Subscription Agency
Exploring and Distributing Knowledge Globally

Pharmaceutical Sciences
Volume 4 Issue 2, 2024
eISSN No.: 2582-8371

Investigating Sitagliptin-Associated Bullous Pemphigoid: A Detailed Case Report

T. Lakshmi Prasanna[1*], Aruna.T [2]
[1]Pharmacovigilance Associate, Pharmacovigilance Programme of India, National Coordination Centre, Indian Pharmacopoeia Commission, Ghaziabad, India.
[2]Coordinator, ADR monitoring center, Govt. Kilpauk Medical college, Chennai-10.

Corresponding Author
Email: yesuprasanna@gmail.com

ABSTRACT
Dipeptidyl Peptidase-4 Inhibitors (DPP-4 Inhibitors) are a class of oral medications used primarily for the management of type 2 diabetes. They work by inhibiting the enzyme dipeptidyl peptidase-4, which plays a role in the breakdown of incretin hormones. Incretins, such as glucagon-like peptide-1 (GLP-1) and glucose-dependent insulinotropic polypeptide (GIP), help regulate blood glucose levels by stimulating insulin release and inhibiting glucagon secretion. studies have indicated that certain individuals using DPP-4 inhibitors, like sitagliptin, have experienced risk of developing Bullous Pemphigoid. This case report delves into the correlation between the antidiabetic drug Sitagliptin and the onset of Bullous Pemphigoid, an autoimmune blistering disorder.

Keywords: - *Sitagliptin, Bullous Pemphigoid, Autoimmune Disease.*

INTRODUCTION
Bullous Pemphigoid (BP) is an uncommon autoimmune blistering disease primarily observed in elderly individuals, characterized by generalized pruritic tense blisters and erosions on the skin. The autoimmune response in BP targets hemidesmosomal proteins, specifically BP180 and BP 230, at the dermo epidermal junction [1]. Dipeptidyl Peptidase 4 (DPP-4) inhibitors constitute a recent class of oral antidiabetic agents used in the treatment of type 2 diabetes. These inhibitors, including the first FDA-approved Sitagliptin in 2006, function by preventing the degradation of incretins [2]. This action leads to decreased glucagon release, increased insulin secretion, and a subsequent reduction in blood glucose levels. The drug-induced form of BP may occur following the oral or, in some cases, topical administration of specific drugs, with DPP-4 inhibitors being implicated. Recognizing this variant of BP is challenging as it closely resembles classic BP clinically [3]. It becomes crucial to consider this possibility in elderly patients who have recently initiated or modified their medication regimen, particularly by adding new drugs. This underscores the importance of vigilant monitoring and prompt medical attention if clinical features of BP or other adverse reactions arise in patients using DPP-4 inhibitors.

CASE REPORT
This was a ICSR (Individual Case Safety Report) reported to our Adverse drugs reactions monitoring center govt Kilpauk Medical College. The report from a healthcare professional presented a 72-year-old female with bullous Pemphigoid crusted erosion over scalp, trunk, feet. She was diagnosed with type II diabetes and with no other comorbidities. Her blood sugar levels were poorly controlled on conventional antidiabetics. So oral sitagliptin therapy was initiated. The dosage was 100 mg twice a day along with other hypoglycemic drugs.

Pharmaceutical Sciences
Volume 4 Issue 2, 2024
eISSN No.: 2582-8371

After three weeks of taking sitagliptin therapy, she developed bullous Pemphigoid crusted erosion over scalp, trunk, feet. The preliminary diagnosis remained as gliptin-induced bullous pemphigoid. The suspected drug was stopped, and medical treatment was initiated. Later the patient started recovering from the event. The reporter has not mentioned the concomitant drugs and rechallenge/rechallenge in the ICSR report.

DISCUSSION

Sitagliptin phosphate belongs to the DPP-4 inhibitor class for hypoglycemic drugs and was approved by the US Food and Drug Administration in 2006 [2]. It is used as a second-line drug for the management of type 2 diabetes mellitus. There are a few reports of cutaneous adverse effects such as bullous reaction, fixed drug eruption, and photosensitivity with sitagliptin. Definite pathogenesis of allergic reactions in the patients taking sitagliptin is unknown. DPP-4 inhibitors are incretin-based drugs used in diabetes mellitus type 2, which act by inhibiting the degradation of incretins and cause increased insulin secretion with alteration of blood glucose levels [4].

The analysis of previously published articles based on pharmacovigilance databases suggests an association between DPP-4 inhibitors and bullous pemphigoid, with most affected patients being over 70 years of age. Older age is one of the important risk factors, and most of the studies have reported the mean age of subjects with DPP-4i induced BP > 70-75 years. Patients with DPP-4 inhibitor-induced bullous reaction may present with inflammatory or a non-inflammatory phenotype of bullous pemphigoid [5]. Clinical improvement after withdrawal of the suspected drug suggests the diagnosis of drug-induced BP in our patient. Discontinuation of DPP-4 inhibitor treatment in patients with diabetes should be done when bullous reactions occur [6].

