Title: SEDATIVE AND HEMODYNAMIC EFFECTS OF DEXMEDETOMIDINE IN HUMANS

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Dexmedetomidine (DEX) is a highly selective centrally acting α_2-adrenergic agonist which has anesthetic sparing qualities in man and animals. Alpha$_2$-adrenergic agonists have 2 predominant hemodynamic effects: 1) a transient peripherally mediated vasoconstriction resulting in increased blood pressure and 2) a centrally mediated decreased sympathetic tone and increased vagal tone resulting in reduced mean blood pressure (BP) and heart rate (HR). This IRB approved study evaluated the effects of 4 doses of DEX in 37 consenting healthy male volunteers on sedation, BP, and HR in a double-blind placebo controlled study. While being monitored with an arterial catheter and ECG, each subject received either a placebo, 0.25, 0.5, 1.0 or 2.0 μg/kg DEX intravenously over 2 minutes. Sedation was measured by a visual analog scale.

Figure A: Sedation was dose related, and shortly after the infusion of higher doses some subjects were briefly unarousable by vocal commands or shaking. Sedation scores were significantly increased for 55 and 190 min after the lowest and highest doses respectively.

Figure B: By 30 min BP for all doses was below control (central effects on sympathetic tone). The maximum decrease in BP for the 0.25, 0.5, 1.0 and the 2.0 DEX doses were 12, 16, 24, and 26 mmHg respectively. BP remained lower than the placebo control for 60, 105, 240, and 360 min in the low to high dose groups respectively.

Figure C: The maximal increase in BP and reduction in HR (although not shown in fig B) occurred transiently during the drug infusion. HR decreased 20, 16, 28 and 26% in the low to high dose groups respectively. Except 2.0 μg/kg the drug-induced elevated BP returned to control by 4 min (transient peripheral vasoconstriction).

All doses of DEX were well tolerated. Sedation at the higher doses was marked. Transient peripherally mediated increased BP was dose related and could likely be reduced by a slower infusion. Maximal reductions in BP and HR (centrally mediated effects) were not dose related indicating a plateau.