Title : EFFECTS OF INDUCTION AGENTS AND NON VOLATILE ANESTHETICS ON CHEMOTAXIS OF POLY_ MORPHONUCLEAR LEUKOCYTES (PMN)

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Introduction. The effects of local anesthetics on the cytoskeletal control of cell mobility has been well established. Reports of a reversible inhibition of chemotactic locomotion of polymorphonuclear cells in vivo during and after general anesthesia, using a modified Boyden chamber technique, have appeared recently [1]. Thus, we have investigated whether the non volatile anesthetics, i.e. induction agents, and drug adjuncts, used during anesthesia, i.e. narcotics, have any effects on the in vitro migration (chemotaxis) of polymorphonuclear leukocytes.

Methods. PMN migration beneath agarose gels was used as an assay. Blood from normal adult volunteers was collected on the day of the experiment in heparinized vacutainer tubes. The cells (PMN) were separated from whole blood by Ficoll hypaque density gradient centrifugation, followed by dextran sedimentation of the PMN-rich cell pellets, using sterile technique. Trypan blue dye exclusion test for viability of the PMN was performed, and the final cell suspension usually contained 95% PMN and 5% mononuclear cells. Approximately $1x10^6$ cells were delivered into each well of a petri dish containing agarose gels. The plates were covered and incubated for 18 hours at 37°C in a chamber with 5% CO_2 and 95% humidified air. At the end of the incubation, the gels were removed. Migration patterns and boundaries were clear and could easily be read with the measuring magnifier. Net migration diameter was calculated by subtracting the standard well diameter which for all control values was greater than 7 mm. Three induction agents, i.e. diazepam, ketamine and sodium thiopental; and two narcotics, fentanyl, which is a short-acting drug and morphine, a long-lasting drug, were investigated at different concentrations. For 3 drugs, exposing the cells for periods of 1-2 to 3 hours and washing the cells subsequently to study the possible reversibility of the action was also done.

Results. As seen in Figure 1, all the induction agents investigated displayed dose-related and statistically significant ($p < 0.05$) inhibition of PMN migration, but usually at doses higher than those encountered clinically. As for the narcotics (Table 1), only morphine displayed a statistically significant inhibition of PMN chemotaxis. Fentanyl seems to produce, at the doses investigated, a slight but not statistically significant increase in PMN migration, which decreases as the concentration increases. Preliminary data indicate that washing the cells after exposure to the drugs reverses the inhibition of PMN migration.

Discussion. Chemotaxis, i.e. the migration of leukocytes toward the locus of inflammation and of infection plays an important role in host defense mechanism. Any inhibition of the migration of PMN cells during or after anesthesia, induced by the anesthetic drugs or their metabolites, may create an increased risk of infection. Our data so far have not supported the in vivo observations [1], i.e. the inhibition of PMN migration at anesthetic concentrations of these drugs, except for morphine, but only at higher doses, not found in vivo. Our preliminary data show that the effect is reversible. Migration inhibition of PMN chemotaxis at the concentrations studied may be related to the indirect effects of the drugs on microtubules. In the earlier study [1], the effect of multiple drugs was investigated, which we have not yet explored.

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Reference.

1. Stanley TH, Hill GE, Portas MR et al.: Neutrophil chemotaxis during and after general anesthesia and operation. Anesth Analg Curr Res 55: 668-672 , 1976

Table: EFFECT OF NARCOTICS ON PMN MIGRATION

Fentanyl	Concentration ug/ml	Percent Migration
	2.0	118
	5.0	114
	10.0	87
	12.5	92
Morphine	100	22
	500	0
	960	0

EFFECT OF INDUCTION AGENTS ON PMN MIGRATION