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Influence of hyperglycaemia on stroke outcomes

It is well recognised that hyperglycaemia in individuals who are previously known to have diabetes, or stress hyperglycaemia in those who are not known to have diabetes, translates into increased mortality and morbidity subsequent to acute coronary syndromes. Likewise, it has been suggested that admission hyperglycaemia may well produce a deterioration in outcome following ischaemic origin stroke (Capes et al, 2001; Diener et al, 2008; Stead et al, 2009). The majority of these previous studies have involved small numbers of individuals with stroke, a mixture of haemorrhagic and ischaemic strokes, and some who have not received thrombolytic therapy.

As expected, baseline hyperglycaemia with stroke is more common in individuals with pre-existing diabetes, but is also noted to be present in significant proportions of people without diabetes. A causal relationship between hyperglycaemia and a reduction in outcomes has, however, not been definitively proven. Indeed, the question arises as to whether hyperglycaemia is a parallel phenomenon of underlying stroke severity, or whether the hyperglycaemia itself is directly deleterious to ischaemic brain tissue. Additional explanations may also need to be considered, such as that hyperglycaemia is purely a stress response with increasing cortisol and catecholamine levels. Alternatively, the hyperglycaemia may simply reflect previously undiagnosed diabetes.

There are, of course, a variety of basic pathophysiological processes that would account for the relationship between hyperglycaemia and increased brain injury. More recent studies suggest that the severity of stroke, subsequent to correction for other confounding parameters, may well increase with rising baseline glucose values (Diener et al, 2008). While many previous studies have evaluated individuals without thrombolysis, the studies in those who have received thrombolysis together with stroke have been very small, and have reported outcomes of varying levels (Bruno et al, 2002; Yong and Kaste, 2008; Stead et al, 2009). However, regardless of methodological limitations, most of these studies have suggested an increasing risk of poor outcomes with elevations of glucose levels in thrombolysed individuals. Thus, some of these studies have suggested that regardless of baseline treatment, as baseline glucose levels increase, the odds of a favourable outcome diminish, and the risk of a symptomatic intracerebral haemorrhage increases.

Most recently, a report from the Canadian ALTEPLASE for Stroke Effectiveness Study of 1098 individuals indicated that 27% had admission hyperglycaemia, including 18% of people without diabetes and 70% of those with diabetes (Poppe et al, 2009). Subsequent to multivariable regression analysis, increased risk of death was independently related to the level of admission glycaemia, and likewise a reduction of the probability of a favourable outcome at 90 days. Thus, as baseline glucose values increased in individuals with and without diabetes, there was an incremental risk of death and symptomatic intracerebral haemorrhage. Consequently, in this large study of people who received thrombolytic therapy, admission hyperglycaemia was incrementally associated with an increased risk of either death or intracerebral haemorrhage and poor residual functional status at 90 days. Therefore, while a causal relationship between admission hyperglycaemia and poor outcome after stroke appears to have been established, further trials are required to establish whether such increased risk is modifiable. In the meantime, it would be prudent to include the treatment of hyperglycaemia in stroke patients in current treatment guidelines.

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