Different genders should be considered for the extraglycemic benefits of oral antidiabetic drugs

Wen-Hsun Chang[a,b], Chia-Hao Liu[b,c,d,*]

[a]Department of Nursing, Taipei Veterans General Hospital, Taipei, Taiwan, ROC; [b]Department of Obstetrics and Gynecology, Taipei Veterans General Hospital, Taipei, Taiwan, ROC; [c]Department of Obstetrics and Gynecology, National Yang Ming Chiao Tung University, Taipei, Taiwan, ROC; [d]Institute of Clinical Medicine, National Yang Ming Chiao Tung University, Taipei, Taiwan, ROC

DEAR EDITOR,

Many patients with type 2 diabetes mellitus (T2DM) need oral antidiabetic drug treatment for blood sugar control and to avoid or delay the T2DM-related complications that could damage the microvascular and macrovascular circulatory systems and subsequently develop various kinds of morbidities and eventually mortality.[1] We read Dr. Chang's study,[2] editorial comments by Dr. Lee et al,[3] and a letter to Editors by Dr. Lee et al[4] to discuss the extraglycemic benefits of oral antidiabetic drugs, including dipeptidyl peptidase-4 inhibitors (DPP-4i) in patients with T2DM. We found with interest that all patients with T2DM treated with DPP-4i took advantage of the lowering risk of the development of osteoporosis, as shown by the authors, but it is important to note that the advantages of decreasing the risk of osteoporosis are different between the male and female populations. Males had an adjusted hazard ratio (HR) of 0.562 (95% confidence interval [CI]: 0.322–0.878), and the females had an adjusted HR of 0.638 (95% CI: 0.364–0.980),[2] suggesting that the extraglycemic benefits of DPP-4i may be more apparent in the male population. A recent meta-analysis enrolling 82 randomized controlled trials with 104,833 participants showed DPP-4i was significantly associated with an increased risk of the composite of gallbladder or biliary diseases with an odds ratio (OR) of 1.22 (95% CI: 1.04–1.43) compared with placebo or nonincretin drugs.[5] Additionally, compared with sodium-glucose cotransporter-2 inhibitors, DPP-4i also increased the risk of the composite of gallbladder and biliary diseases, as well as cholecystitis.[5] The prevalence and incidence of gallbladder or biliary tract diseases differ between male and female populations. The male population may have a higher risk of developing gallbladder or biliary tract diseases than the female population.[6] Moreover, the male population is also strongly associated with a higher mortality rate compared with the female population,[6] contributing to the concern about using DPP-4i as an antidiabetic agent in the T2DM male population. Since the extraglycemic benefits, such as the prevention of osteoporosis, are claimed by the authors, we comment that different genders may have a different impact on using DPP-4i as a choice in the management of patients with T2DM. We wonder about the authors' opinions.

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*Address correspondence. Dr. Chia-Hao Liu, Department of Obstetrics and Gynecology, Taipei Veterans General Hospital, 201, Section 2, Shi-Pai Road, Taipei 112, Taiwan, ROC. E-mail addresses: chliu12@vghtpe.gov.tw; mikeliuu@gmail.com (C.-H. Liu).

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