REPLY to MS#JAAD-D-19-00162

Reply to: Comment on “Oral diabetes medications other than dipeptidyl peptidase-4 inhibitors are not associated with bullous pemphigoid: A Finnish nationwide case control study” and a case report of glucagon-like peptide-1 receptor agonist induced bullous pemphigoid.

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To the editor: We thank Dr. Schwager and his co-authors for their interest in our recent publications.\textsuperscript{1,2} They comment that the title of our article\textsuperscript{2} may mislead the reader into prematurely ruling out oral diabetes medications other than gliptins as a possible aggravating factor for bullous pemphigoid (BP). We agree that our study may have not been able detect the association between the newer diabetes drugs and BP, due to the lack of data on oral diabetes medication used by patients with bullous pemphigoid after the year 2013. This limitation is clearly acknowledged in several parts of our paper including the abstract. We agree with the observation that our study included only a small number of patients using glucagon-like peptide-1 receptor agonists (GLP-1RAs). However, since our data were drawn from a nationwide data set, we consider our sample to be representative and do not share Dr. Schwager’s concern about the small numbers of subjects receiving certain classes of antidiabetic drugs.

Dr. Schwager and his co-workers present a case in which BP manifested six weeks after the initiation of treatment with the GLP-1RA dulaglutide. The patient’s BP resolved with topical corticosteroids after the withdrawal of dulaglutide. However, the authors do not describe the patient’s previous history of diabetes treatment. We have previously shown that the risk for BP is significantly increased by the use of dipeptidyl peptidase-4 inhibitors (DPP-4i), even when initiated more than a year prior to BP diagnosis.\textsuperscript{1} Other studies of DPP-4i-associated BP have described latency periods of over 6 months between DPP-4i initiation and BP onset.\textsuperscript{3,4} Therefore, the argument presented with this case is weakened by the lack of information on prior medication use.

The use of GLP-1RAs is increasing in Europe. However, as of January 2019, the numbers of suspected pemphigoid cases reported by health care professionals to the European database of suspected drug reactions (Eudravigilance, www.adrreports.eu) are low for exenatide (n=8), dulaglutide (n=5), and liraglutide (n=5). No suspected BP cases have been reported for patients receiving albiglutide or lixisenatide. Suspected cases of BP make up only 0–2% of all adverse skin
reactions in patients treated with GLP-1RAs. This is substantially lower than the rate of suspected BP cases associated with gliptin treatment.

A recent study compared the use of antidiabetic medications in 670 patients with BP and diabetes and 670 non-BP diabetic controls. There was no difference between the two groups in the use of antidiabetic agents other than DPP-4is. However, all the antidiabetic drugs aside from DPP-4is were analyzed as a group and therefore any potential association between GLP-1RAs could not be examined. Furthermore, to the best of our knowledge, there are no reports in the English language published literature of GLP-IRA-associated BP. Overall, we agree with the assertion of Dr. Schwager and his co-authors that more studies are needed to further clarify the potential association between the newer diabetes medications and BP.

References:


