

# Citrate Toxicity During CRRT After Massive Transfusion

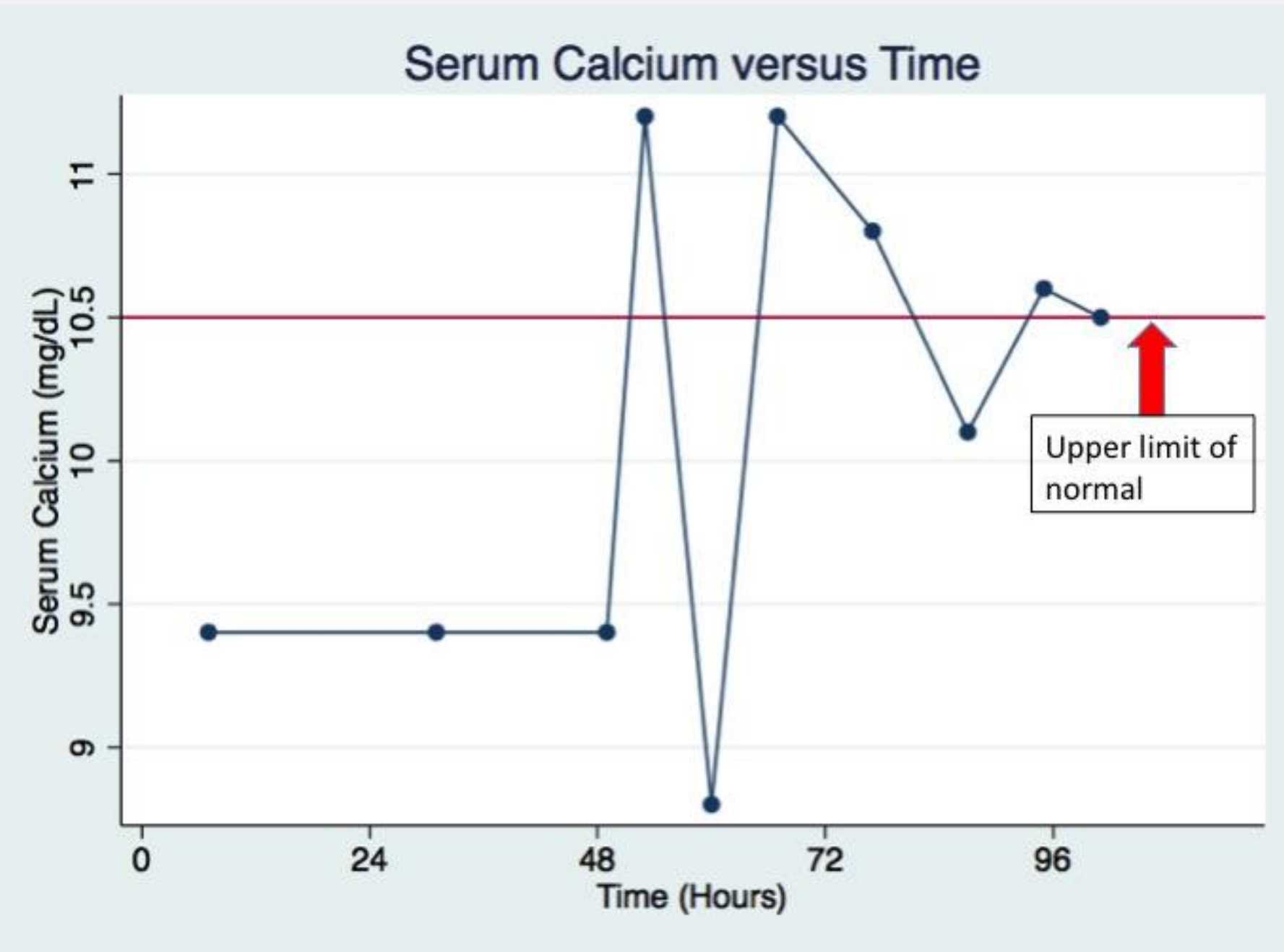
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## Background

Regional citrate anticoagulation (RCA) is commonly used in continuous renal replacement therapy (CRRT). Citrate is also used to inhibit coagulation during storage of blood products by chelating calcium (Ca). Fresh frozen plasma (FFP) has the highest concentration of citrate among blood products at approximately 20 mmol/L.<sup>1,2,3</sup> The normal liver rapidly metabolizes citrate to bicarbonate and releases bound Ca, but liver dysfunction reduces this ability and predisposes to citrate toxicity during CRRT with RCA. Citrate toxicity is detected by an elevation in the total to ionized Ca ratio (TCa/iCa).

