DIABETES RESEARCH AND CLINICAL PRACTICE 141 (2018) 190–199

Contents available at ScienceDirect

Diabetes Research and Clinical Practice

journal homepage: www.elsevier.com/locate/diabres

Probiotics and nutraceuticals as a new frontier in obesity prevention and management

N. Kobyliak [a,*], T. Falalyeyeva [b], N. Boyko [c], O. Tsyryuk [b], T. Beregova [b], L. Ostapchenko [b]

[a] Bogomolets National Medical University, Kyiv, Ukraine
[b] Taras Shevchenko National University of Kyiv, Kyiv, Ukraine
[c] Uzhhorod National University, Uzhhorod, Ukraine

ARTICLE INFO

Article history:
Received 9 March 2018
Received in revised form
17 April 2018
Accepted 8 May 2018

ABSTRACT

Introduction: The beneficial interaction between the microbiota and humans is how bacteria contained within the gut 'talk' to the immune system and in this landscape, probiotics and nutraceuticals play a major role. The study aims to determine whether probiotics plus nutraceuticals such as smectite or omega-3 are superior to probiotic alone on the monosodium glutamate (MSG) induced obesity model in rats.

Methods: Totally, 75 rats divided into five groups were included (n = 15, in each). Rats in group I were intact. Newborn rats in groups II–V were injected with MSG. Group III (Symbiter) received 2.5 ml/kg of multiprobiotic "Symbiter" containing concentrated biomass of 14 probiotic bacteria genera. Groups IV (Symbiter-Omega) and V (Symbiter-Smectite) received a combination of probiotic biomass supplemented with flax and wheat germ oil (250 mg of each, concentration of omega-3 fatty acids 1–5%) or smectite gel (250 mg), respectively.

Results: In all interventional groups, significant reductions of total body and visceral adipose tissue weight as compared to MSG-obesity were observed. However, the lowest prevalence of obesity was noted for Symbiter-Omega (20% vs 33.3% as compared to other interventional groups). Moreover, supplementation of probiotics with omega-3 lead to a more pronounced decrease in HOMA-IR (2.31 ± 0.13 vs 4.02 ± 0.33, $p < 0.001$) and elevation of adiponectin levels (5.67 ± 0.39 vs 2.61 ± 0.27, $P < 0.001$), compared to the obesity group.

Conclusion: Probiotics and nutraceuticals led to a significantly lower prevalence of obesity, reduction of insulin resistance, total and VAT weight. Our study demonstrated that supplementation of probiotics with omega-3 may have the most beneficial antiobesity properties.

Abbreviations: ACAT, acyl-coenzyme A:cholesterol acyltransferases; BSH, bile salt hydrolase; CFU, colony-forming unit; FAS, fatty acid synthase; FXR, farnesoid X receptor; GA, gum Arabic; GLP, glucagon-like peptides; HDL-C, high density lipoproteins cholesterol; HFD, high-fat diet; IL, interleukins; INF-γ, interferon γ; IR, insulin resistance; LDL-C, low density lipoproteins cholesterol; LPS, lipopolysaccharide; MSG, monosodium glutamate; NAFLD, non-alcoholic fatty liver disease; PPAR, peroxisome proliferator-activated receptor; SCFA, short-chain fatty acids; TC, total cholesterol; TG, triglycerides; SREBP1c, sterol regulatory element-binding protein 1c; TGF-β, transforming growth factor β; VAT, visceral adipose tissue; WPI, whey protein isolate; ZO, zonula occludens

* Corresponding author at: Endocrinology Department, Bogomolets National Medical University, Pushkinska 22a str., Kyiv 01601, Ukraine.
E-mail address: nazariikobyliak@gmail.com (N. Kobyliak).

https://doi.org/10.1016/j.diabres.2018.05.005

1. Introduction

Obesity is currently recognized as a condition that belongs to the most wide-spread medical and social problem, playing an outstanding role in human pathology development. Obesity is known to reduce human reproductive potential by having a negative impact on the general human condition, working ability, and patients' quality of life.

Without any exaggeration, obesity can be characterized as a global scale epidemic; the number of people that are overweight, among both the adult and child population is getting ever greater. According to the data of the World Health Organization, 1.9 billion humans of 18 years and above are overweight, 600 million of them are obese patients [43]. During the period between 1980 and 2014, the prevalence of obesity in developed countries has drastically increased among the adult population (from 15% up to 33%). The proportion of overweight children has increased from 6% up to 19% [43]. Both overweightness and obesity promote the rise of metabolic syndromes such as type 2 diabetes and cardiovascular conditions, leading to early disability and significant life span shortening [34].

