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Discrepant post-filter ionized calcium concentrations by 2 common gas analyzers in continuous renal replacement therapy using regional citrate anticoagulation: another piece of the puzzle

To the editor: During continuous veno-venous hemodialysis with regional citrate anticoagulation, ionized calcium (iCa) measurements in pre- and post-filter samples are used to adjust calcium and citrate flows. Post-filter iCa target concentrations are within a low range (0.25–0.34 mmol/L), and blood gas analyzers (BGAs) are mainly calibrated for physiological values (1.12–1.20 mmol/L). Bias between BGAs in these low-value measurements leads to errors in adjusting the citrate dose,^{1,2} yet current regional citrate anticoagulation protocol is used worldwide despite the lack of standardization.^{3,4}

Table 1 | Concordance of citrate dose adaptation induced by ionized calcium measured by ABL 90 Flex Plus (Radiometer, Copenhagen, Denmark) and GEM Premier 4000 (Werfen, Barcelona, Spain) analyzers in 50 post-filter samples, taken from 5 critically ill patients treated with continuous veno-venous hemodialysis with regional citrate anticoagulation

ABL GEM	Citrate dose decreased (Ca < 0.25)	Citrate dose unchanged (Ca = 0.25–0.34)	Citrate dose increased (Ca > 0.34)	Total
Citrate dose decreased (Ca < 0.25)	0	15	0	15
Citrate dose unchanged (Ca = 0.25–0.34)	0	9	26	35
Citrate dose increased (Ca > 0.34)	0	0	0	0
Total	0	24	26	50

Continuous veno-venous hemodialysis with regional citrate anticoagulation was conducted with blood flow rate at 100 ml/min and dialysate flow rate at 2000 ml/h (Multifiltrate, Fresenius Medical Care, Bad Homburg, Germany).

We analyzed 50 post-filter samples taken from 5 critically ill patients treated with continuous veno-venous hemodialysis—regional citrate anticoagulation, on GEM Premier 4000 (Werfen, Barcelona, Spain) and ABL90 Flex Plus (Radiometer, Copenhagen, Denmark) for low iCa concentrations (0.18–0.43 mmol/L). The Institutional Review Board of Montpellier University Hospital approved the study and waived the need for written consent (IRB-MPT_2020_03_202000392). Consents for publication were obtained. Despite a significant linear correlation ($r = 0.928$), the ABL90 results were higher than the GEM results, with a mean difference at 0.09 mmol/L, 95% confidence interval (0.07–0.11; [Supplementary Figures S1 and S2](#)). These discrepancies impacted citrate dose adjustment in 82% of measurements ([Table 1](#)), inducing a poor concordance ($Kappa = 0.24$) between BGAs.

Differences were not explained by BGAs’ analytical performances, as both devices appeared to be reliable and reproducible ([Supplementary Table S1](#)), but potential BGAs calibration differences could be hypothesized. Given that discrepancies were higher in post-filter samples than in CaCl₂ diluted in saline ([Supplementary Figure S1](#)), a matrix effect could be involved. Our results pointed out the need for standardization of iCa monitoring to control risks of metabolic disorders (e.g., alkalosis, acidosis, hypernatremia, dyscalcemia) or filter clotting, in patients treated with continuous veno-venous hemodialysis—regional citrate anticoagulation. We, therefore, suggest calibrating BGAs using a commutable reference material close to the plasma composition (i.e., containing albumin, globulins, sodium, and other such components) but with very low iCa concentrations.

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AUTHOR CONTRIBUTIONS

JPC conceived the study. NK, LP, and RL analyzed the data and drafted the manuscript. All authors revised the manuscript and approved the final version.

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