

Response to Article “Are There Differences in Gut Microbiome in Patients with Type 2 Diabetes Treated by Metformin or Metformin and Insulin?” [Letter]

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Dear editor

Diabetes mellitus is one of metabolic diseases characterized by the elevated blood glucose levels. There are growing studies regarding the effect of diabetes to the development of other diseases such as hypertension, stroke, and even blindness. In the study performed by Dzięgielewska-Gęsiak et al, the comparison of two different treatments in diabetic type-2 patients regarding the effect to the microbiota composition was shown and discussed. Their study compared the microbiota profile in patients treated by metformin only and metformin supplemented with insulin. This study is an interesting and informative study, which gives a novel idea and hint of the different pattern of microbiota composition as the effect of different treatments given to patients. However, certain suggestions are given to the authors as consideration for their future studies.

The alteration of homeostatic gut microbiota composition has been continuously reported to play important role in the health field, especially in metabolic diseases, such as diabetes mellitus.¹ The study performed by Dzięgielewska-Gęsiak, et al, compared the profile of gut microbiota of the patients with diabetes mellitus type-2 given by two different treatments, metformin or metformin and insulin.² Their results showed that there were no significant differences in the gut microbiota profile detected and analyzed from the patients treated with metformin compared to those treated with metformin and insulin. A question addressed here was why and how? Were the patients included in this study maintaining significant diet and life circumstances for that long time? Does insulin as a hormonal agent really do nothing in the gut microbiota alteration? Meanwhile, the microbiota composition was reported as one of the essential aspects in the development of metabolic diseases and one of factors causing the metabolic disorders itself, in which diabetes mellitus is included.³

After a deep reading, we provided several suggestions for the authors of this study or even for other scientists in the field as worth considering suggestions for being hopefully unraveled in the future studies. The long term treatment with metformin only or metformin+insulin, based on this particular study, caused no significant effect on the gut microbiota profile of the patients whom got the treatment for more than five years. However, there could be significant differences in gut microbiota profile if being compared to patients whom were just recently being treated with metformin. The comparison of gut microbiota profile could have been performed in comparing those in patients treated with metformin and other different anti-diabetic agent (treatment).

The abundant bacteria found in the undertreatment type-2 diabetic patients were *Clostridiales*, *Firmicutes* and *Verrucomicrobia*. Meanwhile, *Bacteroidetes* and *Proteobacteria* were in the smaller total proportions. In previous study, *Bacteroidetes* was reported to be associated with the high risk of diabetes mellitus while being compared to the

microbiota composition of healthy individuals.⁴ The profile of *Bacteroidetes* in both groups of patients treated by metformin or metformin+insulin was low in this study, probably due to the effect of the anti-diabetic drug. Anyways, the role of insulin addition under metformin in altering the gut microbiota composition to the healthy composition for type-2 diabetes mellitus cases was not completely unraveled in this study. Therefore, these aspects could be revealed in the future studies.

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Author Contributions

NSDP went through the cited publications and analyzed the reported data. NSDP designed and conceived the critical design of the letter. NSDP wrote the original letter draft. CSWL and MSM recommended required corrections. NSDP, CSWL and MSM did necessary revision for improvement of the manuscript accordingly.

Disclosure

The authors report no conflicts of interest in this communication.

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