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**Different nutrient compositions in diet and taking hypoglycemic drugs can modulate gut microbial flora**

Lin ZJ *et al*. Different nutrient compositions

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**Abstract**

The diet structure of diabetic patients is different from that of normal people. Diabetic patients also need to take hypoglycemic drugs to regulate blood sugar. Both dieting and drugs affect the gut microbiota of diabetic patients. In this letter, we discuss that different dietary patterns and the use of hypoglycemic agents may have an impact on changes in gut microbiota in diabetic patients.

**Key Words:** Diabetic patients; Gut microbiota; Hypoglycemic drugs

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**Core Tip:** Changes in diet can lead to changes in the composition of gut microbiota in diabetic patients. On the other hand, taking hypoglycemic drugs can also change the gut microbiota. Therefore, it is necessary to consider the dietary structure and the use of hypoglycemic drugs in the study of changes in the intestinal flora of patients with diabetes.

**TO THE EDITOR**

Diabetes mellitus (DM) is one of important risk factor for population health in the twenty-first century worldwide. It is of great significance to explore the lifestyle intervention mode for the prevention and treatment of type 2 diabetes mellitus (T2DM). One study found intermittent hypoxia (IH) was associated with metabolic diseases including as obesity and obstructive sleep apnea-hypopnea syndrome (OSAHS)[1]. IH may be involved in selective alterations of the gut microbiota of T2DM patients with OSAHS. Similarly, changes in gut microbiota can affect the development of T2DM.

Gut microbiota is known to change with diet. Especially when someone suffering from T2DM, doctors often recommend dietary changes to curb the progression of the disease. Changes in eating habits can disrupt the balance of gut microbiota when the body's resistance is low[2]. The study by Liu *et al*[3] showed that blood sugar levels in mouse model of T2DM induced by streptozotocin-high-fat diet were changes with gut microbiota. A large number of studies have shown that diet affects the development of diabetes. For example, blackcurrant extract enhanced insulin sensitivity and glucose-stimulated insulin secretion in non-obese type 2 diabetic rats[4]. Therefore, the diet structure will affect the gut microbiota. However, the following questions need to be further clarified in future studies. What nutrition considerations for persons with diabetes that will impact persons? What are the recommendations for persons with diabetes concerning nutrition to be considered? The link between gut microbial, diabetes, nutrition and autoimmunity are important, but still need to be addressed.

In addition, hypoglycemic drugs also affect gut microbiota. In this study, drugs that regulate IH have an effect on the balance of gut microbiota. We strongly agree with this view. However, when taking drugs to regulate IH, hypoglycemic drugs are also used. Therefore, hypoglycemic drugs also have an impact on the balance of gut microbiota. For some patients who require combination therapy to treat diabetes and complications of diabetes, especially after combination therapy with antibiotics and hypoglycemic drugs, the impact on the intestinal flora is significant[5]. Clinically, metformin is widely used in the treatment of T2DM. Studies have shown that gut microbiota is an active site of metformin. The gut is a potential target of metformin. Metformin induce butyrate and propionate involving glucose homeostasis[6]. When diabetics take metformin, the gut microbiota will definitely change. Studies have also shown that treating diabetic mice with oleuropein (OP) is also treated by modulating the gut microbiota. The OP could decrease fasting blood glucose levels and improve glucose tolerance[7]. Hypoglycemic drugs are also taken when taking drugs that regulate IH, so hypoglycemic drugs will also affect the intestinal flora of patients with IH. It is common for IH patients to take hypoglycemic drugs, so the regulation of hypoglycemic drugs on gut microbiota also needs to be discussed.

On the other hand, IH may be associated with changes in gut microbiota, and it is possible that changes in gut microbiota led to IH. In the clinical setting, the effective treatment for IH is usually oxygen therapy. Thus, we can use oxygen inhalation to intervene in changes in gut microbiota. By conducting oxygen supply experiments, the relationship between IH and gut microbiota can be further reflected, which makes the research results more convincing.

The diet structure of diabetic patients is different from that of normal people. Diabetic patients also need to take hypoglycemic drugs to regulate blood sugar. Both dietary structure of patients with diabetes and hypoglycemic drugs taken by the patients with diabetes can alter the gut microbiota of the patients. Therefore, the influence of diet and drugs on the gut microbiota cannot be ignored.

**REFERENCES**

1 **Tang SS**, Liang CH, Liu YL, Wei W, Deng XR, Shi XY, Wang LM, Zhang LJ, Yuan HJ. Intermittent hypoxia is involved in gut microbial dysbiosis in type 2 diabetes mellitus and obstructive sleep apnea-hypopnea syndrome. *World J Gastroenterol* 2022; **28**: 2320-2333 [PMID: 35800187 DOI: 10.3748/wjg.v28.i21.2320]

2 **Song M**, Chan AT, Sun J. Influence of the Gut Microbiome, Diet, and Environment on Risk of Colorectal Cancer. *Gastroenterology* 2020; **158**: 322-340 [PMID: 31586566 DOI: 10.1053/j.gastro.2019.06.048]

3 **Liu S**, Qin P, Wang J. High-Fat Diet Alters the Intestinal Microbiota in Streptozotocin-Induced Type 2 Diabetic Mice. *Microorganisms* 2019; **7** [PMID: 31208113 DOI: 10.3390/microorganisms7060176]

4 **Yang HJ**, Zhang T, Wu XG, Kim MJ, Kim YH, Yang ES, Yoon YS, Park S. Aqueous Blackcurrant Extract Improves Insulin Sensitivity and Secretion and Modulates the Gut Microbiome in Non-Obese Type 2 Diabetic Rats. *Antioxidants (Basel)* 2021; **10** [PMID: 34068659 DOI: 10.3390/antiox10050756]

5 **Zarrinpar A**, Chaix A, Xu ZZ, Chang MW, Marotz CA, Saghatelian A, Knight R, Panda S. Antibiotic-induced microbiome depletion alters metabolic homeostasis by affecting gut signaling and colonic metabolism. *Nat Commun* 2018; **9**: 2872 [PMID: 30030441 DOI: 10.1038/s41467-018-05336-9]

6 **Wu H**, Esteve E, Tremaroli V, Khan MT, Caesar R, Mannerås-Holm L, Ståhlman M, Olsson LM, Serino M, Planas-Fèlix M, Xifra G, Mercader JM, Torrents D, Burcelin R, Ricart W, Perkins R, Fernàndez-Real JM, Bäckhed F. Metformin alters the gut microbiome of individuals with treatment-naive type 2 diabetes, contributing to the therapeutic effects of the drug. *Nat Med* 2017; **23**: 850-858 [PMID: 28530702 DOI: 10.1038/nm.4345]

7 **Zheng S**, Wang Y, Fang J, Geng R, Li M, Zhao Y, Kang SG, Huang K, Tong T. Oleuropein Ameliorates Advanced Stage of Type 2 Diabetes in *db*/*db* Mice by Regulating Gut Microbiota. *Nutrients* 2021; **13** [PMID: 34206641 DOI: 10.3390/nu13072131]

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