Continuous Renal Replacement Therapy Dosing in the Severely Underweight: A Case Report

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Guidelines recommend that patients treated with continuous renal replacement therapy be delivered an effluent dose of 20 to 25 mL/kg/h. There is debate, especially at the extremes of body mass index, as to whether actual or ideal body weight (IBW) should be used in these dose calculations. A middle-aged woman with severe anorexia presented with 48 hours of altered mental status. Laboratory tests showed severe metabolic acidosis necessitating intubation, which was ultimately found to be due to nonprescribed use of metformin for weight loss. The patient became anuric and was initiated on continuous venovenous hemodialysis. Due to refractory acidosis, the modality was converted to continuous venovenous hemodiafiltration by adding postfilter hypertonic bicarbonate solution. Based on changes in sodium and bicarbonate levels over 4 hours with hypertonic bicarbonate solution, we were able to calculate an "effective" volume of distribution for this severely underweight patient. Our calculations suggest that IBW gives a better approximation of effective volume of distribution than actual body weight in a severely underweight woman. Inadequate effluent flow rate calculated based on actual rather than IBW may lead to insufficient correction of metabolic derangements in extremely underweight patients.

INTRODUCTION

Severe acute kidney injury requiring dialysis has an in-hospital mortality rate > 50% in critically ill patients,[1,2] making it one of the deadliest conditions commonly encountered in US hospitals. Continuous renal replacement therapy (CRRT) is generally the preferred dialysis option in the intensive care unit because it is associated with less hemodynamic instability than intermittent therapy.[3]

A major component of the CRRT prescription is dose, which is based on urea clearance. In CRRT, in which dialysate or replacement fluid flow rates are low relative to blood flow, urea clearance is a function of effluent flow rate.[4] KDIGO (Kidney Disease: Improving Global Outcomes) recommended in their 2012 clinical practice guideline that patients treated with CRRT receive an effluent flow rate normalized for body weight of 20 to 25 mL/kg/h (a 1A level recommendation).[5] However, whether effluent flow rate should be normalized for ideal body weight (IBW) or actual body weight is unknown. Differences in IBW and actual body weight can lead to wide discrepancies in weight-normalized delivered doses at the extremes of body mass index.[6,7] In this case report, we provide evidence for use of IBW rather than actual body weight in a severely underweight woman.

CASE REPORT

A middle-aged woman with a history of hypothyroidism and severe anorexia was admitted with a 2-day history of altered mental status. She had no other significant medical, surgical, social, or family history. She had no prescribed medications other than levothyroxine, but was later found to be taking nonprescribed metformin for weight loss.

A timeline of events and laboratory flow sheet are given in Figure 1 and Table 1. Initial vital signs were significant for weight of 27 kg, body mass index of 10.1 kg/m^2, and blood pressure of 70/34 mm Hg. Her IBW was calculated as 57 kg. Laboratory results were notable for the following values: lactate, 21 mmol/L; bicarbonate, 7 mmol/L; and creatinine, 2.1 mg/dL. An arterial blood gas drawn at arrival to the emergency department showed an initial pH < 6.80, P_{CO_2} of 32 mm Hg, and calculated bicarbonate level of 5 mg/dL. Protocolized sepsis management was initiated, including fluid resuscitation, and she was intubated. She became anuric, and approximately 6 hours after arriving at the hospital was initiated on CRRT using continuous venovenous hemodialysis (CVVHD). The initial dialysate dose, prescribed using actual weight, was 800 mL/h (30 mL/kg/h), with dialysate fluid that had a sodium concentration of 140 mmol/L and bicarbonate concentration of 36 mmol/L.

