

# Safety of intravenous administration of hydrogen-enriched fluid in patients with acute cerebral ischemia: initial clinical studies

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## Abstract

**Background:** Most of the results regarding hydrogen (H<sub>2</sub>) therapy for acute cerebral ischemia are derived from in vitro studies and animal experiments, with only a few obtained from human trials with a limited number of subjects. Thus, there is a paucity of information regarding both the beneficial therapeutic effects as well as the side effects of H<sub>2</sub> on acute cerebral ischemia in humans. We designed a pilot study to investigate single dose intravenous H<sub>2</sub>-administration in combination with edaravone, aiming to provide an initial estimate of the possible risks and benefits in select patients presenting with acute ischemic stroke.

**Methods:** An open-label, prospective, non-randomized study of intravenous H<sub>2</sub>-administration was performed in 38 patients hospitalized for acute ischemic stroke. All patients received an H<sub>2</sub>-enriched intravenous solution in addition to edaravone immediately after the diagnosis of acute ischemic stroke. Acute stroke patients within 3 h of onset received intravenous tissue plasminogen activator (t-PA) (0.6 mg/kg) treatment, and patients receiving t-PA had to commence the administration of the H<sub>2</sub>-enriched intravenous solution and edaravone before or at the same time as the t-PA was infused.

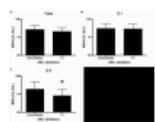
**Results:** Complications were observed in 2 patients (5.3%), which consisted of diarrhea in 1 patient (2.6%) and cardiac failure in 1 patient (2.6%). No deterioration in laboratory tests, urinary tests, ECG, or chest X-ray radiograms occurred in any patient in this study. In all patients, the mean National Institutes of Health Stroke Scale (NIHSS) scores at baseline, and 7, 30, and 90 d after admission were  $8.2 \pm 7.5$ ,  $5.6 \pm 7.1$ ,  $4.9 \pm 6.5$ , and  $4.5 \pm 6.3$ , respectively. The early recanalization was identified in 4 of 11 patients (36.4%) who received intravenous t-PA administration. Hemorrhagic transformation was observed in 2 patients (18.2%). None of the patients in this study that were treated with t-PA developed symptomatic intracranial hemorrhage.

**Conclusions:** Data from the current study indicate that an H<sub>2</sub>-enriched intravenous solution is safe for patients with acute cerebral infarction, including patients treated with t-PA.

**Keywords:** Acute ischemic stroke; Edaravone; Free radical scavenger; Hydrogen; Reactive oxygen species; Safety; Tissue plasminogen activator.

## Figures

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**Figure 1** Changes in the levels of...

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