

Urine-Specific Gravity-Based Hydration Prevents Stroke in Evolution in Patients with Acute Ischemic Stroke

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Background: Early neurological deterioration after ischemic stroke (stroke-in-evolution [SIE]) is associated with poorer outcomes. Previous studies have demonstrated a link between hydration status and the development of SIE. In this study, we tested the hypothesis that rehydration therapy, administered on the basis of urine-specific gravity (USG) findings, might reduce the development of SIE. *Methods:* We conducted a single-arm prospective study of patients with acute ischemic stroke with historical controls. For the study group, a USG higher than 1.010 was taken as an indication for rehydration. Control group patients were rehydrated without referring to USG. An increase in National Institutes of Health Stroke Scale (NIHSS) score of 4 or higher within 3 days was defined as having SIE. *Results:* A total of 445 patients were analyzed, 167 in the study group and 278 in the control group. The proportion of patients who developed SIE was numerically, but not significantly, lower in the study group (5.9%; 10 of 167) compared with the control group (11.5%; 32 of 278). Among patients with a USG higher than 1.010 at admission, the SIE rate was significantly reduced in the study group compared with the control group (6.1% versus 16.0%; $P = .021$), while the rate of SIE was similar in those with a USG of 1.010 or lower at admission. Multivariate logistic regression analysis confirmed that USG-based hydration was an independent factor associated with reducing SIE. *Conclusions:* USG might be a convenient and useful method for guiding fluid therapy in patients with acute ischemic stroke. USG-based hydration reduced the incidence of SIE among patients with a USG higher than 1.010 at admission. **Key Words:** Urine-specific gravity—dehydration—ischemic stroke—therapy—fluid—stroke-in-evolution.

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Introduction

Ischemic stroke is a very common event that is associated with significant morbidity and mortality.¹ One factor known to be linked to poorer outcomes after stroke is early neurological deterioration (stroke-in-evolution [SIE]).^{2,5} Research suggests that up to 40% of patients may experience SIE after ischemic stroke within up to 4 days after the initial event, but typically it occurs within the first 24 hours of hospital admission.^{3,5-7} Clearly, being able to identify patients at risk of experiencing SIE would be of significant benefit for the patient, in terms of clinical outcome, and for reducing the costs associated with medical treatment.

Over the years, numerous factors have been reported to predict SIE/early neurological deterioration among patients who have experienced ischemic stroke.⁸ These factors include stroke severity (as measured using the Canadian Stroke Severity Score and National Institutes of Health Stroke Scale [NIHSS]),^{7,9} hemodynamic factors and perfusion abnormalities,⁸ various biochemical and physiological parameters,^{7,10-14} and medical history.^{3,13} Unfortunately, many of these predictors do not appear to be reliable and are therefore of limited use in the clinical setting.⁸ The lack of consistency/reliability between studies likely reflects differences in study design, participant populations, study eligibility criteria, and, most importantly, the criteria for defining SIE.⁸

The blood urea nitrogen (BUN)/creatinine ratio is a common marker of hydration status. The normal ratio is approximately 10:1,¹⁵ which is raised if there is dehydration.¹⁵⁻¹⁸ We previously reported that a BUN/creatinine ratio higher than 15 was an independent predictor of SIE.¹⁴ Furthermore, Schrock et al reported that a BUN/creatinine ratio of 15 or higher was associated with significantly poorer outcomes 30 days after ischemic stroke.¹⁹ These findings are of interest given that dehydration is a critical issue with regard to the acute phase of ischemic stroke. In another study, we also found that a urine-specific gravity (USG), another indicator of hydration status,²⁰ higher than 1.010 was associated with the development of SIE after ischemic stroke.²¹ Given the evidence that hydration status after ischemic stroke may be associated with SIE, we hypothesized that USG-based hydration therapy might reduce the development of SIE. This study was carried out to test this hypothesis.

Methods

Study Design

This was a single-arm prospective study with historical controls that was conducted at Chang Gung Memorial Hospital (Chiayi, Taiwan). The study group comprised patients who received hydration on the basis of USG findings, whereas the historical control group comprised patients who received standard hydration on the basis

of their physical examination findings. The study protocol was approved by the Institutional Review Board of Chang Gung Memorial Hospital. All patients provided written informed consent.

Patients

Patients were eligible for inclusion in the study if they were hospitalized in the Emergency Department (ED) of Chang-Gung Memorial Hospital between August 2010 and September 2013 (study group) or between October 2007 and June 2010 (control group), and the time between the onset of neurological symptoms and presentation was less than 12 hours.

Patients were excluded from the study if they had received fibrinolytic therapy, an initial NIHSS score of 25 or higher, unilateral or bilateral hydronephrosis, an initial blood creatinine of more than 2 mg/dL, underlying congestive heart failure, or received diuretics. Patients for whom the NIHSS score returned to 0 within 24 hours were classified as having transient ischemic attack (TIA) and were also excluded from the study.

We recruited 200 patients in the study group. Seventeen patients were found not to have ischemic stroke or TIA at discharge. Also, 16 patients were withdrawn from the study; 9 refused further urine testing during admission, and the others requested transfer to another hospital or discharge against medical advice during the first 3 days of admission. Therefore, 167 patients were included in the analysis. A separate group of patients who fulfilled the eligibility criteria from a previously described cohort study¹⁴ were used as a control group.

Study Procedures

All patients underwent a brain computed tomography (CT) scan within 2 hours of being admitted to the ED. During the emergency, the patients were diagnosed by a neurologist according to brain CT and physical examination. After the patient was admitted to the hospital, magnetic resonance imaging (MRI) of the brain was used to confirm the diagnosis. The patients also underwent renal sonography, which was performed and interpreted by a nephrologist to exclude post-renal obstruction.

After admission, urine was collected for analysis during the first 24 hours after stroke on average. Patients' USG findings were immediately forwarded to the attending physician, who prescribed fluids on the basis of these findings. A USG higher than 1.010 was considered to indicate dehydration, and patients were advised to immediately drink water, be fed via nasogastric tube, or receive bolus intravenous fluid support (300 cc normal saline). In the study group, USG was measured daily for the first 3 days. If USG higher than 1.010 was measured, rehydration via the oral or parenteral route was performed. Apart from the rehydration treatment, daily maintenance fluid requirements were adjusted by physicians based on their

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