



CASE STUDY

Journal home page: www.jpadr.com

Safety profile and adverse drug reaction with causality assessment of Dapagliflozin in diabetes

Prabhudatta Mohapatra ^{a,*}, Karmajeet Rath ^b, Priyabrata Pattanayak ^a

^a Sri Jayadev College of Pharmaceutical Sciences, Naharkanta, Bhubaneswar, India-752101

^b IMS & SUM HOSPITAL, Siksha 'O' Anusandhan, Bhubaneswar, India-751003

ARTICLE INFO ABSTRACT



Received 16 February 2022; Revised 26 April 2022; Accepted 15 May 2022.	Introduction: Diabetes mellitus is a metabolic disorder characterized by high blood sugar levels and may damage nerves, kidneys, and other organs in the body. Currently, there are different anti-diabetic drugs prescribed by the physician to treat diabetes mellitus. Among them, dapagliflozin is now commonly prescribed for reducing blood glucose levels along with kidney protection.
Keywords: Dapagliflozin, polychondritis, adverse drug reaction, patient safety profile	Objective: The primary objective of the study was to describe adverse drug reaction (ADR) of dapagliflozin. Methods: This is a clinical observational study of an 81-year-old male patient with a hyperglycemic condition. Here the patient case study was done for the safety purpose in diabetes mellitus. Result: In this case of dapagliflozin intake the patient suffered from itching and rashes with redness in the bilateral external earlobes. The dermatologist labeled it as polychondritis of the ear cartilage. Recurrence of the symptoms when the patient was rechallenged with dapagliflozin. As per the dechallenge and rechallenge done in the patient, the withdrawal of dapagliflozin freed up this particular side effect. Conclusion: The patient was detected with an adverse drug reaction due to the intake of dapagliflozin. So, any administration of dapagliflozin should be followed up with possible polychondritis or itching and rashes in the skin in general and the ear lobe in particular.

An official publication of Global Pharmacovigilance Society.

Introduction

Diabetes mellitus is a chronic metabolic disorder, which causes high blood sugar. In a diabetic patient, the body may not make enough insulin or, can't utilize the insulin produced by the body. Diabetes mellitus is characterized by polyurea, polydipsia, and polyphagia. Diabetes leads to impairment of the nervous system, kidneys, and other organs of the body (Danaei *et al.*, 2011).

Various categories of anti-diabetic drugs or insulin are used for the treatment. Nowadays newer drugs of sodium-glucose co-transporter-2 (SGLT-2) inhibitor are commonly

used by the physician for better response. Dapagliflozin, canagliflozin, empagliflozin, remogliflozin are different drugs which belong to the SGLT-2 inhibitor group (Op den Kamp *et al.*, 2021; Singh *et al.* 2019; Anderson SL 2014; List *et al.* 2009).

Dapagliflozin is widely used to reduce the blood glucose level and also prevents renal reuptake of glucose. Dapagliflozin is mainly used in patients with heart failure and reduces the risk of being hospitalized and death due to heart and blood vessel disease. It is also used to reduce the risk of worsening kidney disease, the need to be



* Corresponding Author

Prabhudatta Mohapatra

E-mail: prabhudattamohapatra8@gmail.com

Contact: +7978637613

* Copyright: 2582-7235 // © 2022 The Author(s).

Published by Global Pharmacovigilance Society.

This is an open-access article under the CC BY-NC-ND license.



Available online 1 June 2022

hospitalized for heart failure, and the risk of death due to heart disease in adults with kidney disease.

Dapagliflozin has few side effects like rashes, itching, urgent, burning or painful urination, swelling of the legs and feet, etc.

Method

An 81-year-old, male patient came for consulting a diabetologist for his hyperglycemic condition with complaints of uncontrolled diabetes, dizziness and knee pain. The patient had fasting blood sugar (FBS) level of 128 mg/dL, and post prandial blood sugar (PPBS) level of 205 mg/dL and was prescribed Metformin 1000 mg, Glimepiride 1 mg, and Dapagliflozin 10 mg by the physician to control the diabetic level. The next day, patient developed rashes on both his earlobes and itching sensation along with intense head reeling and sweating.

Then he consulted a dermatologist and was diagnosed with 'polychondritis' of the ear lobes and advised not to further continue treatment with dapagliflozin. To treat

polychondritis cefuroxime 500 mg and levocetirizine 5mg with montelukast 10 mg was prescribed by the dermatologist. It has been presented in **Figure 1**.

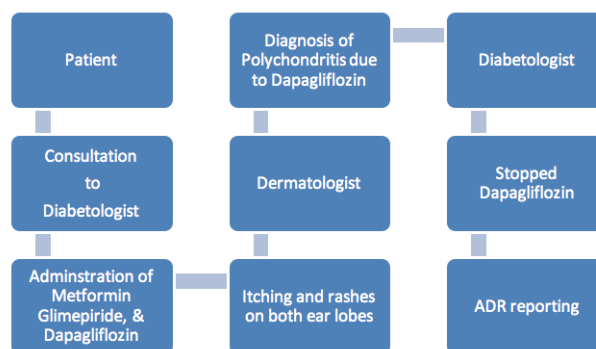


Figure 1: Flow chart of methodology and adverse drug reaction

Polychondritis may be the possible side effect of dapagliflozin (Ptaszynska *et al.*, 2015). The causality assessment of dapagliflozin has been presented in **Table 1**.

