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Title: EFFECT OF VOLATILE ANESTHETICS AND NEUROMUSCULAR BLOCKING AGENTS IN PMN CHEMOTAXIS

Authors: Alix Mathieu, M.D. and Diana Mathieu, Ph.D.

Affiliation: Department of Anesthesia, University of Cincinnati College of Medicine, Cincinnati, Ohio 45267

INTRODUCTION

Polymorphonuclear leukocytes (PMN) play an active role in defense against infections by migrating to the site of injury (chemotaxis), followed by subsequent phagocytosis and intracellular killing of bacteria. During the peri-operative period, patients are exposed to bacteria and to a variety of anesthetic agents. Therefore, anesthesiologists should be interested to know the effect of anesthetic and adjunct drugs used during anesthesia on the parameters of host defenses. In this study, we are reporting the effect of two volatile anesthetics and five commonly used neuromuscular agents in PMN chemotaxis, using the technique of PMN migration under agarose.

METHOD

Halothane 0.5 - 4% and enflurane 1 - 7% were investigated using the technique of PMN migration under agarose under controlled conditions for pH and osmolality. Horse serum (10%) was used as the chemoattractant. Different concentrations of the anesthetic gases were obtained in plexiglass, air-tight chambers. The anesthetic vapors were mixed for five minutes with a mixture of 5% CO_2:95% air. The concentrations of halothane and enflurane were monitored at the start and termination of the experiment by analyzing samples with a gas chromatograph. The petri dishes containing agarose, 10% horse serum and 6 - 7 replicate wells (2.5 mm) each containing 1 x 10^6 PMN were placed inside the chambers for the duration of the experiment. After exposure to the anesthetic, the chambers were placed inside the incubator for 18 hours at 37°C. The five muscle relaxants, four non-depolarizing, i.e., pancuronium, tubocurarine, gallamine triethiodide and alcuronium and one depolarizing, succinylcholine dichloride were investigated. For these experiments, the concentration of drug studied is incorporated directly into the agarose. The results are expressed as either percent inhibition or stimulation and obtained by dividing the net migration obtained with drug/net migration of control (not exposed to drug) X 100.

RESULTS AND DISCUSSION

Halothane displayed a dose-dependent and statistically significant inhibition of chemotaxis between concentrations of 1-4%. Enflurane, at concentrations of 1-7% displayed a mild but consistent stimulation of chemotaxis, ranging from 2-14%, with PMN obtained from six healthy individuals. The results obtained with halothane confirm the observations of previous investigators[1,2] while the difference in effect of enflurane in our assay is of interest. Preliminary data have shown complete reversibility of the effect of either drug, even after an exposure of four hours. The stimulation obtained with enflurane, if validated by further experiments, could suggest that the latter might be the anesthetic of choice in patients with known infection. As for the muscle relaxants, pancuronium and tubocurarine significantly inhibited PMN chemotaxis at concentrations of 125-500 ug/ml. Conversely, alcuronium and gallamine displayed significant dose-related increase of PMN chemotaxis at concentrations of 10-1000 ug/ml. Succinylcholine was noted to produce either of two effects, a mild dose-related increase in PMN migration in certain individuals tested or a significant inhibition of locomotion in others. These effects were observed at concentrations ranging from 125-2000 ug/ml. The dual mechanism of action observed with succinylcholine on PMN chemotaxis is still unclear and warrants further investigation. The effects noted for muscle relaxants occur at concentrations much greater than those used clinically.

TABLE: EFFECT OF HALOTHANE AND ENFLURANE ON PMN CHEMOTAXIS

HALOTHANE CONCENTRATION PERCENTAGE	% INHIBITION
0.5	3
1.5	10
3.0	19
4.0	27

Mean results from four experiments

ENFLURANE CONCENTRATION PERCENTAGE	% STIMULATION
1	8
2	6
4	14
7	2

Mean results from six experiments

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