

HALOTHANE-INDUCED CHANGES IN CONTRACTIONS OF MESENTERIC LYMPHATICS OF THE RAT

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ABSTRACT

The effects of halothane on the contraction of mesenteric lymphatics was examined in rats. Following administration of 0.75% or 1.5% halothane, the contraction rate decreased from 10.6 ± 3.1 to 7.4 ± 2.5 times/minute and from 13.8 ± 3.9 to 4.1 ± 3.5 times/minute, respectively. Halothane caused a dose-dependent suppression of contractile movements of the mesenteric lymphatics.

The lymphatic system plays an important role in the control of extracellular fluid, transporting liquid and protein from the interstitial space to the bloodstream (1). Although lymphatic contractions are thought to be a key mechanism for lymph transport (2), there are few reports on the quantitative effects of general anesthetics on lymphatic contraction. This study was undertaken to examine the effect of halothane on the contraction of rat mesenteric lymphatics.

MATERIALS AND METHODS

Twelve male Wistar rats, weighing 100-140g, were used. Under halothane-oxygen anesthesia, a tracheostomy was performed and the femoral artery and vein were cannulated for direct arterial pressure recording and intravenous fluid and drug administration. Halothane

anesthesia was then discontinued (after an average duration of 30 minutes) and sodium pentobarital (20mg/kg) was administered intramuscularly. After administering pancuronium bromide (0.1mg) intravenously, the lungs were artificially ventilated with 100% oxygen. The PaCO₂ was maintained at 30-40mmHg. The animals were placed on a microscope stage and the rectal temperature was maintained at $37.0 \pm 1.0^{\circ}\text{C}$ by a heating pad. The small intestine was exposed and the mesentery was spread on a transparent plastic block. The mesentery was perfused with mammalian Ringer's solution at 37°C . Using a TV camera attached to the microscope, the lymphatic contractions were observed and recorded on videotape with time markers for later analysis.

Following a 5-minute control period, halothane (0.75% or 1.5%) was administered for 20 minutes through a calibrated vaporizer (Halomatic; AIKA Co.). The contractile movements were averaged for 5 minutes during each observation. The averaged values of 5-10 minutes and 15-20 minutes during the inhalation of halothane were used for the contraction rate at 10 minutes and 20 minutes, respectively. The averaged values of 10-15 minutes after the discontinuation of halothane were used as the contraction rate at 35 minutes.

The statistical significance of the data was assessed by the Student's t-test.

RESULTS

Following 20 minutes at 0.75% halothane administration, the lymphatic contraction rate decreased from a control value of 10.6 ± 3.1 to 7.4 ± 2.5 times/minute ($p < 0.01$), and returned to 9.5 ± 3.6 times/minute at 15 minutes after discontinuation of halothane. Following 20 minutes of 1.5% halothane, the contraction rate decreased from a control value of 13.8 ± 3.9 to 4.1 ± 3.5 times/minute ($p < 0.01$) and returned to 7.5 ± 3.7 times/minute at 15 minutes after discontinuation of halothane. Compared to 0.75% halothane which maximally suppressed contraction by $31 \pm 20\%$ of control, 1.5% halothane suppressed lymphatic contraction by $72 \pm 23\%$ ($p < 0.05$). The effects of these two doses of halothane on lymphatic contractile motion are graphically shown in Fig. 1. The suppression of

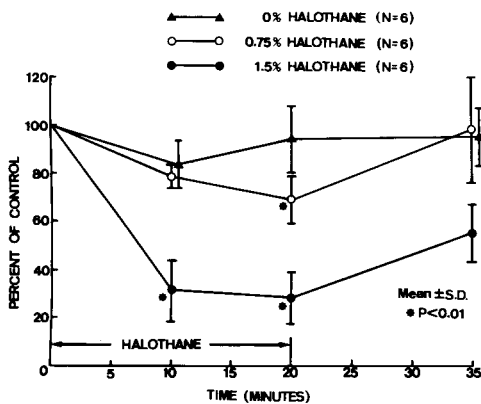


Fig. 1. Time course of the effect of halothane (0.75% and 1.5%) on the contraction rate of rat mesenteric lymphatics. The contraction rates were suppressed significantly by both concentrations and recovered after discontinuation of halothane (see Results).

contractile movement by both concentrations was not only significantly different from control values but the suppression by 1.5% was significantly greater than that following 0.75% ($p < 0.05$).

DISCUSSION

Contractile movements of lymphatics have been observed in sheep, guinea

pigs, bovines, rats and humans (1,3). Kinmonth (4) observed rhythmic contractions of retroperitoneal lymphatics in man. The contraction rate has been reported to be about 19 times/minute in rat mesenteric lymphatics (5). Lymphatic contraction is classified into active and passive contraction; the latter is induced by muscle contractions, respiratory movements, arterial pulsations and intestinal peristalsis (1). Smith (6) demonstrated the existence of active contraction of lymphatics in rats by recording contractile movements independent of respiration and pulsation of adjacent arteries. Mawhinney (7) reported that spontaneous contraction was approximately 2 times/minute in isolated segments of lymphatic vessels. The electrical activity of lymphatic smooth muscles also has been examined. Azuma (8) showed that the action potentials of bovine mesenteric lymphatics resemble the pacemaker potentials recorded from smooth muscles. In our experiment, because the rats were immobilized with a muscle relaxant and contractions were independent of respiration and arterial pulsations, the lymphatic motion undoubtedly was spontaneous.

Concerning the influence of general anesthesia on lymphatic contractions, Guyton (1) maintained that tissue damage or anesthesia was likely to block spontaneous contractions. Hall (2) suggested that the absence of lymphatic contractions during surgery was probably due to the direct inhibitory effects of anesthesia or surgical trauma. In the present study, the administration of halothane caused a significant suppression of the contraction rate in a dose dependent manner.

Because lymphatic contraction seems to have a close relationship to lymph formation and to be regulated by neural and humoral mechanisms, it is reasonable that halothane may influence this phenomenon. Smith (6) noted that the lymphatic contraction rate is proportional to the rate of lymph formation. Whitwan (9), moreover, observed that the administration of halothane prompted a decrease in thoracic duct lymph flow, which from the present study may derive

from reduced lymph formation in the mesentery, a major source of TDL. Lymphatic vessels also have an adrenergic innervation and physiologically vasoactive substances, such as catecholamines, probably play an important role in the control of lymphatic contractions (10,11). Since catecholamines stimulate an increase in the contraction rate (12), the inhibitory effect of halothane on the sympathetic nervous system (13) and the adrenal medulla (14) may indirectly also induce a decrease of the lymphatic contraction rate. Alternatively, halothane may effect the contractile mechanisms of lymphatic smooth muscle directly. Azuma (8) has speculated that the calcium current through cell membranes is the key factor which determines the contractile motion of lymphatics. Accordingly, an inhibitory effect of halothane on the transport of Ca^{2+} through cell membranes (15) may have suppressed lymphatic smooth muscle contractions.

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