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The Reply

We thank Rokutan for his interest in our systematic review.[1] We do agree that the inclusion of case reports of adverse events in systematic reviews hampers the finding of a true causal relationship between a drug and such events. However, for rare adverse events, case reviews may be the only information available.

As Rokutan points out, we did demonstrate that the appearance of symptoms in patients receiving sodium polystyrene sulfonate with sorbitol was shorter than those receiving sodium polystyrene sulfonate alone. This difference may have been imparted by differences in the case mix of the patients receiving each type of therapy. Furthermore, his mention of the study conducted by Lillemoe et al,[2] which demonstrated that sodium polystyrene sulfonate administration alone did not cause any significant pathologic change in rats, does not lend credence to the argument that sodium polystyrene sulfonate itself may not lead to colonic injury because that study was based on an animal model, and thus may not translate into "real-world" situations.

Finally, our systematic review was comprehensive and performed following the guidelines of the Meta-analysis of Observational Studies in Epidemiology.[3] It encompassed the full scope of the literature on gastrointestinal adverse events associated with sodium polystyrene sulfonate use. To strengthen our findings, we attempted to determine a causal relationship between sodium polystyrene sulfonate use and gastrointestinal adverse events using a validated assessment tool, the World Health Organization-Uppsala Monitoring Centre causality assessment system. By using this system, we were only able to categorize all studies into the "possible" rank for causality, because criteria for a "certain" or "probable/likely" causal relationship could not be met because information on the response to withdrawal of sodium polystyrene sulfonate was not described, nor was the effect of rechallenging patients with sodium polystyrene sulfonate for any case. Despite this limitation, we believe we cannot discount the possible role of sodium polystyrene sulfonate in gastrointestinal adverse events because the aforementioned criteria would be difficult to meet from a clinical point of view given the possible catastrophic side effects of sodium polystyrene sulfonate use. Specifically, it would not be advisable to rechallenge a patient with sodium polystyrene sulfonate after the patient has experienced a serious adverse event thought to be related to its use.

In the absence of a randomized control trial adequately powered to detect adverse events related to sodium polystyrene sulfonate use, observational designs offer the best assessment of risk. Given that such designs are prone to bias and confounding, it is not possible to prove a causal relationship with such studies, but rather a correlation. As such, relying on the "unquestionable proof of causality" for adverse events with regard to the decision to use sodium polystyrene sulfonate alone in the management of hyperkalemia is unrealistic. Ultimately, clinicians must be cognizant of the risks associated with sodium polystyrene sulfonate use based on the best available evidence and decide whether use of this therapy is warranted in a particular situation according to its risk-benefit profile.

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