Paramedic Delivery of Magnesium Does Not Improve Outcomes in Patients With Acute Stroke

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Early intervention is critical in patients with acute stroke, and there is a narrow time frame in which to pursue acute therapies [Saver JL. *Stroke* 2006; Saver JL et al. *JAMA* 2013]. Approximately 35% to 70% of patients with stroke arrive by ambulance. Therefore, prehospital personnel are often the first health care providers to come in contact with these patients [Ekundayo OJ et al. *Circ Cardiovasc Qual Outcomes* 2013]. Jeffrey L. Saver, MD, University of California Los Angeles Stroke Center, Los Angeles, California, USA, presented results from the Field Administration of Stroke Therapy–Magnesium (FAST-MAG) trial, a prehospital, multicenter, randomized, placebo-controlled efficacy study whose aim was to test whether intravenous magnesium sulfate given within 2 hours of symptom onset improves the outcomes of patients with acute stroke. Although the researchers did not show that the administration of prehospital magnesium sulfate improved neurologic outcomes in patients with acute stroke, they did show that it was feasible to test a potential neuroprotective agent within the first 2 hours of stroke onset (with treatment being initiated in 74% of patients £1 hour after symptom onset).

According to Dr. Saver, magnesium sulfate is known to dilate cerebral blood vessels, increase blood flow to the brain, and block calcium buildup in neurons [Kemp PA et al. *Clinic Sci (Lond)* 1993; Alborch et al. *Eur J Pharmacol* 1992]. In animal models, magnesium has demonstrated a modest protective effect against stroke, and it has an established safety record in humans [Muir KW. *CNS Drugs* 2001].

The study involved collaboration among 40 emergency medical service agencies, 315 ambulances, 2988 paramedics, 60 receiving hospitals, 952 participating emergency physicians, and >225 neurologists and neurosurgeons throughout Los Angeles and Orange counties.

The study randomized 1700 patients who were within 2 hours of stroke symptom onset to either a loading dose (4 g over 15 minutes) of magnesium sulfate or matched saline placebo in the ambulance. On arrival at the emergency department, a maintenance infusion (16 g) of magnesium sulfate or matched saline placebo was continued over the next 24 hours.

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Participants had a mean age of 69 years (range, 40-95 years), and 42% were women. The median pretreatment stroke severity score on the Los Angeles Motor Scale was 4. The final diagnosis was cerebral ischemia in 73%, intracerebral hemorrhage in 23%, and stroke mimic in 3.9%. Overall, 74% of patients were treated in the golden hour and 25% in the second hour. Median time to treatment was 48 minutes after symptom onset.

The primary study endpoint was having a modified Rankin Scale score of 0 to 6, measured at 90 days. The study showed no statistically significant difference in the degree of disability on the modified Rankin Scale between the 2 treatment groups. Administration of intravenous magnesium sulfate was a safe intervention, with no increase in bradycardia and mild increases in hypertension and respiratory distress. Overall, there was no increase in serious adverse events.

According to Dr. Saver, the potential reasons for these neutral results may include the facts that magnesium passes across the blood-brain barrier slowly, which delays the impact on the central nervous system, and that magnesium alone may be insufficient to suppress the entire ischemic cascade in this environment.

Although the study failed to meet its primary objective, the FAST-MAG trial resulted in the development of a new prehospital research network, which will allow researchers to test other promising neuroprotective therapies for acute stroke care in the future. This study also demonstrated that it is feasible to initiate potential neuroprotective treatment within the first 2 hours of stroke onset.