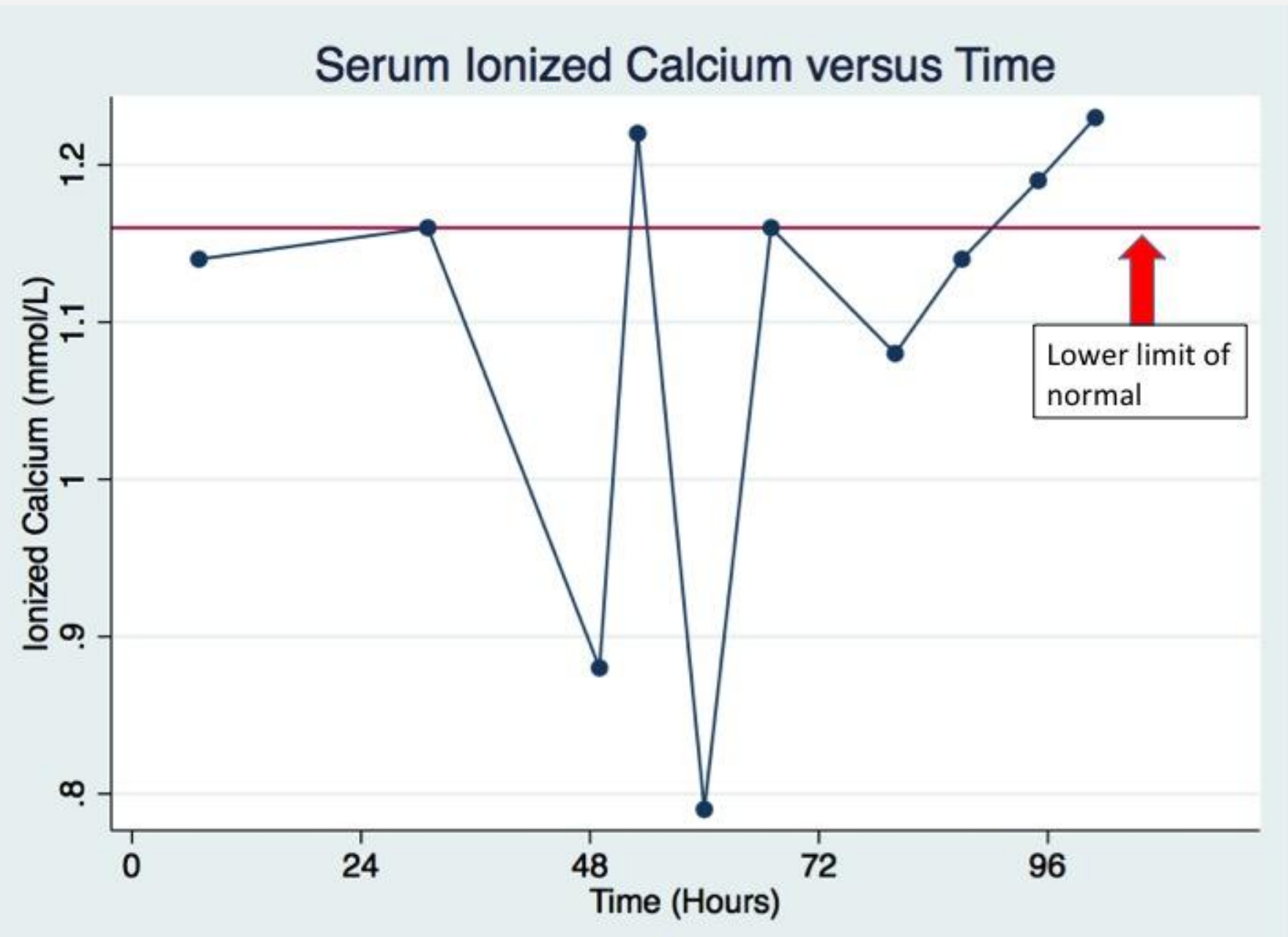


**Figure 1.** Total serum calcium concentration during the reported period.

## Case Report

A 51 year-old woman with cirrhosis due to chronic hepatitis B (HBV) was admitted to the intensive care unit for acute liver failure, thought to be due to rapid HBV replication after she stopped taking antiviral medication because of side-effects. During the next two weeks she developed encephalopathy, coagulopathy, lactic acidosis, and oliguric acute kidney injury.

Continuous veno-venous hemofiltration (CVVH) with Ca 1.5 mmol/L was started without anticoagulation. Because of a gastrointestinal hemorrhage, the patient received 10 units (2.6L) of FFP, and one unit of packed red blood cells (PRBC), for a total of approximately 50 mmol of citrate.



