

## METFORMIN HYPERSENSITIVITY: A CASE REPORT

Abhijit Chowdhury<sup>1</sup> Jannatul Ferdoush<sup>2\*</sup> Amalendu Bikash Chowdhury<sup>3</sup>

### Summary

*Metformin is a popular oral antidiabetic medicine of the Biguanide class. It is widely chosen as the first line therapy for treating Type 2 Diabetes Mellitus. The drug is believed to be a comparatively safer agent for controlling blood sugar. This case report aims at describing an unusual phenomenon of Metformin hypersensitivity in a female patient who presented with perioral lesions.*

### Key words

Metformin; Diabetes; Hypersensitivity.

### Introduction

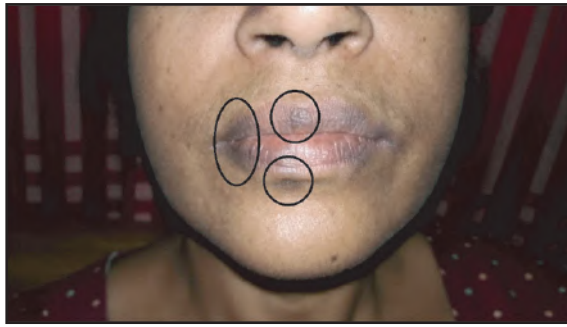
Type 2 Diabetes Mellitus (T2DM) is the pandemic of modern era which comes with dismal consequences. When patients with this metabolic disease fail to maintain adequate blood sugar with proper aerobic exercise, healthy dietary habit and lifestyle modification, then physicians prefer the oral antidiabetic drugs on the very first hand. Metformin is an oral anti-diabetic agent of the Biguanide class [1]. Sometimes it is recommended in pre-diabetes and for obesity. Lactic acidosis being the most severe adverse reaction caused by Metformin, it also has a lower risk of hypoglycaemia and rarely may cause hypersensitivity or allergy [2]. Psoriasis from drug eruption and leukocytoclastic vasculitis are the two most common manifestations of Metformin allergy [3–5]. The patients usually develop itching and rash within a few days of Metformin ingestion and become symptomatically relieved when the drug is stopped. The recurrence of skin lesions after restarting the drug is also notable [5]. The main objective of this write-up is to aware the health professionals on rare yet important metformin hypersensitivity.

1. PhD Research Fellow  
Centre for Clinical Epidemiology and Biostatistics  
Hunter Medical Research Institute  
The University of Newcastle, Australia.
2. Assistant Professor of Pharmacology & Therapeutics  
ChattagramMaa-O-Shishu Hospital Medical College, Chittagong.
3. Medical Superintendent (Retired)  
Chittagong Port Authority Hospital, Chittagong.

\*Correspondence: Dr. Jannatul Ferdoush  
Email : jannat\_fkh@yahoo.com  
Cell : 01856 189977

### Case Report

A 50 year old normotensive married woman hailing from Patiya, Chittagong presented to the physicians complaining of swelling of the upper lip and tingling sensation around the lips for a week. She is post-menopausal with Body Mass Index (BMI) of 29 kg/m<sup>2</sup>. Oral Glucose Tolerance Test (OGTT) 1 week back showed 120 minutes glucose level (Venous plasma) of 10.9 mmol/L. With a diagnosis of Impaired Glucose Tolerance (IGT), she was prescribed Metformin 500 mg once daily by a local general practitioner alongside advice for diet, exercise and lifestyle modifications. Two days after commencing the drug the patient first noticed gradual swelling and warmth of the upper lip alongside perioral itching and tingling. The discomfort persisted all day long, and it interfered with her quality of daily living. No other body area was involved, and all the systematic examinations revealed normal findings. The lady was interviewed explicitly on her food and drug history. She was asked about the quality of cosmetics she used and suspecting Metformin-induced hypersensitivity she was advised to stop the drug immediately. According to the patient, she was on no medication that time but Metformin. For resolution of her symptoms, she was prescribed Tablet Pheniramine Maleate 3 times daily for 7 days and Tablet Dexamethasone 1mg daily in 2 divided doses for 5 days. She was advised to follow up after a week with some routine blood tests and Serum IgE. On the next follow-up visit, her lip swelling and itchiness disappeared with darkening of the areas of lips affected before. Laboratory reports revealed Eosinophilia with RBS- 10 mmol/L and IgE- 850 UI/ml which supported the suspicion of Metformin allergy. The patient was then asked to start Metformin again and the following day she came with the same symptoms with more severity after a single dose of the drug. Clinically confirming the diagnosis of Metformin hypersensitivity she was advised to avoid the drug for the rest of her life and was prescribed oral Pheniramine Maleate and Dexamethasone for another week.