As stated in the WHO-UMC system for standardized case causality assessments, adverse drug reactions are rarely specific. According to the WHO-UMC algorithm, the level of causality of linagliptin-associated BP in our patient is ‘probable/likely.’

CONCLUSION

To conclude, the connection between the use of Dipeptidyl Peptidase-4 inhibitors (DPP-4i) and the development of autoimmune disorder is intricate. Recent research indicates that the utilization of DPP-4i may be linked to a reduction in the incidence of composite autoimmune disorder [7]. Bullous Pemphigoid (BP) is one such type of AD that can be induced by DPP-4i, particularly among the elderly population. studies also reported that females are more likely to develop DPP-4i induced BP [8]. This highlights the complexity of the relationship between DPP-4i and Autoimmune disorder, where the medication may have both positive and negative impacts on different aspects of Autoimmune disorder incidence.

Acknowledgement
The authors acknowledge National Coordination Centre – Pharmacovigilance Programme of India (PVPI) for their technical support provided.

Funding - Nil

Conflict of Interest – None to declare.

Disclaimer: The views here expressed are personnel and does not represent the opinion of NCC-PVPI or its scientific committee /group or other regulatory agencies.

REFERENCES

1) Gornowicz-Porowska J, Seraszek-Jaros A, Bowszyc-Dmochowska M, Kaczmarek E, Pietkiewicz P, Bartkiewicz P, Dmochowski M. Analysis of the autoimmune response against BP180 and BP230 in ethnic Poles with neurodegenerative disorders and bullous pemphigoid. Cent Eur J Immunol. 2017;42(1):85-90. doi: 10.5114/ceji.2017.67322. Epub 2017 May 8. PMID: 28680335; PMCID: PMC5470618.
2) Pathak R, Bridgeman MB. Dipeptidyl Peptidase-4 (DPP-4) Inhibitors in the Management of Diabetes. P T. 2010 Sep;35(9):509-13. PMID: 20975810; PMCID: PMC2957740.
3) Miyamoto D, Santi CG, Aoki V, Maruta CW. Bullous pemphigoid. An Bras Dermatol. 2019 Mar-Apr;94(2):133-146. doi: 10.1590/abd1806-4841.20199007. Epub 2019 May 9. PMID: 31090818; PMCID: PMC6486083.
4) Makrilakis K. The Role of DPP-4 Inhibitors in the Treatment Algorithm of Type 2 Diabetes Mellitus: When to Select, What to Expect. Int J Environ Res Public Health. 2019 Jul 30;16(15):2720. doi: 10.3390/ijerph16152720. PMID: 31366085; PMCID: PMC6696077.
5) Molina-Guarneros JA, Sainz-Gil M, Sanz-Fadrique R, García P, Rodríguez-Jiménez P, Navarro-García E, Martin LH. Bullous pemphigoid associated with the use of dipeptidil peptidase-4 inhibitors: analysis from studies based on pharmacovigilance databases. Int J Clin Pharm. 2020 Apr;42(2):713-720. doi: 10.1007/s11096-020-01003-6. Epub 2020 Mar 5. PMID: 32140915; PMCID: PMC7192859.
6) Thewjitcharoen Y, Wanothayaroj E, Thammawiwat C, Porramatikul S, Vorayingyong C, Nakasatien S, Krittiyawong S, Chanprapaph K, Himathongkam T. Clinical Features and Outcomes of Dipeptidyl Peptidase-4 Inhibitor-Associated Bullous Pemphigoid (DPP4i-Associated BP) in Thai Patients. Case Rep Endocrinol. 2020 Oct 10;2020:8832643. doi: 10.1155/2020/8832643. PMID: 33101737; PMCID: PMC7569454.
7) Roy A, Sahoo J, Narayanan N, Merugu C, Kamalanathan S, Naik D. Dipeptidyl peptidase-4 inhibitor-induced autoimmune diseases: Current evidence. World J Diabetes. 2021 Sep 15;12(9):1426-1441. doi: 10.4239/wjd.v12.i9.1426. PMID: 34630898; PMCID: PMC8472501.
8) Roy A, Sahoo J, Narayanan N, Merugu C, Kamalanathan S, Naik D. Dipeptidyl peptidase-4 inhibitor-induced autoimmune diseases: Current evidence. World J Diabetes. 2021 Sep 15;12(9):1426-1441. doi: 10.4239/wjd.v12.i9.1426. PMID: 34630898; PMCID: PMC8472501.