ORIGINAL RESEARCH PAPER

Diabetology

KEY WORDS: Type 2 diabetes mellitus, barley, beta-glucan, Fructooligosaccharides

BETA-GLUCAN AND FOS ADDED BARLEY SLIMS IMPROVES GLYCEMIA, GUT HEALTH AND INFLAMMATORY STATUS OF TYPE 2 DIABETES MELLITUS INDIVIDUALS RESIDING IN URBAN VADODARA

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ABSTRACT

Aim: To study the impact of barley slims supplementation on glycemic, inflammatory status and gut health of type 2 DM subjects

Method: A randomized, placebo controlled trial was undertaken wherein 47 adult type 2 DM subjects were selected from private clinics of urban Vadodara. The placebo and experimental group were supplemented wheat slims and barley slims (6 grams beta glucan powder and 2 ml of Fructooligosaccharides) respectively for a period of 45 days.

Results: At baseline, a strong correlation was observed between the beneficial microflora and glycemic parameters. Barley slims supplementation showed significant reduction in weight, BMI, SBP, FBS, ABG, HbA1c and fructosamine by 1.1%, 0.7%, 3.5%, 14%, 4.3%, 3.8% and 3% respectively. hs-CRP and homocysteine levels reduced non-significantly by 8% and 9% respectively. Fecal log counts of *Lactobacillus* and *Bifidobacterium* increased significantly by 15% and 11.2% and *E.coli* was reduced significantly by 22% ($p<0.001$).

Conclusion: Intake of barley slims (6 gram of beta glucan and 2 ml of Fructooligosaccharides) in the diets of type 2 diabetic patients improves glycemia, gut health and reduces inflammation.

INTRODUCTION

The global mortality responsible due to NCD are sky rocketing. Early detection and timely intervention can save many lives and reduce the burden of NCDs (IDF, 2017). A large variety of foods are marked as functional food with a variety of components affecting a various of body functions relevant to either a state of wellbeing and health and/or to the reduction of risk of a disease (Noomhorm and Ahmad, 2014). *Hordeum vulgare*, commonly known as Barley encompass Beta glucan, a bioactive compound has been shown to prevent insulin resistance (Bays et al, 2011 & Choi et al, 2010). Fructooligosaccharide (FOS), a type of carbohydrate, has also been recently recognized as a potent prebiotic which is emerging as an important factor in the bacterial ecology of human health (Vuyst de Luk and Leory F, 2011; Mendlik K et al, 2012).

METHODS AND MATERIALS

A randomized placebo control trial was undertaken wherein two private clinics of Vadodara were conveniently selected based on the permission obtained from the doctor to enrol diabetic subjects. A total of 47 subjects were screened and enrolled as per the inclusion and exclusion criteria. Subjects were briefed on the objectives and benefits of the study and written and verbal information were provided. The subjects who willingly signed the written informed consent form were enrolled for the study. The subjects were further randomly divided into experimental group (n=27) and control group (n=20) (Figure 1).

Inclusion criteria for selection of patients

- Adult stable type 2 diabetic subjects.
- Willingness to participate in the study
- Physician's consent.

Exclusion criteria for selection of patients

- History of chronic illness
- Taking any supplements
- Consumption of various functional foods.
- Allergic to supplementation powder
- Smokers or tobacco chewers
- Rapid weight gain or loss
- Thyroid disorder
- $HbA1_c \geq 10$

Baseline information of subjects was obtained using a pretested semi-structured questionnaire and the socio economic status was collected from the subjects using the Kuppuswamy's Socioeconomic Status Scale 2012. Sitting blood pressure of subjects was measured using the standard sphygmomanometer on the right arm. All anthropometric measurements were assessed using the guidelines adopted at the NIH sponsored Arlie Conference (Lohman et al 1988). Trained Laboratory technician from Thyrocare pathology lab helped to draw the blood (5 ml). Fasting blood sugar level, glycated haemoglobin, Fructosamine, hs-CRP, Homocysteine were analysed using GOD/POD Enzymatic Method, Fully automated H.P.L.C, Nitroblue tetrazolium assay, Nephelometry and Chemi luminescent immunoassay. Average blood sugar was derived from glycated haemoglobin. The gut microbial analysis was determined in terms of *Bifidobacterium* and *Lactobacilli* and *E.coli* (FAO/WHO, 2001)

The Beta- glucan powder was procured from Mitushi Biopharma Ltd., Ahmedabad, Gujarat. FOS liquid was procured from TATA chemicals Ltd. Barley slims were composed of barley flour, wheat flour, beta glucan powder, FOS, salt, spices and oil whereas standard slims were composed of 100% wheat flour along with salt, spices and oil.

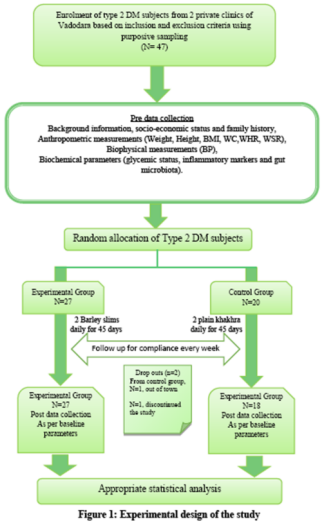

Figure 1: Experimental design of the study

Ethical clearance

The study was approved by The Institutional Ethics Committee for Human Research (IECHR) of the Foods and Nutrition Department, The M.S. University of Baroda and the ethical number allotted for the study was IECHR/2017/6.