**Fig 1 :** Darkening of the involved areas of lips (In dark circles) following resolution of swelling

### Discussion

Now a days Metformin is a widely used oral hypoglycaemic agent [6]. Alongside Type 2 Diabetes Mellitus, it is also prescribed in obesity and in patients with Metabolic Syndrome [7,8]. It is well absorbed requiring no plasma protein binding and excreted in urine. Gastrointestinal upset is the most common adverse reaction of Metformin [9]. As a single agent, it has very slim chance to induce hypoglycaemia in type 2 diabetes patients.

Hypersensitivity to Metformin may also occur which is exceedingly rare. Metformin induced vasculitis reported by Viroj Wiwanitkit a 35 years female patient after starting Metformin developed palpable purpura on the upper part of lower limbs, near the genitalia [10]. The report is similar to this case report. Here, after taking Metformin the patient noticed gradual swelling and warmth of the upper lip alongside perioral itching and tingling and the lesions disappeared after discontinuing the drug and again reappear after restarting the drug.

There are several forms of clinical presentations for Metformin allergy. The lichenoid reaction of the oral mucous membrane may occur beside the leukocytoclastic vasculitis and psoriatic drug eruption. In Metformin hypersensitivity respiratory involvement is rarely seen. Grinspan's Syndrome (Triad of oral lichen planus, diabetes mellitus, and hypertension) could be seen in Metformin allergy [11]. The patient described in this case report had the classical scenario related to a drug allergy which in her case was Metformin. As no skin biopsy was done, it was inconclusive of which type of inflammatory reaction she suffered from. She had the on and off symptoms related to Metformin ingestion, diagnosed clinically with strong biochemical evidences and treated accordingly. Compared to

other Bangladeshi patients the patient we described in this report was atypical. In Bangladesh doctors readily prescribe this drug to their patients for better control of blood sugar as a primary agent but very few cases have been reported to have side effects like Metformin allergy.

### Conclusion

Like any other drug Metformin can cause a hypersensitivity reaction. Though it is rare, this potential drug allergy should always be kept in mind by the physicians while prescribing it.

### Disclosure

All the authors declared no competing interest.

### References

1. Skipper EW, Ormerod TP, Haste AR. Current therapeutics. CCXLVI. Metformin. Practitioner. 1968;200:868–873.
2. Sawin G, Shaughnessy AF. Glucose control in hospitalized patients. Am Fam Physician. 2010;81: 1121–1124.
3. Klapholz L, Leitersdorf E, Weinrauch L. Leucocytoclastic vasculitis and pneumonitis induced by metformin. Br Med J (Clin Res Ed). 1986;293:483.
4. Koca R, Altinyazar HC, Yenidünya S, Tekin NS. Psoriasisiform drug eruption associated with metformin hydrochloride: A case report. Dermatol Online J. 2003;9:11.
5. Ben Salem C, Hmouda H, Slim R, Dengezli M, Belajouza C, Bouraoui K. Rare case of metformin-induced leukocytoclastic vasculitis. AnnPharmacother. 2006;40:1685–687.
6. Langendam MW, Hooijkaas C, Piepenbrink JF. The increase in the use of drug treatment for diabetes mellitus in the Netherlands, 1998–2003. Ned TijdschrGeneesk. 2006;150:1396–1401.
7. Pelikánova T. Treatment of diabetes in metabolic syndrome. VnitrLek. 2009;55:637–645.
8. Svacina S. Obesity treatment in metabolic syndrome patients. VnitrLek. 2009;55:622–625.
9. Krentz AJ, Ferner RE, Bailey CJ. Comparative tolerability profiles of oral antidiabetic agents. Drug Saf. 1994;11:223–241.
10. Wiwanitkit V. Metformin Allergy. Indian J Pharmacol. 2011;43(2): 216–217.
11. Lamey PJ, Gibson J, Barclay SC, Miller S. Grinspan's syndrome: A drug-induced phenomenon? Oral Surg Oral Med Oral Pathol. 1990;70:184–185.