Title : HALOTHANE AND CNS MODULATION OF CIRCULATION

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Introduction. Circulatory effects of inhalation anesthetics have been extensively investigated but the response to surgical stimulus as a function of anesthetic concentration has not been well delineated. A rat model was developed utilizing the cardiovascular change with stimuli as a graded response. The effect of anesthetic concentration and the role of the autonomic nervous system on the circulatory response were studied in this model.

Methods. Six groups of 5 CD rats (mean wt. 352 gms. ± 6 SEM) underwent tracheostomy with halothane/oxygen anesthesia. Maintenance was with nitrous oxide/oxygen,curare and controlled ventilation for placement of arterial and central venous lines. All incisions had xylocaine infiltrated. Phasic arterial, mean arterial, central venous pressure and stimulusvoltage were recorded. Electric shock was delivered by nerve stimulator to the tail or cheek. The stimulus duration was 5 seconds and the interval 3 minutes. Curarized rats were sequentially ventilated with oxygen alone and three increasing halothane concentrations (1/3,2/3,and 1%) for 25 minutes each. Inspired concentration was changed 15 minutes prior to stimulation and "end tidal" halothane confirmed by gas chromatography. The first group explored the relation between stimulus strength and blood pressure response with 7 stimuli (range 0.375-7 volts) at each halothane level.Group 2 had three 7 volt shocks applied at each halothane level. Group 3 had two 5 µg boluses of IV phenylephrine at each halothane percentage. Groups 4 and 5 had 7 volt electric shocks identical to Group 2;Group 4 had bilateral cervical vagotomies and Group 5 had atropine 1 mg/kg IV 10 minutes prior to each batch of stimuli. Group 6 had C1-C2 cordotomy to interrupt sympathetic outflow. Baroreceptor vagal axis function was confirmed by bradycardia resulting from phenylephrine induced hypertension. Shocks were applied to the cheeks of the spinal animals.

Results. The correlation coefficient between blood pressure increase and the log of stimulus voltage was 0.96 or better for each halothane concentration in Group 1. The greater the inspired halothane concentration the less the rise in blood pressure induced by the 7 volt shocks (Table). Neither vagotomy nor atropinization altered this attenuation of blood pressure rise by halothane. C1-C2 cord transection abolished the blood pressure rise caused by shock of the cheek despite this rise being essentially identical when cheek or tail is shocked in rats without cord transection. The increase in blood presure caused by phenylephrine was unchanged by halothane. Heart rate was always increased by shocks — an increase attenuated progressively by higher concentrations of halothane except in cord transected rats where shocks caused no increase in heart rate.

Response to 7 Volt Shocks

Mean Arterial Pressure Increase ± SEM (Torr)

Halothane %	O_2	1/3%	2/3%	1%
Shock Alone	56 ±2	47 ±2	23 ±1	13 ±1
Phenylephrine Bolus	41 ±2	42 ±2	42 ±2	41 ±4
Vagotomy & Shock	28 ±6	46 ±7	24 ±3	9 ±1
Atropine & Shock	49 ±4	36 ±3	22 ±3	11 ±1
C1-C2 Section & Shock	1 ±2	2 ±1	-1 ±3	2 ±3

Discussion. A reproducible dose-response curve was observed for the effect of low dose halothane on blood pressure rise due to electric stimulation in the rat. Halothane concentrations below minimum alveolar anesthetic concentration produced significant decreases in the cardiovascular response. The effect was apparently mediated within the CNS, since the peripheral effects of phenylephrine were unaltered. Mediation was predominantly sympathetic since the heart rate changes persisted despite atropine induced vagal blockade or vagotomy. Vagal effects (baroreceptor function) were observed independent of competing sympathetic responses in spinal rats. The absence of heart rate changes in these spinal rats suggested that the parasympathetic system did not contribute significantly to the circulatory changes in the intact rats.