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Prevalence of Pruritus in Type 2 Diabetic Patients on GLP-1 Agonist Therapy

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INTRODUCTION

Chronic pruritus is a commonly underestimated comorbidity in type 2 diabetes mellitus (T2DM) patients, affecting between 18.4% to 27.5% of diabetics.[1] Glucagon-like peptide-1 (GLP-1) agonists have reportedly decreased itch in diabetics with concurrent psoriasis[2]; however, their role in targeting itch specifically remains unknown. To investigate the association of GLP-1 agonists and pruritus prevalence in T2DM, we conducted a retrospective cohort study utilizing the TriNetX database.

Four cohorts were defined as T2DM patients prescribed semaglutide, dulaglutide, liraglutide, or tirzepatide. The control cohort included T2DM patients without any GLP-1s. GLP-1 therapy was also compared with T2DM patients prescribed metformin. Additionally, the effects of GLP-1 therapy were analyzed between diabetics without neuropathy versus those with neuropathy. Sources of infectious itch and injection site pruritus were excluded from all groups. Cohorts were propensity matched for demographics, comorbidities, and comedications. Pruritus prevalence was evaluated at 14 days, 3 months, 6 months, and 12 months post-GLP-1 therapy (Table 1).

Compared to controls, all GLP-1 medications were associated with significantly decreased pruritus after two weeks. Following one year, semaglutide, dulaglutide, and tirzepatide further decreased itch prevalence versus 14 days. Relative to metformin, liraglutide did not significantly decrease pruritus at any point. Conversely, after two weeks, semaglutide, dulaglutide, and tirzepatide all lowered itch rates. After one year, semaglutide and tirzepatide were again associated with significantly decreased itch compared to two weeks. Additionally, semaglutide, dulaglutide, and liraglutide significantly improved pruritus in diabetics without neuropathy compared to those with neuropathy. Tirzepatide was associated with similar itch improvement in both groups.

Compared to controls, GLP-1 agonists were effective in decreasing pruritus prevalence. Semaglutide, dulaglutide, and tirzepatide also demonstrated superior itch relief relative to metformin. This suggests that these GLP-1 agonists' benefits on pruritus extend beyond glucose or hemoglobin A1c improvement. Additionally, approximately 50% of diabetics experience pruritus in the context of diabetic neuropathy.[1] However, diabetics without neuropathy were associated with greater or similar itch improvement after

TABLE 1.

Pruritus Prevalence at Various Time Points After GLP-1 Treatment

Cohorts	GLP-1 agonist	14 days	6 months	1 year
GLP-1 vs Control	Semaglutide	0.32 (0.33-0.36)	0.29 (0.28-0.31)	0.23 (0.22-0.25)
	Liraglutide	0.58 (0.54-0.63)	0.56 (0.51-0.60)	0.51 (0.47-0.56)
	Dulaglutide	0.46 (0.44-0.49)	0.43 (0.41-0.46)	0.39 (0.36-0.41)
	Tirzepatide	0.23 (0.21-0.25)	0.15 (0.13-0.17)	0.09 (0.08-0.11)
GLP-1 vs Metformin	Semaglutide	0.50 (0.46-0.54)	0.42 (0.39-0.47)	0.34 (0.30-0.38)
	Liraglutide	0.95 (0.81-1.12)	0.88 (0.74-1.05)	0.94 (0.77-1.14)
	Dulaglutide	0.79 (0.70-0.88)	0.72 (0.64-0.82)	0.66 (0.57-0.76)
	Tirzepatide	0.29 (0.25-0.35)	0.11 (0.08-0.15)	0.11 (0.08-0.14)
GLP-1: No Diabetic Neuropathy vs. Diabetic Neuropathy	Semaglutide	0.67 (0.60-0.75)	0.65 (0.56-0.75)	0.64 (0.53-0.76)
	Liraglutide	0.69 (0.57-0.82)	0.73 (0.59-0.91)	0.61 (0.48-0.78)
	Dulaglutide	0.63 (0.56-0.70)	0.59 (0.51-0.67)	0.64 (0.55-0.74)
	Tirzepatide	0.79 (0.55-1.13)	1.38 (0.87-2.17)	1.41 (0.76-2.63)

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GLP-1 therapy compared to diabetics with neuropathy. As such, it is unlikely that GLP-1s decrease itch through neuropathy relief. Instead, although the exact mechanism is currently unclear, it is possible that GLP-1 agonists' anti-inflammatory effects dampen itch. These medications downregulate inflammatory markers, such as interleukin (IL)-6 and IL-17, which play a role in pruritus pathogenesis.[3,4] GLP-1 therapy decreases expression of IL-23, IL-22, and tumor necrosis factor-α, key pro-inflammatory cytokines linked to inflammatory skin diseases associated with both diabetes and itch.[5]

Limitations include unaddressed confounding variables, patient medication adherence, dosage details, ICD code misclassification bias, and lack of causal conclusions. However, our findings strongly suggest an association between semaglutide, tirzepatide, and dulaglutide therapy with decreased pruritus prevalence. Semaglutide and tirzepatide also appear to have a stronger effect on itch over time.

DISCLOSURES

There are no potential conflicts or conflicts of interest.

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