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LETTER

Awareness of Genetic Polymorphism in Drug Metabolizing Enzymes and Transporters May Promote Personalized Type 2 Diabetes Management [Letter]

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Dear editor

We read with great interest the study by Williams et al,[1] which shows that the use of personalized medicine in people with type 2 diabetes mellitus (T2D) could improve medication adherence, patient satisfaction, and quality of life. We especially appreciate the viewpoint that factors affecting the intensity of treatment and choice of pharmacotherapy should include medical and patient influences. However, we found one point worthy of discussion and we would like to share our perspectives in the following paragraphs.

Mutations in genes important in drug absorption, distribution, metabolism, and excretion play a critical role in pharmacogenetics of diabetes.[2] There is an extreme need to consider the genetic polymorphism when low efficacy and side effects occur. For example, CYP2C9 is the major metabolizing enzyme responsible for sulfonylureas' biotransformation and the number of *CYP2C9*2* and **3* alleles is associated with nearly three-fold increased risk of hypoglycemic events.[3] *CYP2C8*3* polymorphisms result in significantly lower exposure and higher clearance of thiazolidinediones (eg, pioglitazone and rosiglitazone), and lower odds ratio of developing edema during rosiglitazone treatment.[4,5] The *SLCO1B1*1B* haplotype reduces plasma concentrations of repaglinide, but has limited effects on the pharmacokinetics of nateglinide.[6] Two genetic variations in *SLC22A1* that are in strong linkage disequilibrium increase prevalence of the side effects of metformin in patients with T2D.[7]

Williams et al examined the personal factors, phenotypic characteristics, biomarkers and genetic markers that may have a role in personalizing the management of T2D, and their work is very enlightening and beneficial for the international community. Their recommendations along with our perspectives may provide a more detailed guide for personalized anti-diabetic therapy.

Disclosure

The authors report no conflicts of interest in this communication.

References

1. Williams DM, Jones H, Stephens JW. Personalized type 2 diabetes management: an update on recent advances and recommendations. *Diabetes Metab Syndr Obes*. 2022;15:281–295. doi:10.2147/DMSO.S331654
2. Glamočlija U, Jevrić-Čaušević A. Genetic polymorphisms in diabetes: influence on therapy with oral antidiabetics. *Acta Pharm*. 2010;60(4):387–406. doi:10.2478/v10007-010-0040-9
3. Dujic T, Zhou K, Donnelly LA, Leese G, Palmer CNA, Pearson ER. Interaction between variants in the CYP2C9 and POR genes and the risk of sulfonylurea-induced hypoglycaemia: a GoDARTS study. *Diabetes Obes Metab*. 2018;20(1):211–214. doi:10.1111/dom.13046

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4. Stage TB, Christensen MMH, Feddersen S, Beck-Nielsen H, Brøsen K. The role of genetic variants in CYP2C8, LPIN1, PPARGC1A and PPARγ on the trough steady-state plasma concentrations of rosiglitazone and on glycosylated haemoglobin A1c in type 2 diabetes. *Pharmacogenet Genomics*. 2013;23(4):219–227. doi:10.1097/FPC.0b013e32835f91fc
5. Tornio A, Niemi M, Neuvonen PJ, Backman JT. Trimethoprim and the CYP2C8*3 allele have opposite effects on the pharmacokinetics of pioglitazone. *Drug Metab Dispos*. 2008;36(1):73–80. doi:10.1124/dmd.107.018010
6. Kalliokoski A, Backman JT, Neuvonen PJ, Niemi M. Effects of the SLCO1B1*1B haplotype on the pharmacokinetics and pharmacodynamics of repaglinide and nateglinide. *Pharmacogenet Genomics*. 2008;18(11):937–942. doi:10.1097/FPC.0b013e32830d733e
7. Tarasova L, Kalnina I, Geldnere K, et al. Association of genetic variation in the organic cation transporters OCT1, OCT2 and multidrug and toxin extrusion 1 transporter protein genes with the gastrointestinal side effects and lower BMI in metformin-treated type 2 diabetes patients. *Pharmacogenet Genomics*. 2012;22(9):659–666. doi:10.1097/FPC.0b013e3283561666

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