

**Title:** PLASMA ATRIAL NATRIURETIC PEPTIDE AND ANGIOTENSIN II CONCENTRATIONS DURING ANESTHESIA IN THE RAT.

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**Introduction.** Angiotensin II (AII) and atrial natriuretic peptide (ANP) appear to have opposite effects in several physiological functions. AII is released by hypovolemic stimuli while ANP is released by acute hypertension and hypervolemia. In addition, the cardiovascular and renal effects of AII and ANP are opposite. Here, we have investigated the effects of halothane and fentanyl on the circulating levels of these two peptide hormones.

**Methods.** Male Sprague-Dawley rats were anesthetized with halothane and chronic saline-filled catheters were inserted into the femoral artery and jugular vein. These catheters were tunneled under the skin and exited from the back of the neck. Each rat was allowed 3 hours to recover from the surgical and anesthetic effects. At the end of this period arterial blood pressure, heart rate and blood gases were measured and a 2 ml blood sample was drawn for measurement of ANP and AII. Blood was collected with inhibitors to inhibit proteolytic inhibition. Samples were centrifuged, the plasma eluted and frozen at  $-80^{\circ}\text{C}$ . The withdrawn blood was replaced with donor rat blood. The above measures and blood samples were repeated 30 minutes (sample 2) and one hour later (sample three). On day two, samples were taken in the same rats during halothane anesthesia. The first sample was obtained under control unanesthetized conditions. The second sample was obtained 30 minutes after the rat was intubated and ventilated with 1.1% halothane in 100%  $\text{O}_2$ , equivalent to 1 MAC for the rat. The third sample was obtained 30 minutes later during ventilation with 2.2% halothane. Blood was replaced with donor blood as before. On day three the effects of fentanyl anesthesia was tested in each rat. The first sample was taken under control unanesthetized conditions. The second sample 30 minutes after intubation, paralyzation with pancuronium and infusion of fentanyl at a rate of  $50 \mu\text{g}/\text{kg}/\text{hr}$ . The third sample was obtained following a 30 minute infusion of  $200 \mu\text{g}/\text{kg}/\text{hr}$  fentanyl. AII was extracted from plasma using an acetone, HCl, water mixture, and ANP was extracted using a Sep Pak. AII and ANP were measured by separate radioimmunoassays using a double antibody technique. Data were analyzed by repeated measures ANOVA and paired t-tests.

**Results.** Arterial blood pressure, heart rate and blood gases remained at control levels when measured under unanesthetized conditions. Plasma ANP and AII levels also did not change (Table 1). Blood pressure decreased significantly with both 1.1% and 2.2% halothane. AII showed a dose-related increase with halothane. ANP decreased with 1.1% halothane and returned to control levels with 2.2% halothane. Fentanyl produced an increase in blood pressure and an increase in AII at both anesthetic levels. Plasma ANP concentrations did not change.

**Discussion.** These results show that both halothane-induced hypotension and fentanyl-induced cardiovascular stimulation are coincident with an increase in plasma AII. Halothane produces a decrease in ANP at 1.1% but not 2.2%, whereas fentanyl did not alter ANP at any level. The data suggest that the normal regulation of ANP release may be inhibited by both halothane and fentanyl, since it would be expected to rise in the face of increased blood pressure and to decrease when blood pressure is lowered.

Table 1. Blood pressure, AII and ANP changes during halothane and fentanyl anesthesia.

	BP	AII	ANP
<u>Unanesthetized</u>			
control	108 $\pm$ 3	11 $\pm$ 1	312 $\pm$ 18
sham	105 $\pm$ 3	9 $\pm$ 1	332 $\pm$ 22
sham	107 $\pm$ 4	8 $\pm$ 1	271 $\pm$ 17
<u>Halothane</u>			
control	109 $\pm$ 3	10 $\pm$ 1	270 $\pm$ 16
1.1% HAL	92 $\pm$ 3 *	20 $\pm$ 5 *	187 $\pm$ 11 *
2.2% HAL	57 $\pm$ 2 *	50 $\pm$ 7 *	332 $\pm$ 21
<u>Fentanyl</u>			
control	98 $\pm$ 3	10 $\pm$ 2	283 $\pm$ 18
50 $\mu\text{g}/\text{kg}$ fent.	121 $\pm$ 4 *	25 $\pm$ 2 *	342 $\pm$ 24
200 $\mu\text{g}/\text{kg}$ fent.	126 $\pm$ 4 *	49 $\pm$ 6 *	310 $\pm$ 21

\* =  $P < 0.05$  compared to control. Number of rats in each treatment group = 7. Data reported as mean  $\pm$  SE.