Brewer's Yeast Improves Glycemic Indices in Type 2 Diabetes Mellitus

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Original Article

ABSTRACT

Background: Brewer's yeast may have beneficial effects on insulin receptors because of itsglucose tolerance factor in diabetic patients. This study was conducted to investigate the effects of brewer's yeast supplementation on glycemic indices in patients with type 2 diabetes mellitus.

Methods: In a randomized double-blind controlled clinical trial, 84 adults (21 men and 63 women) aged 46.3 ± 6.1 years old with type 2 diabetes mellitus were recruited and divided randomly into two groups: Supplement group receiving brewer's yeast (six 300mg tablets/day, total 1800 mg) and control group receiving placebo (six 300mg tablets/day) for 12 weeks. Body weight, height, body mass index, food consumption (based on 24h food record), fasting blood sugar (FBS), glycosylated hemoglobin, insulin sensitivity, and insulin resistance were measured before and after the intervention. Data analysis was performed using the Statistical Package for Social Sciences (version 18.0).

Results: The changes in FBS, glycosylated hemoglobin, and insulin sensitivity were significantly different between the two groups during the study (respectively $P < 0.001$, $P < 0.001$, $P = 0.02$ independent sample *t*-test). There was a significant difference in FBS, glycosylated hemoglobin, and insulin sensitivity at the end of the study between the two groups after removing the effects of baseline values (respectively $P = 0.002$, $P < 0.001$, $P = 0.02$, analysis of covariance). Changes in body mass index, 24h food record, insulin resistance were not significant.

Conclusions: Dietary supplementation with brewer›s yeast besides the usual treatment of diabetes can ameliorate blood glucose variables in type 2 diabetes mellitus.

Keywords: Brewer's yeast, HbA1c, type 2 diabetes

INTRODUCTION

Diabetes mellitus is one of the most common metabolic disorders and noninfectious diseases in the world.[1] In diabetic individuals, long-standing hyperglycemia leads to nephropathy, neuropathy, and cardiovascular diseases.[2]

World Health Organization reports state that more than 246 million people are affected by noninsulin-dependent diabetes mellitus[3] and this could go up to 438 million by 2030.[4] In *Iran*, one out of five persons is diabetics and 10%-15% of these patients die every year.[5,6] In 1958, Mertz discovered that brewer's yeast reinforces hypoglycemic activity of insulin.[7] As a result, glucose tolerance factor (GTF) was extracted from brewer's yeast. The next studies provided more insight into the extent to which this biologically active component is pharmacologically or nutritionally related to brewer's yeast. Also, the comparison between brewer's yeast and CrCl3 had been studied in some investigations.[8-10] Their results unanimously showed that brewer's yeast supplementation was more effective than CrCl3 in diabetics and not in nondiabetics. Consequently, brewer's yeast was known as the best and accessible substance providing GTF in recent studies.[11] It has drawn the attentions due to its ability of making improvement in diabetic patients and preventing cardiovascular diseases.[1] This yeast is dried and inactive cells of *Saccharomyces cerevisiae* which does not have fermenting activity.[6] Its mechanism is via contributing of GTF in insulin function. It seems GTF structure as a complex compound contains organic chromium which is biologically active. Moreover, some amino acids (Cis, Glu, Gly) and vitamin B3 are present in GTF structure in association with Cr+3. Therefore, the absorption of chromium is longer and more consistent in the case of GTF structure. It creates a triple complex composed of insulin and insulin receptors on target cell membranes. GTF contains achromodulin molecule which binds to the insulin-activated receptor raising its tyrosine kinas activity up to 8 times.[12] Some studies on the potential health benefits of yeast have found that brewer's yeast may favorably affect carbohydrate in diabetic patients, but there were a discrepancy in their outcomes.[13,14] The majority of research studies on supplementation with brewer's yeast showed fasting blood sugar (FBS)[8,14,15] and insulin resistance reduction.[16] The influence of brewer's yeast on HbA1c has been explored in a few studies.[14,17] In 2009, Nahas and Moher evaluated the efficacy of different formulations of yeast with dissimilar doses for 2 to 26 weeks on type 2 diabetes in a meta-analysis on 41 trials (*N*:1198). There was strong evidence of HbA1c and FBS levels reduction in present review; however, this article remarked on further clinical trials.[18] Notwithstanding, these investigations have been implemented in far-flung regions that their populations have different racial, social, and dietary habits.[8,19,20] On top of that, just one experimentation has been done in Iran until now.[21] So, we hypothesized that supplementation with brewer's yeast may well ameliorate diabetes.

