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Association between GLP-1 receptor agonists and nail disorders: results from a multinational case-control study

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Introduction

GLP-1 receptor agonists (GLP-1 RA) are experiencing considerable growth in the treatment of type 2 diabetes and obesity. While their association with alopecia has already been reported, nail disorders remain largely unexplored, with rare and anecdotal pharmacovigilance reports. Since the nail matrix shares rapid cell turnover mechanisms with the hair follicle, an impact of these treatments on nail health constituted a legitimate line of investigation.

Materials and Methods

A multinational cross-sectional study (France, United States, Brazil, Mexico) including 575 GLP-1 RA users and 1,329 controls (type 2 diabetes and/or obesity, BMI >30) with no exposure to GLP-1 RA, recruited from a representative sample in each country. Targeted assessment: unusual hair loss, loss of hair volume/density, dandruff and scalp erythema, nail fragility, dyschromia, changes in thickness, onycholysis and ridges/grooves. Weight loss was measured over a 3-month period, and a stratified analysis was performed to distinguish the drug effect from the weight loss effect.

Results

GLP-1 RA users (mean treatment duration 18.5 months; median 9 months) reported weight loss over 3 months more frequently than controls (76.3% vs 47.3%; $p < 0.001$). At least one nail disorder was reported by 66.3% of GLP-1 RA users versus 52.8% of controls ($p < 0.001$). Nail detachment was the most prominent nail disorder, with a prevalence multiplied nearly sevenfold in the exposed group (39.3% vs 8.7%, OR = 6.84 [5.30-8.81], $p < 0.001$). Other parameters were also significantly more frequent: dyschromia (45.6% vs 17.0%, OR = 4.09 [3.29-5.08], $p < 0.001$), onycholysis (49.2% vs 29.7%, OR = 2.29 [1.87-2.80], $p < 0.001$), fragility (58.3% vs 51.1%, OR = 1.34 [1.09-1.65], $p = 0.005$) and ridges/grooves (46.8% vs 31.8%, OR = 1.89 [1.55-2.31], $p < 0.001$) (all $p < 0.001$). When the analysis was restricted to patients who had actually lost weight, the differences between the two groups remained significant.

Conclusions

This large-scale case-control study reveals a novel nail signal under GLP-1 RA, dominated by onycholysis with a

prevalence multiplied nearly sixfold. The persistence of the associations after stratification by weight loss suggests a specific pharmacological mechanism affecting keratinized structures with rapid turnover. Systematic dermatological screening including nail examination should be integrated into the follow-up of patients treated with GLP-1 RA.

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