Understanding the metabolic complications of Regional Citrate Anticoagulation for CRRT – a basic guide

The basic premise is that if you infuse citrate into blood, it will chelate the free, ionized calcium. This will halt the coagulation cascade and inhibit platelet activation. To achieve effective anticoagulation of the CRRT circuit, there is a fixed delivery of citrate, proportionate to the blood flow, into the afferent limb of the circuit. The fixed ratio of citrate to blood results in a citrate concentration which will therapeutically anticoagulate but can be easily reversed.

The citrate solution we use is rich in acid and sodium too, and a proportion of this anticoagulant solution (AC-A) is delivered back to the patient down the efferent limb of the CRRT circuit. The ACCUSOL buffers much of the acid effect, and there is little or no risk of significant hypernatraemia.

Citrate-calcium complexes are filtered away within the CRRT system, and therefore you should give additional calcium to the patient to correct for this. ACCUSOL-35 has some calcium in it already to at least partially correct the citrate effect before the blood returns to the patient.

Citrate is acidic, but when metabolised it generates bicarbonate. Therefore RCA can cause both acidosis and alkalosis.

Citrate continues to bind calcium in the blood, until the citrate is metabolised through the Kreb’s cycle in mitochondria of liver, muscle, kidney etc. Once the citrate is metabolised, this calcium is once again measurable as ionized Calcium (iCa).

**Common Problems**

**Hypocalcaemia** – there is loss of calcium in the CRRT circuit, and this must be replaced. The ACCUSOL-35 substitution fluid has some calcium already in it. Follow the protocol for calcium replacement (guided by iCa results from the blood gas machine). The Aquarius software will automatically compensate the fluid removal volume for the change in calcium infusion, and deliver the fluid balance goal you have already set. If your patient is needing large quantities of additional calcium and has a worsening acidosis, consider whether they are failing to metabolise citrate (see below)

**Alkalosis** – the citrate infused into the patient is being metabolised and generating bicarbonate. If the pH gets to 7.50 or the bicarbonate to 40 mmol/L then you should act. The solution to the alkalosis is to lower the amount of citrate getting into the patient. To do this, swap from protocol 1 to protocol 2 (or if you were on protocol 3, change to protocol 1). Moving from protocol 1 to protocol 2 increases the amount of citrate removed within the CRRT circuit, and hence the flow of citrate to the patient, without hugely affecting the overall “dose” of renal replacement therapy. Moving from protocol 3 to protocol 2 reduces the amount of citrate that the patient receives by bringing down the blood and citrate flow rates and the “dose” of RRT. If the alkalosis does not improve despite being on Protocol 2, then discontinue RCA.

**Acidosis** – remember that your patient may have many reasons for an acidosis already. However, the acidosis driven by RCA is a raised anion gap acidosis driven by failure to metabolise the delivered citrate. It is most likely to occur in those with severe shock or severe acute liver failure. In addition, patients with poisonings which either affect mitochondrial function (e.g. ethylene glycol or cyanide) or cause combined muscle, renal and liver injuries (e.g. amphetamines or heat-injury), or with underlying mitochondrial disease or taking medications which affect mitochondrial function (e.g. certain anti-retrovirals), may be predisposed to citrate toxicity.

If there is an excess of unmetabolised citrate, there will be reduction in ionized calcium. You may have had to repeatedly correct this with increasing volumes of calcium replacement solution; although the iCa may be correcting, your patient could now have a raised total blood calcium (the sum of free ionized calcium, protein bound calcium, and now citrate-chelated calcium too). Compare the total serum calcium (NB NOT the adjusted or corrected calcium, but the total calcium from the laboratory sample) to the ionized calcium on the blood gas sample. If the ratio between the two is greater than 2.5, then this is consistent with excess unmetabolised citrate. To treat citrate-driven acidosis, reduce the systemic citrate delivery in the same way that alkalosis is managed (see above). However, given the patient may have severe underlying acute illness, be prepared to cease RCA-based CRRT and use another anticoagulation choice.