1. Heras M, Saiz A, Fernández-Reyes MJ, Sánchez R, Zurita P, Urrego C. Brote lúpico durante la inducción con ciclofosfamida en la nefropatía lúpica proliferativa difusa. Nefrologia 2011;31(2):231-3.
2. Burchadi C, Schlöndorff D. Induction theraphy for active lupus nephritis: mycophenolate mofetil versus cyclophosphamide. Nat Clin Pract Nephrol 2006;2:314-5.
3. Houssiau FA. Cyclophosphamide in lupus nephritis. Lupus 2005;14:53-8.

M. Heras[1], A. Saiz[2], M.J. Fernández-Reyes[1], R. Sánchez[1], P. Zurita[3], C. Urrego[3]
[1] Nephrology Department.
General Hospital of Segovia. Spain.
[2] Anatomical Pathology Department.
Ramón y Cajal Hospital. Madrid. Spain.
[3] Rheumatology Department.
General Hospital of Segovia. Spain.
Correspondence: M. Heras
Servicio de Nefrología.
Hospital General de Segovia.
40002 Segovia.
manuhebe@hotmail.com
mherasb@saludcastillayleon.es

B) BRIEF PAPERS ON RESEARCH AND CLINICAL EXPERIMENTS

Metformin-induced lactic acidosis: usefulness of measuring levels and therapy with high-flux haemodialysis

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To the Editor,

Lactic acidosis in metformin-treated diabetes mellitus patients is a very rare complication, with a high mortality rate and is often associated with an underlying condition, which alone could cause this very severe hydroelectrolytic imbalance. Metformin is a widely-used oral antidiabetic agent, which is eliminated by active tubular secretion, but accumulates in patients with kidney failure.[1] Clinically, metformin-associated lactic acidosis (MALA) develops abruptly and is accompanied by overbreathing, abdominal pain, drowsiness and coma. Abnormal laboratory MALA indicators are a high anion gap, base excess in the arterial blood gas and high plasma lactate levels (prognostic value) and metformin plasma levels. Monitoring the lactate and metformin levels is a very useful way of evaluating the evolution and the possible modifications in the treatment. MALA treatment is controversial; using bicarbonate is usual although there is no scientific evidence associating it with a better prognosis. Low metformin binding to plasma proteins allows haemodialysis techniques with bicarbonate solutions to be used when it has been overdosed. This technique has proven to be effective in eliminating plasma metformin and also allows acidosis to be corrected.[2,3] Dialysis seems to contribute significantly to treating this severe pathology and improving results where MALA is associated with acute renal failure.[4] If we were to compare MALA to severe lactic acidosis located elsewhere, MALA prognosis is significantly better. Its diagnosis should be considered in all metformin-treated patients that present with lactic acidosis.[5]

Eighty-one year old patient with high blood pressure, dyslipidaemia, type 2 diabetes and dilated myocardiopathy (ejection fraction [EF] 30%). Usual treatment: telmisartan, torsemide, metformin 850mg/8hrs, atorvastatin, carvedilol and omeprazole. She arrived at the emergency department with diarrhoea with mucus and blood, and vomiting, which had lasted for one week, as well as oligoanuria for 24 hours.

Physical examination: blood pressure: 120/70mm Hg, heart rate (HR): 95bpm, temperature (T): 36ºC.

Neurological examination: Glasgow score 12, time/space disorientation and bradypsychia, with no signs of focusing. Rhythmic heart beat, no murmur, crackling until the middle field. No signs in the abdomen and lower limbs.

Biochemical tests showed: haemoglobin: 11.7g/dl; leukocytes: 18 030 (78.9% neutrophils); platelets: 307 000; glucose: 68mg/dl; urea: 133mg/dl; creatinine: 6.89mg/dl; sodium: 134mEq/l; potassium: 4.4mEq/l; pH: 6.89; pCO_2: 29mm Hg; bicarbonate: 6.9mmol/l; ionic calcium: 3.85mg/dl; anion gap: 28. Normal coagulation. Urine: pH: 6; creatinine: 71mg/dl; proteinuria: 400mg/dl; 100 red blood cells/field; 60 leukocytes/field; positive ketone bodies and negative drugs (benzodiazepines, barbiturates). Normal abdominal ultrasound with symmetrical kidneys (12cm); good corticomedullary delimitation.

