Title: ADVERSE EFFECTS OF SOME ANESTHETICS ON SPINAL CORD ISCHEMIC INJURY

Authors: M. Koike, M.D., M.F. Roizen, M.D., J. Zivin, M.D., Ph.D., B. Johnston, B.A., J. Joyce, M.D.

Affiliation: Departments of Anesthesia, Medicine and Pharmacology, University of California School of Medicine, San Francisco, California, and Department of Neurology, University of Massachusetts, Worchester, Massachusetts

Introduction: Studies indicate that biologic amines might contribute to neurologic damage after ischemia or trauma. We hypothesize that anesthesia might ameliorate the stress response to ischemia and, hence, neurologic damage secondary to activation of biologic amine systems. To test this hypothesis, we used ischemia of the rabbit spinal cord as a model of stroke. This lesion is highly reproducible and does not damage other organ systems.

Methods. One hundred twenty-five male New Zealand rabbits (2-3 kg) were randomly divided into five groups. The first received halothane (2.5% in O_2). We placed a Tycron snare around the aorta distal to the left renal artery and occluded the aorta. We anesthetized the rest of the rabbits with halothane for placement of the snare, but allowed them to awaken and exhibit normal neurologic function. Later that day, snare ligature was pulled tight and the aorta occluded. One min after occlusion, intraperitoneal injection of ketamine (100mg/kg), fentanyl (50µg/kg), naloxone (0.4mg/kg), or saline (controls) was made. For all rabbits the aorta was occluded for 15-45 min, after which time the snare was released and aortic blood flow restored. In six to eight rabbits in each group, blood pressure and plasma levels of catecholamines were measured every 3 min during occlusion using catheters that had been placed in femoral and ear arteries. We observed all rabbits during occlusion and for three days after, grading neurologic impairment as follows: 1=Total neurologic impairment of hindquarters and incontenance of urine and feces; 2=Any neurologic defect, such as abnormal hopping, less-than-normal responsiveness to pinching of the hindlimbs or variable bowel or bladder function; 3=No neurologic damage. Data for animals having some neurologic function on day 3 (grades 2 and 3) were compared with those for animals having total neurologic impairment. The mean time of occlusion for 50 percent of animals to have no hindlimb function was determined usind Waud iterative analysis (1).

Results. The time to neurologic damage after aortic occlusion was significantly shorter in animals receiving halothane or ketamine than in control animals, despite the fact that these agents ameliorated the plasma catecholamine response to aortic occlusion (Table 1). The time to neurologic injury was prolonged by naloxone, but was not affected by analgetic doses of fentanyl.

Discussion. These results disprove our hypothesis that reducing stress decreases neurologic defect after ischemia. Therefore, anesthesia may be detrimental for patients having recent strokes. Although fentanyl analgesia did not alter the time to neurologic deficit after ischemia, the prolongation of this interval by the narcotic antagonist naloxone indicates that anesthetic doses of narcotics may also shorten the time to neurologic damage. The anesthetic agent that increases serotonergic activity (ketamine) shortened the time to neurologic damage, while the agent that decreases such activity (naloxone) prolonged it. Perhaps the ideal anesthetic for the patient who has just had or is about to have, ischemia of the CNS is one that decreases serotonergic activity. However, the hypothesis remains to be proven.

References.

1. Waud DR: On biological assays involving quantal responses. J Pharmacol Exp Ther 183:577-607, 1972

TABLE 1

Group	Time to total neurologic deficit in 50% of animals (min)±SEM	Maximum level of plasma catecholamine (percent of baseline)
Saline (control) n = 32	35.1 ± 0.15	210 ± 30 (n=8)
Ketamine n = 25	22.5 ± 0.1*	143 ± 15* (n=6)
Halothane n = 22	23.3 ± 0.1*	103 ± 18* (n=8)
Naloxone n = 23	51.3 ± 0.5*	220 ± 26 (n=8)
Fentanyl n = 18	37.5 ±0.12	-

* significantly different from control $P \leq 0.05$.