MANAGEMENT OF HYPERGLYCEMIA AND HYPERTENSION IN ACUTE STROKE

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Hyperglycemia: Hyperglycemia in acute stroke has been related to increased morbidity and mortality in numerous studies. Hyperglycemia as early as 3 hours after stroke onset is associated with poor outcome (1). However, blood glucose increases following stroke and this increase relates to stroke severity(2), as also found in animal models (3;4). Hyperglycemia is associated with a worse prognosis in rt-PA treated patients (5;6).

Hyperglycemia may reflect a stress response to stroke (7;8) or it may independently contribute to stroke outcome by inducing secondary brain damage (9;10). These two hypotheses are not mutually exclusive. Since blood glucose increases more in severe stroke, late blood glucose measurements will show higher blood glucose values in patients with severe stroke who are most likely to have unfavorable outcome. However, already before arriving in hospital, the severity of the cerebrovascular event seems to have influenced the level of blood glucose (2). We found that blood glucose on admission within 6 hours was highest in those who died within 7 days and in those with more severe stroke as measured by the Scandinavian Stroke Scale. Further, blood glucose increased in the following 12 hours and the increase was higher in patients with the more severe cerebrovascular events. Blood glucose also increased in TIA patients. Serial measurements have shown a temporal profile where the early hyperglycemia is followed by a decrease at 14-16 h poststroke (11).

In the GIST trial (12), 933 patients with admission plasma glucose 6.1 – 17.0 mMol/L within 24 hours of stroke onset were randomized to receive glucose/potassium/insulin (GKI) infusions or placebo. Mean age of patients was 75 years and mean time from onset to randomization was 13h 53 mins. Baseline plasma glucose was 8.38 mMol/L in the GKI group and 8.17 mMol/L in the control group. A significant lowering of plasma glucose was achieved in the treatment group, but glucose also fell in the control group resulting in a mean difference of 0.57 mmol/L, p> 0.0001. Systolic blood pressure decreased in both groups, more so in the insulin group with a mean difference of 9 mm Hg. No differences were observed in mortality or avoidance of disability. Modified Rankin Scale was equal in the two groups at follow-up at 3 months.

The results of the GIST trial question that hyperglycemia directly affects outcome in acute stroke. However, several points of criticism have been raised against this study: The trial was terminated early, recruitment into the trial was slow, the inclusion window of 24 hours after stroke onset was too wide. The infusion period of 24 hours was too short, the mean glucose level between the control and the treatment group was small. Therefore, new studies in patients with higher blood glucose values treated earlier after stroke onset for longer periods will be relevant. Until then the guidelines (13,14) recommending start of insulin treatment, when blood glucose is ≥ 10 mmol/L can be maintained.

Hypertension: In acute stroke 50% - 70% of patients have hypertension on admission with systolic blood pressures above 140 mmHg. With serial measurements of blood pressure over the first 6-10 hours after admission blood pressure will decrease spontaneously in the majority (15). The spontaneous decrease of blood pressure is most pronounced in patients with mild stroke, whereas blood pressure often remains elevated in patients with severe stroke. In observational studies it has been shown that systolic blood pressure in the range of 140 – 180 mmHg is associated with better outcomes than lower or higher levels (16). The reason could be that a low blood pressure could lead to a decreased perfusion of the ischemic border zone while a high blood pressure could promote cerebral oedema and also lead to cardiac complications. The ACCESS study (17) suggested a beneficial effect of the angioyensin receptor blocker Candesartan in the acute phase of stroke, although it did not reduce the blood pressure significantly. An ongoing study: Scandinavian Candesartan Acute Stroke Trial will further explore this in a larger sample.

In spite of paucity of evidence, guidelines (13,14) recommend antihypertensive treatment in the acute setting of stroke in patients scheduled for thrombolysis if blood pressure is above 185/110 mmHg. If thrombolysis is not indicated antihypertensive treatment is recommended when blood pressure is above 220/110 mm Hg. If treatment is not urgently indicated as in thrombolysis, patients should be closely monitored to observe if a spontaneous fall in blood pressure occurs.

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