TITLE: VENTILATORY EFFECTS OF DEXMEDETOMIDINE IN HUMANS

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Introduction. Dexmedetomidine (DEX), a centrally acting α₂ adrenergic agonist, produces complete or nearly complete anesthesia in animals (1). Thus, it is potentially a new anesthetic agent in humans.

Methods. We studied the ventilatory effects of placebo and 0.25, 0.5, 1.0, and 2.0 μg·kg⁻¹·h⁻¹ of DEX infused over two minutes in 37 normal male subjects (consented and IRB approved). Prior to the infusion, two control CO₂ ventilatory response curves were determined while the subjects were breathing 60% O₂. The CO₂ challenge was repeated every 45 minutes starting approximately 10 minutes after the infusion. The slope and intercepts were determined by linear regression on the ventilation and P₄CO₂ breath-by-breath data. Room air arterial blood gases were obtained prior to each CO₂ challenge. Ventilation, P₄CO₂, and P₅CO₂ were measured continually during and immediately after DEX infusion and during normoxia just prior to each CO₂ challenge.

Results. DEX caused marked sedation in all subjects. No adverse reactions occurred. By four hours after the infusion, all subjects were fully awake and alert. Compared to the average of the two control periods, the peak ventilatory depression was seen on the second and third measurements after DEX. The maximum decrease in ventilation was 2.44 ± 1.33 l·min⁻¹ (mean ± s.d.) in the 2.0 μg·kg⁻¹·h⁻¹ group by a reduction in tidal volume with little change in respiratory frequency. The P₄CO₂ increased by 1.3 ± 1.2, 1.4 ± 0.9, 5.0 ± 4.7, and 6.5 ± 3.9 mmHg for the four increasing DEX doses (placebo showed an increase of 0.61 ± 2.4 mmHg). The increases for the two highest doses were significantly different from placebo. Figure 1 gives the results for the arterial P₄CO₂ and the P₅CO₂ response slopes and intercepts at the 2.0 μg·kg⁻¹·h⁻¹ dose for all time periods.

There was a right shift and depression of the hypercapnic response. The hyperventilation slowly returned to normal and by the last two tests (4.5 and 8.25 hours after the infusion) there was no significant difference from the control experiments.

Discussion. DEX is a potent new α₂ adrenergic agonist, more specific and selective than either the antihypertensive agent clonidine or the animal anesthetic xylazine. We did not study DEX’s analgesic properties in these experiments; however, all subjects showed a marked decrease in sedation. The amount of respiratory depression was quite small considering the amount of sedation. Since there did not seem to be any significant difference in the degree of ventilatory depression between the two highest drug doses, this may indicate a ceiling effect. This lack of major ventilatory depression from DEX may make it useful as a perioperative anesthetic adjuvant. 1. Anesthesiology 90:818-823, 1988.

Figure 1: Mean (± s.e.m.) of the ventilation at a P₄CO₂ of 55 mmHg, the slope of the CO₂ response and the P₅CO₂ for the 10 subjects receiving 2.0 μg·kg⁻¹·h⁻¹ DEX. Two control runs (C) were made 45 minutes apart; DEX was infused at 1, and the subsequent measurements were made at 30-minute intervals. * p < 0.05 different from the two control runs by ANOVA and Duncan’s range test.