

RESEARCH LETTER

Prevalence of Pruritus with Use of Metformin and Other Oral Hypoglycemic Agents

Lauren Sattelle, BS¹, Courtney Linkous, BA^{1,2}, Laura Andrews, MD, MSCR², Chelsea Shope, MD, MSCR², Nicholas Strat, MSCR¹, Lara Wine Lee, MD, PhD³

¹ College of Graduate Studies, Medical University of South Carolina, Charleston, SC

² College of Medicine, Medical University of South Carolina, Charleston, SC

³ Department of Dermatology & Dermatologic Surgery, Medical University of South Carolina, Charleston, SC

ABSTRACT

Introduction: Metformin is being prescribed with increasing frequency for many dermatologic indications. This has resulted in anecdotal evidence correlating metformin use with pruritus, but the evidence is limited to case reports. We aimed to investigate the association between metformin use and pruritus.

Methods: Using the FDA Adverse Event Reporting System (FAERS), we performed a retrospective review of patients taking metformin, canagliflozin, insulin lispro, and insulin glargine between January 1, 2012, and November 14, 2022. Data was analyzed using Chi square and Fisher's exact testing, with Bonferroni adjusted column proportions.

Results: Prevalence of pruritus for patients taking metformin was 0.7%, canagliflozin 0.9%, insulin lispro 0.4%, and insulin glargine 0.6%. Canagliflozin was significantly more likely to cause pruritus than both insulin lispro and glargine ($p < 0.05$). Reports of pruritus by metformin users was not significantly different than the other three oral hypoglycemics ($p > 0.05$).

Conclusion: Our results suggest that metformin is not significantly associated with pruritus and may be used for treatment of dermatologic conditions with little concern for this adverse event. Canagliflozin, however, was significantly likely to cause pruritus. General practitioners should consider counseling canagliflozin users on this significant adverse event.

INTRODUCTION

Metformin is being prescribed with increasing frequency for many dermatologic indications, including skin cancer prevention, acne, psoriasis, and hidradenitis suppurativa, among others.¹ Increased prescribing of metformin by dermatologists has resulted in anecdotal evidence correlating metformin use with pruritus.^{2,3} However, existing evidence is limited to case reports, and larger scale data investigating this association is

lacking. As such, we aimed to investigate the association between metformin use and pruritus.

METHODS

Using the FDA Adverse Event Reporting System (FAERS), we performed a retrospective review of patients taking an oral hypoglycemic medication between January 1, 2012, and November 14, 2022. The occurrence, or absence, of pruritus was

January 2024 Volume 8 Issue 1

recorded for each patient. In efforts to control for confounding of pruritus caused by diabetic polyneuropathy itself, canagliflozin, insulin lispro, and insulin glargine were evaluated in addition to metformin.⁴ These medications were chosen as representatives of their respective medication class; medications with less than 10 reports of pruritus were excluded. Patients on multiple medications were excluded from our analysis. Data was analyzed using Chi square and Fisher's exact testing, with Bonferroni adjusted column proportions. A Bonferroni adjusted p-value of <0.05 was considered significant. Statistical analysis was performed using SPSS Statistics (IBM, Armonk, NY).

RESULTS

A total of 29,698 patients prescribed one of the four oral hypoglycemic medications included in our analysis reported an adverse event to the FAERS database during the study period. Of these patients, 178 (0.6%) reported pruritus. Among patients reporting pruritus, 30 cases (16.9%) were attributed to metformin, 48 (27.0%) to canagliflozin, 23 (12.9%) to insulin lispro, and 77 (43.3%) to insulin glargine. Prevalence of pruritus among patients taking metformin was 0.7%, canagliflozin 0.9%, insulin lispro 0.4%, and insulin glargine 0.6 percent. Canagliflozin was significantly more likely to cause pruritus than both insulin lispro and glargine (p-value<0.05). Reports of pruritus by metformin users were not significantly different than the other three oral hypoglycemics (p-value>0.05). These results are outlined in **Table 1**.

DISCUSSION

Our results suggest that metformin is not significantly associated with pruritus and may

be used for the treatment of dermatologic conditions with minimal concern for this adverse event. Canagliflozin, however, was significantly associated with pruritus. While canagliflozin is not prescribed for cutaneous disease, it is prescribed with increasing frequency for patients with heart failure and is often used for weight loss.⁵

Limitations of this study include its retrospective design, the potential for duplicate or incomplete reports in FAERS system, and the exclusion of patients on multiple oral hypoglycemic medications. Additionally, adverse events may be self-reported by patients. Therefore, submitted reports may not be medically confirmed nor establish causation between the suspected drug and adverse event.

Given the widespread use of canagliflozin, and the high frequency of pruritus as a presenting symptom to dermatology, general practitioners and dermatologists should consider counseling canagliflozin users on this significant adverse event.

Acknowledgements: A special thank you to Dr. Mathew Gregoski, PhD, MS for his statistical analysis contribution to this study.

Conflict of Interest Disclosures: None

Funding: This project was supported, in part, by the National Center for Advancing Translational Sciences of the National Institutes of Health under Grant Number UL1 TR001450. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

Corresponding Author:

Lauren Sattelle, BS
135 Rutledge Ave, 11th floor
Charleston, SC, 29425
Email: lauren.sattelle@uscmcd.sc.edu

References:

1. Badr D, Kurban M, Abbas O. Metformin in dermatology: an overview. *J Eur Acad Dermatol Venereol.* 2013;27(11):1329-1335. doi:10.1111/jdv.12116
2. Voore P, Odigwe C, Mirrakhimov AE, Rifai D, Iroegbu NA. DRESS Syndrome Following Metformin Administration: A Case Report and Review of the Literature. *Am J Ther.* 2016;23(6):e1970-e1973. doi:10.1097/MJT.0000000000000292
3. Díaz JM, Bruñén JMG, Cameo RB, González AM. Erythroderma and Chronic Lichenification Due to Metformin. *Eur J Case Rep Intern Med.* 2019;6(6):001119. Published 2019 May 29. doi:10.12890/2019_001119
4. Lima AL, Illing T, Schliemann S, Elsner P. Cutaneous Manifestations of Diabetes Mellitus: A Review. *Am J Clin Dermatol.* 2017;18(4):541-553. doi:10.1007/s40257-017-0275-z
5. Rådholm K, Figtree G, Perkovic V, et al. Canagliflozin and Heart Failure in Type 2 Diabetes Mellitus: Results From the CANVAS Program. *Circulation.* 2018;138(5):458-468. doi:10.1161/CIRCULATIONAHA.118.034222

Table 1. Reports of Pruritus in the FAERS Database Among Patients Taking Oral Hypoglycemic Agents.

	Metformin	Canagliflozin	Insulin Lispro	Insulin Glargine	Total
Users within FAERS database (n)	4,312	5,154	6,422	13,810	29,698
Users reporting pruritus (n, %)	30 (16.9%) _{a, b} *	48 (27%) _a *	23 (12.9%) _b *	77 (43.3%) _b *	178
Prevalence of pruritus among all AEs	0.7%	0.9%	0.4%	0.6%	0.6%
Prevalence of pruritus among users	0.1%	0.2%	0.1%	0.3%	0.6%

*Each subscript letter denotes a subset of medication categories whose column proportions do not differ significantly from each other at the .05 level.

AEs: Adverse events