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ORIGINAL ARTICLE

Study on Diabetic Rats Comparing the Effects of Sitagliptin and Probiotics on Serum Glucose

NAGHMANA LATEEF[1], IRUM REHMAN[2], MUHAMMAD TAHIR[3], IMRAN MEHBOOB BAIG[4], ARJUMAND[5], FAYAZ AHMED MEMON[6]
[1]*Associate Professor, Deptt of Physiology, Fatima Jinnah Medical University Lahore.*
[2]*Associate Professor, Deptt of Physiology, Margalla Institute of Health Sciences Rawalpindi*
[3]*Assistant Professor, Department of Pharmacology, Mekran Medical College, Turbat Balochistan*
[4]*Assistant Professor, Deptt of Physiology, Shahida Islam Medical College, Lodhran, Punjab*
[5]*Associate Professor, Deptt of Pathology, Liaqat College of Medicine & Dentistry, Karachi*
[6]*Professor, Department of Medicine, Muhammed Medical College & Hospital, Mirpurkhas, Sindh*
Corresponding author: Naghmana Lateef, Email: naghmanalateef@hotmail.com.

ABSTRACT

Objective: Probiotics were compared to Sitagliptin in this research in order to see whether they might lower blood glucose levels in diabetic rats more effectively.
Study Design: Quasi experimental study
Place and Duration: Fatima Jinnah Medical University Lahore. Jan, 2021 to June, 2021
Methods: There were 80 male rats were presented in this study. We used Streptozotocin to inflict diabetes in rats, and after one week, the results were validated by measuring Fasting Blood Glucose (FBG) (>7 mmol/L was termed diabetic). Rats were divided in four groups. Group I had 20 diabetic control rats, group II had 20 rats and received probiotics (250 mg/Kg), group III received sitagliptin (10 mg/Kg) among 20 rats and group IV received combination of probiotics and sitagliptin. Blood glucose was measured at baseline and after 6-weeks. Results among all groups were compared. SPSS 24.0 was used to analyzed all data.
Results: We observed that rats given probiotics in group-II saw a substantial drop in their fasting blood glucose levels, with an effectiveness that was on par with that of rats given sitagliptin in group-III (p 0.05). Sitagliptin and probiotics had a synergistic impact in group IV that was stronger ($p<0.05$) than either of their individual effects in groups II and III.
Conclusion: We concluded that Sitagliptin plus Probiotics lowers diabetic rats' blood glucose more than individual medicines. Probiotics reduce fasting blood glucose in diabetic rats like Sitagliptin. Diabetes treatment can include probiotics.
Keywords: Diabetes mellitus, Fasting blood glucose, Sitagliptin, Probiotics, Rats

INTRODUCTION

Approximately 422 million individuals have been diagnosed with diabetes mellitus, compared to 180 million in 1980 [1]. Increasing numbers of people are being diagnosed with type 2 diabetes (T2DM) as the obesity pandemic continues to spread [2]. T2DM can cause a wide range of health issues, including vision loss, neuropathy, kidney damage, and a shorter life expectancy, if uncontrolled or inadequately treated. [3]. The osteoblastic dysfunction associated with both forms of diabetes (T1DM and T2DM) increases the incidence of bone fractures, particularly at the hip (primarily in T1DM) [4].

Type 2 diabetes mellitus patients with poor glycemic control can benefit from a variety of treatments that alter the bacterial community structure.[5] Metformin, -glycosidase inhibitors, and dipeptidyl peptidase 4 (DPP-4) inhibitors are examples of oral antidiabetic medications that work by affecting the gastrointestinal tract in some way. As a first-line hypoglycemic medication, Metformin inhibits intestinal glucose absorption and hepatic glycogen production via AMPK-dependent and non-amphetaminergic mechanisms. Emerging data shows that metformin's anti-diabetic actions are mediated by changes in gut microbiota [6]. There was an increase in bacteria that produce short-chain fatty acids (SCFAs) and degrade mucin in individuals with type 2 diabetes who were taking metformin. [7,8] Glucose intolerance was alleviated in mice by transplanting the intestinal microbiota of metformin-treated individuals. It is thought that acarbose, an Actinoplanes-produced complex oligosaccharide, may reduce postprandial hyperglycemia by suppressing -glycosidase activity in the brush border of the small intestine and so decreasing intestinal epithelial cell absorption of monosaccharides.[9,10]

