Effects of Dietary Fiber on Glycemic Control, Incretins, and Microbiota in Patients with Type 2 Diabetes Mellitus

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Background

Fiber supplements such as psyllium are known to be beneficial to glycemic control in patients with type 2 diabetes (T2DM). Gut microbiota can regulate host energy metabolism by several pathways such as short-chain fatty acid production, fasting-induced adipose factor expression, endocannabinoid system, and gut epithelial permeability. As dietary component can influence on the composition of microbiota, we hypothesized that fiber supplement intake can modify gut microbiota and consequently affect glycemic control and inflammatory status in patients with T2DM.

Aims

The effect of dietary fiber supplement (AGIO®; mixture of plantago seed and ispaghula husk; BUKWANG PHARM. CO., LTD) on glycemic control markers, incretins, and microbiota in patients with T2DM.

- Primary outcome
 - insulin sensitivity (Matsuda index) and insulin resistance (HOMA2-IR) change
- Secondary outcome
 - inflammatory markers [CRP, lipopolysaccharide (LPS)], incretins, microbiota change

Methods

- Open, single-arm pilot trial
- T2DM patients who visited Diabetes Center, Samsung Medical Center, Seoul, Korea
 - Age ≥ 50 years
 - ≥ 2 components of metabolic syndrome (ATP III criteria)
 - ≥ 6 months of treatment with combination of metformin and sulfonylurea

Table 1. Study design

Visit	1	2	3	4
Week	Week –1	Week 0	Week 4	Week 8
Screening	O			
Informed consent	O			
AGIO® intake		Start	Finish	No
Diet diary	Start	O	O	Finish
Mixed meal test		O	O	O
Fecal sampling		O	O	O

- 4 weeks of AGIO® intake → 4 weeks of cessation
- The difference in AUC of glucose between week 0 and 4, during mixed meal test (MMT)
 - The first quartile: *Responders* (R; n=3)
 - The fourth quartile: *Non-responders* (NR; n=3)
- Wilcoxon signed rank test
- LEfSe was adopted to estimate taxonomic composition and characterize differences between paired groups.

Figure 1. AGIO® granule

Results

- All 10 participants
- 6 males, Median age 61-year-old, median BMI 25.8 kg/m², median 15 years of T2DM, median hemoglobin A1c 8.0%

Table 2. Laboratory outcomes in all participants

Variables	Week 0	Week 4	Week 8
Glycemic markers			
Matsuda index	4.1 (2.3 - 5.2)	2.6 (2.2 - 4.9)	3.4 (2.5 - 4.9)
HOMA2-IR	0.8 (0.6 - 1.5)	1.3 (0.8 - 1.6)	1.0 (0.6 - 1.5)
Glycoalbumin	19.8 (17.0 - 27.3)	19.4 (17.4 - 25.7)	21.1 (17.3 - 25.5)
Inflammatory marker			
CRP	0.05 (0.03-0.06)	0.06 (0.05-0.12)	0.05 (0.04-0.13)
LPS (log)	81.0 (47.4 - 259.2)	72.0 (32.8 - 455.7)	93.7 (45.2 - 376.6)

* Values are described in median (interquartile range).
* Wilcoxon signed rank test was adopted for the analysis, all p > 0.05.

Figure 2. Changes of incretin AUCs during MMT

* Wilcoxon signed rank test was adopted for the analysis, all p > 0.05.

Table 3. Laboratory outcomes in R and NR

R (n=3)	Week 0	Week 4	Week 8
Matsuda index	5.0 (2.0-5.6)	5.6 (2.2-6.9)	4.2 (3.0-12.9)
HOMA2-IR	0.6 (0.6-2.1)	0.6 (0.5-1.8)	0.6 (0.2-1.6)
Glycoalbumin	18.8 (17.0-28.9)	18.4 (16.1-26.6)	18.5 (17-25.4)
CRP	0.05 (0.03-0.05)	0.03 (0.03-0.22)	0.04 (0.03-0.05)
LPS (log)	92.8 (36.6-524.5)	81.4 (19.3-453.8)	92.1 (20.0-362.9)
NR (n=3)	Week 0	Week 4	Week 8
Matsuda index	4.1 (2.5-7.0)	2.4 (2.0-4.4)	2.5 (2.4-5.6)
HOMA2-IR	0.8 (0.6-1.3)	1.4 (0.9-1.5)	1.0 (0.6-1.5)
Glycoalbumin	19.8 (14.9-26.8)	20.2 (15.1-25.0)	21.4 (14.8-23.9)
CRP	0.06 (0.03-0.13)	0.09 (0.06-0.19)	0.12 (0.03-0.22)
LPS (log)	69.3 (42.4-606.4)	62.7 (57.3-596.8)	95.3 (47.2-600.0)

* Values are described in median (range).
* Wilcoxon signed rank test was adopted for the analysis, all p > 0.05.

- In overall analysis, the abundance of metabolically unfavorable family *Coriobacteriaceae*, genus *Blautia* decreased at week 4 and restored at week 8.
 - Week 0: phylum *Cyanobacteria* (R > NR)
genera *Bautia*, *Lachnospiraceae* (NR > R)
 - Week 4 compared to week 0:
 - Responder: *Roseburia intestinalis* increased
 - Non-responder: family *Coprobacillus* decreased

Discussion / Conclusion

4 weeks of AGIO® administration induced a beneficial change in the microbiota composition, e.g., the reduction of the abundance of metabolically unfavorable microbiota and the subsequent reversal was observed after 4 weeks of discontinuation. The increased abundance of butyrate forming *Roseburia intestinalis* at week 4 in R might be associated with the tendency of increment in insulin sensitivity and decrement in insulin resistance in this group.