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Late Breaking Clinical Trial
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ESC 2025: POTCAST: Increasing potassium level in patients at high risk for ventricular arrhythmias

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Evidence from observational studies suggests that hypokalemia or even low-normal plasma potassium levels increase the risk of ventricular arrhythmias among patients with cardiovascular diseases. The multicenter, open-label, event-driven POTCAST trial tested whether increasing potassium levels in patients at high risk for ventricular arrhythmias would decrease cardiovascular events.

Eligible participants (n=1200; mean age, 62.7 years, 19.8% women) had an ICD or cardiac resynchronization therapy defibrillator and had a baseline plasma potassium ≤4.3 mmol/L. Participants were randomized to a treatment regimen aiming at increasing plasma potassium levels to a high-normal level (4.5–5.0 mmol/L), using dietary guidance, potassium supplements, and/or mineralocorticoid receptor antagonist (MRA) therapy, or to standard care. The trial was conducted at three sites in Denmark.

From mean baseline levels of 4.01 mmol/L, plasma potassium levels dropped to a mean of 4.36 mmol/L in the study arm compared with 4.05 mmol/L in the control arm after 6 months.

During a median follow-up of 39.6 months, there were significantly fewer primary endpoint events (documented sustained ventricular tachycardia or appropriate ICD therapy, unplanned hospitalization of >24 hours for arrhythmia or heart failure, or death from any cause) in the high-normal potassium groups, compared to the standard-care group (22.7% vs. 29.2%; hazard ratio [HR], 0.76; 95% confidence interval [CI], 0.61 to 0.95; p=0.01).

The effect of raising serum potassium was consistent across prespecified subgroups, including those with ischemic heart disease and heart failure and regardless of the method used to increase potassium levels (e.g. supplementation or MRAs).

The difference between groups was primarily driven by a lower incidence of any appropriate ICD therapy (shock therapy or anti-tachycardia pacing) in the high-normal potassium arm (15.3% vs. 20.3% in the control group; HR 0.75; p<0.05). Unplanned hospitalizations for cardiac arrhythmias occurred in 6.7% and 10.7% of study and control participants, respectively (HR, 0.63; p<0.05), and unplanned hospitalizations for heart failure occurred in 3.5% and 5.5%, respectively (HR 0.62; 95% CI 0.37 to 1.11).

All-cause death was seen in 5.7% and 6.8%, respectively (HR, 0.85; 95% CI 0.54 to 1.34).

The incidence of hospitalization for hyperkalemia or hypokalemia was similar in the two groups at about 1% for both outcomes in both groups.

Summary

Among patients with cardiovascular disease who had an ICD and were at high risk for ventricular arrhythmias, increasing potassium levels to “high-normal” reduced the risk of arrhythmias, hospitalization for heart failure or arrhythmia, and death, as compared with no intervention. There were no safety concerns.

“In several landmark heart failure trials, the improvements in cardiovascular outcomes seen with MRAs were accompanied by increases in potassium levels,” noted senior author H Bundgaard in an ESC press release. “The findings of POTCAST lead us to

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speculate that increased potassium levels may, at least partially, be responsible for MRAs' positive outcomes, rather than merely being a side effect. We believe the time is right to consider increasing potassium levels to the mid-to-high normal range as an inexpensive and widely available treatment strategy in patients with a broad spectrum of cardiovascular diseases associated with a high risk of ventricular arrhythmia."

Comments

In his discussion of the trial, Dr. J.C. Nielsen noted that very few patients met the target serum potassium level of 4.5 to 5 mmol/L but given the "impressive" 24% reduction in the primary endpoint, he suggested that the 0.35 mmol/L increase achieved may be sufficient.

Asked whether the results can be extended to other patient groups, Dr. Jons, the principal investigator, noted that in the pre-specified subgroup analysis, no significant difference in the primary endpoint was noted in the subgroups of patients with ischemic heart disease and low left ventricular ejection fraction. "But, with that in mind, I think we can extend it to a great proportion of our cardiovascular patients, and I don't think we can say anything yet about extending beyond cardiovascular."

In a press conference, Dr. Bundgaard, the senior author on the paper, suggested this: "With a broader view, we can say that higher dietary intake of potassium may not only benefit patients with heart diseases, but probably all of us. So, maybe we should all reduce sodium and increase potassium content in our food."

References:

https://pubmed.ncbi.nlm.nih.gov/40879429/