Table 1: Causality assessment of dapagliflozin

Sr. No.	WHO Scales	Certain	Probable	Possible	Unlikely	Unclassified	Unclassifiable
1	Time Relation	Yes	Yes	Yes	NA	NA	NA
2	Pharmacology	Yes	Yes	Yes	NA	NA	NA
3	Alternate Option	No	No	Yes	Yes	NA	NA
4	Dechallenge	+ve	+ve	Yes	NA	NA	NA
5	Rechallenge	+ve	NA	NA	NA	NA	NA

From these relational studies we found that Dapagliflozin relates to the adverse drug reaction, because after the rechallenge of dapagliflozin for five days, similar side effects recurred. In this study patient confidentiality has been properly maintained under due ethical practices.

Discussion

Long-term administration of anti-diabetic drugs requires proper drug monitoring by the physician and regular visits by the patient. To rule out kidney affliction and hepatic involvement, regular renal function test and liver function test are to be done (Ptaszynska *et al.*, 2015; Fioretto *et al.*, 2015). Few side effects occur which are rare and found only during long-term follow-up and monitoring of the patient. In this case of dapagliflozin intake, the patient suffered from itching and rashes with redness in the bilateral external earlobes. The dermatologist labelled it as polychondritis of the ear cartilage. As per the dechallenge and rechallenge done in the patient, the withdrawal of dapagliflozin freed up this particular side effect. These effects have not occurred by the use of the other anti-diabetic drugs, metformin and glimepiride as after their continuation, the patient did not have similar side effect.

Conclusion

Although dapagliflozin has been developed to treat type 2 diabetes mellitus (T2DM), polychondritis or itching and rashes on the skin in general and ear lobe in particular was observed. So, any administration of dapagliflozin should be followed-up with possible adverse drug reaction.

Conflict of Interest

Authors declare that there are no conflict of interest.

References

- Anderson S. L. (2014). Dapagliflozin efficacy and safety: a perspective review. *Therapeutic advances in drug safety*, 5(6), 242–254.
- Danaei, G., Finucane, M. M., Lu, Y., Singh, G. M., Cowan, M. J., Paciorek, C. J., Lin, J. K., Farzadfar, F., Khang, Y. H., Stevens, G. A., Rao, M., Ali, M. K., Riley, L. M., Robinson, C. A., Ezzati, M., & Global Burden of Metabolic Risk Factors of Chronic Diseases Collaborating Group (Blood Glucose) (2011). National, regional, and global trends in fasting plasma glucose and diabetes prevalence since 1980: systematic analysis of health examination

surveys and epidemiological studies with 370 country-years and 2.7 million participants. *Lancet (London, England)*, 378(9785), 31–40.

Fioretto, P., Giaccari, A., & Sesti, G. (2015). Efficacy and safety of dapagliflozin, a sodium glucose cotransporter 2 (SGLT2) inhibitor, in diabetes mellitus. *Cardiovascular diabetology*, 14, 142.

Heerspink, H., Stefansson, B. V., Correa-Rotter, R., Chertow, G. M., Greene, T., Hou, F. F., Mann, J., McMurray, J., Lindberg, M., Rossing, P., Sjoström, C. D., Toto, R. D., Langkilde, A. M., Wheeler, D. C., & DAPACKD Trial Committees and Investigators (2020). Dapagliflozin in Patients with Chronic Kidney Disease. *The New England journal of medicine*, 383(15), 1436–1446.

List, J. F., Woo, V., Morales, E., Tang, W., & Fiedorek, F. T. (2009). Sodium-glucose cotransport inhibition with dapagliflozin in type 2 diabetes. *Diabetes care*, 32(4), 650–657.

Op den Kamp, Y., de Ligt, M., Dautzenberg, B., Kornips, E., Esterline, R., Hesselink, M., Hoeks, J., Schrauwen-Hinderling, V. B., Havekes, B., Oscarsson, J., Phielix, E., & Schrauwen, P. (2021). Effects of the SGLT2 Inhibitor Dapagliflozin on Energy Metabolism in Patients With Type 2 Diabetes: A Randomized, Double-Blind Crossover Trial. *Diabetes care*, 44(6), 1334–1343.

Ptaszynska, A., Cohen, S. M., Messing, E. M., Reilly, T. P., Johnsson, E., & Johnsson, K. (2015). Assessing Bladder Cancer Risk in Type 2 Diabetes Clinical Trials: the Dapagliflozin Drug Development Program as a 'Case Study'. *Diabetes therapy: research, treatment and education of diabetes and related disorders*, 6(3), 357–375.

Singh, M., Sharma, R., Kumar, A. (2019). Safety of SGLT2 Inhibitors in Patients with Diabetes Mellitus. *Current Drug Safety*, 14(2), 87–93.