

## Metformin high dosage and bleeding episode: A clinical case study

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### ABSTRACT

Although metformin is a widely used anti-diabetic drug, it has certain side effects. This case reports a bleeding episode which occurred after up- titration of metformin while trying to achieve adequate glycemc control.

**Key words:** Bleeding, episode, metformin

### INTRODUCTION

Metformin is a widely used antidiabetic drug that is well-known among general practitioners.<sup>[1]</sup> This drug is considered a safe drug; however, adverse effects are noted.<sup>[2,3]</sup> In addition to its adverse effects, such as, induction of hypoglycemia, there are also other adverse effects, which include induction of bleeding. Such bleeding episodes can be mild or severe.<sup>[2,3]</sup> In this specific case report, the author reports a case of an old male diabetic patient presenting to the physician with the problem of a bleeding episode after getting the new adjusted high dosage of metformin, for controlling the blood glucose level.

### CASE REPORT

A 66-year-old man presented to the physician with a complaint of bleeding lesions. This case was of a diabetic patient with a long history of diabetes mellitus, about 20 years. The blood glucose level of this patient had been under control for a long time. His diabetes mellitus was controlled by oral metformin 1000 mg per day. However,

the patient visited the physician in the previous week and presented with a significantly increased blood glucose level. At that time, he denied any undesired behavior that could increase the blood glucose level, hence, the physician in charge decided to adjust his drug dosage. The new dosage was oral metformin 1700 mg per day. After taking this new dosage of metformin for three days, the patient's wife noticed that the patient has spontaneous painless epistaxis and told the patient to visit the physician again, but the patient rejected. However, on the seventh day the patient himself observed that he had painless epistaxis several times, hence, he decided to visit the physician.

At this time, the blood was analyzed and revealed that the patient had a normal platelet count with normal PT and aPTT. After careful history taking, the new evidence that the patient had not disclosed to the physician in charge on the previous visit, when he had stated that he had no undesired behavior that could increase the blood glucose level, came to light. On the previous visit, he had had a soft drink before getting fasting blood sugar determination. This patient was finally diagnosed as having a bleeding episode as an adverse effect of high dosage of oral metformin.

### DISCUSSION

Metformin is a widely used drug for diabetic patients. For sure, its adverse effects can be expected. In this report, the author described an interesting case study of a bleeding episode in a patient, due to the high dosage of oral metformin. In general, epistaxis has been reported in

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very few subjects taking metformin. Only 0.04% of the people who report adverse effects of metformin have epistaxis.<sup>[4]</sup> It usually occurs early in the course, with a high dose, commonly in subjects aged more than 50-years, with equal frequency in male and female. As this is an unusual adverse drug reaction, this is an interesting case report.

As already discussed, epistaxis in the diabetic patients using metformin is very rare. The epistaxis normally occurs only in cases on high dosage of metformin.<sup>[4]</sup> The above-mentioned patient had no aggravating activity or history of nasal trauma.<sup>[4]</sup> Also, it is usually painless.<sup>[4]</sup> These characteristics can be seen in the present case report. Focusing on the associated risk factors for developing the epistaxis, there is no evidence that having an underlying nasal abnormality increases the chance of bleeding. Also, there is no sexual preference. However, the identified risk factor is old age.<sup>[4]</sup> This may be due to the generalized generation of the vascular system in the elderly, especially those who are chronic sufferers of diabetes mellitus. In addition to epistaxis, other bleeding disorders such as eye bleeding and gastrointestinal bleeding as adverse effects of metformin intake can also be found.<sup>[1,2,4-9]</sup> The underlying mechanism leading to epistaxis as well as other bleeding disorders, in cases on metformin, is believed to be due to platelet malfunctioning.<sup>[5,6]</sup>

Indeed, there are some previous reports mentioning the platelet function aberration induced by metformin.<sup>[5,6]</sup> Actually, metformin is approved for the prevention of platelet aggregation.<sup>[7,8]</sup> It is considered that this effect of metformin is helpful in the control of cardiovascular complications in diabetic patients.<sup>[7,8]</sup> However, one coin has two sides. This action can be an unwanted adverse effect in some cases, especially for those who get unnecessary excessive metformin dosage. In addition, metformin also has a fibrinolytic nature on account of diminished plasminogen activator inhibitor 1 activity.<sup>[9]</sup> Bleeding as an

adverse effect of metformin is rare and should be kept in mind by general practitioners. Interestingly, a fatal bleeding case such as gastrointestinal bleeding can also be seen in patients taking metformin.<sup>[9]</sup>

In this case, we also learn the lesson that adjustment of the antidiabetic drug for a diabetic patient who was previously in good control to correspond to a single episode of undesired hyperglycemia should be carefully performed. In this case, the patient had concealed information and the danger to him was the outcome.

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