



OLGU SUNUMU / CASE REPORT

Metformin associated lactic acidosis in a renal transplant patient

Böbrek nakil hastasında metforminle ilişkili laktik asidoz

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Abstract

Although metformin is a well tolerated anti-hyperglycemic drug it may cause lactic acidosis which has high mortality. In this paper we reported a renal transplant patient with lactic acidosis. Fifty-five year old renal transplant patient was admitted to our hospital with confusion and lactic acidosis. Her confusion improved dramatically after restoring blood glucose, supportive therapy and hemodialysis. Her obstructive ureteral stone was removed with ureteral catheterization. In follow up period her renal function was similar to baseline. In summary rapid diagnosis and also appropriate treatment including hemodialysis can prevent morbidity/ mortality in a patient with metformin associated lactic acidosis. Metformin users, especially renal transplant receivers who have high risk of acute renal failure, should be educated about the discontinuation of the drug when their urine volume decreased.

Key words: Metformin, lactic acidosis, renal transplant receiver, hemodialysis

Öz

Metformin iyi tolere edilen bir anti-hiperglisemik ilaç olmasına rağmen tedavisi sırasında mortalitesi yüksek laktik asidoza neden olabilir. Burada laktik asidoz ve böbrek yetersizliği gelişen bir böbrek nakil hastası rapor edilmiştir. Ellibeş yaşında böbrek nakil hastası hastanemize şuur bozukluğu, hipoglisemi ve laktik asidoz ile getirildi. Hastada postrenal akut böbrek yetersizliği saptandı. Hipoglisemi ve destek tedavisini takiben hemodiyaliz sonrası hastanın konfüzyonu dramatik olarak düzeldi. Üreteral taşın çıkarılmasından sonra böbrek fonksiyonları önceki değerlerde normal seyretti. Metformine bağlı gelişen laktik asidozda erken tanı ve geciktirilmeden hemodiyaliz dahil destek redavisi ile morbidite ve mortaliteyi önleyebilir. Ayrıca, akut böbrek yetersizliği gelişme riski yüksek transplant hastaları dahil metformin kullanan hastaların idrar azalması durumunda metformine ara vermesi konusunda eğitilmesi önemli olabilir.

Anahtar kelimeler: Metformin, laktik asidoz, böbrek nakil hastası, hemodiyaliz

INTRODUCTION

Metformin is a first-class oral anti-hyperglycemic agent used for treatment of type2 diabetes mellitus (T2DM). The most common side effects of metformin are diarrhea, nausea and vomiting. Lactic acidosis is a rare but serious side effect of this drug¹. Here we presented uremia and severe lactic acidosis and acute renal failure secondary to ureterolithiasis associated with metformin using in a case with renal transplant receiver.

CASE

55 year-old-woman admitted to intensive care unit

(ICU) with confusion. She had been transplanted 7 years ago. She had the history of nausea, vomiting and decreased urine output in the last three days. On physical exam Glasgow Coma Scale was 9-10. Blood pressure was 140/80 mmHg, pulse 92 was per minute, temperature was 37⁰C.

There was crepitant rales at lungs and moderate pretibial edema. She had been treated with tacrolimus, mycophenolate mofetil, prednisolone, metformin and glimepiride for the last 7 years. She had been operated for lumbal disc hernia at another center two weeks ago. Her renal function tests were normal and blood glucose, HbA1c and serum tacrolimus levels were within targeted limits. Laboratory tests in the last 30 days and during

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clinical follow up in the last 5 days were summarized on Table 1. Blood glucose was found as 17mg/dl in ICU. Blood glucose returned to normal level after dextrose infusion but her confusion did not improve. Abdominal ultrasound showed slightly enlarged transplanted kidney, dilatation at renal pelvis (2 cm) and grade 2 hydronephrosis. Her condition dramatically improved following

immediate hemodialysis. Following 6 hours of hemodialysis, confusion and lactic acidosis improved. Ureteral calculi causing hydronephrosis was removed by catheter. After catheterization oliguria and uremia disappeared. Her blood sugar was regulated with insulin. The maintenance immunosuppressive medications were re-started. In follow up period any adverse event did not develop.