In Chinese individuals with type 2 diabetes, acarbose had weight reduction and HbA1c effects equivalent to metformin. Carbohydrate hydrolysis was decreased in type 2 diabetic patients by acarbose, which may have changed the microbial fermentation and lowered the amounts of lipopolysaccharides and inflammatory cytokines. [11] Postprandial blood glucose levels are reduced by sitagliptin, a DPP-4 inhibitor, since it prevents the breakdown of incretin hormones. Gut microbiota has yet to be studied in relation to DPP-4 inhibitors. Sitagliptin and vildagliptin may correct the microbial diversity of diabetic rats, according to two animal investigations. Few studies have examined the differences between different hypoglycemia medications and their impact on gut flora, with the exception of comparisons between monotherapy and a placebo [12,13].

A considerable portion of Pakistan's population lives below the poverty line, hence expensive treatment options are not warranted. In addition to the financial constraints, the negative effects of these medications urge us to search for a safe alternative. [14] For treating diabetes and its consequences, the use of Probiotics with strong metabolic capabilities might be an alternative treatment. [15] There is a paucity of information about the potential benefits of commercially available Probiotics in Pakistan. For the time being, no Pakistani study has compared the effects of Probiotics with Sitagliptin. This research will help close the diabetes treatment gap by making commercial Probiotics formulations available to the general public for usage.

MATERIAL AND METHODS

This Quasi experimental study was conducted at Fatima Jinnah Medical University Lahore and comprised of 80 rats. The National Institutes of Health (NIH) animal house provided rats measuring 200–250 grammes, without any physical abnormalities and with normal baseline measurements.

They had unrestricted access to running water. It was necessary to keep the temperature in the animal housing facility at 202°C, the relative humidity at 50–70%, and a 12-hour light/dark cycle. We used Streptozotocin to inflict diabetes in rats, and after one week, the results were validated by measuring Fasting Blood Glucose (FBG) (>7 mmol/L was termed diabetic). Rats were divided in four groups. Group I had 20 diabetic control rats, group II had 20 rats and received probiotics (250 mg/Kg), group III received sitagliptin (10 mg/Kg) among 20 rats and group IV received combination of probiotics and sitagliptin.

Serum glucose levels were checked after three weeks to assess how medication was affecting them. All groups underwent final sample by heart puncture after four weeks to assess the effect on serum glucose levels. The SPSS-24 statistical software was

used for the study. According to the data, mean differences were recorded. One way ANOVA (post hoc Tuckey test) was used to compare quantitative parameters across the groups, and a p-value of 0.05 was considered significant.

RESULTS

In group I mean fasting glucose level among diabetic rats were 478.9±13.41 mg/dl. Mean fasting blood glucose level in group II was reduced significantly to 93.13±5.16 mg/dl and in group III mean glucose level reduced to 94.7±3.25 mg/dl. Sitagliptin and probiotics had a synergistic impact in group IV that was stronger 89.6±10.62 mg/dl ($p<0.05$) than either of their individual effects in groups II and III.(table 1)

Tabe-1: Comparison of FBG levels among all groups

FBG (mg/dl)	Mean	Std	P Value
Group I	478.9	13.41	0.005
Group II	93.13	5.16	0.012
Group III	94.7	3.25	0.015
Group IV	89.6	10.62	0.008