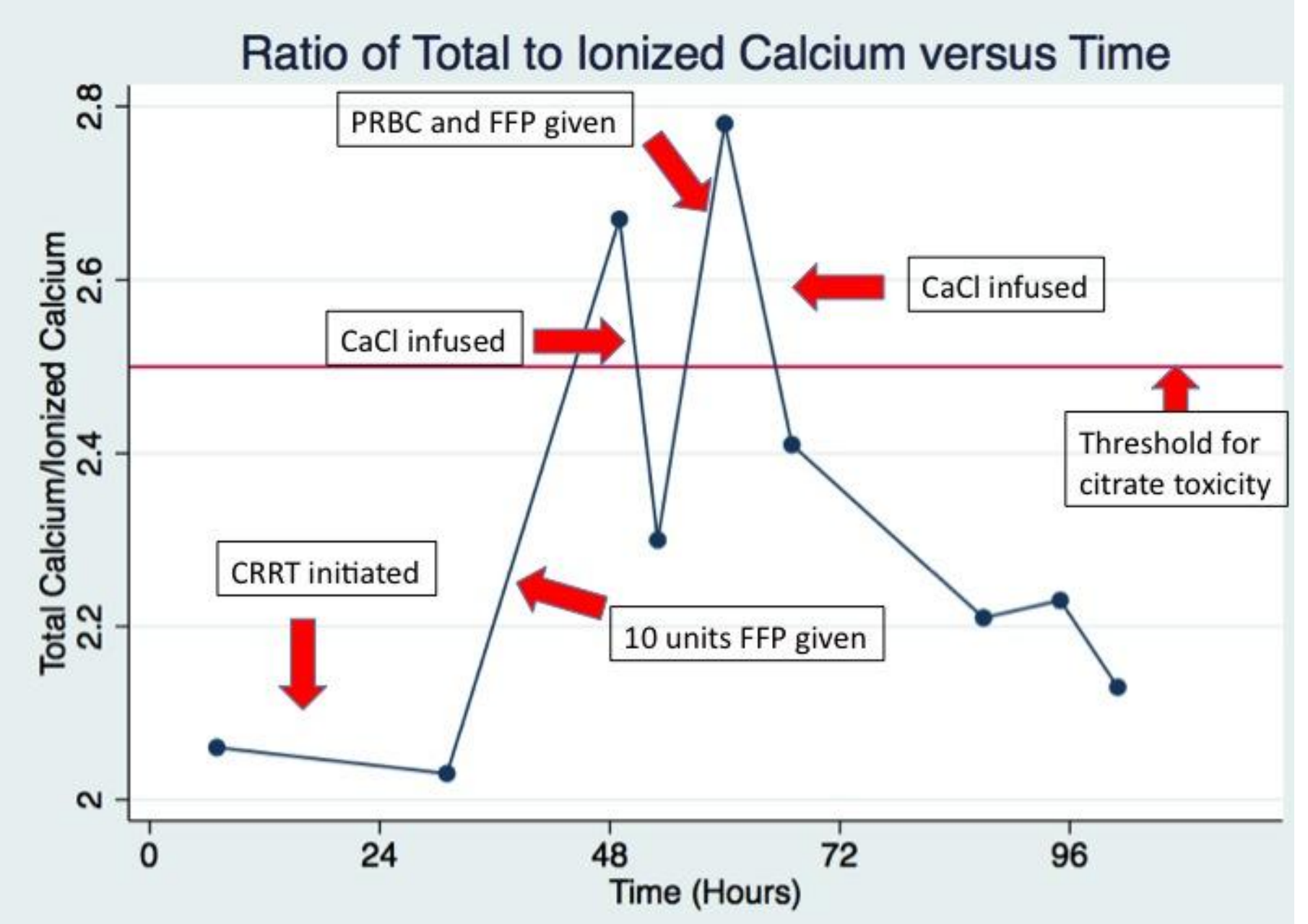
**Figure 2.** Serum ionized calcium concentration during the reported period.

She developed hypotension and was found to have an iCa level of 0.88 mmol/L, a TCa level of 9.4 mg/dL, and an elevated TCa/iCa ratio of 2.67. This ratio was significantly higher than prior to the administration of blood products and is above the threshold value for citrate toxicity of 2.5. Two grams (14 mmol) of calcium chloride (CaCl<sub>2</sub>) were given, and an infusion of CaCl<sub>2</sub> at 1 mmol/hr was started. After the patient received a total of 22 mmol of Ca, iCa was normalized, with reduction of the TCa/iCa ratio below 2.5. The CaCl<sub>2</sub> infusion was stopped. The following day she was given 4 units PRBC and 4 units FFP (approximately 20 mmol citrate), and developed elevated TCa (Figure 1), low iCa (Figure 2) and elevated TCa/iCa ratio, and was re-treated with another bolus and infusion of CaCl<sub>2</sub>, for a total of 26 mmol Ca (Figure 3).

The bleeding eventually resolved without intervention. With no further large-volume transfusions, the calcium derangements did not recur. CVVH was continued, but the patient deteriorated and subsequently was transitioned to comfort care.

## Conclusion

Citrate toxicity is not uncommon in patients with liver failure undergoing CRRT with RCA and is monitored by measuring the TCa/iCa ratio. However, as this case illustrates, patients with liver failure who receive massive amounts of blood products should also be monitored for the development of citrate toxicity.



**Figure 3.** Ratio of total to ionized calcium during the reported period.

## References

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