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TITLE: THE EFFECT OF ETHANOL ON MAC OF HALOTHANE IN HUMANS.

AUTHORS: TA Slee, MD, BF Cullen, MD, J Unadkat, PhD, EG Pavlin, MD

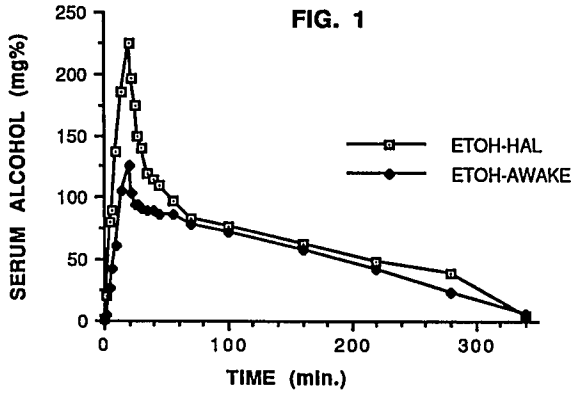
AFFILIATION: Department of Anesthesiology and Pharmaceutics, University of Washington, Seattle, WA, 98104

Acute ethanol intoxication is commonly associated with traumatized patients requiring surgical intervention.[1] A decrease in anesthetic requirement has been documented in animals[2,3,4] administered ethanol intraperitoneally but this has not been correlated with blood levels nor are quantitative data available in humans. The purpose of this study was to quantify the effect of a steady state level of ethanol on MAC in humans anesthetized with halothane and to assess the effect of halothane on ethanol pharmacokinetics.

METHODS: Institutional approval and informed consent were obtained. All patients were unpremedicated, non-alcoholic, ASA I-II of comparable weights and ages. Twelve patients (Group I) underwent inhalational induction with halothane (HAL) and oxygen; followed by intubation. Ventilation was controlled. Endtidal PCO_2 and HAL were measured by mass spectrometer. Movement or lack of movement to surgical incision by the prior patient determined the $P_{ET}HAL$ by adjusting HAL up or down in .10% increments respectively. End tidal HAL stabilized for a minimum of 15 minutes prior to surgical incision. In 10 other patients (Group 2) HAL anesthesia was followed by a 20 minute infusion of ethanol (ETOH) of 572 mg/kg followed by a maintenance infusion to achieve a blood level of 100 mg% by 40 minutes. Multiple blood samples were obtained. MAC was determined as in the first group. Group 3 subjects were unanesthesized controls receiving intravenous ETOH at the same rates and sampling schedules as the patients in Group 2.

RESULTS: Halothane MAC for sober anesthetized patients was .78% which compares favorably with the values in the literature[5]. The average ETOH level in Group 2 was 94 ± 15 mg% at time of MAC determination. MAC for the ethanol group was .53%. Figure 1 shows the blood levels during and after identical rates of infusions of ETOH in Groups 2 and 3. The peak level for Group 2 (ETOH-HAL) was 230 ± 17 mg% at twenty minutes, which was 85% higher than the 124 ± 6 mg% in Group 3 (ETOH-awake).

FIG. 1



DISCUSSION: A blood Ethanol level of approximately 100 mg% lowers MAC of halothane by 32%. This should be taken into account when anesthetizing intoxicated patients. The peak ethanol level after a short rapid infusion is considerably higher under halothane anesthesia than during the awake state. One explanation might be a lower volume of distribution for ethanol during halothane anesthesia.

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TITLE: INFLUENCE OF L-DOPA ON MINIMUM EFFECTIVE DOSE (MED) OF HALOTHANE IN THE RAT

Authors: JL Horn, MD, BVR Sastry, PhD and JJ Franks, MD

Affiliation: Depts. of Anesthesiology and Pharmacology, Vanderbilt University, Nashville, TN 37232

INTRODUCTION: The precursor regulation of the synthesis of S-adenosyl-L-methionine (SAM) plays an important role in several clinical situations.[1] During treatment of Parkinson's disease with L-dopa (L-3,4-dihydroxyphenylalanine) SAM is utilized for the conversion of L-dopa to 3-O-methyldopa. Therefore, SAM will be depleted to about 30% of normal levels in brain.[1] SAM-mediated enzymatic N-methylation of membrane phosphatidylethanolamine (PE) is enhanced in rat brain synaptosomes and myelin by the minimum effective dose (MED) of halothane (abolition of response to tail clamping).[2] There is an inverse relationship between SAM-mediated phospholipid methylation and transmitter release which might be relevant to central synapses during anesthesia.[3] A question arises as to whether brain SAM levels influence the MED of halothane. Therefore, we have determined the MED of halothane in rats in which brain SAM levels were lowered by administration of L-dopa.

METHODS: Animal use was approved by the Animal Care Committee of Vanderbilt University. One experimental group (N=6) of male Sprague-Dawley rats (255-325 g) was anesthetized for 20 min with halothane in humidified air and oxygen (FI_{O2}, 0.3). The MED of halothane was determined for each rat.[2] The rats were allowed to recover from anesthesia. Five to ten days later, they were treated with L-dopa (100 mg/kg as a hydrochloride, i.p.). Thirty min after treatment with L-dopa, they were anesthetized with halothane, and the MED for each rat was again determined. This experiment was repeated with a second group of control rats (N=6) injected with saline instead of L-dopa.

RESULTS: The MED (mean ± SE) of halothane in the first group of rats before treatment with L-dopa was 1.35 ± 0.01% (M1). It decreased to 1.22 ± 0.01% after L-dopa treatment (M2). The difference between M1 and M2 was significant at $p < 0.01$. The MED for halothane in the control group of rats after treatment with saline (1.33 ± 0.02%) was not different from the MED before treatment (1.33 ± 0.02%).

DISCUSSION: This study indicates that L-dopa treatment decreases the MED for halothane in rats. It has already been demonstrated that L-dopa (100 mg/kg) decreases brain SAM levels by about 70% and methionine levels by 20%.[1] SAM availability may be one of the limiting factors in the depth of anesthesia achieved with halothane. The pattern of precursor control of brain SAM and its modification by pharmacological agents may serve as an experimental tool for understanding relationships between phospholipid methylation and actions of inhalational anesthetics.

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