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Bioenergetic gain of citrate anticoagulated continuous hemodiafiltration—a comparison between 2 citrate modalities and unfractionated heparin☆,☆☆

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Abstract

Purpose: To determine bioenergetic gain of 2 different citrate anticoagulated continuous hemodiafiltration (CVVHDF) modalities and a heparin modality.

Materials and Methods: We compared the bio-energetic gain of citrate, glucose and lactate between 29 patients receiving 2.2% acid-citrate-dextrose with calcium-containing lactate-buffered solutions (ACD/Ca^{plus}/lactate), 34 on 4% trisodium citrate with calcium-free low-bicarbonate buffered fluids (TSC/Ca^{min}/bicarbonate), and 18 on heparin with lactate buffering (Hep/lactate).

Results: While delivered CVVHDF dose was about 2000 mL/h, total bioenergetic gain was 262kJ/h (IQR 230-284) with ACD/Ca^{plus}/lactate, 20 kJ/h (8-25) with TSC/Ca^{min}/bicarbonate ($P < .01$) and 60 kJ/h (52-76) with Hep/lactate. Median patient delivery of citrate was 31.2 mmol/h (25-34.7) in ACD/Ca^{plus}/lactate versus 14.8 mmol/h (12.4-19.1) in TSC/Ca^{min}/bicarbonate groups ($P < .01$). Median delivery of glucose was 36.8 mmol/h (29.9-43) in ACD/Ca^{plus}/lactate, and of lactate 52.5 mmol/h (49.2-59.1) in ACD/Ca^{plus}/lactate and 56.1 mmol/h (49.6-64.2) in Hep/lactate groups. The higher energy delivery with ACD/Ca^{plus}/lactate was partially due to the higher blood flow used in this modality and the calcium-containing dialysate.

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Conclusions: The bioenergetic gain of CVVHDF comes from glucose (in ACD), lactate and citrate. The amount substantially differs between modalities despite a similar CVVHDF dose and is unacceptably high when using ACD with calcium-containing lactate-buffered solutions and a higher blood flow. When calculating nutritional needs, we should account for the energy delivered by CVVHDF.

1. Introduction

Citrate inhibits coagulation through chelation of ionized calcium. When administered in the extracorporeal circuit, regional anticoagulation is obtained because part of the citrate is removed through the filter while the other part is rapidly metabolized after entering the patient's circulation. As a result, the use of citrate does not increase the patient's risk of bleeding and this is the main benefit of citrate anticoagulation for continuous renal replacement therapies (CRRT). Compared to heparin, anticoagulation with citrate showed less bleeding and superior circuit life enabling the delivery of high quality CRRT [1-7]. We have implemented citrate anticoagulation in our intensive care unit in 1999 as standard of anticoagulation for all patients at risk of bleeding [8].

Citrate anticoagulation has metabolic consequences, which mainly depend on the amount of citrate reaching systemic circulation, its subsequent metabolism in the citric acid cycle, composition of the dialysis, or replacement fluids and the protocol used. The literature on the systemic effects of citrate focuses on the risk of accumulation if its metabolism fails, on dysnatremia or acid base imbalance. However, the bioenergetic impact of citrate has not been clarified yet.

Up to now, there is no standard citrate protocol. Different solutions and modalities are used. The most frequently used solutions are trisodium citrate (TSC) [9,10], acid-citrate-dextrose (ACD) [11-16] and an isotonic calcium-free predilution replacement fluid containing citrate in a concentration corresponding to the desired bicarbonate equivalent [17]. In a recent study, we found that the use of ACD as citrate source in combination with calcium-containing lactate-buffered fluids (ACD/Ca^{plus}/lactate) provided a daily energetic load to the patient in the form of citrate, glucose and lactate of more than 5000 kJ (1190 kcal) [18]. We therefore implemented a citrate anticoagulation modality using 4% TSC with a calcium-free, bicarbonate-buffered replacement fluid (TSC/Ca^{min}/bicarbonate).

The primary aim of the present study was to compare the patient's bioenergetic gain of our previously adopted ACD/Ca^{plus}/lactate modality with our newly implemented TSC/Ca^{min}/bicarbonate modality and our heparin/lactate modality. We additionally measured metabolic control, circuit life and costs.

2. Materials and methods

This prospective observational study was performed in a 20 bed intensive care unit in the university hospital from January 2008 until April 2011. The study was approved by the university hospital Ethical Board which waived the need for informed consent.

We compared the bioenergetic gain between 2 modalities of citrate anticoagulation in postdilution continuous venovenous hemodiafiltration (CVVHDF) and heparin anticoagulation as a control using commercially available fluids. The ACD group received 2.2% ACD as citrate source in combination with a calcium-containing lactate-buffered solution (ACD/Ca^{plus}/lactate). The TSC group received 4% TSC with a calcium-free, low-sodium, low bicarbonate solution (TSC/Ca^{min}/bicarbonate). The heparin group received anticoagulation with unfractionated heparin and a lactate buffered solution (Hep/lactate).

We additionally compared the rates of hypo- and hypernatremia, acid-base derangements, circuit survival time, and costs between the three modes of anticoagulation.

2.1. Continuous venovenous hemodiafiltration

Indications for renal replacement therapy were renal failure with elevated levels of uremic toxins and/or loss of response to diuretics. For CVVHDF, we used the Aquarius device (Baxter, Irvine, CA) and a 1.9 m^2 polysulfone filter (Aquamax, Bellco, Mirandola, Italy). CVVHDF on Aquarius device exclusively uses the postdilution mode. Prescribed CVVHDF dose was 20 to 25 mL/kg per hour [19,20]. Patients with a risk of bleeding received citrate anticoagulation, while heparin was used in patients without a risk of bleeding. Lactate buffering was used as long as the arterial lactate remained <3 mmol/L. Initially, all patients with hyperlactatemia received ACD with another bicarbonate buffered fluid. These patients were not included in this study. After changing the department's citrate protocol in late 2009, all citrate patients received TSC/Ca^{min}/bicarbonate. Citrate dosage in both study groups was titrated in increments to maintain the postfilter ionized calcium (Ca^{2+}) less than 0.4 mmol/L. Ca^{2+} was checked every hour until stable and thereafter 4-hourly. Calcium chloride (10%) was infused into a port distal from the venous bubble trap to maintain arterial Ca^{2+} within normal range (0.8-1.3 mmol/L). Arterial Ca^{2+} was monitored every 6 hours.

In the *ACD/Ca^{plus}/lactate group*, 2.2% ACD (Fenwal, Baxter Healthcare, Deerfield, IL) was used as anticoagulant. ACD contains 113 mmol citrate/l and 138.9 mmol glucose/l (2.5% glucose). Blood flow (Qb) was set initially at 150 mL/min and ACD infusion was initiated at 300 mL/h (33.9 mmol/h) to the port after the prefilter sampling port of the