Title: EFFECT OF HYPOGLYCEMIA ON CEREBRAL METABOLISM AND CEREBROVASCULAR RESPONSIVITY

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Introduction. Numerous studies have shown the adverse effects which alterations in blood glucose levels may have on the brain during ischemia.[1] However, these results are difficult to interpret because the effects that blood glucose levels may have on cerebral blood flow (CBF) and metabolism reactivity have not been fully delineated. This study examined the effect of hypoglycemia(HG), on cerebral metabolism and cerebrovascular reactivity to carbon dioxide.

Methods. Male dogs (15-25Kg) were anesthetized with pentobarbital (30 mg/kg, iv), intubated and ventilated. Mean vascular pressures (mm HG) were measured in the intrathoracic aorta (MABP) and sagittal sinus (SSP). CBF (ml/min/100g) was determined by the radiolabeled microsphere technique. Cerebral O_2 uptake ($CMRO_2$, ml O_2/min/100g) was calculated using the arterial-sagittal sinus O_2 content difference times CBF. The fraction of oxygen extracted by the cerebrum (E) was calculated as the arterial-sagittal sinus O_2 content difference divided by the arterial O_2 content. Cerebral glucose, lactate, pyruvate, acetoacetate and beta-hydroxybutyrate uptakes were calculated using the respective metabolite concentrations measured in arterial and sagittal sinus blood samples. Bilateral electroencephalographic (EEG) readings were recorded throughout each experiment. HG was induced with insulin to obtain a blood glucose < 30 mg/dl. Animals underwent 2 successive hyper- or hypocapnic challenges. Hypercapnia was studied in 10 animals (3 control, 7 HG) by increasing $PaCO_2$ from control (35±4; X±SEM) to 54±2 mmHg by ventilating the animal for 10 minutes with a 5% CO_2-air gas mixture in normoglycemic (NG) and HG situations. Hypocapnia was studied in 11 animals (3 control, 8 HG) by decreasing $PaCO_2$ from control (39±1) to 14±1mmHg by 10 minutes of hyperventilation with air in NG and HG situations. In both groups, HG was induced after the first respective CO_2 alteration. Measurements were taken after reaching steady state $PaCO_2$ in both groups at each control and altered $PaCO_2$ states.

Results. Blood glucose was decreased from 87±6 to 29±3 mg/dl in the hypercapnic, HG group. CBF increased with hypercapnia to 175% of control in both NG and HG. (fig. 1) EEG slowing occurred in 3 out of 7 hypercapnic, HG animals. E decreased from .46±.04 to .29±.001 during control and hypercapnia, respectively and there were no changes in $CMRO_2$. In the HG, hypocapnic group, blood glucose was decreased from 71±2 to 20±2mg/dl during the control and HG situations, respectively. CBF decreased with hypocapnia to 62±5% in NG animals but remained at control (100±4) in HG animals. (Fig. 1) E increased from .39±.02 to .60±.04 during NG, but did not change with HG. There were no alterations in $CMRO_2$. A flat line EEG occurred in all HG hypocapnic animals. No changes occurred in uptake of other cerebral metabolite measured in any group.

Discussion. This study sustantiates previous work showing an intact CBF hypercapnic response during HG.[2] Thus, increased CO_2 tensions should improve oxygen and glucose delivery to the brain during hypoglycemia. However, in this dog model, the brain may be harmed by the interaction of HG and hypocapnia. This combination causes an attenuation of the cerebrovascular response to hypocapnia and severe disturbance in EEG. The EEG flattening without alterations in $CMRO_2$ or E is a similar finding to the rat hypoglycemia model where cerebral metabolism did not decrease until 15 minutes after the production of hypoglycemic coma.[3] However, in maintaining the level of cerebral metabolism, vasoconstriction does not occur and the neurophysiologic state is altered.

References.

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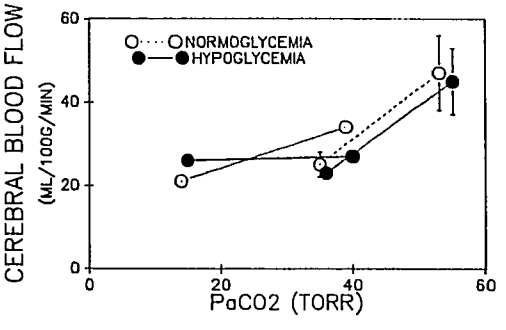

FIG. 1

Effect of $PaCO_2$ on cerebral blood flow in normo- and hypoglycemia