

**Title: Esmolol reduces halothane MAC in rats**

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**Introduction:** Esmolol is a short-acting cardio-selective ( $B_1$ ) beta blocking agent which is finding increasing use in the control of intra-operative hypertension and tachycardia. Studies of its use to ameliorate the stress response to electroconvulsive therapy have suggested that it may reduce the length of seizures produced (1). One mechanism for this might be that esmolol acts as a general anesthetic. We measured the MAC of halothane in rats before, during and after infusion of esmolol.

**Methods:** After institutional Animal Care Committee approval, six female Sprague-Dawley rats were studied. Rats were anesthetized with 4% halothane (H), then intubated and ventilated with 0.5-2.0% H in 100% O<sub>2</sub>. Endtidal CO<sub>2</sub> was maintained at 30-35mm Hg. Inspired and end-tidal gases were measured with an Ohmeda 6000 MGM mass spectrometer. Left carotid artery and internal jugular vein were cannulated for pressure measurement and infusion of study drugs, respectively. MAC for H was determined for each rat by the step-up, step-down method in response to standardized tail clamping (2). Fifteen min of steady end-tidal measurements were made between steps. Esmolol was then infused at the rate of 500  $\mu\text{g}/\text{kg}/\text{min}$  for 30 min and MAC was measured again. Finally, esmolol was discontinued for 30 min and MAC was measured a third time. Data were

analyzed by Wilcoxon signed-ranks matched pairs test with  $P < 0.05$  considered significant.

**Results:** Although this is a larger dose than is usually given to humans, administration of 500  $\mu\text{g}/\text{kg}/\text{min}$  resulted in no significant change in mean arterial pressure and a decrease of approximately 15 percent in heart rate in the rats studied (Table I). MAC for the rats used in this study was  $0.82 \pm 0.09$  percent (mean  $\pm$  S.E.) Five of six rats showed a reduction in MAC following esmolol administration (MAC =  $0.73 \pm 0.09$  percent, Table I,  $P < 0.05$ ) which was reversed by discontinuation of esmolol (Table I, ns from control).

**Discussion:** Centrally acting alpha agonists have been shown to have anesthetic properties (3), but beta blockers have not been thought to affect anesthetic requirement and esmolol is not thought to act centrally. Esmolol in a dose of 500  $\mu\text{g}/\text{kg}/\text{min}$  reliably decreased halothane MAC by 10-15% in this model, suggesting that it does in fact have anesthetic properties. Whether this is a direct central effect or an indirect effect, perhaps due to lowering of circulating catecholamines remains to be determined.

**References:** 1) Partridge BL, Weinger MB, *Anesth Analg* 60:301, 1990; 2) White PF et al., *Anesthesiology* 40:52, 1974. 3) Bloor BC, Flacke WE, *Anesth Analg* 61: 741, 1982.

TABLE I: Halothane MAC in rats (\* =  $P < 0.05$ )

	MAC	MAP	HR
Before	$0.82 \pm 0.09$	$123 \pm 4$	$386 \pm 18$
Esmolol	$0.73 \pm 0.09^*$	$120 \pm 5$	$325 \pm 20^*$
After	$0.79 \pm 0.09$	$126 \pm 8$	$375 \pm 24$

**A334**

**TITLE:**  $\alpha_2$ -AGONIST, DEXMEDETOMIDINE AS ANALGESIC AFTER LAPAROSCOPIC TUBAL LIGATION

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**Introduction:** Medetomidine is an anesthetic in domestic animals<sup>1</sup> and in human volunteers it is sedative and well tolerated.<sup>2</sup> The racemic composition of medetomidine has dose-dependent analgesic effect in various animal models.<sup>3</sup> Dexmedetomidine, a pharmacologically active d-isomer of medetomidine, is selective  $\alpha_2$ -adrenergic agonist.<sup>4</sup> We evaluated the analgesic potency of intravenous dexmedetomidine after laparoscopic tubal ligation.

**Methods:** The study was approved by the Ethical Committee of the Hospital and comprised 96 consenting healthy women. Anesthesia was induced with propofol  $2.0\text{mg}\cdot\text{kg}^{-1}$  and maintained with 0.3% end-tidal isoflurane. At the PACU the patient was given i.v. a blinded drug, when she estimated her pain to be moderate or severe on Visual Analog Scale. She either received dexmedetomidine 0.2 or 0.4  $\mu\text{g}\cdot\text{kg}^{-1}$ , diclofenac  $0.25\text{mg}\cdot\text{kg}^{-1}$  or oxycodone  $0.06\text{mg}\cdot\text{kg}^{-1}$ . The doses were repeated until the pain subsided or disappeared. No more than three consecutive doses were given during one hour. If adequate pain control was not achieved with the test drugs, morphine was administered at  $0.06\text{mg}\cdot\text{kg}^{-1}$  doses. Once treated with morphine the patient did not receive additional doses of the test drugs. The intensity of pain was evaluated before each trial drug administration and at 5 minute intervals until another trial drug dose. The sedation scores (1=awake, eyes open; 2=asleep easy to arouse; 3= asleep, difficult to arouse; 4=asleep, not arousable) were estimated at the same time intervals.

**Results:** 20 of the 24 patients in the diclofenac group needed extra morphine. This contrasts with only 8 cases in the patient group receiving either oxycodone or the larger dose of dexmedetomidine.

Furthermore, the morphine doses needed were fewest in number in the larger dose dexmedetomidine group. Visual Analogue Scale indicated that substantial pain relief was achieved already after the first dose of oxycodone. A corresponding pain relief was achieved after the third administration of dexmedetomidine. Dexmedetomidine was far more sedative than oxycodone or diclofenac. 8 of the 24 patients given the larger dose dexmedetomidine needed atropine because of bradycardia.

**Discussion:** Repeated doses of dexmedetomidine produced pain relief and sedation, but caused transient bradycardia, which may set limits for its clinical use in certain patient groups.

Table 1	Main results			
	dexmed 0.4 $\mu\text{g}/\text{kg}$	dexmed 0.2 $\mu\text{g}/\text{kg}$	oxycodone 0.06mg/kg	diclofenac 0.25mg/kg
No of patients	24	24	24	24
Age (years)	$38 \pm 0.9$	$40 \pm 0.6$	$39 \pm 0.9$	$39 \pm 0.9$
VAS before drug	$61 \pm 3$	$59 \pm 3$	$56 \pm 4$	$57 \pm 2$
$\Delta$ VAS after -1st drug	$10 \pm 3$	$12 \pm 4$	$24 \pm 3^*$	$6 \pm 3$
- 2nd drug	$20 \pm 3$	$11 \pm 4$	$29 \pm 4^*$	$11 \pm 4$
- 3rd drug	$29 \pm 4^*$	$20 \pm 4^*$	$31 \pm 4^*$	$7 \pm 3$
Patients given Morphine	8*	17	8*	20
Sedation scores	$2.7 \pm 0.1^*$	$1.9 \pm 0.1^*$	$1.9 \pm 0.1^*$	$1.5 \pm 0.1$
Patients given atropine	8*	0	0	0

1. *Anesth Analg* 1988; 67:611-615
2. *Clin Pharmacol Ther* 46:33-42, 1989
3. *Acta Vet Scand* 1989; 85:29-37
4. *Eur J. Pharmacol* 150:9-14, 1988

\* $p < 0.01$  vs diclofenac