Table 1. Laboratory findings during hospitalization and pre-post hospital period

	BUN mg/dL	Creatinine mg/dL	Glucose mg/dL	Na mEq/L	K mEq/L	Ca mg/dL	pH	HCO ₃ mmol/dL	pCO ₂ mmHg
-30th day	13	0,61	115	138	4	9,9			
Admission	105	7.95	17	134	5.96	8.62	7.15	10.6	26.6
Day 1	30	5.59	129	125	4.5	8.1	7.39	16.8	27.9
Day 2	36	5.3	124	119	3.6	7.9	7.37	19.3	35.6
Day 3	47	3.55	125	131	3.1	8.3	7.40	25.4	41.8
Day 4	45	1.79	126	140	3	8.7	7.38	25.5	43.7
Day 5	28	1.11	123	134	3.4	8.2	7.34	22.3	42
Day 6							7.37	23.3	41.2
+ 90th day	16	0.91	117	139	3.9	8.1			

DISCUSSION

Metformin improves hyperglycemia by reducing hepatic gluconeogenesis and stimulating intracellular glucose uptake. Major routes of metformin elimination are glomerular filtration and tubular secretion. Metformin related adverse events may develop due to decreased clearance and metformin dosage must be reduced in patients with decreased glomerular filtration rate (GFR) (<30-45 ml/minute).

The most serious side effect of metformin use is lactic acidosis. This side effect is more common in patients with co-morbid diseases such as renal failure and liver dysfunction³. Lactate is substrate for hepatic gluconeogenesis and can be eliminated from kidneys. For this reason blood lactate level does not increase significantly in healthy people. However in the presence of renal dysfunction lactate and metformin clearance decrease and their blood levels increase⁴. Clinically significant lactic acid accumulation occurs in cases with renal insufficiency (serum creatinine > 1.4 mg/dL [124 µmol/L] in women and 1.5 mg/dL [132 µmol/L] in men), or low creatinine clearance, and also in cases with concurrent liver disease, alcohol abuse, heart failure, history of lactic acidosis, decreased tissue perfusion or hemodynamic instability, hypoxic states or severe acute illness. In our case, predisposing factor was

acute renal failure due to ureteral calculus in transplanted kidney.

Metformin-associated lactic acidosis (MALA) is defined as a syndrome of high blood lactate level with acidemia in patients treated with metformin, after excluding other causes of lactic acidosis. It can also develop in cases receiving toxic doses of metformin and even in therapeutic doses. The incidence of MALA is not clearly documented with estimated 3 and 9 cases per 100,000 patient year. However its mortality is extremely high, more than half of the patients die. Mortality and morbidity decrease with the early hemodialysis⁵. The treatment involves correction of acidosis and also to remove the causes of lactic acidosis and supportive therapy. Hemodialysis relieves lactic acidosis and also efficiently removes metformin and lactate from plasma and prevents further lactate accumulation. Following 6 hours of hemodialysis, impairment of consciousness and lactic acidosis improved in our patient. Confusion and lactic acidosis recovered after glucose infusion and hemodialysis. Previously we successfully treated a hemodialysis patient with coma and Metformin induced lactic acidosis⁶.

In conclusion, lactic acidosis and hypoglycemia due to metformin using in a renal transplant case, dramatically improved with hemodialysis and supportive care. After removing the obstruction, function of transplanted kidney regained to baseline

levels at follow-up period. Therefore we must be careful in the use of metformin in cases with renal transplantation who are high risk for acute kidney injury including obstructive renal disease. Metformin users especially renal transplant patients who have high risk of acute renal failure, should be educated about the discontinuation of the drug when their urine volume decreased.

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