

## CASE REPORT

# Erectile dysfunction as a possible important side effect of metformin: A case report

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### Abstract

Metformin-induced sexual dysfunction is rare in patients with diabetes mellitus. Herein, we present the case of a 57-year-old man newly diagnosed with type 2 diabetes mellitus who developed erectile dysfunction following treatment with metformin 500 mg BD. Prior to taking metformin, he had well-controlled hypertension, hyperlipidaemia and normal sexual function. Two weeks after beginning metformin therapy, he was diagnosed with erectile dysfunction after experiencing persistent difficulty achieving an erection. After discontinuation of metformin, his sexual function returned to normal. To determine whether sexual dysfunction is caused by metformin, we rechallenged the patient with metformin 500 mg BD. After 15 days, he became impotent again, confirming that metformin was the most likely cause of his sexual problem. Metformin was stopped, and his sexual function returned to normal after 3 weeks. The adverse reaction is 'probable' according to the World Health Organization–Uppsala Monitoring Centre.

### Introduction

Metformin has been the first-line treatment for diabetes mellitus for several years, and its gastrointestinal side effects are well known. Metformin-induced sexual dysfunction has rarely been reported. It is crucial that doctors inquire about patients' general health, including their sexual history, during consultation. This case report highlights metformin-induced erectile dysfunction, which is fortunately reversible.

### Case presentation

A 57-year-old man with normal sexual function who had been treated for hypertension and hyperlipidaemia for the past 2 years was recently diagnosed with diabetes mellitus. His blood pressure and lipid level were well controlled with telmisartan 80 mg OD and atorvastatin 40 mg OD. He did not smoke, consume alcohol or take herbal supplements. Prior to taking metformin, he did not experience erectile dysfunction.

Metformin 500 mg BD was prescribed. In the first week of treatment, the patient experienced mild nausea, which completely subsided thereafter.

In the second week of taking metformin, he had difficulty achieving an erection despite having adequate arousal. In the Erection Hardness Scale (Table 1),<sup>1</sup> his erection hardness, which was rated as 3 prior to

treatment with metformin, decreased to 1, which significantly impacted his sexual life: He was unable to engage in sexual activity.

**Table 1.** Erection Hardness Scale.

0:	The penis does not enlarge.
1:	The penis is larger but not hard.
2:	The penis is hard but not hard enough for penetration.
3:	The penis is hard enough for penetration but not completely hard.
4:	The penis is completely hard and fully rigid.

Physical examination revealed a normal abdomen, external genitalia and testicular volume (20 mL). There were no indications of peripheral vascular disease, as the ankle-brachial index was normal at 1.2.

We screened the patient for anxiety and depression, which were not significant in this instance. He had a random blood glucose level of 9.2 mmol/L, normal sinus rhythm on electrocardiogram and negative urine microalbumin result. Thorough blood examinations were also performed. His glycated haemoglobin level was 7.8% (uncontrolled but still below 8.0%), and his liver, kidney and thyroid functions as well as his testosterone level were normal. The blood examination outcomes are detailed in Table 2. During follow-ups, his random blood glucose levels ranged between 7.8 and 9.0 mmol/L.

**Table 2.** Blood examination outcomes, including the liver and renal functions, thyroid-stimulating hormone level and serum testosterone level.

Outcomes	Detected value	Normal reference range	Unit
Alanine aminotransferase level	53	30–65	U/L
Aspartate aminotransferase level	24	13–35	U/L
Creatinine level	83	41–115	μmol/L
Urea nitrogen level	4.9	3.6–8.5	mmol/L
Fasting blood glucose level	7.4	<7	mmol/L
Glycated haemoglobin level	7.8%		
Thyroid-stimulating hormone level	2.49	0.4–4	mIU/L
Serum testosterone level	12.3	6.07–27.10	nmol/L

Throughout the study, we charted his sexual function using the International Index of Erectile Function (IIEF)<sup>2</sup> (Table 3).

**Table 3.** Changes in the International Index of Erectile Function before and after metformin therapy.

Area	Before starting metformin	Two weeks of metformin	Three weeks of metformin withdrawal	Two weeks of metformin rechallenge	Three weeks of metformin withdrawal
Erectile function	26	13	27	14	26
Orgasmic function	8	6	9	5	9
Sexual desire	9	9	9	9	9
Intercourse satisfaction	12	6	12	6	13
Overall satisfaction	9	3	9	3	9

After exhaustion of other possibilities, metformin-induced erectile dysfunction was suspected. We discontinued metformin, changed the treatment to gliclazide MR 120 mg OD and then added vildagliptin 50 mg BD to the regimen. Three days after stopping metformin, his sexual function began to improve, and 2 weeks later, both his sexual function and IIEF score returned to normal.

To determine whether metformin causes erectile dysfunction, we obtained informed consent from the patient to rechallenge him with metformin 500 mg BD. Within 10 days of taking metformin, he once again experienced difficulty achieving an erection, as indicated by a decrease in his IIEF score. On day 15, he was rendered completely impotent. Thereafter, metformin was withdrawn.