Laboratory tests 2 hours later showed serum bicarbonate level of 3 mmol/L, prompting an increase in dialysate flow rate to 1,750 mL/h (30 mL/kg/h), which was calculated using IBW of 57 kg. Laboratory tests assessed 12 hours after arrival showed that bicarbonate level was stable at 3 mmol/L, with lactate level of 22 mg/dL and pH 6.87. Given that pH had not improved despite 6 hours of CVVHD, the CRRT modality was converted to continuous venovenous hemodiafiltration, with 1,500 mL/h of dialysate and 250 mL/h of postfilter hypertonic bicarbonate solution, which was composed of 6 ampules of
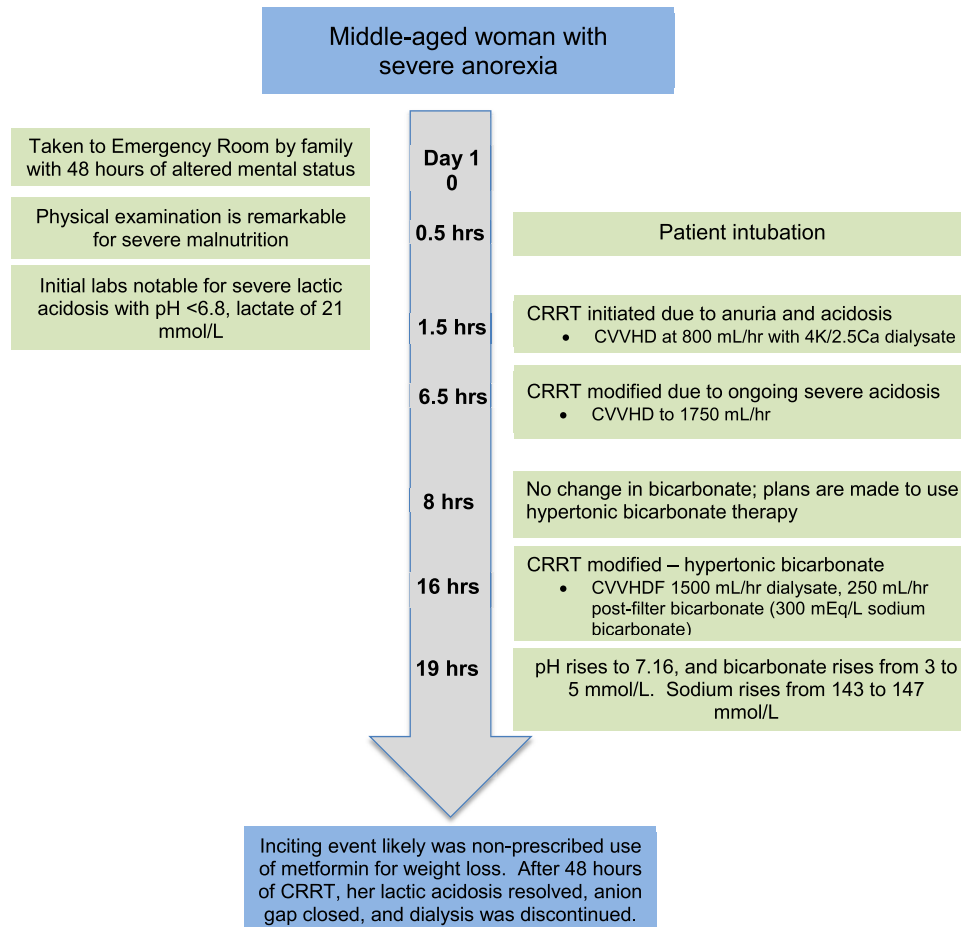
Figure 1. Timeline of events on treatment day 1. Abbreviations: CRRT, continuous renal replacement therapy; CVVHD, continuous venovenous hemodialysis; CVVHDF, continuous venovenous hemodiafiltration.

bicarbonate in 1 L of water (300 mmol/L of sodium bicarbonate). Four hours after initiation of hypertonic bicarbonate solution administration, pH increased to 7.16 and bicarbonate level increased to 5 mmol/L.

DISCUSSION

This case describes a severely underweight woman with lactic acidosis due to metformin toxicity who was initiated on CRRT. Because the patient was anuric, changes in

Table 1. Arterial Blood Gas, Basic Metabolic Panel, and Lactate Values on Day 1

Time Since Admission	0	0.5 h	1.5 h	6.5 h	8 h	12 h	16 h	19 h
Key events	Admission	Intubation		CRRT initiated	CRRT modified		CRRT, hypertonic bicarbonate initiation	CRRT, post–hypertonic bicarbonate
Arterial blood gas								
pH	<6.80	6.84		6.83	6.87			7.16
PCO₂, mm Hg	32	15		10	10			10
Calculated bicarbonate, mmol/L	5	3		2	2			5
Basic metabolic panel and lactate								
Sodium, mmol/L	146		143		143	145	143	147
Potassium, mmol/L	2.7		2.5		4.2	4.1	4.4	3.9
Chloride, mmol/L	104		104		106	107	107	103
Bicarbonate, mmol/L	7		2		3	3	3	5
Creatinine, mg/dL	2.0		2.1		1.8	1.6	1.5	1.4
Lactate, mmol/L	21		23		22	22	21	21

Abbreviation: CRRT, continuous renal replacement therapy.

sodium and bicarbonate levels were assumed to be due to CRRT alone, allowing for an estimation of the patient's effective volume of distribution (V_D). We found that IBW better estimated V_D than actual body weight.

V_D Based on Changes in Sodium

Expected changes in sodium levels while on CRRT can be calculated using the following equation[8]:

$$[Na^+](t) = [Na^+]_i + ([Na^+]_{RF} - [Na^+]_i) \times (1 - e^{\frac{-Dt}{V}}) \qquad (1)$$

$[Na^+]_i$ is sodium concentration at initiation, $[Na^+]_{RF}$ is sodium concentration of the replacement fluid (or dialysate), D is effluent flow rate in L/h, and $[Na^+](t)$ is sodium concentration after t hours of treatment.

