Indian J Med Res 141, March 2015, pp 266-268

Commentary

Early neurological deterioration, easy methods to detect it

Early neurological deterioration (END) is defined as the clinical worsening or recurrence during the first 72 h after ischaemic stroke. It is a common complication, although incidence is variable across studies due to differences in the population studied and in the definition of END. The incidence rate ranges between 13-37 per cent of all ischaemic strokes[1]. The consequences of END can be serious, as it is associated with a worse functional outcome measured at three months[2].

By definition, the causes of END are related to the pathophysiology of ischaemic strokes. Alternatively late neurologic deterioration is generally due to systemic causes like infections, metabolic disorders, or other vascular complications. The pathophysiological mechanisms that can produce END may vary between patients and in some cases it is not possible to establish a specific cause. Described mechanisms of END are failure of collateral circulation in patients with critical stenosis or occlusion of a large vessel, either intra- or extra-cranial; progression of thrombosis with consequential increase in the ischaemic area; early recurrence especially in atherothrombotic strokes ; the development of cerebral oedema in patients with large strokes and finally haemorrhagic transformation in patients treated with fibrinolytic drugs[1].

Several studies have focused on the search for predictors of END, and with the result we have been able to acknowledge the influence of a number of variables such as the initial severity measured by the NIHSS stroke scale (severe strokes have an increased risk of END compared with mild strokes); the stroke aetiology (atherothrombotic strokes have a higher risk of recurrence than lacunar or cardioembolic strokes); metabolic factors such as hyperglycaemia on admission, increased urea in plasma, markers of inflammation, excitotoxicity and oxidative stress; haemodynamic factors such as blood pressure at admission (both high and low); radiological data such as the existence of extensive lesions (> 1/3 area of MCA) and the presence of vascular occlusions in the neurovascular study[3-5].

Identifying predictors of END is crucial because early treatment can help to prevent this serious complication. The fundamental measure to prevent END is the admission of patients with acute stroke in a Stroke Unit with comprehensive management by neurologists who are also experts in cerebrovascular diseases. Strokes Units have proved not only to prevent END but to improve the patient's outcome[6]. For this and other reasons the implementation of stroke units in hospitals although seemingly costly has shown to result in a reduction of overall health expenditure.

In this issue Bhatia and colleagues[7] present a new study conducted in New Delhi, India, on the search for predictors of END. This study was focussed on determining the role of relative dehydration measured by two simple parameters *viz*. the blood urea nitrogen (BUN)/creatinine ratio and the urine specific gravity (USG) in the development of END. It is well known that acute stroke patients are at increased risk of dehydration because of multiple factors such as the low level of consciousness, the existence of initial dysphagia and motor problems. In a large study, 36 per cent of patients were dehydrated on the day of admission and 62 per cent were dehydrated at some point during their admission[8]. Dehydration has been shown to be associated with a higher mortality and worse functional outcome after acute ischaemic stroke[8,9]. However, the relationship between baseline dehydration status and the risk of END has not been studied in depth.

In the previous studies the methodology used to measure the dehydration status has been variable[9,10]. Dehydration can be detected with biomarkers of reduced blood water, most commonly using the

BUN/creatinine ratio and plasma osmolality. In the present study[7], dehydration was assessed by the BUN/creatinine ratio in a blood test and USG measured with urine dipsticks at the time of patient's arrival at the hospital and subsequently on days 1, 2, and 3.The study showed that the BUN/creatinine ratio > 15 at arrival was independently associated with the END after adjustment for other clinical predictors, whereas no independent association was found for USG. Patients with BUN/creatinine >15 were almost six times more likely of having END.

END rate in this study[7] was about 22 per cent, which was consistent with previous literature. It was noticed that patients' mean age was lesser than the average age in European stroke study[3]. Moreover, stroke aetiology was also different with higher prevalence of lacunar and atherothrombotic stroke compared to cardioembolic strokes in this Indian cohort. Besides the BUN/creatinine ratio, in multivariate analysis other previously known predictors of END were confirmed, such as the initial severity (NIHSS> 12), the initial glucose and the presence of extensive infarction (hypodensity > 1/3 in the MCA territory) in the basal CT. Bun/creatinine ratio>15 and USG <1.010 have been found to be strong independent predictors of END in previous studies[10,11]. However, USG was not associated with END in the current study probably due to the method used for measurement (urine dipsticks), which is not very reliable, as is also pointed out by the authors[7].

The mechanisms why dehydration would be associated with an increased risk of END are many. On one hand, it would increase blood viscosity with higher likelihood of expanding initial thrombosis and on the other hand, it could decrease blood pressure with higher risk of collateral circulation failure[9].

Though this study by Bhatia *et al*[7] had some limitations, mainly the size of the cohort (n=114), this study was well designed and developed. The confirmation of previous predictors of END like the stroke severity or radiological data, indicates the reliability of results. The merit of this study is the clinical relevance of its results since the measurement of BUN/creatinine ratio is easy and inexpensive and can be performed in any Emergency department. This parameter, along with other simple data like basal glycaemia, initial blood pressure or stroke extension in the basal CT, could help to select those patients at higher risk of END. These patients would benefit from intensive therapeutic measures and longer clinical observation.

International guidelines of acute stroke management clearly establish that the degree of body fluid volume status is important for the prognosis of patients[12]. Hypovolaemia or dehydration should be corrected by the use of intravenous fluids. The goal is to achieve euvolaemia since hypervolemia can have damaging effects such as increasing brain oedema and myocardial stress. The work conducted by Bhatia *et al*[7] could help to identify patients who should immediately be put onto endovenous fluid repletion to prevent END and eventually improve their neurological status.

Elisa Cuadrado-Godia
Department of Neurology
Neurovascular Research Group
IMIM-Hospital del Mar (Institut Hospital del Mar d'Investigacions Mèdiques)
Universitat Autonoma de Barcelona/DCEXS-Universitat Pompeu Fabra,
Barcelona 08003, Spain
ECuadrado@parcdesalutmar.cat

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