*LETTER TO THE EDITOR*

# INFLUENCE OF PREBIOTIC ADMINISTRATION ON INFLAMMATORY AND GLYCAEMIC MARKERS IN TYPE-2 DIABETES

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To the Editor,

Prebiotics are often administered with the daily diet: they have been widely investigated in recent years, and several researchers have assessed that they can favorably affect health and cell aging. Prebiotics seem to actively enhance several antioxidant pathways that overall improve the immune homeostasis, also increasing the suppression of chronic inflammation and the prevention of insulin resistance (1).

Prebiotics may promote changes in the bacterial composition and/or in the main activities of the gastrointestinal tract; moreover, they have been shown to improve the gut environment and its microbiome, often closely associated with the onset and severity of type-2 diabetes mellitus (T2DM). Furthermore, prebiotics can modulate the production of haemoglobin-A1c (HbA1c), thus modulating the glycaemic values detected just after lunch. Finally, prebiotics have been associated with a slight reduction of the main inflammatory markers, in T2DM patients (1,2).

Growing evidence links prebiotics to better control of glycemia, thanks to their action on the gut microbiota (3). Both animal and human studies have linked gut microbiota to metabolic dysregulation. Patients with diabetes have a different gut microbiota, in comparison to healthy individuals (3-5), characterized by a high Gram-negative and Gram-positive bacterial ratio, and a low presence of bifidobacteria, which is a microbial population able to give several health benefits (5). Changes in gut microbiota composition, and their impact on gut permeability and glycaemic control, have not been well investigated; in particular, the mechanisms working in humans are still quite unknown (6).

There are currently several strategies for reducing the glycaemic markers in humans: prebiotics are a potentially novel, economic, and safe treatment for T2DM, able to improve the control of T2DM by modulating gut microbiota, gut permeability and local inflammation (7). The aim of this pilot study was to evaluate the influence of prebiotic administration on inflammatory and glycaemic markers in patients affected by type-2 diabetes.

## MATERIALS AND METHODS

Twenty patients with body mass index (BMI) 25–40kg/m$^2$, 40–65 years of age, reporting a high risk of developing T2DM were enrolled in our study. All participants

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followed a standardized diet (55% carbohydrates, 30% fats, 15% proteins) isocaloric, for 7 weeks. Prebiotic foods (e.g., yogurt) and/or superfoods were not allowed. Written and verbal informed consent was also obtained from each participant.

A randomized double-blinded, placebo-controlled, parallel-groups experimental design was carried out. In the first stage, the participants were allocated into two groups: a) Group using a supplementation with Hyperbiotics Prebiotic Powder (1 scoop/day), or b) Group using a supplementation with 10g/day of a placebo (maltodextrin; 4kcal/g) for 7 weeks.

Measurements of key outcomes, such as body weight or glycaemic markers, were performed at baseline, and at the following time-points.

All measurements were taken during the time-lapse 7:00 to 11:00 a.m. Blood samples were collected at baseline, and after 7 weeks. The samples were stored at −80°C.

The product tested in the experimental group was Hyperbiotics Prebiotic Powder, a soluble dietary formula containing organic fibers from acacia, Jerusalem artichoke and green banana flour (ZuviiTM), with non-GMO ingredients, free of gluten, sugar, wheat, psyllium, and dairy.

*Statistical analysis*

Outcome measures of the exploratory study were analysed with a *t*-test for paired samples for pre–post differences with time as the factor using Statistical Package for Social Sciences (SPSS for Windows, Version 11.5, Chicago, Ill) software, to detect significant differences between pre-test and post-test scores.

## RESULTS

In this study, 20 patients were selected, and randomly enrolled into a treated group (4 females and 6 males) and a placebo Group (3 females and 7 males).

*Blood glucose and HbA1c analysis.*

The results showed that the administration of prebiotics may significantly induce a better glucose tolerance, mainly demonstrated by a fast and significative reduction of glycaemic markers and glycated hemoglobin (Fig. 1). In fact, in the treated group there was a decrease of 4% in HbA1c values, and a reduction of 2% of glycemia. On the other hand, in the placebo group the variations did not exceed 0.5% in the two time-points.

