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LETTER TO THE EDITORS

Response to the Letter to the Editor "Preventing heme-induced nephropathy in children with glucose 6 phosphate dehydrogenase deficiency: is there a role for acetazolamide?"

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Dear Editors,

We thank Drs. Qian, Chen, and Chen [1] for their interest and valuable comments on our article entitled "Normal saline, the known but least-examined fluid therapy method for preventing heme-induced nephropathy in children with glucose 6 phosphate dehydrogenase deficiency: a randomized controlled clinical trial" [2]. We are pleased to read their comments regarding our published article, and to provide the following response.

So far, clinical and experimental studies have suggested heme-induced nephropathy occurs due to the combination of renal ischemia and direct tubular epithelial cell toxicity mediated by the generation of reactive oxygen species. It has been shown that the activation of cytokine-induced inflammatory mediators damages proximal tubular cells and this activation is influenced by tissue hypoxia and intracellular medullary acidosis. Therefore, the current study aimed to assess the hypothesis of whether acetazolamide would protect against heme-induced nephropathy due to its carbonic anhydrase inhibitory and cellular energy conservation properties.

As we mentioned, there is a lack of documented randomized clinical trials comparing the efficacy and safety of acetazolamide in the prevention of heme-induced nephropathy due to favism in children with glucose 6 phosphate dehydrogenase deficiency (G6PDd). Due to the similarity of heme-induced nephropathy and contrast-induced nephropathy (CIN), the current study was designed based on a previous study of CIN.

In response to the first question about safety of acetazolamide in children under two years, we acknowledge the authors' concern regarding the risk of acute kidney injury (AKI) following the administration of > 1 g/day. Although there is no absolute contraindication for this administration, we prescribed only 5 mg/kg/day acetazolamide. For instance, 60 mg/day acetazolamide was administered for a 2-year-old child weighing 12 kg, which is approximately 1/15 of 1 g/day.

Regarding the second question, on the lack of significant difference in serum potassium among the three groups, it is noteworthy that the consequent decrease in potassium level usually happens after long-term consumption. As we mentioned, the treatment period in our patients was about 2 to 3 days, and the potassium level was checked periodically to monitor its safety.

Regarding the third question, the authors addressed a retrospective study reporting AKI in ICU patients after intravenous acetazolamide treatment [3]. These results may have occurred due to various inclusion criteria and the study design. As we declared, we assessed patients with only acute hemolytic anemia due to G6PDd. In contrast, the referenced article investigated critically ill patients who may have suffered from multi-organ dysfunctions or comorbidities. Therefore, the prevalence of AKI in the retrospective study may be due to the abovementioned factors.

In conclusion, we are thankful for the comments and for pointing out further research possibilities.

References

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