Title : EFFECTS OF KETAMINE ON REGIONAL CEREBRAL BLOOD FLOW IN THE ASPHYXIATED FETUS

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Introduction. Fetal asphyxia is a common cause of neurological damage in the newborn infant. The normal adaptive response of the fetus to hypoxemia is to increase cerebral blood flow by elevating perfusion pressure[1]. During asphyxia fetal cerebral blood flow increases dramatically with maximal cerebral vasodilatation to maintain normal oxygen delivery to the brain. There is no evidence of autoregulation during asphyxia[2]. Previous studies have shown that barbiturates and inhalation anesthetics administered to maternal animals reduce fetal cerebral perfusion by decreasing fetal blood pressure during asphyxia. For these reasons we decided to study the effects of ketamine anesthesia on fetal blood pressure and cerebral blood flow (CBF) in the asphyxiated fetus.

Methods. Under halothane-oxygen anesthesia 8 near-term fetal lambs were prepared by insertion of:

1. Femoral arterial catheter for monitoring fetal blood pressure.
2. Axillary artery catheter for monitoring fetal blood gases and sampling microspheres in CBF measurements.
3. Femoral venous catheter for injection microspheres.
4. Maternal arterial and venous catheter for monitoring blood gases, blood pressure and injection of drugs.
5. Umbilical cord occlusion loop for producing partial fetal asphyxia.

Following surgery both mother and fetus were allowed 24 hours to recover before any study was performed.

On the day of a study, fetal pH was reduced to 7.05-7.15 by slow incremental inflation of the umbilical cord occlusion loop. Blood flow to the cerebral cortex, brain stem, cerebellum and basal ganglia were determined using the radioactive microsphere technique. Ketamine 2 mg/kg or 4 mg/kg was then administered to the mother and CBF measurements repeated. When the animal had recovered from the initial dose of ketamine, the other dose of ketamine was administered and CBF measurements repeated. Fetal blood pressure was monitored continuously and blood gases measured intermittently throughout the study.

Results. The onset of asphyxia resulted in a slight increase in fetal blood pressure and heart rate, while fetal base deficit and oxygen saturation decreased dramatically. Both the 2 and 4 mg/kg doses of ketamine did not significantly change these variables from the asphyxiated state (Table 1).

The 2 mg/kg dose of ketamine maintained regional cerebral blood flow (rCBF) at near asphyxial levels. The 4 mg/kg dose produced a profound decrease in rCBF in all 4 regions of the brain studied (Table 2).

TABLE I

FETAL VITAL SIGNS AND ARTERIAL BLOOD GASES (±S.E.)

	Control	Asphyxia	Ketamine 2mg/Kg	Ketamine 4mg/Kg
$\overline{BP}$	64 ±3	71 ±5	*66 ±6	*64 ±7
HR	144 ±12	186 ±19	199 ±23	187 ±22
pH (units)	7.39 ±.03	**7.09 ±.03	**7.08 ±.01	**7.03 ±.03
BE (mEq/l)	-1.5 ±1.5	**-15.9 ±1.2	**-16.5 ±.07	**-16.7 ±2.1
SaO_2 (%)	43 ±5	**21 ±2	**19 ± 2	**18 ±4

*Significantly reduced from asphyxia

**Significantly reduced from control

TABLE 2

FETAL REGIONAL CEREBRAL BLOOD FLOW (ml/100gm/min) (±S.E.)

Region	Asphyxia	Ketamine 2mg/Kg	% Change	Ketamine 4mg/Kg*	% Change
Cerebral Cortex	178±34	166±33	-6	121±31	-34
Cerebellum	264±31	261±40	-3	195±39	-31
Brain Stem	408±74	356±66	-13	252±60	-41
Basal Ganglia	347±69	325±72	-12	220±52	-39

*All cerebral blood flow values after 4mg/Kg significantly reduced from asphyxial levels.

Discussion. Following the 2 mg/kg dose of ketamine rCBF was maintained in the asphyxiated fetus, while the 4 mg/kg dose was associated with a reduction in flow despite maintenance of fetal blood pressure. This likely indicated cerebral vasoconstriction occurred with the higher dose of ketamine but not with the lower dose. Since the asphyxiated fetus depends on a high CBF to maintain oxygen delivery, low dose ketamine may be indicated as an induction agent in the presence of fetal asphyxia. High dose ketamine would obviously be detrimental. In addition ketamine may increase cerebral metabolic rate, so that although flow is maintained, oxygen delivery may not meet demand with cerebral hypoxia the result.

References.

1. Lou HC, et al: Impaired autoregulation of cerebral blood flow in the distressed newborn infant. J Ped 94:118-21,1979

2. Johnson G, et al: Regional cerebral blood flow changes during severe fetal asphyxia. Am J Obstet Gynecol In Press 1979