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CORRESPONDENCE

Evidence-based medicine to solve the mysteries of citrate anticoagulation for continuous renal replacement therapy

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We thank da Hora Passos et al. [1] for their interesting comments on our recently published article [2]. When it comes to regional citrate anticoagulation (RCA) in continuous renal replacement therapy (CRRT), we do agree with the authors that several additional "gaps" remain and deserve attention, although it is a difficult task to tackle them all in a brief overview with the constraints of a limited word count [2]. As underlined by da Hora Passos and colleagues, it is indeed very clear that adequate nutritional support is required in case of RCA and all CRRT modalities exhibit a significant impact on the body's metabolism and nutrition [3]. The superiority of indirect calorimetry in these patients over formulas to determine accurately the energy requirements has been reported by Jonckheer et al. [4]. As CRRT clearance is not specific, there is a loss of some nutritional elements (such as amino acids, peptides, proteins, trace elements and vitamins) and a gain of others (such as dextrose and non-nutritional calories like citrate and lactate) both of which need to be taken into account when prescribing nutritional support [3]. The authors questioned how citrate infusion impacts energy balance during CRRT. Each gram of citrate that is metabolized yields 2.5 kcal [3]. Depending on the citrate solution, the gain can be as much as 1434 kcal/day, resulting in significant overfeeding [3]. Selecting specific modalities can also limit caloric gain from citrate. For example, if we increase the effluent, the entry of citrate into the patient will decrease and limit caloric gain to 100–300 kcal/day [3]. However, to establish clear guidelines on nutritional adjustments for patients under RCA-CRRT, evidence-based data are lacking to strongly determine the optimal nutritional support, the energy and protein requirements, and the type, if any, of micronutrient additives [3].

Regarding the hypothesis of an alternative metabolic pathway for citrate outside the hepatic mitochondria, we have proposed a robust plan in designing experimental future studies to clinically validate or not this hypothesis which is indeed of upmost importance [2].

We also agree that serum citrate level could be a good tool to diagnose early citrate accumulation along with other parameters such as lactate kinetics [1]. Some authors also advocate the measurement of citrate levels in the blood and in the effluent where the citrate losses in the effluent can be efficiently modulated by increasing the effluent flow rate [5].

Lastly, it is indeed known that infection rate increases with longer filter lifespan [1]. However, this is most likely related to the increased filter lifespan (whatever the anticoagulant used), rather than to the specific use of the citrate molecule.

In conclusion, evidence-based medicine is certainly the only way to go to better understand pathophysiology related to citrate anticoagulation and to provide scientific answers to the remaining gaps in our knowledge of RCA for CRRT (metabolic pathways, nutritional impact, strategies to better anticipate metabolic complications).

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