

# Is Continous Dialysis Effective to Treat Metformin Toxicity?

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## Abstract

**Case presentation** In this case, we are presenting 26-year-old young patients, who took 60-gram metformin plus 900 mg pioglitazone, presenting with abdominal pain, nausea, confusion, and lethargy. And lactic acidosis was treated with continuous hemodialysis >15 hours. Our aim, in this case, is to highlight the importance of continuous hemodialysis in the treatment of metformin poisoning. **Discussion** Metformin is an oral antidiabetic drug which is used as a first line treatment in the treatment of DM. Metformin poisoning is a rare condition seen by clinicians. One of the severe side effects of metformin poisoning is lactic acidosis and it can be fatal without on-time treatment due to acidosis-related complications. **Conclusion** Metformin toxication is a rare condition seen in clinical practice. Metformin associated lactic acidosis is one of the expected complication. The continous dialysis can be effective to treat the lactic acidosis caused by metformin toxication. **What's already known about this topic?** Lactic acidosis might be caused by metformin toxicity. Without on-time treatment for metformin toxicity, it can cause life-threatening condition. **What does this article add?** The treatment of hemodialysis, especially continous hemodialysis, might be beneficial to treat the patients with metformin toxicity. **Key words:** Metformin Toxicity, Dialysis, Lactic acidosis

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### Abstract

#### Case presentation

In this case, we are presenting 26-year-old young patients, who took 60-gram metformin plus 900 mg pioglitazone, presenting with abdominal pain, nausea, confusion, and lethargy. And lactic acidosis was treated with continuous hemodialysis >15 hours. Our aim, in this case, is to highlight the importance of continuous hemodialysis in the treatment of metformin poisoning.

#### Discussion

Metformin is an oral antidiabetic drug which is used as a first line treatment in the treatment of DM. Metformin poisoning is a rare condition seen by clinicians. One of the severe side effects of metformin poisoning is lactic acidosis and it can be fatal without on-time treatment due to acidosis-related complications.

#### Conclusion

Metformin toxication is a rare condition seen in clinical practice. Metformin associated lactic acidosis is one of the expected complication. The continous dialysis can be effective to treat the lactic acidosis caused by metformin toxication.

#### What's already known about this topic?

Lactic acidosis might be caused by metformin toxicity. Without on-time treatment for metformin toxicity, it can cause life-threatening condition.

### What does this article add?

The treatment of hemodialysis, especially continuous hemodialysis, might be beneficial to treat the patients with metformin toxicity.

**Key words:** Metformin Toxicity, Dialysis, Lactic acidosis

**Introduction:** Metformin is an oral anti-diabetic drug, which is a biguanide used to treat Diabetes Mellitus(1). Biguanides can be used as a monotherapy or combination with other drugs. Metformin increases the sensitivity of insulin, decreases the output of glucose from the liver, and increases the uptake of glucose by muscles(2). Common side effects are gastrointestinal such as metallic taste, bloating, abdominal discomfort, nausea, mild anorexia, and diarrhea(2). And one of the major side effects of metformin is lactic acidosis(3).

**Case :** A 26-year-old young patient after digesting 60 g metformin plus 900 mg pioglitazone for the suicidal purpose was admitted to the emergency ward. He presented with abdominal pain and discomfort, nausea, agitation, confusion, and lethargy 3 hours after digestion of drugs. His vital signs were as follows: blood pressure:115/85, pulse:110 beat/min, respiratory rate: 18 RR/min, oxygen saturation in room air: 96%. His laboratory results were glucose:123 mg/dL, creatinine:1,75 mg/dL, urea:27 mg/dL, alanine transferase(ALT):29 U/L, aspartate transferase(AST):17 U/L. Arterial blood gas (ABG) analysis showed acidosis pH:7.15, which was caused by elevated lactate levels. The lactate level was 7,8 mmol/L. The anion gap was calculated at 11 mmol/L(6 hours after the suicide attempt)(Table 1). The patient was transferred to the intensive care unit(ICU). At the time of admission to ICU, confusion, and lethargy worsened and blood glucose levels lowered to 64 mg/dL. IV dextrose (1 g/kg) was administered. IV saline was administered due to polyuria. A central venous catheter was performed and continuous dialysis was initiated. Hemodialysis was performed with Fresenius 4008 S device, 1.5 m2 high-flux FX-60 membrane (Fresenius), 300 ml/min blood flow rate, 500 mL/min dialysis fluid rate, 32 mmol/L bicarbonate, without ultrafiltration. At the 4th hour of dialysis, the patient was more oriented and cooperated. Continuous dialysis was performed for 15 hours. Lactate levels lowered and at the 48th hours following admission to ICU, lactate levels were completely normalized. The patient was discharged 3 days after admission to the hospital.

**Table 1:** The results of ABG

ABG following suicide attempt	pH	pCO2 (mmHg)	HCO3 (mmol/L)	Lactate (mmol/L)	Base Exc
6th hour (ABG at the time of admission)	7,15	48,5	13,8	7,8	-11
11th hours (2 hours after initiation of dialysis)	7,11	50,8	13,2	20	-12,2
14th hour	7,25	45,1	17,8	12,2	-6,7
17th hour	7,38	40,3	23,3	7,2	-0,7
20th hour	7,46	34,7	25,4	6	1,2
22th hour	7,40	32,9	21,5	7,9	-3,9
24th hour (After 15-hour dialysis)	7,40	38,3	23,5	6,7	-0,7
48th hour	7,40	44,8	26,5	1,8	3

**Discussion:** Metformin is an oral anti-diabetic drug used in the treatment of type 2 DM as a first-line treatment. It is absorbed from the upper part of the intestine and is excreted unmetabolized from the kidney via transporters in the proximal tubules. Elimination of metformin from the kidney takes 5 hours in those who have good renal function. But it can be accumulated in patients with acute or chronic kidney disease(4). One of the major complications of metformin is lactic acidosis despite the fact that it is rarely seen in patients with normal kidney function. Lactic acidosis is generally seen in patients with glomerular filtration rate lower than 30 mm/min. Moreover, It can be also seen in patients with metformin poisoning(5-6). Metformin-associated lactic acidosis(MALA) is a rare condition. Without diagnosis and on-time treatment, it might

have detrimental consequences. The diagnosis of MALA is based on lactic acidosis following metformin exposure. Metformin levels assessment is not easy and available in most centers. And because metformin is mostly intracellular toxin, measuring levels of metformin has no value to diagnose MALA(7). The mainstay of MALA treatment is supportive. Gastrointestinal clearing with activated charcoal and treatment with sodium bicarbonate or hemodialysis are suggested. The treatment is to remove the offending agent, balance acid-base status in the normal range, and buffer to acidosis by removing lactate through dialysis. Although removal of metformin by dialysis is uncertain due to high volume (63–646 l/kg) and it is mostly intracellular toxin, dialysis has importance to treat the complications of lactic acidosis(7-8). In one of the biggest studies conducted by Peter and et al., there was no significant difference in dialyzed and undialyzed MALA patients in terms of mortality. But the patients in the dialyzed group had the higher simplified acute physiology score II (SAPSII) and need for vasopressor compared to undialyzed group. Dialyzed group were more disadvantaged compared to undialyzed group in terms of SAPS II and the need for vasopressor. Because of these two factors, there was no difference in terms of mortality between the two groups. This indicates that dialysis might be beneficial in the treatment of MALA(7). **Conclusion:** Continuous dialysis might be beneficial in patients with MALA not to remove the metformin but especially to treat the lactic acidosis, which might be detrimental and life-threatening.

### Data Availability Statement

All datasets are available from the corresponding author upon reasonable request.

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