Plasma Cortisol as a Measure of Stress Response in Acute Stroke

To the Editor:

Mulley et al¹ suggest that hyperglycemia following stroke is an epiphenomenon reflecting a stress response and may not independently predict outcome. I would argue to the contrary that hyperglycemia in the acute phase of stroke indicates an underlying diabetic state, which makes the outcome worse in these patients.

We can diagnose diabetes (i.e., a patient has sustained abnormal levels of blood glucose over weeks or months) by measuring glucose binding to the hemoglobin A molecule. Of the three major glycosylation sites, HbAla, HbAlb, and HbAlc, the fraction of the latter predominates. HbAlb sites are a possible source of error in the diagnosis of diabetes, which can be avoided by utilizing an isoelectric focusing chromatographic technique. This technique eliminates elevated glycosylated fractions produced by transient blood glucose elevations such as the short duration “stress” effects of hyperglycemia.

An earlier study of patients with acute myocardial infarction showed a highly significant correlation between glycosylated HbAlc measurements and frankly diabetic glucose tolerance tests obtained 3 months later.² Using the isoelectric focusing technique, we studied glycosylated HbAlc levels in 100 consecutive acute stroke admissions³ and demonstrated a highly significant correlation between the random blood sugar and the HbAlc value (p<0.0001). This result strongly supports the existence of diabetic glucose levels for several weeks before the stroke and not acutely in the days surrounding the event.

Of those patients with HbAlc values in the clearly diabetic range, 27% had not been previously diagnosed with the condition and 64% died within the first week, compared with 16% of the nondiabetic group (p<0.001). The stroke scores and demographic profiles of the two groups showed no statistically significant differences. Therefore, the poorer prognosis of the high blood sugar group was more likely to depend on premorbid diabetic state than on stroke severity. This result led us to speculate that HbAlc measured by isoelectric focusing could be a useful predictor of stress response and that a measurement of 7.8% or above indicates a diabetic state that may not have been diagnosed previously.

We respectfully suggest that the concept of stress hyperglycemia has outlived its usefulness.

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References

Animal Models in Stroke

To the Editor:

In a recent editorial, Wiebers et al¹ noted the failure of several pharmacologic studies to translate from the experimental cerebral ischemia model to the clinical setting. The authors suggested that deficiencies in current animal models of stroke were primarily responsible for these shortcomings. In our view, a principal and obvious deficiency in most current stroke models is that they rely on mechanical occlusion of brain arteries and therefore do not simulate the clinical condition of this disease. To model stroke per se requires the induction of thrombotic occlusions at suitable arterial sites, resulting in the generation of cerebral infarction.

Over the past several years, we have developed models of photochemically induced vascular thrombosis for the purpose of investigating the consequences of thrombotic stroke on brain structure and function.²⁻⁴ These studies have shown that thrombotic events in cerebral vessels produce not only cerebral infarction, but also widespread hemodynamic, metabolic, and structural abnormalities, which may be absent in more conventional infarct models yet potentially important in terms of stroke outcome. For example, we have shown that thrombosis of the common carotid artery releases circulating humoral factors, which acutely alter cerebral vascular permeability and blood flow at remote sites.⁵⁻⁷ These findings have recently been duplicated for the case of heat-mediated arterial thrombosis (photocoagulation), further indicating that thrombosis per se is involved intrinsically in generating remote consequences (unpublished observations). In a recent pharmacologic study, the remote hemodynamic consequences of acute cortical thrombotic infarction were inhibited without affecting infarct size.⁸ Thus, although the size of a pathological lesion is an important indicator of stroke outcome, we also need functional and behavioral probes to assess pharmacologic trials adequately.⁹

Finally, recent data demonstrate that ischemic brain injury may be enhanced when ischemia is induced by arterial thrombosis, in comparison to ischemia induced by mechanical arterial occlusion.¹⁰¹¹ Our findings also suggest that the temporal profile of neuronal and vascular injury may be different from that induced by ischemia alone and may help explain the current clinical inadequacy of drugs found to be protective in animal models. We therefore believe it useful to call attention to these experimental findings, inasmuch as this work demonstrates the consequences of a methodology that was invented to simulate stroke directly, thereby facilitating a direct approach to developing strategies to alleviate this widespread clinical problem.

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