Elvir Mučić[1], Damir Peličić[1,2]

LAKTATNA ACIDOZA POVEZANA SA METFORMINOM

Sažetak: U ovom radu dali smo kratak osvrt na laktatnu acidozu povezanu sa metforminom kod bubrežnih bolesnika, trećeg do četvrtog stadijuma hronične bubrežne bolesti . Prikazan je bolesnik muškog pola, starosti 70 godina, koji je unazad dvadeset godina lečen od dijabetesa tip 2. Kako je uzimao visoke doze metformina u kućnim uslovoma, bez nadzora porodice i lekara, primljen je urgentno na Klinici za Nefrologiojunefrologiju, Kliničkog centra Crne Gore u Podgorici, gde je momentalno urađena dijagnostika i pacijent je uključen na hemodijalizu, uz ostalu simptomatsku i konzervativnmu terapiju. Tokom hospitalizacije kod pacijenta je došlo do poboljšanja opšteg stanja i laboratorijskih analiza aztotnih materija i kalijuma. U našem slučaju, pacijentovo lečenje hemodijalizom dovelo je do brze korekcije metaboličkih poremećaja i hemodinamske stabilizacije, te na kraju do oporavka, tako da nije bilo potrebe za njegovim daljim lečenjem hemodijalizom. Pacijent je otpušten kući dobrog opšteg stanja, pa se može zaključiti da je pravovremena dijagnoza laktatne acidoze povezane sa metforminom, od velikog značaja za lečenje hemodijalizom, kojom se uspešno koriguje težakški metabolički poremećaj. Ovaj slučaj predlaže značaj ranog prepoznavanja i lečenja pacijenata sa laktatnom acidozom kod dijabetičara i bubrežnih bolesnika koji nekontrolisano ili neadekvatno uzimaju terapiju metformina za lečenje dijabetesa tip 2.

Ključne reči: Hronična bubrežna bolest, DM 2, mlečna kiselina, hemodijaliza

Uvod

Laktatna acidoza povezana s metforminom (MALA) je retka i ozbiljna neželjena komplikacija, koja se manifestuje visokom stopom smrtnosti, od 30–50%. Njeno rano prepoznavanje i pravovremeno započinjanje dijagnoze i lečenja mogu smanjiti morbiditet i smrtnost kod pacijenata s MALA (1). To je ozbiljno medicinsko stanje koje nastaje zbog nakupljanja mlečne kiseline u krvi i drastičnog pada pH plazme (1).

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U literaturi, MALA je rijetka komplikacija koja se javlja kod pacijenata lečenih od od dijabetesa tipa 2 (DM2), koja može biti uzrokovana visokim unosom lekova ili komorbiditetima, poput insuficijencije bubrega (2). Manifestuje se gastrointestinalnim simptomima, izmenjenim mentalnim stanjem i povišenim azotnim materijama u serumu i čestro zahtijeva lečenje hemodijalizom (2).

Iako se upotreba metformina preporučuje u liječenju DM2, potreban je veliki oprez pri propisivanju ovog leka pacijentima sklonim sistemskim hipoperfuzijskim stanjima, jer može dovesti do nakupljanja štetnih produkata metabolizma u telu pacijenta i metaboličkih poremećaja koji mogu rezultirati laktičnom acidozom povezanom s metforminom (3).

Prikaz bolesnika

Pacijent B. R., starosti 70 godina, primljen je u Nefrološku kliniku putem Urgentnog centra kasno navečer 4. jula 2026. goidine, u stanju opasnom po život zbog laktične acidoze.

Dan pre prijema, pacijent je razvio gastrointestinalne simptome, poput mučnine i povraćanja, kao i učestalo štucanje. Povraćao je oko deset puta u dvadeset četiri sata. U posljednja dva dana, prijavljuje ređe mokrenje, bez dizuričnih smetnji. Pri prijemu, analize krvi uključuju povišen serumski kreatinin od 980 mmol/l, s hiperkalijemijom i laktičnom acidozom. Pacijent se leči od DM2 više od 20 godina, na inzulinskoj je terapiji, ali je uzimao i metformin samoinicijativno, te ga dugo nije pratio endokrinolog.