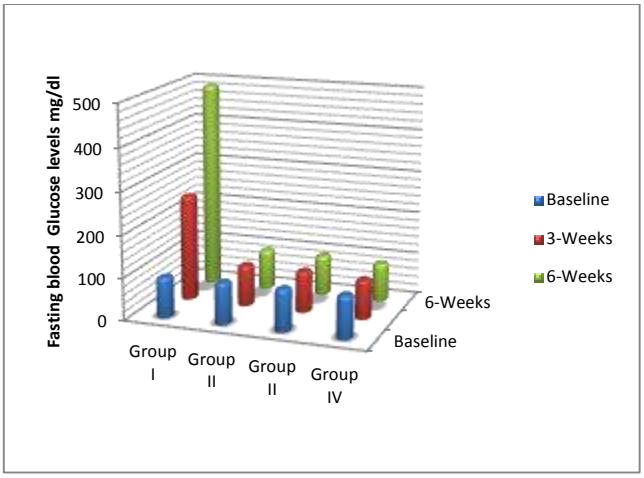

Figure-1: Comparison of mean fasting blood Glucose levels at baseline and after 6-weeks

DISCUSSION

A lot of attention is being paid to the relationship between medicines and gut microbiota [16]. Non-antibiotic and anti-diabetic medications have been shown to affect the microbiome and ameliorate diabetes, as have antibiotics [17,18]. A wide range of medications and chemicals are affected by the baseline microbiota, which can have both favourable and negative effects on their pharmacokinetics and pharmacodynamics [19,20]. However, few research have studied how pre- and/or probiotics might influence the efficacy of anti-diabetic medications by changing gut flora. Diabetic mice were given Bifidobacterium animalis ssp. lactis 420, polydextrose as a prebiotic, and sitagliptin as a combination in a recent research [21]. T2D characteristics were reduced when sitagliptin and pre- and probiotics were used together. Combining prebiotic polysaccharide with metformin and sitagliptin lowered hyperglycemia and obesity in Zucker diabetic rats [22] compared to taking the medicines alone. A combination of a prebiotic and metformin was used to treat diabetic mice in another investigation. Compared to metformin or MOS alone, the combination treatment improved fasting blood glucose, glucose tolerance, and insulin resistance [23].

In this study 80 male rats were presented. Rats were divided in four groups. Group I had 20 diabetic control rats, group II had 20 rats and received probiotics (250 mg/Kg), group III received sitagliptin (10 mg/Kg) among 20 rats and group IV received combination of probiotics and sitagliptin. We observed that rats given probiotics in group-II saw a substantial drop in their fasting blood glucose levels, with an effectiveness that was on par with that of rats given sitagliptin in group-III (p 0.05). Sitagliptin and probiotics had a synergistic impact in group IV that was stronger ($p<0.05$) than either of their individual effects in groups II and III. These results were comparable to the previous studies.[24,25] The results of this study show that streptozotocin-induced hyperglycemia may be alleviated by Probiotics with equal efficacy to sitagliptin. According to a slew of research, probiotics can significantly reduce the risk of developing type 2 diabetes. [26] Sohag MSU et al[27] found that treatment of Probiotics reduced FBG in diabetic rats, which is consistent with our findings. Streptozotocin-induced diabetic mice were fed Probiotics, and their anti-hyperlipidemic effects were examined by Aggarwal J et al[28]. Supplementation with Probiotics improved the metabolic profile of diabetic individuals and reduced FBG, HbA1c, triglycerides, according to a research conducted by Yadav R et al[29].

Most of the investigations on the benefits of Probiotics on diabetes were done on either cultures of Probiotics[30] or Probiotics fermented products, such as probiotic fermented milk or yogurt[31,32]. Because it was so readily available, we utilised a commercially prepared Probiotic. Patient compliance is improved because of the ease of oral administration and the low cost of these medications. When a research was done using commercially available Probiotics called "Protégé," the results were in line with those of Campos LF et al. [33]. There were Lactobacillus and Bifidobacterium Probiotics in the commercial Protégé formulation. Besides Lactobacillus and Bifidobacterium, HifloraTM is a commercial and locally accessible probiotic preparation in Pakistan that we employed for our study.

Preliminary researches show that probiotics supplementation significantly decreased fasting plasma glucose, glycated haemoglobin and fasting insulin levels in diabetes patients.[34,35]

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