METHODS

Patients and research design

This double-blind, randomized, clinical trial study was carried out from autumn to winter 2010. Ninety-two well-controlled type 2 diabetic patients were enrolled at the beginning. After explaining the study aims, 89 patients were recruited. During the intervention, five volunteers were excluded and 84 subjects (63 women and 21 men volunteers) finished the research finally [Figure 1]. Inclusion criteria were history of at least 2 years clinically diagnosed type 2 diabetes mellitus and aged 35-55 years. On the contrary, a history of heart, liver, kidney, intestinal disorders or gout, stroke and Parkinson, recent intake of brewer's yeast supplement, continual consumption of antidepressant drugs, and treatment with insulin were exclusion criteria. The subjects were allocated into brewer's yeast and placebo groups by sequential randomly preloaded coded envelopes in a 1:1 ratio after blocking based on sex and glycosylated hemoglobin (HbA1c). The members of the two groups received equal education about consumption of both anti-diabetes drugs and current tablets. Participants of the brewer's yeast group received 1800 mg brewer's yeast (two 300 mg tablets three times daily; *N*:42) for 12 weeks and placebo group (*N*:42) received equal quantities of pills containing excipient without brewer's yeast for the same period of time. Placebo tablets consisted of cellulose microcrystalline compounds, magnesium stearate, caramel, malt, and stearic acid. Supplements and placebos were the same in size, color, and taste. They were manufactured by (Health Aid Co., Marlborough Hill, UK). Compliance of participants was assessed by tablet counting at the meetings held each month and they were given a new monthly supply of tablets. Subjects were instructed by two nutritionists how

