High Volume Continuous Venovenous Haemodiafiltration For The Treatment Of Metformin Induced Lactic Acidosis

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Objective

To describe the use of high volume continuous venovenous haemodiafiltration (HV-CVVHDF) for the treatment of lactic acidosis following an intentional metformin overdose.

Clinical Features

A 50 year old female patient presented to our emergency department following an intentional overdose with approximately 150-180g of immediate release metformin and 250mg of doxylamine.

Past Medical History	Medication
Non-insulin dependent diabetes mellitus	Metformin Immediate Release 1g BD Gliclazide Modified Release 120mg daily
Hypertension	Irbesartan 300mg daily Metoprolol 50mg BD
Previous deep vein thrombosis	Rivaroxaban 20mg daily
Hypercholesterolaemia	Untreated
Schizo-affective depression	Untreated

Table 1: Past medical history and regular medications.

She only admitted to taking metformin and doxylamine but we did not suspect other co-ingested medications given her coagulation parameters were normal (making rivaroxaban overdose unlikely) and was hyperglycaemic on presentation (making gliclazide overdose unlikely). Although she was vasoplegic, this was attributed to her significant acidosis.

Interventions

Due to her profound degree of lactic acidosis (pH=6.93) and deteriorating conscious state, she was subsequently intubated and transferred to our intensive care unit (ICU) for further treatment. A vascular access catheter was then inserted in preparation for renal replacement therapy (RRT) using our standard Fresenius 5008 system with a polysulfone high-flux filter (AV600s).

We initially commenced RRT with continuous venovenous haemodiafiltration (CVVHDF) with an effluent flow rate (or RRT dose) of 75ml/kg/hour (in contrast 30-40ml/kg/hour typically found in other ICUs). Despite several hours of aggressive filtration, her lactate failed to improve and remained above 20mmol/L (the limit of detected at our center). RRT was then escalated to HV-CVVHDF with an effluent flow rate of 135ml/kg/hour which was eventually increased to a peak of 240ml/kg/hour. Approximately 10 hours after increasing her RRT dose, her lactate began to fall and her acidosis improved, allowing us to wean and eventually cease HV-CVVHDF.

She required CVVHDF (effluent rate = 30ml/kg/hour) 36 hours later for solute clearance from new anuric renal failure.

She eventually recovered sufficient renal function and RRT was ceased completely 6 days later.

Apart from RRT, she also received 2 doses of activated charcoal and supportive care in the form of vasopressor therapy (noradrenaline, dobutamine and methylene blue) intravenous sodium bicarbonate for her acidosis and invasive mechanical ventilation.

