

## A Patient with Glucophage-Induced Sexual Dysfunction: Case Presentation and Review of the Literature

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### Abstract

**Background:** Attention to Glucophage induced impotence has attracted the attention of doctors. Optimal drugs for diabetes maximize therapeutic response and minimize adverse effects. Sexual activities in diabetes might decrease because of medications or sickness. So far there are no report to show the possible adverse effect of Glucophage-induced impotence.

**Case presentation:** We present a case of Type 2 diabetes mellitus with sexual dysfunction. Through self-control studies, we guessed that his impotence was due to the use of Glucophage. A 39-year-old male patient with diabetes without sexual dysfunction treated with Glucophage 500 mg bid. After 3 months, he became libido with impotence/anejaculation/anorgasmia. He was diagnosed with impotence. When off Glucophage for 2 weeks, his sexual function basically returned to the past. To verify whether Glucophage induced impotence, the patient was given Glucophage (500 mg bid) again after obtaining his consent. 17 days later, he became impotent again. When off 3 weeks, his sexual function/impotence returned to normal again.

**Conclusion:** Glucophage can cause sexual dysfunction, but it can be recovered after withdrawal. This indicates that Glucophage induced hypothyroidism or impotence can be reversed. Attention should be paid to drug related sexual dysfunction.

**Keywords:** Type 2 diabetes mellitus; Glucophage; Sexual dysfunction

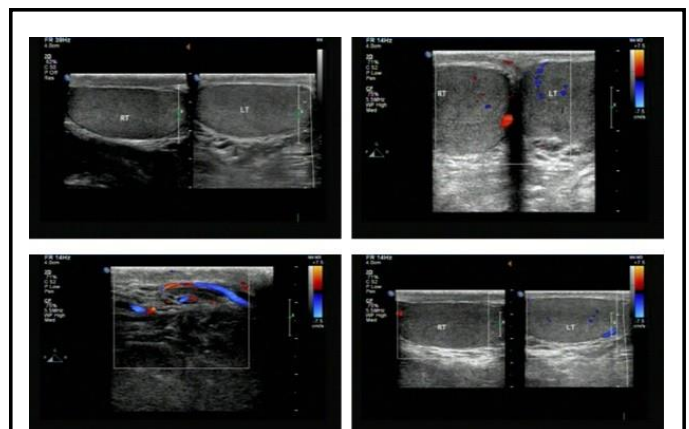
### Introduction

Optimal drugs for diabetes maximize therapeutic response and minimize adverse effects. Diabetes is a chronic disease with many complications, value and key to therapeutic drug treatment is adherence. Failure to adhere in treatment may lead to serious sexual dysfunction. Drug induced impotence is a cause of withdrawal or irregular medication. So far there are no report to show the possible adverse effect of Glucophage-induced sexual history. But, sexual activities in diabetes might decrease because of medications or sickness. It is important for the general physician to ask the patients about general conditions including sexual history while on medications. This case presentations that Glucophage induced sexual dysfunction.

### Case Presentation

A 39-year-old male Chinese patient with diabetes without sexual dysfunction treated immediately with Oral Glucophage (500 mg bid) after diagnosis of diabetes, without a personal history of diabetes or chronic disease, nor any special surgical or psychosocial background or toxic habits, and with a familial history of diabetes. There was only a mild gastrointestinal reaction during the treatment, such as mild nausea and mild appetite. The patient had diarrhea at the beginning of treatment. He continued to take the drug; the symptoms of diarrhea disappeared after 1 week. He insisted on taking the

Glucophage for half a year. In the past 3 months, his sexual function declined. His penile was often no obvious congestion and swelling during sleep. He also has no morning breek. when the patient had sexual intercourse, the penis often has no reaction, the penis volume often did not increase significantly, which motivated the patient to consult in my clinic. After night penile erection and hardness testing, he was diagnosed as impotence. Genital ultrasound showed no abnormalities in the testis and epididymis, and no varicocele was seen (Figure 1).



