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TITLE: EFFECT OF HALOTHANE ON CANINE TRACHEAL SMOOTH MUSCLE; ROLE OF CYTOSOLIC Ca²⁺, CAMP AND PROTEIN KINASE C M.YAMAKAGE,MD, A.NAMIKI,MD

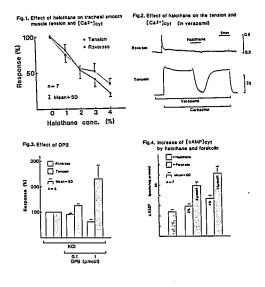
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Recently, it has been reported that the tension of various smooth muscles does not parallel cytosolic Ca^{2+} concentration($[Ca^{2+}]cyt$). In the present study, we examined the effect of halothane on $[Ca^{2+}]cyt$ and cAMP, and the role of protein kinase C(PKC).

Effect of halothane on $[Ga^{2+}]$ cyt of tracheal smooth muscle strips was monitored by measuring light emission ratio(R340/380) of Fura-2 and simultaneously monitored the isometric tension. Contractions were evoked by carbachol(1µmol/1) with or without verapamil(10nmol/1), and halothane (1%-4%) was introduced. Next, contractions were evoked by high K⁺ solution(72.7mmol/1) and DPB (0.1, 1µmol/1), a PKC activator, was administered. Cytosolic concentration of cAMP([cAMP]cyt) was measured using RIA technique, when halothane(2,4%) was introduced. When forskolin(8,14µmol/1), a adenylate cyclase activator, was administered, [cAMP]cyt was measured as described above. The concentrations of forskolin were decided which showed identical suppression with halothane(2,4%).

Halothane decreased both the tension and R340/380. However, the decrease of the tension was remarkable compared with the decrease of R340/380 (Fig. 1). In verapamil, carbachol moderately increased the muscle tension(60-70%), but R340/380 did not change. When halothane was applied again, the muscle tension decreased remarkably, but R340/380 did not change(Fig. 2). DPB enhanced the muscle tension without increasing R340/380(Fig. 3). Halothane moderately but significantly increased [cAMP]cyt, whereas forskolin increased it to much greater extent(Fig. 4). Halothane decreased [Ca²⁺]cyt by increasing

Halothane decreased $[Ga^{2+}]$ cyt by increasing [cAMP]cyt, but this only partly explains its inhibition of contraction of tracheal smooth muscle. Because carbachol also activates PKC activity, halothane may modify PKC activity and thereby partially inhibit the contraction of tracheal smooth muscle.



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TITLE: ISOFLURANE ANESTHESIA AT DEPTHS PRODUCING A BURST-SUPPRESSION EEG PATTERN DOES NOT ATTENUATE THE HEMODYNAMIC RESPONSE TO INTUBATION

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<u>Introduction:</u> Rampil et al reported that in 32 patients anesthetized with a combination of pentothal, fentanyl, lidocaine, and droperidol, a spectral edge frequency (SEF) less that 14 Hz was associated with a more attenuated hemodynamic response to laryngoscopy and intubation than occurred when the SEF was greater than 14 Hz.¹ The authors suggested that the EEG effects of some anesthetics could predict the sympathetic response to intubation. Isoflurane is known to cause increasing suppression of the EEG. Does EEG suppression by isoflurane attenuate the hemodynamic response to intubation? Failure to do so would suggest that its anesthetic action may be different from that of some intravenous anesthetics and that anesthesia and suppression of the sympathetic nervous system are mediated by separate mechanisms.

<u>Methods:</u> With the approval of the Institutional Review Board and patients consent, six patients who were scheduled for craniotomy for resection of a focus of intractable seizures were studied. Intravenous and arterial cannulae were inserted prior to induction. ECG and arterial pressures were recorded continuously using a strip chart, and the EEG was recorded continuously on an eight-channel Grass recorder. Anesthesia was induced with thiopental 3-5 mg/kg, and pancuronium 0.1 mg/kg was administered. Isoflurane in 100% oxygen was given in increasing concentrations until the EEG pattern showed moderate burst suppression. This level was maintained for an additional 10 minutes before laryngoscopy and intubation were performed.

<u>Results:</u> The mean rise in systolic blood pressure (SBP) with intubation was 39% (range 19-60%) and the mean heart rate (HR) increase was 38% (range 19-60%).

<u>Conclusions:</u> The inability of isoflurane to attenuate the hemodynamic response to intubation at a depth which causes burst suppression of the EEG strongly supports the premise that anesthesia and analgesia are mediated by different mechanisms. Although the doses of fentanyl in the study by Rampil et al were small (94 \pm 80 mcg, or 72 \pm 108 mcg), they may explain the differences between their study and ours. Other work has indicated that in addition to the effects of opioids on specific receptors, a membrane effect may be involved in their anesthetic action.^{2,3} We hypothesize that the dual effect of opiates would explain the correlation between EEG suppression and hemodynamic response for fentanyl and the lack of correlation between these parameters for isoflurane. References: 1. Anesthesiology 67:139, 1987. 2. Anesth Analg

<u>References:</u> 1. Anesthesiology 67:139, 1987. 2. Anesth Analg 67:663, 1988. 3. Anesthesiology 62:615, 1985.

Changes in BP and HR with Laryngoscopy and Intubation

Parameter	Pre-laryngoscopy	Maximum Increase
Systolic BP (mmHg)	92 ± 10	128 ± 25 *
Mean BP (mmHg)	58 ± 7	91 ± 22 *
Diastolic BP (mmHg)	42 ± 6	72 ± 20 *
HR (beats/min)	86 ± 9	119 ± 26 *
Values are mean \pm SD		*p <.01