Title: Effect of Esmolol on Cerebral Blood Flow During Intracranial Hypertension and Hemorrhagic Hypovolemia.

Authors: L. Bunegin, B.S., M.S. Albin, M.D., and E. F. Gelineau, B.S.

Affiliation: Neuroanesthesia Laboratory, Department of Anesthesiology, University of Texas Health Science Center at San Antonio, 7703 Floyd Curl Drive, San Antonio, Texas 78284-7838

Introduction: Arterial hypertension can be hazardous to the brain in the face of decreased intracranial compliance and imminent hemorrhage in the case of neurovascular pathology. Anti- hypertensive agents in themselves may be hazardous to cerebrovascular homeostasis because precipitous drops in cerebral perfusion pressure below autoregulatory levels may enhance the possibility of developing cerebral ischemia. Because of its selectivity as a Beta-1 adrenergic receptor blocker and its ultrashort acting potency (half life 9 min.), Esmolol Hydrochloride may have significant advantages over other agents used to lower arterial pressure in the face of a compromised cerebral circulation. This study describes the effects of Esmolol Hydrochloride on cerebral hemodynamics in normal and low compliant brains.

Methods: Following a protocol previously approved by the Laboratory Animal Care Committee, twenty dogs weighing 18 to 25 kg were anesthetized with an intravenous dose of 25mg/kg Pentobarbital with additional doses of 5mg/kg provided for maintenance as needed. The animals were intubated and ventilated to maintain normoxia and normocarbia. A balanced electrolyte solution was administered IV at a rate of 3ml/kg/hr. Arterial and left ventricular lines were inserted through the femoral arteries and a Swan- Ganz catheter inserted through the external jugular vein. ECG and heart rate as well as arterial, right atrial, pulmonary artery, and intracranial pressure via the cisterna magna were monitored continuously. Blood gases, electrolytes, hematocrits, cardiac output and pulmonary capillary wedge pressures were also measured. CBF was measured by injecting 15u radioactive microspheres (57Co, 113Sn, 103Ru, 46Sc) into the left ventricle via the left ventricular catheter. The experimental animals were divided into four groups of 5 animals each.
Group I and III animals were maintained at normotension with ICP being normal in Group I and elevated to 30mmHg by an epidural balloon in Group III. After a stabilization period of one hour, 500mcg/kg-/min of Esmolol was infused intravenously for one hour. In Groups II and IV, the animals were bled to a mean arterial pressure of 50mmHg with the volume of shed blood returned after a half hour delay using 6% Hetastarch. After half this volume was infused, 500mcg/kg/min of Esmolol was given IV for one hour. Group II animals had normal ICP and in Group IV the ICP was elevated to 30mmHg by an epidural balloon for one hour prior to hemorrhage. Data was collected just prior to infusion, 30 and 60 min after the start of infusion of Esmolol. Significance between intragroup parameters were determined by a paired t-test with alpha splitting.

Results: Arterial blood gases remain within normal limits in all groups for all time periods. Heart rates for all groups at all time periods showed a statistically significant decrease following Esmolol infusion. Arterial pressure and cerebral perfussion pressure were significantly ($P<0.05$) reduced in Group I and at 60' after Esmolol infusion in Group IV. These parameters were not statistically significant. Cardiac output, pulmonary artery and pulmonary capillary wedge pressures showed no significant alterations in any of the groups following Esmolol. Sixty min after Esmolol infusion was initiated, CBF in Group IV was reduced by 80% $P<0.05$, in addition to a 70% decline in hematocrit.

Discussion: During intra and post operative neurovascular procedures, the brain may not tolerate blood pressure fluctuations above the upper limits of autoregulation. Currently available agents for blocking acute arterial hypertension surges make rapid reversal of the block difficult when faced with deteriorating hemodynamic conditions. Esmolol as an utrashort highly selective Beta-1 blocking agent appears to provide adequate blockade without significant alteration of cerebrovascular dynamics in either the normal or low compliant brain under normal cardiovascular conditions, and a normally compliant brain under hemorrhagic hypovolemia. However, the steady decline in CBF during Esmolol infusion under hemorrhagic hypovolemia and low intracranial compliance appears to be related to the decline in perfusion pressure suggesting a possible impairment of autoregulation.