*Analysis of inflammatory markers*

In the both the control group and the treated group, it was seen that the serum concentration

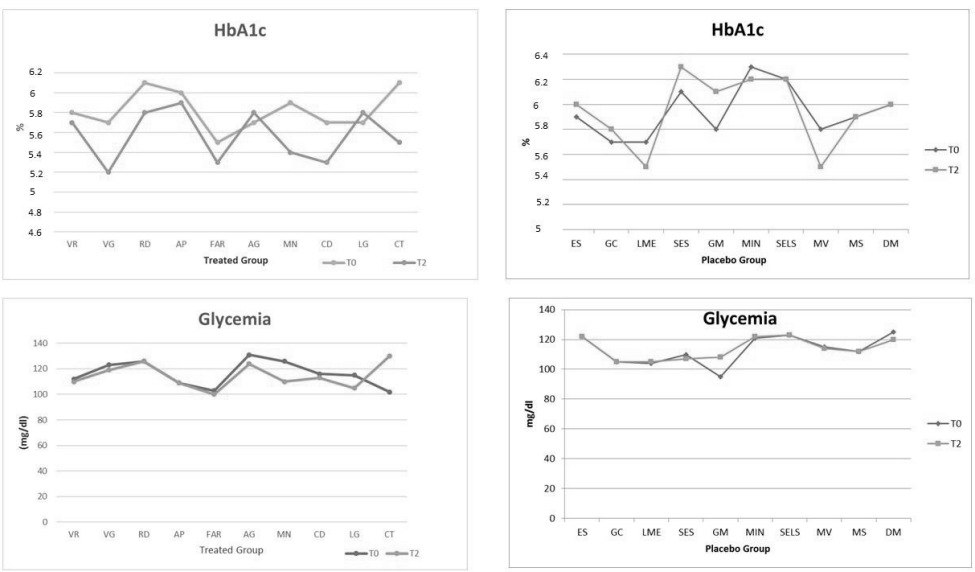


**Fig. 1.** *HbA1c and glycemia levels in treated/placebo groups.*

of the main pro-inflammatory markers remains almost unchanged. IL-6 and TNF-α parameters remain almost the same (Fig. 2): these data suggest that prebiotics added in a normal alimentary diet administered to diabetic patients do not positively impact the inflammatory state, but seem to slightly improve such parameter over time. After careful evaluations of Fig. 2, it can be seen how the levels of IL-6 decrease 3% in the treated group; on the contrary, in the placebo group they remain constant. Additionally, in the treated group, the TNF-α values appear to be substantially constant.

