Dexmedetomidine Infusion Decreases Cerebral Blood Flow in Humans

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Introduction: DEX is a potent, selective ∀$_2$-agonist with sedative, anxiolytic, and analgesic properties that produces minimal respiratory depression. Activation of ∀$_2$-adrenergic receptors on both large and small cerebral vessels, causes direct cerebral vasoconstriction in anesthetized animals, and the degree of vasoconstriction varies with different anesthetics.[1] DEX is being used as a sedative in the intensive care unit; however, no studies have evaluated the effects of DEX on CBF in conscious humans. We hypothesized that therapeutic doses of DEX would decrease cerebral blood flow (CBF) in normal volunteers.

Methods: After IRB approval, 7 supine human subjects underwent radial artery catheterization, cardiac output (CO) measurement via bioimpedance (Sorba, CIC-1000), and CBF via positron emission tomography (PET). After $H_2{}^{15}O$ injections, timed arterial samples were collected during a dynamic PET scan, and used to calculate CBF (mL/100 gm/min) from 14 predetermined brain regions. Global CBF was calculated as the mean of the 14 regional CBFs, and cortical CBF was the mean of 8 cortical regions. Determinations were made at baseline, after DEX loading dose (1Φg/kg over 20 min); 30 min after a low-dose infusion (0.2 Φg/kg/min x 30 min); and 45 min after DEX was increased to 0.6 Φg/kg/min (HIGH DEX). Data are mean∀SEM, with P#0.05 = significant (*), compared to baseline. Data were analyzed by repeated ANOVA, and SNK post-hoc tests.

Results: Three males and 1 female, age 24-43, weighing 77∀3 kg, completed the study (2 males and 1 female were deleted due to technical problems). All patients were sedated but easily arousable by voice at both doses. One subject required 0.4 mg atropine for bradycardia (35 bpm) after the loading dose of DEX. No other adverse effects were noted. DEX decreased HR at both LOW and HIGH doses, with variable effects on CO and MAP. (See Table.)

Parameter	Baseline	20-min Load	Low DEX	High DEX
CO (L/min)	6.8∀0.6	5.9∀0.9	5.9∀0.7	5.4∀0.8*
MAP	92∀3	94∀3	80∀4*	85∀5
HR	75∀4	63∀3*	67∀4*	64∀4*
CBF (Global) ml/100 gm/min	89∀13	N/A	66∀3*	59∀4*
CBF (Cortical) mL/100 mg/min	95∀14	N/A	73∀3	64∀3*

Carbon dioxide tension increased at HIGH dose DEX (39.3-44.0 mmHg, P=0.03). DEX significantly decreased global CBF at both LOW (by 27%) and HIGH (by 34%) doses, and decreased cortical CBF at the HIGH dose by 33%.

Discussion: DEX significantly decreases global and cortical CBF in humans despite a small, but significant increase in carbon dioxide tension. The reduction in CBF could be due to direct ∀$_2$ cerebral vasoconstriction, or DEX-induced reduction in cerebral metabolic rate. Additional studies are underway to confirm these findings, and future studies are needed to determine the mechanisms causing the reduction in CBF in humans.

References:
[1] Anesth Analg 1994;79:892-8.

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