Title: COMPARISON OF THE EFFECTS OF ISOFLURANE AND THIOPENTAL ON NEUROLOGIC OUTCOME FOLLOWING FOCAL ISCHEMIA IN PRIMATES

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Introduction. It has recently been demonstrated that thiopental in doses sufficient to produce burst suppression on EEG provided better neurologic outcome (and significantly less infarction by histopathology) than did isoflurane in baboons exposed to temporary focal ischemia (middle cerebral artery occlusion for 6 h). Because it was assumed that thiopental and isoflurane produced equal cerebral metabolic depression, it was hypothesized that changes in regional cerebral blood flow produced by thiopental might have influenced the results. However, the two groups were not comparable with respect to blood pressure or the use of vasoactive drugs. The thiopental animals had significantly higher blood pressure than the isoflurane animals despite the fact that all thiopental animals received near maximal doses of nitroprusside, a known cerebral vasodilator, and all isoflurane animals received large doses of phenylephrine and metaraminol, both cerebral vasoconstrictors. The more accurate conclusion of the study is that thiopental + increased blood pressure + cerebral vasodilators produces better outcome than isoflurane + normal blood pressure + cerebral vasoconstrictors. It is important to clearly determine whether one anesthetic agent might be clearly advantageous in clinical situations of temporary focal cerebral ischemia. The purpose of the present study was to compare the effects of thiopental and isoflurane on neurologic outcome and histopathology in primates following 5 h middle cerebral artery occlusion (MCA_0), keeping all other variables equal.

Methods. Following approval by the Animal Care Committee, 17 fasted pigtail monkeys were anesthetized with 1.15% halothane in O_2/N_2; paralyzed with 1 mg pancuronium, intubated and ventilated to $PaCO_2$ 35 mmHg. Surgical preparation included placement of peripheral IV lines, a right femoral artery catheter, and electrodes for EEG recording; and right eye enucleation for transorbital approach to the MCA. Thereafter the halothane was discontinued and animals were randomly assigned to one of two groups: thiopental or isoflurane. Half the animals received 5 mg/kg thiopental while the remainder received 1 MAC isoflurane. With exposure of the MCA, the anesthetic was increased to produce burst suppression for 15 min prior to MCA_0. Occlusion was confirmed by failure of IV methylene blue to pass the clip. Mean arterial pressure (MAP), ECG, EEG, arterial blood gases, Hb, glucose lactate, and body temperature were measured continuously; and electrolytes were measured periodically pre-, during, and post-ischemia. MAP was maintained 85-90 mmHg with phenylephrine. After 5 h occlusion the clip was removed, reflow confirmed by methylene blue, and the orbit filled with methyl methacrylate. The isoflurane was decreased to 1 MAC and thiopental infusion was discontinued following MCA reflow and isoflurane was discontinued at the end of the procedure. Ventilation was continued until the animals could breath adequately maintaining a PO_2 > 60 mmHg and PCO_2 < 45 mmHg. They were extubated when they demonstrated pharyngeal reflexes. The animals were followed for 8 days, and given supportive care as needed. The animals were graded daily by an observer blinded to the anesthetic and assigned a neurologic deficit score of 0-5 (0=normal, 1=minimal damage, 2=hemiparesis, 3=hemiplegia, 4=coma, and 5=death due to brain damage). At 8 days the animals were anesthetized with ketamine, killed with KCl, and the brains removed for histologic examination.

Results. MAP, blood gases and chemistries, and temperature in each group were similar. Animals in both groups received phenylephrine but the isoflurane group required significantly more phenylephrine to maintain MAP (MAP = 88 ± 1 mmHg in isoflurane group and 91 ± 3 in thiopental group). The figure displays the final neurologic deficit score in each animal. The scores ranged from 0-5 in each group. Mean NDS was 3.0 for both the isoflurane and thiopental groups. There were no differences between groups. The histopathology results are pending.

Discussion. This study demonstrates that equal neurologic deficits occur following 5 h MCA_0 when either thiopental or isoflurane is given in amounts sufficient to produce burst suppression on EEG and MAP is maintained solely with phenylephrine. The insult sustained by both groups is identical to that sustained by the isoflurane group in the previous study.[1] We conclude that in situations of temporary focal ischemia, thiopental offers no advantage over isoflurane.

References.

1. Nehls DG, Todd MM, Spetzler RF, Drummond JC, Thompson RA, Johnson PC: Comparison of the cerebral protective effects of isoflurane and barbiturates during temporary focal ischemia in primates. Anesthesiology 66:453-464, 1987