Drug lowers high potassium levels associated with potentially lethal cardiac arrhythmias

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Mikhail Kosiborod, M.D., of Saint Luke's Mid America Heart Institute, Kansas City, and colleagues evaluated the efficacy and safety of the drug zirconium cyclosilicate in patients with hyperkalemia (higher than normal potassium levels). The study appears in *JAMA* and is being released to coincide with its presentation at the American Heart Association's Scientific Sessions 2014.

Hyperkalemia is a common electrolyte disorder which can cause potentially life-threatening cardiac arrhythmias and is associated with chronic kidney disease, heart failure, and diabetes mellitus. There is a lack of effective and safe therapies for the management of this disorder in the outpatient setting. Sodium zirconium cyclosilicate (zirconium cyclosilicate) is an agent designed to entrap potassium in the intestine, according to background information in the article. In previous studies, this drug was well tolerated and effective in lowering potassium within 48 hours of administration; for this study, outcomes for 28 days were evaluated.

In this phase 3 trial, ambulatory patients with hyperkalemia (n = 258) received zirconium cyclosilicate three times daily in the initial 48-hour open-label phase. Patients (n = 237) achieving normal potassium levels were then randomized to receive zirconium cyclosilicate, 5 g (n = 45 patients), 10 g (n = 51), or 15 g (n = 56), or placebo (n = 85) daily for 28 days. Patients were recruited from 44 sites in the United States, Australia, and South Africa.

The researchers found that zirconium cyclosilicate was effective both in rapidly lowering potassium to normal range and maintaining normal potassium levels for up to 4 weeks in patients with various degrees of hyperkalemia. The potassium-lowering effect of zirconium cyclosilicate was consistent across all patient subgroups and observed immediately (after 1 hour of the first dose), and normal levels of potassium was achieved in 84 percent of the patients within 24 hours and 98 percent within 48 hours of treatment initiation. Compared with placebo, all three doses of zirconium cyclosilicate resulted in significantly higher proportions of patients with normal potassium levels for up to 28 days. These outcomes occurred with a tolerability profile that was comparable with that of placebo.

"Further studies are needed to evaluate the efficacy and safety of zirconium cyclosilicate beyond 4 weeks and to assess long-term clinical outcomes," the authors write.

Bradley S. Dixon, M.D., of the Veterans Administration Medical Center and the University of Iowa, Iowa City, comments on the findings of this study in an accompanying editorial.

"The findings reported by Kosiborod et al suggest that zirconium cyclosilicate may represent a promising new therapy for the acute and short-term (i.e., 28-day) treatment of outpatients with mild hyperkalemia. However, longer-term studies are needed to assess the clinical benefits and risks that may be related to more extended use of this product, especially among hospitalized patients, as well as those with more severe hyperkalemia, other medical conditions, and other medications that affect potassium [levels]."

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