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Dipeptidyl Peptidase 4 Inhibitors for Type 2 Diabetes and Relationships to Diabetic Macular Edema

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Abstract

Purpose : Diabetic retinopathy (DR) is a common cause of vision loss in working-age adults and a complication of type 2 diabetes mellitus (T2DM). Dipeptidyl-peptidase 4 inhibitors (DPP-4i) are commonly used to treat T2DM, but there are limited studies on the relationship between DPP-4i on diabetic macular edema (DME) development and progression. We performed a retrospective study to compare the development of DME among patients who had used DPP-4i versus those who had not used DPP-4i prior to a DME diagnosis.

Methods : Medical records of patients with diabetes evaluated at the University of Wisconsin between 2010-2022 were reviewed. Proportional hazard models were used to evaluate the association between use of DPP-4i medication and DME development. Separate models were used for each DR status and adjusted for age at DR diagnosis, T2DM duration, glycated hemoglobin (HbA1c), gender, and ethnicity. Participants were excluded if they did not receive DPP-4i and were treated with glucagon-like peptide 1 or sodium glucose cotransporter-2 medications, did not have a DR diagnosis, the DR diagnosis occurred less than a year before the first DME diagnosis, or had missing HbA1c values. A p-value ≤ 0.05 was considered statistically significant.

Results : 2,541 were included in the study: 158 participants were given DPP-4i prior to the first DME diagnosis and 2383 were never given DPP-4i or were given DPP-4i after the first DME diagnosis. 386 (15.2%) of included participants developed proliferative DR and 2,155 (84.8%) developed non-proliferative DR at the time of first DR diagnosis. Participants were 52.2% male, 83.4% white non-Hispanic, average age was 65.8 ± 14.33 years, with mean HbA1c of $7.8 \pm 1.43\%$. In patients with T2DM who had non-proliferative DR, the hazard ratio of developing DME was 1.13 (CI= 0.82 to 1.55; p= 0.447) and among patients who had proliferative DR, the hazard ratio was 1.44 (CI= 0.81 to 2.54; p= 0.213) after adjusting for covariates. HbA1c level was independently associated with a higher risk of DME among patients with non-proliferative DR (HR=1.27; CI= 1.18 to 1.37; p <0.0001) and proliferative DR (HR= 1.22; CI= 1.11 to 1.34; p < 0.0001).

Conclusions : We found no evidence of an association of DPP-4i use and increased hazard for the development of DME among patients with non-proliferative or proliferative DR.

This abstract was presented at the 2023 ARVO Annual Meeting, held in New Orleans, LA, April 23-27, 2023.

Variable	All	Macular Edema and DPP-4i Use	Macular Edema and No DPP-4i Use	No Macular Edema and DPP-4i Use	No Macular Edema and No DPP-4i Use
n	2541	19	327	139	2056
Age (years), mean (SD)	65.8 (14.33)	67.4 (10.31)	65.2 (11.62)	70.8 (10.26)	65.6 (14.92)
T2DM Duration (years), mean (SD)	15.8 (8.36)	12.5 (7.22)	13.7 (7.96)	15.3 (6.8)	16.2 (8.47)
HbA1c, mean (SD)	7.8% (1.43)	8.3 (1.56)	8.1 (1.46)	7.9 (1.07)	7.7 (1.44)
Proliferative DR Diagnosis	15.2%	15.8%	17.1%	2.2%	15.8%
Non-Proliferative DR Diagnosis	84.8%	84.2%	82.9%	97.8%	84.2%
Female	47.8%	47.4%	44%	53.2%	48%
White non-Hispanic	83.4%	73.7%	79.8%	89.9%	83.6%

Summary of all Included Subjects.

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