Pri prijemu, svestan, orijentisan, komunikativan, blago dispnoičan u mirovanju, afebrilan, acijanotičan, antikteričan, dehidriran. Disanje normalno. srčani ritam ritmičan, jasni tonovi, sistolni šum iznad prekordijuma. Abdomen mekan, blago osetljiv u epigastrijumu. Pacijent je dugogodišnji dijabetičar, a heteroanamnezom je utvrđeno da uzima lijek Metformin u visokim dozama. Po prijemu su verifikovane izuzetno povišene vrednosti azotnih materija u serumu sa oligurijom. Odmah nakon prijema, postavljen je centralni venski kateter (CVC) za hemodijalizu, u desnu femoralnu venu i pristupilo se hitnoj hemodijalizi. Propisana je parenteralna rehidratacijska terapija, terapija antibioticima širokog spektra i druga neophodna konzervativna terapija. Propisana terapija rezultirala je oporavkom bubrežne funkcije, uz očuvanu diurezu i serumski kreatinin od 248 mmol/l, optimizaciju diureze i dobro opšte stanje, ali je neophodno dalje kontinuirano praćenje od strane nefrologa i endokrinologa.

Konsultovan je endokrinolog na osnovu glikemijskog profila i započeta je modifikovana inzulinska terapija. Na dan otpusta, CVC je uklonjen iz desne femoralne vene.

Pacijent je otpušten 10. jula 2026. godine sa dobrim opštim stanjem. Terapija je propisana i zakazan je kontrolni pregled kod endokrinologa i nefrologa u ambulantnim uslovima.

Diskusija

Metformin se koristi u lečenju DM2 više od 60 godina, a ravnoteža između njegovih koristi i nus pojava ostaje predmet rasprave (4).

Literatura sugeriše da je laktatna acidoza zaista redak i vrlo ozbiljan neželjeni događaj kod dijabetičara lečenih metforminom, sa incidencom od 0,03–0,1 slučaja na 1000 pacijenata-/godina i visokom stopom smrtnosti od približno 50% (5).

Liberalizacija smernica za propisivanje metformina u Sjedinjenim Američkim Državama i Evropskoj uniji, posebno u pogledu upotrebe u uznapredovanim stadijimima stadijumima hronične bolesti bubrega (KBB), dovela je do ponovnog interesa za temu MALA (6).

Uprkos prilagođavanju doze metformina kod pacijenata s oštećenom funkcijom bubrega, pacijenti s DM2 i bubrežnom insuficijencijom stadijuma III–IV, imaju veći rizik od brzog pada funkcije bubrega, a toksičnost metformina može se javiti ako se lek primenjuje nekontrolisano i bez redovnog praćenja od strane endokrinologa i nefrologa (6).

Literatura takođe sugeriše da MALA čini manji udeo slučajeva, nego laktična acidoza, koja nije povezana s metforminom (7–9).

Zaključak

U našem slučaju, pacijentovo lečenje hemodijalizom dovelo je do brze korekcije metaboličkih poremećaja i hemodinamske stabilizacije, te na kraju do oporavka, tako da nije bilo potrebe za njegovim daljim lečenjem hemodijalizom. Pacijent je otpušten kući dobrog opšteg stanja.

Može se zaključiti da je pravovremena dijagnoza MALA, od velikog značaja za lečenje hemodijalizom pute, kojim se uspešno koriguju teški metabolički poremećaj.

Ovaj slučaj predlaže značaj ranog prepoznavanja i lečenja pacijenata sa laktatnom acidozom kod dijabetičara i bubrežnih bolesnika koji nekontrolisano ili neadekvatno uzimaju terapiju metformina za lečenje DM2.

Konflikt interesa

Autori se izjašnjavaju da nena nema sukoba interesa.

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METFORMIN – ASSOCIATED LACTIC ACIDOSIS

Abstract: In this paper, we provide a brief review of metformin-associated lactic acidosis in renal patients with stage 3 to 4 chronic kidney disease. A 70-year-old male patient is presented, who has been treated for type 2 diabetes for the past twenty years. Since he was taking high doses of metformin at home, without the supervision of his family or doctor, he was urgently admitted to the Nephrology Clinic of the Clinical Center of Montenegro in Podgorica, where diagnostics were immediately performed and the patient was included in hemodialysis, along with other symptomatic and conservative therapy. During hospitalization, the patient's general condition and laboratory analyses of nitrogenous substances and potassium improved. In our case, the patient's treatment with hemodialysis led to rapid correction of metabolic disorders and hemodynamic stabilization, and ultimately to recovery, so there was no need for his further hemodialysis treatment. The patient was discharged home in good general condition, and it can be concluded that timely diagnosis of metformin-associated lactic acidosis is of great importance for hemodialysis treatment, which successfully corrects a severe metabolic disorder. This case suggests the importance of early recognition and treatment of patients with lactic acidosis in diabetics and renal patients who are taking uncontrolled or inadequate metformin therapy for the treatment of type 2 diabetes.