**Figure 1:** Genital ultrasound: no abnormalities in the testis and epididymis, and no varicocele was discovered.

In order to understand the degree of impotence, we carried out Erection hardness scale, his Erection hardness scale is 4, indicating that impotence is a serious. Erection hardness scale shows in Table 1.

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

**Table 1:** Erection hardness scale (EHS).

**Note:** 1) How would you rate the hardness of your erection?  
2) His scale is 4.

We further evaluate his mental disorders associated with impotence by SEAR questionnaire survey. SEAR score shows in Table 2.

Domain	With Glucophage	After Glucophage withdrawal	With Glucophage again	After Glucophage withdrawal again
Sexual relationship	48.89	78.89	42.22	76.67
confidence	58.89	81.11	55.56	77.78
Self-Esteem subscale	54.44	82.22	52.22	78.89
Overall relationship subscale	67.78	77.78	65.56	82.22
Overall (total) score	52.89	77.67	51.11	76.12

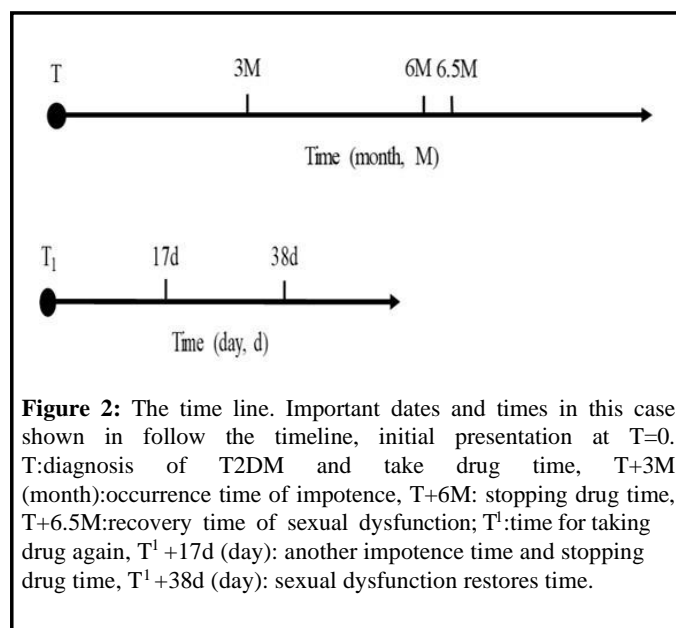
**Table 2:** The changes in SEAR domain, subscale, and overall scores for the patient with or without Glucophage.

Liver and kidney function, blood sugar, glycosylated hemoglobin, thyroid function and testosterone levels were not abnormal, the outcome show in Table 3.

Check item	Detected value	Normal range	reference	Unit
Alanine aminotransferase	23	7 to 40		U/L
Aspartate aminotransferase	19	13 to 35		U/L
Creatinine	62	41 to 115		$\mu$ mmol/L
Urea nitrogen	6.3	2.6 to 7.5		mmol/L
fasting glucose	5.6	3.9 to 6.1		mmol/L
2h Postprandial glucose	7.2	>7.8		mmol/L
Glycosylated hemoglobin	5.6	>7.8		mmol/L
Free triiodothyronine	5.48	3.80 to 6.00		pmol/L
Free thyroxine	9.25	7.86 to 14.41		pmol/L
Growth hormone	2.25	0.34 to 5.6		$\mu$ IU/ml
Testosterone	17.31	14 to 25.40		nmol/L