Development of obesity is associated with the disturbance of the organism's energetic balance including regulation of intake of nutritious substances and energy expenditures. Different weight-regulating mechanisms including peripheral and central signals of hunger and satiation and complex response of the gastrointestinal tract organs following food intake are subjects of numerous scientific studies [17]. Besides genetic susceptibility, environmental conditions and human life style as well as gut microbiota play a very important role in these processes [18].

The problem of the effect of probiotics on lipid metabolism and obesity is a burning issue that is currently being discussed in scientific literature [17,16,27]. Gut microbiota may be considered as an ecological factor modulating obesity development. The use of a high-fat diet (HFD) in mice has been shown to significantly change the intestine microbiota composition, demonstrating the decrease of *lacto-* and *bifidobacteria* levels which are responsible for many positive physiological processes, e.g. improving the barrier function of the intestinal mucosa [27]. The microbiome analysis of mice with genetically-determined obesity demonstrates a drastic quantitative decrease of *Bacteroidetes* representatives, the proportion of *Firmicutes* becoming, on the contrary, increased [25]. Similar changes have also been found in humans: intestines of 12 obese patients contained decreased quantities of *Bacteroidetes* and higher contents of *Firmicutes* compared to control, lean persons [26].

Prebiotics and probiotics are now of great interest [13]; they have been shown to change the microbiota components and to influence food digestion, regulating the appetite and body weight [17,39]. Our choice of probiotic for the present study is based on a previously realized comparative experimental investigation of different probiotic strains intended for treatment and prevention of non-alcoholic fatty liver disease (NAFLD) and obesity [19,40]. Administration to animals of poly-probiotic mixtures containing both live and lyophilized strains beginning from the rats' infancy led to significant decreases of total and visceral adipose tissue (VAT) weight, steatosis and liver lobular inflammation, increased insulin sensitivity and induced hypolipidemic effect; all these processes assured a preventive defense from the NAFLD development in animals with experimental monosodium glutamate (MSG) induced obesity [19,40]. Furthermore, more pronounced changes were seen following administration of a probiotic mixture containing mostly live strains compared to lyophilized ones. Our data also suggest failure of preventive action concerning obesity and NAFLD development in cases when monostrain lyophilized probiotics have been used [19].

Nutraceuticals are substrates-pharmaceuticals supporting normal functional activity of intestinal mucosa. They are able to realize immunomodulating, cytoprotective, and antioxidant functions, to take part in metabolic processes, to deliver energetic and plastic materials to epitheliocytes. This is turn influences hormone metabolism. Nutraceuticals are, in particular, short-chain and polyunsaturated fatty acids belonging to omega-3 and omega-6, sorbents. It is worth using nutraceuticals together with probiotics, as then it is possible to simultaneously improve mucosa cytoprotection and to restore its symbiosis with intestine physiological microflora.

This study aims to determine whether probiotics plus nutraceuticals, such as smectite or omega-3, are superior to probiotic alone on the MSG-induced obesity model in rats.

2. Materials and methods

2.1. Experiment design

Seven animals were maintained in each polycarbonate cage for rats and mice; the cages were with galvanized steel covers and contained *ad libitum* drinking water in glass bottles. The animals were fed by standard chow delivered by the firm ≪REZON-1≫ (Ukraine).

All the animals selected for experiments were examined by a vet, their acclimatization was carried out during the first five days; the animals were then randomly divided into groups and labeled with numbers.

The rats were divided into 5 groups, each group containing 15 animals (n = 75). Group 1 control rats were administered neonatally with hypertonic saline (1.25 mg/g body weight per day, control group) subcutaneously (s.c.) at 2nd, 4th, 6th, 8th and 10th postnatal days. To obtain an experimental obesity model, all newborn rats except control were injected with monosodium glutamate - MSG (4 mg/g body weight per day) at 2–10th days of life to induced obesity [24,20,21]. Were standardized six pups per mother to ensure better lactation. After the weaning one-month aged MSG-treated animals were randomly divided into 4 groups, treated and untreated with probiotics/nutraceuticals. From weaning (30 days) to 120 days of age, rats had free access to standard rodent chow (PurinaW) and water during the entire experimental period.