ジルコニウム環状珪酸塩による高カリウム血症治療 (Abstract 20737)

HARMONIZE：致死的な心臓不整脈に関連する可能性のある高カリウムレベルの低下に薬物が役立つ

HARMONIZE: Drug helps reduce high potassium levels associated with potentially lethal cardiac arrhythmias

ジルコニウム環状珪酸塩はカリウムレベルを急速に正常範囲内に低下させ、様々な程度の高カリウム血症患者の正常カリウムレベルを最長4週間維持することができる、との研究結果が2014年American Heart Association年次集会で発表され、同時に*JAMA*に掲載された。ナトリウムジルコニウム環状珪酸塩（ZS9）は、腸内のカリウムに選択的に結合する非吸収性薬剤である。第III相HARMONIZE臨床試験において、高カリウム血症患者（258人）が初回の48時間オープンラベル相にZS9を1日3回投与された。正常カリウムレベルを達成した患者（237人）がその後、5 g（45人）、10 g（51人）、または15 g（56人）のZS9またはプラセボ（85人）を毎日28日間投与される群にランダムに割り付けられた。ZS9のカリウム低下作用は全ての患者サブグループにおいて一貫しており、迅速に認められた（初回投与後1時間）。84%の患者において24時間以内に、98%の患者において48時間以内に、正常カリウムレベルに達した。プラセボと比較し、3用量全てのZS9の方が、最長28日間にわたり正常カリウム値患者の割合が高かった（全ての比較でp=0.0001）。

Full Text

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. They reported that the drug 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 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 that 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 (ZS9) is a non-absorbable agent that selectively binds 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 the phase III, HyperkAlemia RandoMized interventiON multI-dose ZS-9 maintEnance (HARMONIZE) clinical 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 ZS9, 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 ZS9 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 ZS9 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 (P =0.0001 for all comparisons). Compared with placebo, all three doses of ZS9 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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Cardiology特集
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