Statistical analysis

The data was entered in an excel spreadsheet. The data was cleaned and verified and subjected to appropriate statistical analysis. Statistical analysis was performed using Microsoft Excel 2013. Results were expressed as mean values ± standard deviations. Paired't' test was used to assess the differences between the means of the same group before and after intervention period. Student t test was performed for the comparison between control and experimental group. The significance levels were set at 5% by two sided tests. Correlation coefficient was computed amongst the parameters of interest.

RESULTS

At the baseline, out of forty seven subjects screened, 38.3% were males and 61.7% were females. Out of these, 38.9% of the males were above 65 years of age and 62.1% of the females were in the age group 51-65 years. About 14.8% and 72.5% subjects were overweight and obese respectively and 70% of the subjects had abdominal obesity indicating high risk for development of NCDs.It was observed that 40.5% of the subjects had hypertension. Males were more hypertensive than females.

The inflammatory marker hs-CRP was found to be positively correlated with HbA1c and Average blood sugar whereas homocysteine was found to be positively correlated with FBS and fructosamine. Correlation was observed between the gut microbiota and glycemic status of type 2 DM subjects. *Bifidobacteria* was found to be negatively correlated with FBS, Average blood sugar and HbA1c. *E.coli* was positively correlated with average blood sugar, HbA1c, fructosamine and homocysteine (Table 1).

Table 1: Correlation amongst biochemical parameters and gut health parameters of type 2 DM subjects:

	FBS	ABS	A1c	FSA	Hs-CRP	HC	*Ecoli*	LAB	BIF
FBS	-	0.8**	0.81**	0.6**	0.44**	0.3*	NS	NS	-0.3*
ABS	0.81**	-	NS	0.73**	.42**	NS	0.37**	NS	-0.33*
A1c	0.81**	0.9**	-	0.76**	0.40**	NS	0.39**	NS	-0.35*
FSA	0.6**	0.6**	0.7**	-	NS	0.45**	0.33*	NS	NS
Hs-CRP	0.44**	0.42**	0.4**	NS	-	NS	NS	NS	NS
H.C	0.3*	NS	NS	0.45**	NS	-	0.38*	NS	NS
E.coli	NS	0.37**	0.39**	0.33*	NS	0.38*	-	-0.55**	-0.57**
LAB	NS	NS	NS	NS	NS	NS	-0.55**	-	NS
BIF	-0.3*	-0.33*	-0.35*	NS	NS	NS	-0.57**	NS	-

Post intervention, experimental group showed significant reduction in weight ($p<0.001$) and BMI ($p<0.01$). Reduction in SBP was observed by 3.5% in the experimental group. The glycemic response of the subjects reduced by 14%, 4.3%, 3.8% and 3% in terms of fasting blood sugar ($p<0.001$), average blood glucose ($p<0.05$), HbA1c ($p<0.05$), and fructosamine ($p<0.05$) (Table 2). Also, uncontrolled diabetic (HbA1c ≥8) had significant reduction in FBS, HbA1c and Average Blood glucose by 14%, 7.6% and 9.3%. Significant reduction in FBS values were observed in 15th day, 30th day and 45th day from the 0th day indicating consistent reduction in the FBS levels during the supplementation (Table 2). Subjects having hyperhomocysteinemia (>30µmol/L) had significant reduction in homocysteine levels by 23.6% (Table 3). The fecal log counts of Lactobacillus and Bifidobacteria showed a significant increase by 15% ($p<0.001$) and 11.2% ($p<0.05$) respectively whereas there was a significant reduction by 22% in the fecal log counts of *E.coli* ($p< 0.001$) of diabetic subjects after supplementation (Table 2).

Table 2: Impact of barley slims supplementation on Glycemic, inflammatory status and gut profile of type 2 DM subjects (mean±SD)

