).

Figure 1

Figure 1: Effects of Dexmetomidine on oxyhemoglobin (OHb, uMol/L) and deoxyhemoglobin (HHb), uMol/L) in a patient anesthetized with desflurane. The arrow indicates the start of dexmedetomidine bolus injection.

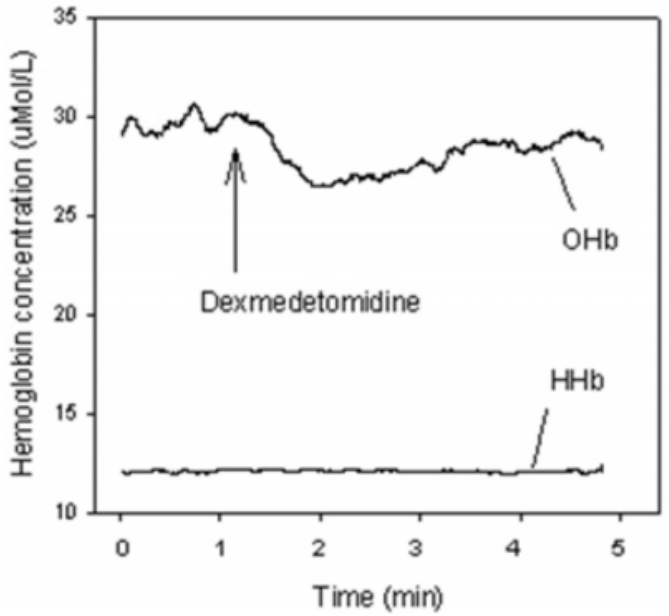

Figure 2

Table 1: Brain oxyhemoglobin (OHb), deoxyhemoglobin (HHb), total hemoglobin (tHb) and oxygen saturation (SO2) during dexmedetomidine (DEX) treatment.

Treatment	n	OHb (uMol/L)	HHb (uMol/L)	tHb (uMol/L)	SO2 (%)
Baseline	4	17.7 ± 6.0	10.5 ± 2.6	28.3 ± 5.1	61.1 ± 12.3
DEX (1 min)	4	16.1 ± 5.7*	10.5 ± 2.4	26.6 ± 4.9*	58.8 ± 12.5*
Change		-1.6 + 0.3*	0.0 + 0.2	-1.7 + 0.3*	-2.3 + 0.4
DEX (5 min)	4	17.3 ± 5.8	10.5 ± 2.3	27.8 ± 5.4	60.8 ± 11.0
Change		-0.4 + 0.8	0.0 + 0.3	-0.4 + 0.7	-0.3 + 1.4

Mean + SD, * = P < 0.05 compared to baseline
Baseline measures during Desflurane anesthesia

The change in brain oxygenation compared to baseline is presented under the absolute values for DEX 1 and 5 minutes.

After injection of DEX, there was an increase in the mean arterial blood pressure from 115 14 mmHg to 124 13 mmHg at two minutes that decreased to 112 + 17 mmHg at 6 minutes after DEX. Heart rate decreased from 86 13 beats per minute (bpm) to 78 10 bpm at 2 minutes and 81 + 11 bpm at 6 minutes after DEX injection

DISCUSSION

The focus of this study was a preliminary examination of the absolute regional brain tissue oxygenation changes produced by intravenous DEX using real time, non-invasive FD-NIRS. This methodology has been introduced in the neuroscience field, allowing a quantification of hemoglobin fractions in the brain[11,13]. The results show that DEX produced a short term decrease in OHb in brain without a change in HHb. These results are consistent with previous reports that DEX produced direct cerebral vasoconstriction without a change in oxygen consumption[10]. The specific decrease in OHb is an indication of arterial constriction, while the lack of change in HHb confirms that oxygen consumption is stable.

We assume that the effects of DEX on brain OHb is an indication of direct cerebral vasoconstriction [14,15,16]. Direct effects of -adrenoreceptors on brain pial vessel vessels have been studied after the injection of DEX[17]. After the infusion of the DEX, more intense vasoconstriction was noted in cerebral arterioles than observed with epinephrine. Decreased OHb concentrations were probably related to the reduction of the arteriolar compartment due to arteriolar vasoconstriction. However, these changes are transient, lasting approximately 4-5 minutes. These changes were consistent with the short term increase in blood pressure produced by DEX. This suggests that direct arterial vasoconstriction decreased OHb and produced peripheral hypertension at the same.

It is interesting to note that HHb was stable after DEX. This may indicate that brain oxygen delivery is adequate to supply demand. HHb may increase if oxygen delivery is inadequate. McPherson et al [16] indicated that DEX inhibits oxygen delivery during hypoxia and decreased cerebral oxygen consumption. If we assume that HHb is an indicator of oxygen utilization, our results indicate that oxygen consumption was stable even though OHb decreased. This is consistent with Zornow et al[10] that DEX decreased cerebral blood flow but did not change brain oxygen consumption. We conclude that even though DEX may decrease OHb by direct brain arterial constriction, this does not inhibit oxygen utilization and HHb production in normal brain.

Total Hb can be assumed to be closely related with the regional cerebral blood volume [18]. In our study, a transitory decrement in tHb fraction was observed after the bolus injection. This effect was observed for less than 5 minutes.

Our data suggest that vasoconstriction occurred primarily in brain arteries. Because HHb did not change, it is unlikely venous constriction occurred. These results suggest that decreased OHb but not HHb during DEX indicate arterial vasoconstriction. This specific action of DEX could be of value to evaluate cerebral hemodynamics in patients with cerebrovascular disease.

It is a weakness of this study that only 4 patients were evaluated. The purpose of this preliminary evaluation was to determine if DEX had an effect on brain oxygenation that could be measured by FD-NIRS and was consistent with reports that it produces cerebral vasoconstriction [14]. The results indicate that DEX produced a small but significant decrease in OHb bilaterally in the 4 patients measured. Although the results were not clinically significant, they are consistent with previous reports that DEX has a central cerebrovascular action[10,16]. Prospective clinical studies should evaluate whether these effects are magnified in patients with cerebral pathology.

In conclusion: This preliminary work shows that non-invasive evaluation of DEX effects in human brain tissue can show consistent and specific short term decreases in OHb. This is likely due to direct cerebral arterial vasoconstriction with DEX. In contrast, HHb did not change probably due to the fact that oxygen consumption did not change. Future studies in patients with brain pathology may be considered in order to understand how cerebral hemodynamics may change during DEX treatment.

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