Revisiting Hyperkalemia Guidelines

Rebuttal

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"And don't criticize
What you can't understand"
The Times They Are A-Changin, Bob Dylan

We read the rebuttal to our viewpoint by Bayes-Genis and colleagues with great interest. We agree on the facts. The issue at hand is what action to take given the data available today. Bayes-Genis et al give four reasons as to why there is no need to change current guidelines. We respectfully argue that these arguments, while scholarly, do not obviate the need for reassessing guidelines.

1. We agree that revising guidelines may risk sub-optimal prescription of renin-angiotensin-aldosterone system inhibitors (RAASi). We also agree that a large part of RAASi suboptimal use is driven by high-risk patient characteristics for adverse effects. But isn't this a reason to revise guidelines to safeguard patients at high-risk for adverse effect to a given therapy?
2. We agree that the causal relationship between the U-shape serum potassium concentration and outcomes is not well understood. Obviously *hypokalemia* should be avoided, but that is not a reason to not revise *hyperkalemia* guidelines. We explicitly state that the risk association between potassium levels and adverse outcomes is a combination of patient phenotype and comorbidity burden, lack of optimal medical therapy due to hyperkalemia, and risk directly attributable to hyperkalemia. We need to elucidate these associations and their causal relationships better, but should we not be focus on patient safety while such research is being conducted when in the meantime study after study is raising concerns, granted they are observational?

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3. We agree with the erudite recap of the effect of valsartan-sacubitril on risk of hyperkalemia. Less risk of hyperkalemia with this drug is a welcome addition to heart failure therapies that may help optimization of mineralocorticoid receptor antagonists (MRA) use. However, this issue is not relevant to our concern, i.e. how to proceed once you do develop hyperkalemia.
4. We completely agree that we need outcomes studies with novel potassium binders, however, while we await such data, how do we address patient risk today?

Clinicians face management conundrums daily where there are risks in both action and inaction, and the guide in such scenarios is to lean in favor of patient safety. If serum potassium concentration between 5.0-5.5 mmol/l was not of clinical concern, then it is curious to note that uniformly all clinical trials in heart failure with RASSi uniformly excluded patients with baseline serum potassium concentration of >5.0 mmol/l. We suggest that patients not on an MRA maintain their serum potassium to < 5.0 mmol/l. We also appreciate that patients who develop hyperkalemia on MRA therapy nevertheless benefit from MRA, and therefore until further prospective data with potassium binders become available, MRA perhaps should be continued for patient with serum potassium concentration up to 5.5 mmol/l (1, 2). However, even in these studies, while there was a relative risk reduction, the risk for adverse outcomes was higher in those with higher serum potassium concentration even in the presence of MRA therapy. Also, the trajectory of potassium changes once hyperkalemia developed in given individuals is not known from these studies.

We appreciate the potential for sub-optimal medical therapy due to hyperkalemia and urge investigators and sponsors to conduct clinical trials with potassium binders to guide optimization of therapy to reduce cardiovascular risk compared to current approaches as soon as possible. However, until we better understand the relationship between elevated serum potassium levels and outcomes, we recommend erring on the side of caution.

Primum non nocere!

Reference

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