Parameters		Control group N=18	Experimental group N=27	Student 't' value
Fasting Blood sugar mg/dL	Pre	135.13±31.1	155.89±36.4	0.14^{NS}
	Post	147.28±37.8	133.02±26.9	2.2*
	Paired 't' test	1.4*	4.28***	
	% change	5.9↑	14↓	
Average Blood glucose mg/dL	Pre	200.5±58.9	182.7±43.2	0.9^{NS}
	Post	196.6±50.1	174.7±37.7	1.2^{NS}
	Paired 't' test	0.73^{NS}	2.3*	
	% change	2.2↓	4.3↓	
HbA1c %	Pre	8.6±2.05	7.7±1.28	1.5^{NS}
	Post	8.4±1.74	7.4±0.94	2.1*
	Paired 't' test	0.74^{NS}	0.48*	
	% change	2.3↓	3.8↓	
Fructosamine µmol/L	Pre	310.18±52.1	261.84±43.2	2.7**
	Post	297.53±46.6	253.79±34.9	3.1**
	Paired 't' test	1.4^{NS}	2.2*	
	% change	3↓	3.09↓	
hs-CRP (mg/L)	Pre	2.4±2.4	2.4±4.1	1.36^{NS}
	Post	2.2±2.0	2.2±4.4	1.58^{NS}
	Paired 't' test	0.4^{NS}	0.4^{NS}	
	% change	8↓	8↓	
Homocysteine µmol/L	Pre	26.3±15.2	19.4±9.6	1.6^{NS}
	Post	25.1±14.7	17.7±7.6	1.9^{NS}
	Paired 't' test	1.17^{NS}	1.4^{NS}	
	% change	4.6↓	8.9↓	
***E.coli* (log_{10} CFU/g)**	Pre	4.23±1.47	4.95±1.34	2.36^{NS}
	Post	4.70±1.06	3.84±1.53	2.51*
	Paired 't' test	1.65^{NS}	4.84***	
	% change	11↑	22↓	
BIF (log_{10} CFU/g)	Pre	5.32±1.63	6.20±1.63	2.1*
	Post	5.50±1.27	6.91±1.37	4.22***
	Paired 't' test	0.64^{NS}	2.83*	
	% change	3.39↓	11.2↑	
LAB (log_{10} CFU/g)	Pre	4.98±1.67	5.95±1.67	1.78^{NS}
	Post	5.16±1.85	6.83±1.91	2.68*
	Paired 't' test	1.01^{NS}	4.49***	
	% change	3↑	15↑	

Note: level of significance: * p-value <0.05** p-value<0.01,*** p-value<0.001,NS=not significant

Table 3: Impact of barley slims khakhras on homo cysteine levels of type 2 DM subjects based on their initial values

Parameter		Control group		Experimental group	
		Homocysteine <30 N=12	Homocysteine >30 N=6	Homocysteine <30 N=19	Homocysteine >30 N=8
Homo-cysteine (µmol/L)	Pre	21.2±14.7	40.1±7.6	15.5±15.5	30.9±9.4
	Post	20.8±14.5	37.4±8.5	15.1±15.1	23.6±9.4
	Paired 't' test	0.55 NS	0.94 NS	0.62 NS	2.91*
	% change	1.8↓	6.7↓	2.5↓	23.6↓

DISCUSSION

Post supplementation resulted in significant reduction in systolic blood pressure by 3.5% in the experimental group. Under the effect of dietary fibre, beta-glucan and FOS, it is assumed that glucose from a typical diet will be absorbed slowly due to formation of viscous gel. This may have led to slower release of insulin and thus preventing the triggering of the SNS which controls the blood pressure (Landsberg L, 1986). This could be the putative mechanism for reduction in SBP in type2 DM subjects. The present study revealed that there was significant decrease in FBS, HbA1c and fructosamine levels by 14%, 3.8% and 3% respectively upon feeding barley slims khakhras. Previous studies have shown that barley consumption prevent insulin resistance and may also improve insulin sensitivity among those with impaired glucose tolerance (Bays et al., 2011 & Choi et al., 2010). One of possible mechanism is via lowering of carbohydrate absorption. These polysaccharides form a gelatinous layer that works as a barrier that renders carbohydrate absorption difficult and thus leading to lower concentrations of glucose in the blood (Kiho et al, 1995). Another possible mechanism for beta-glucans to reduce blood glucose level is mediated by signal pathway through PI3K/Akt activation. Decreased PI3K/Akt activity has been shown to play a key role in the pathogenesis of diabetes. Beta-glucans have been demonstrated to increase PI3K/Akt through several receptors (Hsu et al 2002; Chen and Seviour 2007).Similar study found that FOS supplementation had significant reduction in FBS and HbA1c by 6.3% and 10.6% respectively in hypertensive type 2 DM subjects (Sheth M. and Thakuria A, 2015). The possible mechanism of FOS lowering the glycaemic responses can be by elevating the secretion of gastric inhibitory polypeptide (GIP) and glucagon like polypeptide (GLP-1) that stimulates the release in insulin.

A reduction in homocysteine levels by 23% was found in hyperhomocysteinemia subjects. High insulin levels seem to influence homocysteine metabolism, possibly through effects on glomerular filtration or by influencing activity of key enzymes in homocysteine metabolism, including 5,10-methylenetetrahydrofolate reductase (MTHFR) or cystathione -synthase (CBS) (Gallistl et al, 2000).

In addition, the present study also revealed positive shift in the colonization of gut microflora where *Bifidobacterium* and *Lactobacillus* bacteria improved drastically by 11% and 15% respectively and a decrease in *E. Coli* by 22%. Beta glucan and FOS has been reported of having prebiotic property and is known to increase the beneficial gut microflora (Arena et al., 2014, Sheth M and Thakuria A., 2015; Assudani A and Sheth M. 2014).

CONCLUSION

Beta glucan and FOS added barley slims has definitely proved to be a potential means of controlling the type 2 DM and such foods can be used on a regular basis in the diets of diabetic subjects

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Conflict of Interest

The authors declare that they have no conflict of interest.

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