Keywords: Kidney renal disease, DM 2, Lactic acid, Hemodialysis

Introduction

Metformin-associated lactic acidosis (MALA) is a rare and serious adverse complication, with a high mortality rate of 30–-50%. Its early recognition and timely initiation of diagnosis and treatment can reduce morbidity and mortality in patients with MALA (1).

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It is a serious medical condition caused by the accumulation of lactic acid in the blood and a drastic drop in plasma pH (1). In the literature, MALA is a rare complication that occurs in patients treated for type 2 diabetes (DM2), which may be caused by high drug intake or comorbidities such as renal insufficiency (2).

It is manifested by gastrointestinal symptoms, altered mental status and elevated nitrogenous substances in the serum and often requires treatment with hemodialysis (2).

Although the use of metformin is recommended in the treatment of DM2, great caution is required when prescribing this drug to patients prone to systemic hypoperfusion conditions, as it may lead to the accumulation of harmful metabolic products in the patient's body and metabolic disorders that may result in metformin-related lactic acidosis (3).

Presentation of the Patient

Patient B. R., age 70, was admitted to the Nephrology Clinic via the Emergency Center late on the evening of July 4, 2026, in a life-threatening condition due to lactic acidosis. The day before admission, the patient developed gastrointestinal symptoms, such as nausea and vomiting, as well as frequent hiccups. He vomited about ten times in twenty-four hours. In the last two days, he reports less frequent urination, without dysuric disturbances.

On admission, blood findings include an elevated serum creatinine of 980 mmol/l, with hyperkalemia and lactic acidosis. He has been treated for type 2 diabetes for more than 20 years, he is on insulin therapy, but he also took metformin on his own initiative, and was not monitored by an endocrinologist for a long time.

On admission, conscious, oriented, communicative, slightly dyspneic at rest, afebrile, acyanotic, anticteric, dehydrated. Breathing normally. heart rate rhythmic, clear tones, systolic murmur above the precordium. Abdomen soft, slightly sensitive in epigastrium. The patient is a long-term diabetic, and the heteroanamnesis revealed that he was taking Metformin in high doses. Upon admission, extremely elevated values of nitrogen substances in the serum with oliguria were verified. Immediately after admission, a central venous catheter (CVC) for hemodialysis was placed in the right femoral vein and emergency hemodialysis was started. Parenteral rehydration therapy, broad-spectrum antibiotic therapy and other necessary conservative therapy were prescribed.

The prescribed therapy resulted in the recovery of renal function with preserved diuresis and serum creatinine of 248 mmol/l, optimization of diuresis and good general condition, but further continuous monitoring by a nephrologist and endocrinologist is necessary. An endocrinologist was consulted based on the glycemic profile and

modified insulin therapy was started. On the day of discharge, the CVC was removed from the right femoral vein.

The patient was discharged on July 10, 2027 with a good general condition. Therapy is prescribed and a control examination is scheduled with an endocrinologist and a nephrologist in outpatient settings.

Discussion

Metformin has been used in the treatment of DM2 for more than 60 years, and the balance between its benefits and side effects remains a matter of debate (4).

The literature suggests that lactic acidosis is indeed a rare and very serious adverse event in diabetic patients treated with metformin, with an incidence of 0.03–0.1 cases per 1000 patient-years and a high mortality rate of approximately 50% (5).

The liberalization of metformin prescribing guidelines in the United States of America and the European Union, particularly with regard to its use in advanced stages of chronic kidney disease (CKD), has led to renewed interest in the subject of MALA (6).

Despite adjusting the dose of metformin in patients with impaired renal function, patients with diabetes and stage III-IV renal insufficiency have a higher risk of rapid decline in renal function, and metformin toxicity may occur if the drug is administered uncontrolled and without regular monitoring by endocrinologists and nephrologists. In our case, the patient's treatment with hemodialysis led to a rapid correction of metabolic disorders and hemodynamic stabilization, and finally to recovery, so there was no need for his further treatment with hemodialysis (6).

The literature also suggests that MALA accounts for a smaller proportion of cases than non-metformin-related lactic acidosis (7–-9).

Conclusion

In our case, the patient's hemodialysis treatment led to rapid correction of metabolic disorders and hemodynamic stabilization, and ultimately to recovery, so that there was no need for his further hemodialysis treatment. The patient was discharged home in good general condition.

It can be concluded that timely diagnosis of MALA is of great importance for hemodialysis treatment, which successfully corrects severe metabolic disorders.

This case suggests the importance of early recognition and treatment of patients with lactic acidosis in diabetics and renal patients who are uncontrolled or inadequately taking metformin therapy for the treatment of DM2.

Conflict of Interest

The author declares no conflict of interest.

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