

Letter

**Combined renal replacement therapy for severe metformin-induced lactic acidosis**

Sir,

This report is on a 68-year-old woman with a history of type 2 diabetes mellitus treated with metformin 850 mg thrice daily, and mild chronic renal failure, who underwent cardiopulmonary resuscitation for cardiovascular collapse because of severe metformin-associated lactic acidosis. Even after 12 h of continuous venovenous haemofiltration (CVVH), lactic acidosis persisted and the patient required increasing doses of norepinephrine. After starting simultaneous haemofiltration via a second vascular access, lactic acidosis resolved, norepinephrine infusion was discontinued and the patient subsequently made a complete recovery.

Metformin is the only medication for type 2 diabetes mellitus which has been demonstrated to reduce the risk of macrovascular complications of diabetes [1]. Lactic acidosis is a rare but potentially fatal adverse effect of metformin (30–50% mortality rate [2]) with an estimated risk of 1–15/100 000 patient-years [2]. The significance of lactic acidosis due only to accumulation of metformin in renal insufficiency in the absence of other precipitating factors is the subject of controversial debate [2,3]. Tissue hypoxia triggering lactic acidosis is presumed to be present in most cases.

The patient was admitted to the stroke unit for sudden visual loss, nausea, vomiting and faintness. Soon after diagnosis of a severe metabolic acidosis (pH 6.5), the patient had a cardiovascular collapse. After successful resuscitation, she was transferred to our medical ICU, mechanically ventilated and placed on norepinephrine infusion. Blood gas analysis revealed severe lactic acidosis: pH 6.83, base excess –28 mmol/l, bicarbonate 7.9 mmol/l, lactate 35.3 mmol/l. History and clinical presentation led to the suspicion of a

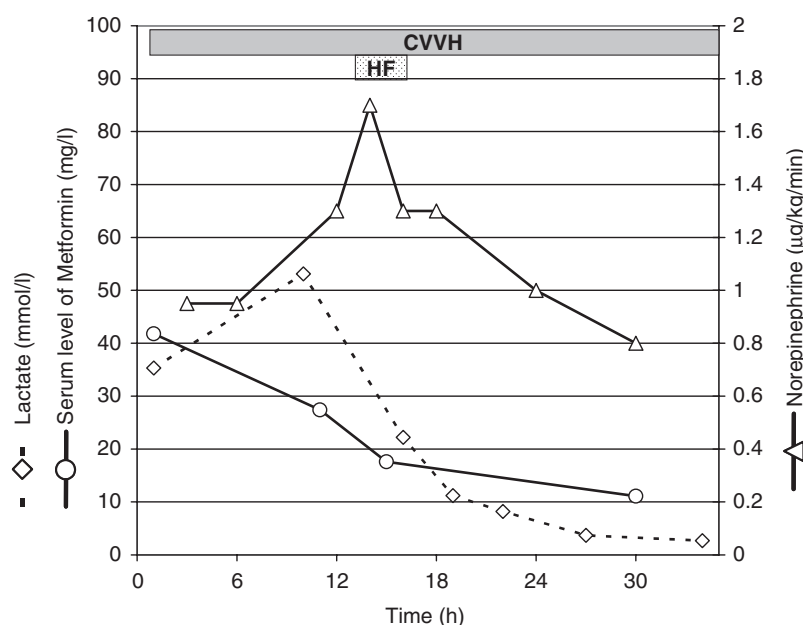
metformin-associated lactic acidosis [4]. Other possible causes for lactic acidosis and circulatory failure, specifically cardiogenic or hypovolaemic shock, bowel or limb ischaemia, severe sepsis or septic shock were ruled out. The plasma level of metformin was 41.9 mg/l (therapeutic range 0.3–1.2 mg/l) and confirmed our diagnosis. Despite immediate CVVH (AV 400, with an ultrafiltration rate of 1500 ml/h and bicarbonate-based substitution solution), the patient's condition deteriorated, the norepinephrine dose had to be increased to 1.65 µg/kg/min, the serum lactate level rose (Figure 1). Since vascular access did not allow for higher ultrafiltration rates, and following the suggestion of Panzer *et al.* [5], we started an additional discontinuous haemofiltration (highflux) via a separate venous catheter. Under this combined renal replacement therapy, serum lactate decreased promptly and norepinephrine doses could be tapered off (Figure 1). Subsequently, the patient recovered completely from the acute illness.

The benefit of simultaneously combining intermittent and continuous renal replacement therapy in case of severe metformin-induced lactic acidosis with circulatory failure, as described by Panzer *et al.* [5], was confirmed in our case. Thus, the approach may be considered in other cases of this frequently fatal complication of diabetes therapy.

*Conflict of interest statement.* None declared.

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**Fig. 1.** Vasopressor dose, serum levels of metformin and lactate during renal replacement therapy.

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