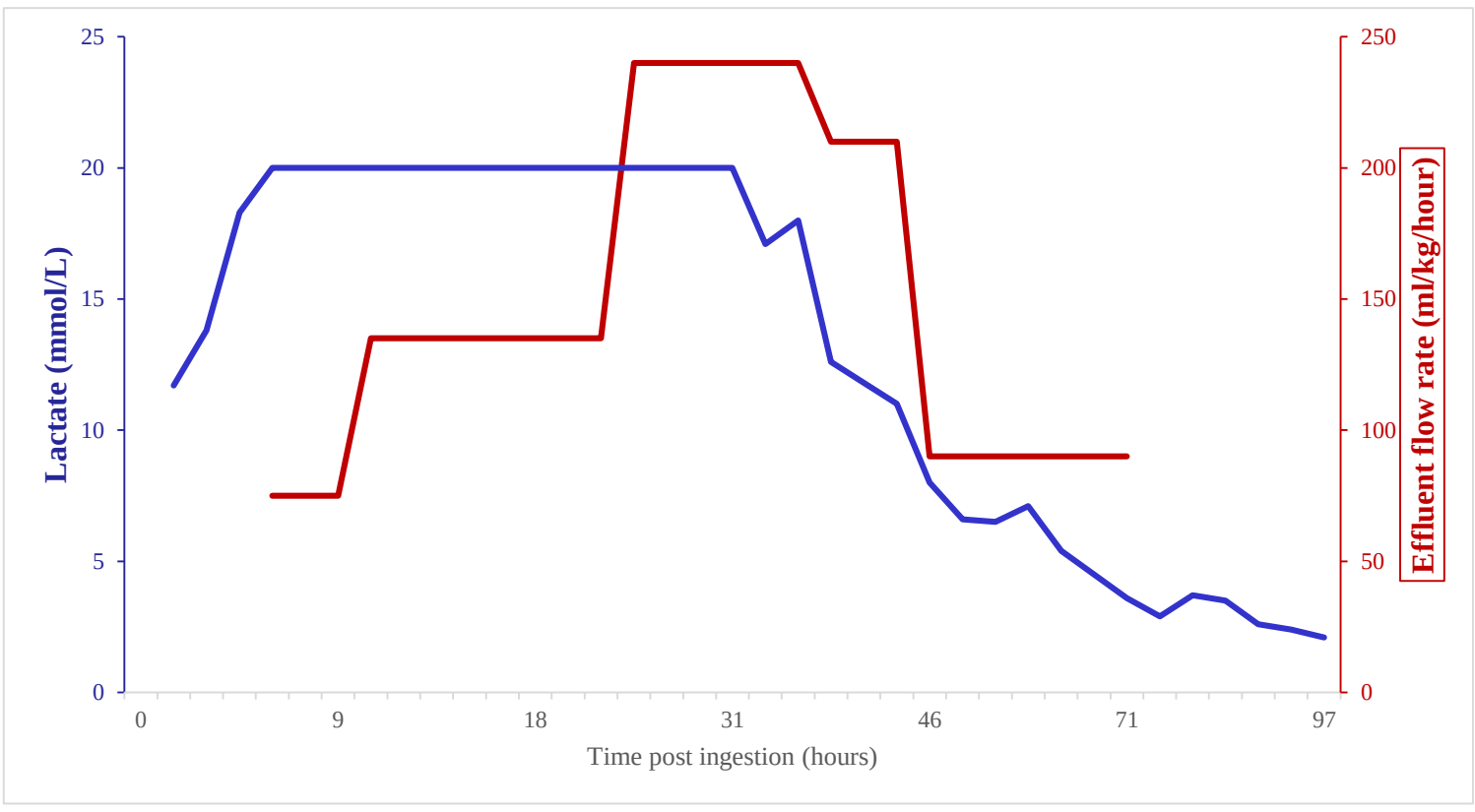

Table 2: Graph comparing lactate levels and response to dose of RRT delivered.

Image 1 : Fresenius 5008 RRT system. The machine is directly connected to a reverse osmosis purifier which generates the large amount of dialysate needed for HV-CVVHDF. Spent ultrafiltrate and dialysate is plumbed directly to the sewerage negating the need for dialysis bag changes.

Discussion

Given the reported lethal dose of metformin without RRT treatment is around 35g, our case described here represents a massive overdose. We were unable to locate another case describing an overdose above 100g.

CVVHDF is an established modality offered by most ICUs for treating metformin overdoses, but as described in this case, may be insufficient if large quantities are ingested.

Although not widely available, HV-CVVHDF enables us to use much larger dialysate flow rates to improve clearance. In our center, benefits of this includes shorter filtration times, reduced manual handling from changing dialysis bags and as described in this case, superior removal of toxins or metabolites. Metformin levels which were not done in our patient would have been useful to help determine if success with this system was due to efficiency at removing plasma metformin or lactate (or both).

Despite these benefits, it is important to consider the impact of higher RRT doses with HV-CVVHDF and it's effects on other therapeutic agents. Our patient was empirically treated with piperacillin-tazobactam for sepsis. We elected to use a dose of 4.5g 4-hourly (in contrast to the recommended dose of 6-hourly in severe sepsis) due to the anticipated losses through HV-CVVHDF. Although unavailable in our center, therapeutic drug monitoring would have been useful to help optimise drug dosing.

Conclusion

CVVHDF may be insufficient at treating large metformin overdoses. HV-CVVHDF should be considered as an alternative and early referral to centers capable of providing this is crucial. Pharmacists should consider the impact of HV-CVVHDF on clearance of therapies such as antibiotics which may result in treatment failure.