Letters to the Editor

Effect of Hyperglycemia on Infarct Size After Cerebrovascular Occlusion in Cats

To the Editor,

The recent paper, “Hyperglycemia Decreases Acute Neuronal Ischemic Changes After Middle Cerebral Artery Occlusion in Cats,” merits discussion since its results directly contradict the findings of our previously reported study. The findings of the two studies were opposite, that is, hyperglycemic compared to normoglycemic middle cerebral artery (MCA) occlusion resulted in significantly less damage in Zasslow’s study, while in ours it resulted in more.

The morphometric methods used by the two studies to assess ischemic tissue damage differed. Thus, Zasslow et al determined the percentage of acute (6-hour) cortical ischemic tissue changes as evaluated from a single coronal brain section, while de Courten-Myers et al determined the percentage of the MCA territory that was infarcted in animals after 2 weeks of survival as assessed from six representative coronal sections throughout the brain. Although the former method ignores white matter and basal ganglia involvement and depicts only two-dimensional cortical damage, our testing of the relation between extents of cortical infarct at the midchiasma level (as percentage of cortex present at that level) and three-dimensional infarct measurements (as percentage of hemisphere volume) in 25 cats shows the two to be highly correlated (r = 0.93, p < 0.001). Thus, differences in morphometric methods seem not to explain the differences in results.

Perhaps the reason for the discrepancy in results between the two studies is brain pathologic assessment following markedly different durations of survival after blood vessel occlusion. Zasslow et al sacrificed their animals after 6 hours compared to our 2 weeks. However, another study has demonstrated that restoring blood flow by clip release after 4 hours of MCA occlusion leads to a markedly different outcome from permanent occlusion. About one half of hyperglycemic and 92% of normoglycemic cats showed no or minimal infarcts (<1/30 the mean infarct size after permanent occlusion), while 54% and 8%, respectively, died acutely after clip release from total territory infarction, hemispheric edema, and brain stem compression. The death rate from edema increased significantly over that following permanent occlusion. Thus, defining cortical morphologic changes as early as 6 hours after occlusion seems not to differentiate reliably reversible from irreversible damage. It follows that Zasslow’s study fails to demonstrate that elevated serum glucose concentrations confer a lasting protective effect in focal ischemia.

Yet even if not indicative of permanent tissue damage, Zasslow’s study demonstrated less acute morphologic alterations in animals receiving 50% glucose infusion throughout the 6 hours of MCA occlusion compared to animals receiving hypotonic (0.45%) saline. Because a 50% glucose solution is about 9X higher in its osmolality (2,780 mosm/l) than plasma, the infusion of such a hypertonic solution may have temporarily reduced brain edema—a major component of acute tissue change.

When comparing osmotic stimulation, the two studies differ markedly. Zasslow et al administered 155 mosm/kg body wt over 6 hours and 5 minutes, while we administered only 23 mosm/kg over 7 hours. Because hyperglycemia’s detrimental effects on markedly ischemic brains can be identified only after more prolonged survival, the extent of acute morphologic changes, the appearance of which may be reduced osmotically, are probably irrelevant and, in themselves, fail to support the view that hyperglycemia acts protectively. We therefore strongly disagree with the authors’ conclusion that insufficient data are available to restrict the administration of glucose solutions during neurosurgical procedures.

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References

The following is in response:

To the Editor:

We appreciate the comments of Drs. de Courten-Myers, Myers, and Wagner regarding our recent paper. They appropriately point out that the results of our study showing that hyperglycemia may protect against focal ischemic damage are not in agreement with their findings that hyperglycemia increases infarct size. There are several methodological differences between these studies that may account for these discrepant results.

The postocclusion survival duration was 6 hours in our experiment, compared with 2 weeks in the study by de Courten-Myers et al. We did not attempt to draw any conclusions concerning the effect of hyperglycemia on late histopathological changes or functional impairment from our study. In the study by de Courten-Myers et al, it is possible that delayed abnormalities in systemic variables (after termination of the 8-hour monitoring period) influenced the final infarct size with a preferential adverse effect in the hyperglycemic animals. Furthermore, differences between the two studies in anesthetic technique (halothane vs. pentobarbital), core body temperature (37.2°C vs. 38.2°C), brain temperature (unmeasured in these studies), strains of cat, and serum glucose levels (561 mg/dl vs. 360 mg/dl) may also have contributed to differences in outcome for the hyperglycemic animals by influencing the degree of ischemia or offering protection in the ischemic penumbra.

Consistent with our results, other groups have also demonstrated a decrease in cerebral infarction with hyperglycemia. We continue to suggest that unequivocal recommendations regarding administration of glucose solutions in clinical settings cannot yet be made.

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