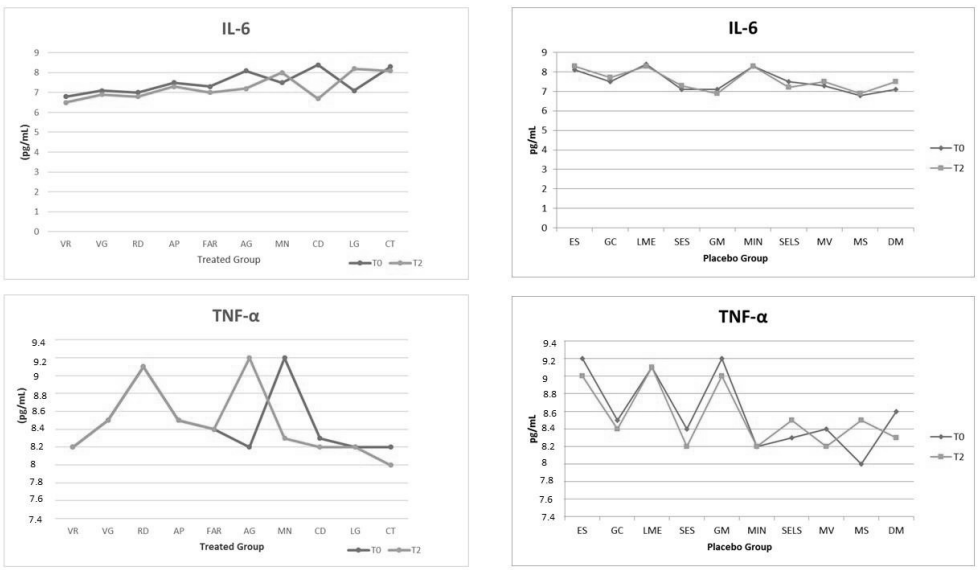


**Fig. 2.** *IL-6 and TNF- α levels in treated/placebo groups.*

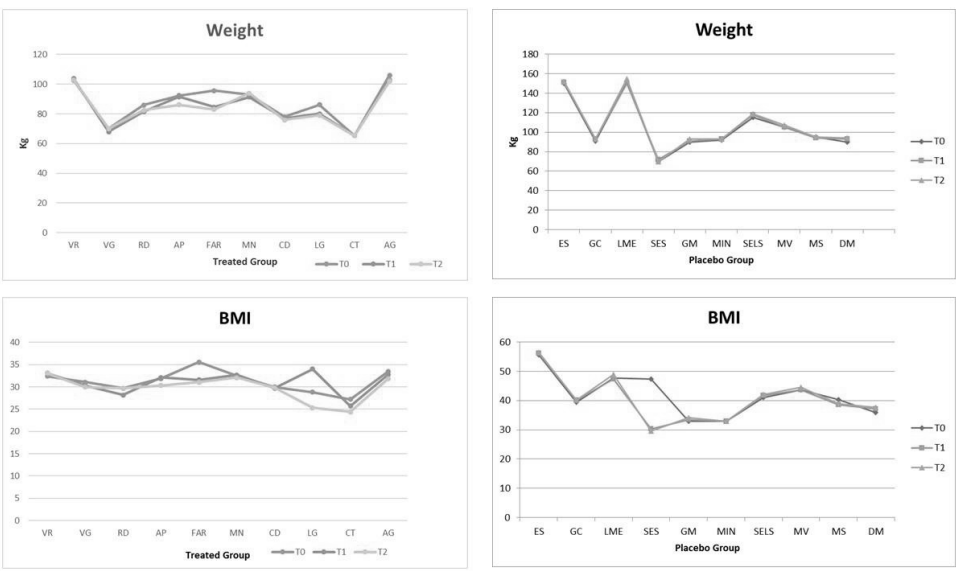


**Fig. 3.** *Weight and BMI values in treated/placebo groups.*

*Bioimpedance analysis*

T2DM patients enrolled in the prebiotics group achieved a better weight reduction. The analysis of bioimpedance data revealed that patients within the treated group showed a weight reduction of about 4%, while the placebo group seemed to maintain the same weight (Fig. 3). On the other hand, the body mass index (BMI) of treated subjects remained unchanged, just like the placebo group.

## DISCUSSION

Patients affected by diabetes mellitus have impaired neutrophil and macrophage activity, thus leading towards an acute inflammatory state. Prebiotics may improve blood sugar levels in patients with type 2 diabetes. A deep and systematic evaluation of clinical trials reported in the scientific literature has clearly revealed that the use of prebiotics can have anti-inflammatory and anti-diabetic effects (8).

It is hypothesized that the anti-inflammatory properties of some prebiotic strains may act by reducing inflammation, through the modulation of cytokine levels and other inflammatory mediators, as reported in some in vitro and in vivo studies (9).

One recentclinical study found that the daily assumption of *L. reuteri* enriches the human intestinal microbiota and modifies the intestinal production of locally active factors that increase insulin secretion. This study was based on a daily administration of *L. reuteri* strain (ATCC SD-5865) in tablets (10). A randomized double-blind placebo-controlled study compared the secretion of insulin and proglucagon-derived P peptides and the function of pancreatic beta cells in glucose-stimulated non-diabetic participants (11). However, the consumption of prebiotics did not lead to any significant clinical results, although it was possible to understand that the consumption of prebiotic-enriched bread by diabetic patients had positive effects on the insulin metabolism (12).

In conclusion, it could be possible to improve glycaemic management in T2D, and to decrease the inflammatory cytokines in prediabetic subjects, if selected prebiotics are administered, within a safe and healthy diet. Numerous other studies on this matter showed that prebiotics undoubtedly give benefit to patients with type 2 diabetes mellitus. This is only a pilot study, therefore we still need to understand the molecular mechanisms involved in the clinical and biological interaction between prebiotics and diabetes.

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