Fortunately, 3 weeks after he stopped taking metformin, his sexual function returned to normal.

### Discussion

Compared with men without diabetes mellitus, those with diabetes mellitus have a threefold increased risk of erectile dysfunction.<sup>3</sup>

Metformin is not known to cause erectile

dysfunction. It has been shown to improve endothelium-dependent vasodilation and may modulate sympathetic activity.<sup>4,5</sup> The beneficial effects of metformin are based on the hypothesis that this medication enhances erectile function by increasing the bioavailability of nitrite oxide in the corpus cavernosum. Despite the established evidence of vasodilation and sympathetic modulation of the vasculature in animal studies and human trials, only few studies have evaluated the use of metformin in the treatment of erectile dysfunction in humans.<sup>6</sup>

A recent randomised controlled trial found that metformin may lower the testosterone level and sex drive and cause low testosterone level-induced erectile dysfunction in patients with diabetes mellitus.<sup>7</sup>

Unfortunately, metformin caused erectile dysfunction in our patient. The dysfunction occurred during metformin treatment, and after the drug was stopped, the patient's sexual function returned to normal. This result suggests that metformin is most likely the cause of our patient's sexual dysfunction, which is fortunately reversible. This adverse drug reaction is classified as 'probable' in the World Health Organization–Uppsala Monitoring

Centre causality assessment system. An identical incident has been reported in Korea.<sup>8,9</sup>

Further research should examine the relationship between insulin resistance, nitrite oxide regulation and erectile dysfunction as well as the efficacy of metformin in treating erectile dysfunction.

### Conclusion

Metformin is a potential cause of impotence in our patient. The mechanism of metformin-induced sexual dysfunction is unclear. The patient's sexual function recovered after drug withdrawal, suggesting that metformin is the cause and that his sexual dysfunction is

reversible. Therefore, clinicians should be aware of this potential adverse effect. The relationship between metformin and erectile dysfunction should be the subject of additional research.

### Acknowledgements

We thank the patient who agreed to the publication of his case.

### Conflicts of interest

All authors declare no conflicts of interest.

### Patient's consent for the content for publication

The patient provided written consent.

### What is new in this case report compared to the previous literature?

- Metformin is commonly prescribed as the first-line treatment for type 2 diabetes mellitus; clinicians should be made aware of the potential erectile dysfunction this medication may cause.

### What is the implication to patients?

At the beginning of new treatments, it is crucial to inquire about patients' experience with medications, including their sexual function. Our patient was hesitant to inform doctors of the rare side effect he experienced (sexual dysfunction), which made him feel upset and frustrated. Fortunately, the side effect is reversible, and we switched the treatment to other oral hypoglycaemic agents.

## References

- Mulhall JP, Goldstein I, Bushmakina AG, Cappelleri JC, Hvidsten K. Validation of the erection hardness score. *J Sex Med*. 2007;4(6):1626–1634. doi:10.1111/j.1743-6109.2007.00600.x
- Rosen RC, Cappelleri JC, Gendrano N, 3rd. The International Index of Erectile Function (IIEF): a state-of-the-science review. *Int J Impot Res*. 2002;14(4):226–244. doi:10.1038/sj.ijir.3900857
- Maiorino MI, Bellastella G, Esposito K. Diabetes and sexual dysfunction: current perspectives. *Diabetes Metab Syndr Obes*. 2014;7:95–105. doi:10.2147/dmso.S36455
- Mather KJ, Verma S, Anderson TJ. Improved endothelial function with metformin in type 2 diabetes mellitus. *J Am Coll Cardiol*. 2001;37(5):1344–1350. doi:10.1016/s0735-1097(01)01129-9
- Manzella D, Grella R, Esposito K, Giugliano D, Barbagallo M, Paolisso G. Blood pressure and cardiac autonomic nervous system in obese type 2 diabetic patients: effect of metformin administration. *Am J Hypertens*. 2004;17(3):223–7. doi:10.1016/j.amjhyper.2003.11.006
- Patel JP, Lee EH, Mena CI, Walker CN. Effects of metformin on endothelial health and erectile dysfunction. *Transl Androl Urol*. 2017;6(3):556. doi:10.21037/tau.2017.03.52
- Al-Kuraishy HM, Al-Gareeb AI. Erectile dysfunction and low sex drive in men with type 2 DM: The Potential Role of Diabetic Pharmacotherapy. *J Clin Diagn Res*. 2016;10(12):Fc21–Fc26. doi:10.7860/jcdr/2016/19971.8996
- World Health Organization. The use of the WHO-UMC system for standardised case causality assessment. 2018. Accessed June 2022. [https://who-umc.org/media/164200/who-umc-causality-assessment\\_new-logo.pdf](https://who-umc.org/media/164200/who-umc-causality-assessment_new-logo.pdf).
- Dai W, Lee D. A patient with glucophage-induced sexual dysfunction: case presentation and review of the literature. *J Clin Exp Pathol*. 2020;10:375. doi:10.4172/2161-0681.1000375.