Electrocardiogram: left bundle branch block (LBBB) at 93bpm. Chest X-ray: cardiomegaly and normal cranial computerised tomography (CT). She was diagnosed with stage 2 chronic kidney failure secondary to acute prerenal hypertensive and diabetic nephropathy in a tubular necrosis phase and high anion gap lactic metabolic acidosis. Repletion treatment with physiological saline solution (PSS) at 0.9%, and dextrose solution at 5%, loop diuretics and 1M sodium bicarbonate. Despite this treatment, she continued with anuria and her cognitive function continued to

Table 1. Evolution of metformin levels

Evolution	Metformin levels (mg/l)
Upon admission (predialysis)	34.4
24 hours	21.3
48 hours	10.2
96 hours	4.8

deteriorate. We therefore decided to perform her first 2-hour haemodialysis session without ultrafiltration. Having confirmed hyperlactacidaemia (10.7mmol/l), high metformin levels (34.4mg/l; therapeutic levels 1.3-5) and symptoms of heart overload with haemodynamic disorder, we decided to perform dialysis for four days and then every 48 hours until reaching a constant lactate decrease and non-toxic levels of metformin (Table 1). She received 7 sessions in total. She received empirical antibiotic therapy with third-generation cephalosporin; the urine and faecal cultures were negative.

She was discharged without any neurological and renal symptoms, with creatinine at 1.6mg/dl and the following treatment: carvedilol at a dosage of 6.25mg/24hrs, repaglinide at a dosage of 1.5mg/8hrs, telmisartan, atorvastatin, torsemide at a dosage of 10mg/24hrs and omeprazole at 20mg/24hours.

She currently presents with 1.26mg/dl creatinine and is neurologically stable.

1. Gainza FJ, Jimeno I, Muñiz R. Acidosis láctica asociada con la utilización de metformina: Papel de la hemodiálisis en el tratamiento. Nefrologia 1998;18(5):427-30.
2. Solano M, González C, Álvarez M. Acidosis láctica en paciente diabético tratado con metformina. An Med Interna (Madrid) 2004;21(6):288-90.
3. Holanda MS, Suberviola B, González A. Acidosis láctica grave asociada a intoxicación por metformina. Nutr Hosp 2007;22(1):124-5.
4. Devetzis V, Passadakis P, Panagoutsos S. Metformin-related lactic acidosis in patients with acute kidney injury. Int Urol Nephrol 2010. doi: 10. 1007/s11255-010-9845-1.
5. Friesecke S, Abel P, Roser M. Outcome of severe lactic acidosis associated with metformin accumulation. Critical Care 2010;14:R226. doi: 10.1186/cc9376.

M.A. Martín Gómez[1], M.D. Sánchez Martos[1], S.A. García Marcos[1], J.L. Serrano Carrillo de Albornoz[2]

[1] Nephrology Unit. Poniente Hospital. El Ejido. Almería. Spain.

[2] Department of Internal Medicine. Poniente Hospital. El Ejido, Almería. Spain.

Correspondence: M.A. Martin Gómez
Unidad de Nefrología. Hospital de Poniente.
Ctra. de Almerimar, s/n.
04700 El Ejido. Almería.
doritamg@gmail.com
mda2505@gmail.com

Warning against unexpected medication in haemodialysis

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To the Editor,

As nephrologists we are used to having to be extremely careful with the medications given to advanced kidney failure patients. However, our patients tend to have multiple disorders, meaning that we must obtain second opinions from other specialists. There are different types of consultations, and often very complex patients have a reduced visit time. Drugs are prescribed, sometimes correctly, but on other occasions without considering the degree of the renal function. It is our responsibility to supervise the dose of these drugs that are added to their usual medication, to prevent any surprises from occurring, such as the ones that we are to describe.

Seventy-eight year old male, diagnosed with end-stage kidney failure, undergoing regular haemodialysis. He arrived at the emergency department because of motor discoordination. Neurologically, he presented with ataxia, motor aphasia and visual hallucinations. Five days before, he presented pain in his left side, and erythematous and vesicular lesions in the same area. We prescribed acyclovir at a dosage of 400mg, and subsequent dosages of 200mg every 24 hours. The patient incorrectly ingested 400mg every 8 hours. After receiving a haemodialysis session, he improved rapidly and was discharged the following day. Alcohol poisoning was first suspected in the emergency department, but was dismissed given that ethanol levels were zero.

Seventy-five year old male undergoing regular haemodialysis for diabetic nephropathy, but who needed daily haemodialysis due to intense cramps, especially during the sessions. Suffering from polyneuritis, a specialist visit was arranged and he was prescribed treatment with baclofen (muscle relaxant). Two days after starting the treatment, he arrived at the emergency department presenting with intense tremors. We observed greatly intense fixed miotic and myoclonic pupils, which initially ceased with clonazepam. He then underwent dialysis and his pupils improved. He was discharged in 24 hours. The first diagnostic suspicion at the emergency department was uraemic myoclonus.

With these two cases, which are repeatedly referred to in the literature[1-6] and reported in our journal NEFROLOGÍA,[3,4] we aim to remind readers of how easily our patients become intoxicated and how difficult it is to reach a diagnosis in the emergency department. Unnecessary examinations are required (cranial computerised tomography, etc.) if data