The patient's dialysate $[Na^+]$ was 140 mmol/L, and postfilter sodium bicarbonate $[Na^+]$ was 300 mmol/L. At rates of 1,500 and 250 mL/h, the effective $[Na^+]_{RF}$ was 163 mmol/L.

$$Effective\ [Na^+]_{RF} = \frac{(140\ mmol/L \times 1,500\ mL/h + 300\ mmol/L \times 250\ mL/h)}{1,750\ mL} = 163\ \frac{mmol}{L} \qquad (2)$$

Given that the initial sodium level at the time of hypertonic bicarbonate solution initiation was 143 mmol/L and that 4 hours later sodium level was 147 mmol/L, we can estimate the effective V_D as follows:

$$147 = 143 + (163 - 143) \times (1 - e^{-\frac{(1.75) \times 4}{V}}) \qquad (3)$$

Solving for V, "effective" V_D is 31 L. If we assume that V_D in this patient is similar to that of an elderly woman (55% of body weight), her effective weight is 57 kg, which is identical to IBW and more than double her actual body weight of 27 kg.

V_D Based on Changes in Bicarbonate

We can similarly use bicarbonate level changes to estimate "effective" volume of distribution using the following equation:

$$\Delta HCO_3^- = \frac{Total\ HCO_3^-\ Given - Endogenous\ Acid\ Production}{V_D} \qquad (4)$$

At bicarbonate levels < 10 mmol/L, V_D for bicarbonate approximates body weight,[9] so calculated V_D was used to find the patient's effective body weight.

To calculate total bicarbonate, we add the dialysate contribution to the postfilter replacement fluid bicarbonate contribution. The bicarbonate gradient used was 32 mmol/L, based on a bicarbonate level before starting

hypertonic bicarbonate solution administration of 3 mmol/L and 5 mmol/L afterward. The gradient was calculated by subtracting the average serum bicarbonate level (4 mmol/L) from the dialysate concentration (36 mmol/L). Based on dialysate and postfilter bicarbonate flow rates, her bicarbonate load was 123 mmol/h:

$$1.5\ L/h \times 32\ mmol/L + 0.25\ L/h \times 300\ mmol/L = 123\ mmol/h \qquad (5)$$

We can calculate endogenous acid production based on the fact that serum bicarbonate level did not change after 4 hours of CVVHD at 1.75 L/h with a bicarbonate gradient of 33 mmol/L.

$$1.75\ L/h \times 33\ mmol/L = 57.75\ mmol/h \qquad (6)$$

Endogenous acid production must be at least this rate to counteract the administered bicarbonate. Acid production may have been higher because buffering from other sources such as bone (phosphate) could not be calculated.

Acid production during administration of hypertonic bicarbonate solution was assumed to be unchanged because lactate level was unchanged following this 4-hour period. If we subtract acid production from the bicarbonate given, we get 65.25 mmol/h net bicarbonate, which over 4 hours is a net gain of 261 mmol of bicarbonate.

Over 4 hours, bicarbonate level increased by 2 mmol/L. The difference in calculated arterial blood gas bicarbonate level was 3 mmol/L. V_D calculations are as follows:

$$\textbf{Increase of 2 mmol/L}: 261\ mmol \div 2\ mmol/L = 130.5\ L \qquad (7)$$

$$\textbf{Increase of 3 mmol/L}: 261\ mmol \div 3\ mmol/L = 87\ L \qquad (8)$$

These calculated V_D values are much higher than IBW or actual body weight, which suggests that there was more endogenous acid production that was buffered by alternative pathways than anticipated, illustrating the possible far-reaching consequences of sustained severe acidosis. These calculations also illustrate that as bicarbonate levels decrease, V_D increases.[9] It is also notable that at extremely low bicarbonate levels, small changes in bicarbonate levels lead to large differences in calculated V_D.

To further illustrate that IBW better predicted bicarbonate level changes that actual body weight, we can calculate expected increases in bicarbonate levels based on actual versus IBW.

Expected increase based on actual body weight :

$$261 \text{ mmol} \div 27 \text{ L} = 9.7 \text{ mmol/L} \quad (9)$$

Expected increase based on IBW :

$$261 \text{ mmol} \div 57 \text{ L} = 4.6 \text{ mmol/L} \quad (10)$$

Given that the actual change was 2 to 3 mmol/L, it is clear that using IBW gave an estimation that was much closer to the observed outcome.

There are several limitations in this case report. V_D was not directly measured. As noted in the discussion, slight changes in values, especially in bicarbonate, would have a marked effect on the calculated V_D. The bicarbonate calculations are based on 1 set of laboratory tests following hypertonic bicarbonate solution administration, and the margin of error for bicarbonate can be up to 2 mmol/L. In addition, endogenous acid production did not account for nonbicarbonate sources of buffer. Finally, it is unclear whether IBW better predicts V_D in patients with extremely high body mass index, which is the much more common scenario in the United States.

Nonetheless, this case report has several strengths; notably, analyses based on clinical data of an anuric patient on CRRT. Because the patient was anuric, all changes during the 4 hours of hypertonic bicarbonate solution therapy could reasonably be attributed to CRRT alone, which allows for calculation of effective body weight. We were also able to show that lactate levels were constant over the course of treatment, making our assumptions of constant acid production plausible.

This case illustrates that in a severely underweight woman treated with CRRT, IBW rather than actual body weight provides a better approximation of the V_D of sodium and bicarbonate. IBW therefore appears to be more appropriate to use when normalizing the effluent flow rate for patient weight when prescribing dialysis therapies.

ARTICLE INFORMATION

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