

Title: A COMPARISON OF THE EXTENT OF ISCHEMIA FOLLOWING MIDDLE CEREBRAL ARTERY OCCLUSION DURING THREE INDUCED HYPOTENSIVE TECHNIQUES

Authors: D.J. Cole, M.D., J.C. Drummond, M.D., H.M. Shapiro, M.D., M. Zurnow, M.D.

Affiliation: Department of Anesthesiology (V-151), Veterans Administration Hospital, San Diego, CA 92161; and University of California at San Diego, CA 92093

Introduction: Induced hypotension is frequently employed during intracranial neurovascular procedures. During such a procedure the patient may be at risk for focal cerebral ischemia. There is little information to indicate whether the choice of hypotensive technique influences the size of the ischemic zone in the event of cerebral vascular occlusion. This study compared the size of ischemic territory occurring during three different hypotensive techniques following middle cerebral artery occlusion (MCAO).

Methods: With prior approval by the Institutional Animal Studies Subcommittee, male, Sprague-Dawley rats (n=18) of similar weights (350-400 grams) were surgically prepared in the following manner. Each rat was anesthetized with 3.0% isoflurane and orotracheally intubated. 1.2 MAC isoflurane (1.87%) was administered during the surgical preparation with an inspired oxygen concentration of 40%, and a balance of nitrogen. The femoral vessels were cannulated for continuous blood pressure monitoring, isotope administration, and blood collection. The left middle cerebral artery (MCA) was exposed via a subtemporal craniotomy.⁽¹⁾ Each rat was then randomly assigned to one of the following groups: 1) Nitroprusside-during 1.2 MAC isoflurane anesthesia the mean arterial pressure (MAP) was decreased to 40-50 mm Hg with a nitroprusside infusion, 2) Isoflurane-end-tidal isoflurane concentration was increased as required to achieve a MAP of 40-50 mm Hg, or 3) Hypovolemia-aliquots of blood were withdrawn to achieve a MAP of 40-50 mm Hg. In all groups hypotension was gradually achieved and maintained for 5 minutes prior to MCAO. Physiological parameters (pH, PaCO₂, PaO₂, MAP, serum glucose, hematocrit, and temperature) were monitored. A proximal MCAO was performed according to Bederson⁽²⁾ using microbipolar coagulation at a low power setting, and a continuous saline irrigation.

Eight minutes after MCAO cerebral blood flow was determined as follows. ¹⁴C-iodo-antipyrine (IAP), 100 uCi/kg, was infused over 40 seconds. At T=39 seconds the rat was decapitated and the brain and spinal cord were rapidly removed and frozen. 20 micron sections of brain and spinal cord were placed on Kodak OM-1 film with ¹⁴C standards for 21 days. The area of zero blood flow (zero ¹⁴C concentration) was read with the Drexel/DUMAS image processing system. Three standard sections were used for measurement corresponding to -0.2mm, -2.2mm, and -4.2mm posterior to the bregma (the point at which the coronal suture crosses the sagittal suture), according to Pelligrino.⁽³⁾ The area in the 4mm span was recorded and reported as a percentage of total brain read for each rat. Statistical analysis was performed using analysis of variance and, as appropriate, mean values were compared by t-tests with a Bonferroni correction.

Results: The requirement within each group necessary to establish hypotension was as follows: 1) Nitroprusside-7.7 ±2.5 ug/kg/min, 2) Isoflurane-3.62 ±0.57%, or 3) Hypovolemia-9.3 ±1.2 ml (approximately 1/3 of the blood volume). There were no between groups differences in the physiological data (P<0.05). The area of no flow in each hypotensive group is presented in Table 1. There were no differences between groups in the area of zero blood flow as presented as a percentage of total brain (P<0.05).

Discussion: We had speculated that different induced hypotensive regimens with unique cerebral vascular effects, would have variable influences in the periphery of a region of focal ischemia. For instance, we theorized that the vasodilatory effect of nitroprusside and isoflurane would improve flow in the ischemic periphery, and that the sympathetic activation associated with hypovolemia would result in an extension of the zero blood flow area.⁽⁴⁾ Our data do not support these hypotheses, and appear inconsistent with previous studies of induced hypotension.⁽⁵⁾ However, a major difference was present in the present study, as the hypotension occurred in the context of focal rather than global ischemia. Our study raises the possibility that data obtained in studies of global ischemia should not be extrapolated to focal ischemic circumstances where 'steals' and other undefined phenomena may be operative. If evaluation of the area of zero flow is relevant, further investigation in this model is warranted to determine differences in the low flow (penumbral) zone. In addition treatment regimens to reverse focal cerebral ischemia should be evaluated.

	<u>Zero Flow Area, %</u>
Nitroprusside	11.6 ±0.4
Isoflurane	10.7 ±1.7
Hypovolemic	10.1 ±2.0

Table 1-Zero Flow Area (mean ±SD). Value is the area of zero flow as a percent of the total brain evaluated. There was no difference between groups (P<0.05).

References:

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