**Table 3:** The outcome of blood test in the patient.

Microalbumin creatinine ratio in urine is 11 and microalbumin in urine is 13.5  $\mu$ mol/L, which were normal. No abnormalities, ankle-brachial index is 1.1, were found in his peripheral vessels by arteriosclerosis noninvasive detector. ECG, cardio color doppler ultrasound, evoked potentials and electromyography were not abnormal. I just stopped using Glucophage and did not use any other hypoglycemic drugs. During the withdrawal period, his blood glucose level was higher than normal, fasting blood glucose was more than 7.5 mmol/L, postprandial blood glucose was more than 10.8 mmol/L. After stopping use of the drug, we observed his change in sexual function. When off metformin for 3 days, his sexual dysfunction was slightly improved. When off metformin for 1 week, his penis can be erectile but not permanent. When off metformin for 2 weeks, his sexual function basically returned to the past. The scales in SEAR was better than before. To verify whether Glucophage induced impotence, the patient was given Glucophage (500 mg bid) again after obtaining his informed consent through meticulous mutual understanding. 12 days, the patient's sexual desire began to decrease, 17 days later, he became impotent again. When off 3 weeks, his sexual function/impotence returned to normal again. Important dates and times in this case shown in follow the timeline (Figure 2), initial presentation at T = 0.



**Figure 2:** The time line. Important dates and times in this case shown in follow the timeline, initial presentation at T=0. T:diagnosis of T2DM and take drug time, T+3M (month):occurrence time of impotence, T+6M: stopping drug time, T+6.5M:recovery time of sexual dysfunction; T<sup>1</sup>:time for taking drug again, T<sup>1</sup>+17d (day): another impotence time and stopping drug time, T<sup>1</sup>+38d (day): sexual dysfunction restores time.

## Discussion

Type 2 diabetes mellitus (T2DM) is encountered in millions of people worldwide, with continuously rising incidence during the past decades, affecting their quality of life despite the increase of life expectancy in these patients. Erectile dysfunction (ED) associated with T2DM is therefore a more prevalent problem. ED is a common and distressing complication of diabetes with about 35% to 90% of diabetic men reported to suffer from ED [1]. The incidence of diabetes has increased year by year. Glucophage, product by the Bristol-Myers Squibb, is a proprietary, prescription- only preparation of biguanide metformin hydrochloride. Metformin is a cheap and efficacious Hypoglycemic agent with T2DM. In addition, evidence is mounting to support that metformin can reduce cardiovascular disease (CVD) [2-4]and reduce the risk of cancer and can increase lifespan and delay the onset of age-associated decline [5-17].

Therefore, it is unknown whether metformin can induce the risk of ED. Through humoral and instrumental testing, we did not find the patient with diabetic nervous system, macrovascular and microvascular complications. In this paper, we found that metformin was associated with impotence by self-control study. His penile blood flow was normal by color doppler ultrasound, which indicated that his ED maybe functional. After stopping the drug, sexual dysfunction can recover. Sexual dysfunction occurred again during he was retreated with the drug. After the withdrawal, the sexual relationship score, confidence score, self-esteem subscale score, overall relationship subscale and overall (total) score of SEAR score improved significantly; the scores of each part of the re-administration decreased and increased after drug withdrawal. Stopping the drug, the improvement of erectile function, the patient's emotional and the success rate of sexual intercourse were improved. The outcome suggesting that impotence caused by Glucophage is reversible.

## Conclusion

Because we have only observed one patient, the conclusion cannot represent universality. Whether not all of them are reversible, it is not clear. The pathophysiological mechanism of Glucophage-induced impotence is not clear. Is it psychological or drug? These need further study. We speculate that it may be this "no desire" state that perpetuates youth, and that this is one reason metformin slows aging and prolongs life span. This also needs further research to confirm.

Glucophage can cause sexual dysfunction, but it can be recovered after withdrawal. This indicates that Glucophage induced hypothyroidism or impotence can be reversed.

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## Declaration

## Ethics approval and consent to participate

The manuscript involves retrospective reporting of a clinical case managed inward of the said hospital by the author and the team and the hospital ethical committee was informed regarding the publication and consent was obtained from the patient for publication without personal identification details. Name of the ethics committee: Hainan Provincial People's Hospital ethics committee.

## Consent for publication

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by Editor-in Chief of this journal.

## Availability of data and materials

Available upon request.

## Competing interests

The authors declare that they have no competing interests.

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## Author's contributions

Wenxin dai management of the patient and writing the article, Dongwon lee overall supervising and management; the manuscript was prepared by the first author. All authors read and approved the final manuscript.

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