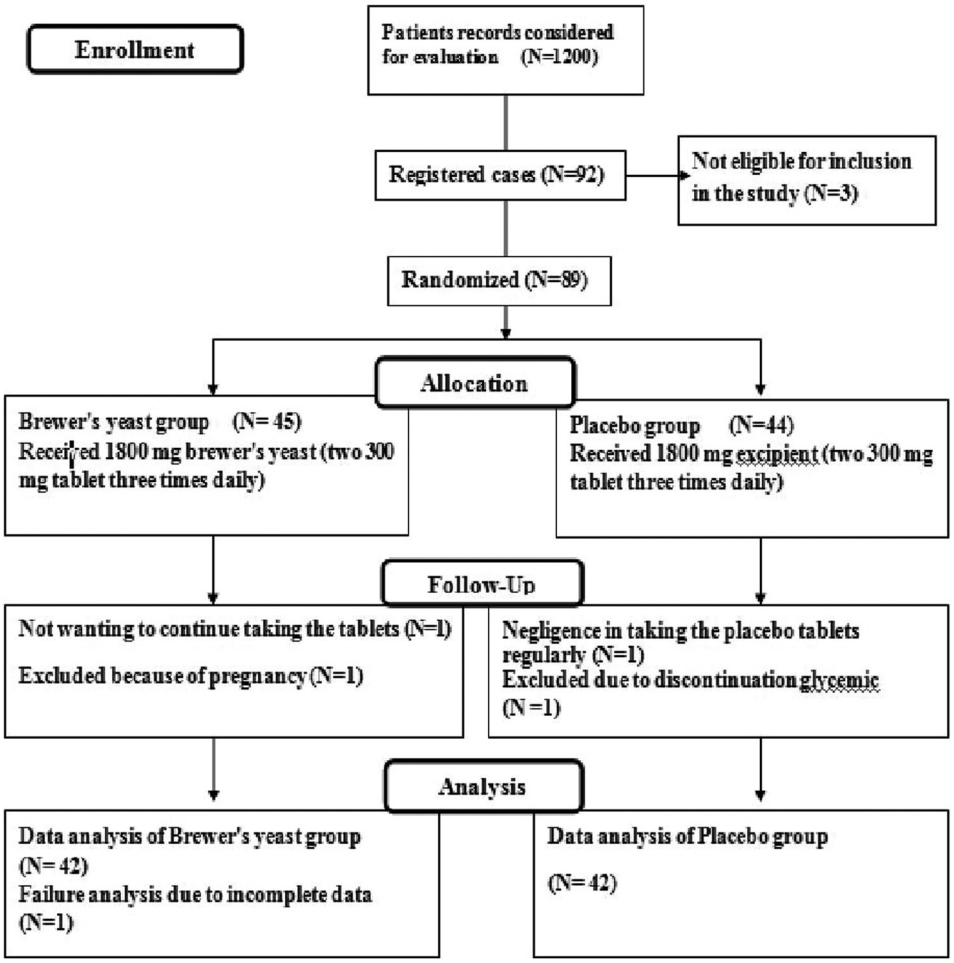

Figure 1: Flow diagram

to record their daily foods and beverages. Dietary intake was assessed by three 24 h diet records. Energy, macronutrients, sodium, potassium, and chromium intakes were computed by means of Food Processor II software (FPII, version 2. ESHA Research, Salem, Oregan). All participants were weighed (seca762, secagmbh and co. kg. Hammer Steindamm 9-25 22089 Hamburg, Germany) with light clothes and without shoes in the fasting state at the baseline and the end of 12th week. Their heights were measured by stadiometer (seca 206, secagmbh and co. kg. Hammer Steindamm 9-25. 22089 Hamburg, Germany). A total of 5 mL of blood samples were taken from antecubital vein. And 4 mL of blood were transferred to a tube without anticoagulant using for FBS; insulin and lipid profile measurements and 1 mL was transferred to a tube containing ethylene diamine tetra acetic acid (K3EDTA) as an anticoagulant using for (hemoglobin A1c) HbA1c test. Tubes without anticoagulants were left at room temperature for half an hour and then centrifuged at 2400 g for 5 min/4°C to separate sera. The sera were transferred to microtubes and placed in −70°C freezer for further analysis. A questionnaire about personal information, medical history, drug, and supplement consumption was filled for each volunteer initially. The patients were advised not to change their medications, dietary, and exercise habits during the course of the study. All the participants signed an informed consent. Authors stated that the protocol for the research project has been approved by Tehran University of Medical Sciences Ethics Committee and that it conforms to the provisions of the Declaration of Helsinki (as revised in Edinburgh 2000).

This trial was registered with Iranian Registry of Clinical Trials, no.IRCT138807062513N1.

This randomized controlled trial followed the guidelines of the consolidated standards of reporting trials statement.

Laboratory measurements

Serum glucose, HbA1c, and insulin resistance indices

Serum glucose was measured by autoanalyzer (Hitachi 911, Japan). FBS was measured by GOD/PAP method (kitno. 10-505, ZiestChem Diagnostics Co., Tehran, Iran) with sensitivity: 3.3 mg/dL. Glycosylated hemoglobin was determined in K3EDTA whole blood tubes and was measured by an ion exchange chromatography using a NycoCard® Reader II instrument (Catalog ref 1042184, Axis-Shield poC AS, Oslo, Norway). For measurement of plasma insulin, we used "Sandwich" immunoradiometric assay, (Kit no. IM 3210-sensitivity 0.5 μIU/mL, Immunotech, Beckman Coulter Co; Murmanská 1475/410005 Prague, Czech Republic). The homeostatic model assessment of insulin resistance (HOMA-IR) was computed as fasting plasma glucose (mmol/L) × fasting serum insulin (mU/L)/22.5[22] and quantitative insulin sensitivity check index (QUICKI) was calculated as 1/[log insulin (μIU/mL) + log glucose (mg/dL)].[23]

Data analyses

We used Statistical Package for Social Science Version 18.0 (SPSS Inc., Chicago, IL) for the statistical analyses. To compare all values between the brewer's yeast and placebo groups at baseline, independent sample *t*-test was performed. In addition, Paired *t*-test was done on the variables of each group at baseline and after 12 weeks of supplementation. To remove the effect of the baseline values from final parameters, we used analysis of covariance (ANCOVA). $P < 0.05$ was considered statistically significant.

RESULTS

There were no significant differences between the brewer's yeast and placebo groups at baseline with regard to sex, body mass index (BMI), and age [Table 1]. Dietary intakes were also similar at the beginning and at the end of the study. Moreover, the groups showed no change in dietary intakes during the intervention [Table 2]. FBS decreased by 12.4 g/dL in the brewer's yeast group for the period of supplementation ($P = 0.02$), whereas in the placebo group it rose by 13.5 mg/dl ($P = 0.002$). The percent of changes in FBS was significantly different between the two groups during the study [$P < 0.001$, Figure 2]. There was a significant difference in FBS at the end of the study between the two groups after removing the effects of baseline values [$P = 0.002$, ANCOVA, Table 3]. HbA1c during the period of supplementation in the brewer's yeast group declined significantly ($P = 0.001$). HbA1c decreased by 1.1% in brewer's yeast group compared with an increase of 0.1% in placebo group. Furthermore, differences between the two groups were statistically significant at the end

Table 1: Baseline characteristics of the two treatment groups

Variables	Brewer's yeast	Placebo	Total
Number of patients	42	42	84
Sex (men/women)	10/32	11/31	21/63
‡Age (year)	46.8±6.21	45.7±6.11	46.2±6.16
†‡BMI (Kg/m^2)	30.0±4.4	29.9±4.7	29.9±4.5

†‡BMI=Body mass index, ‡Data are expressed as mean±standard deviation

Table 2: Dietary intakes at the beginning and at the end of the study between the two treatment groups

†Variables	Brewer's yeast		Placebo	
	Baseline	12w	Baseline	12w
Energy (Kcal)	1431.0±416.7	1329.0±389.8	1447.0±484.8	1374.0±386.3
Carbohydrate (g)	172.1±60.6	168.3±57.6	170.1±53.0	171.0±61.5
Protein (g)	57.4±16.3	50.0±14.3	53.4±20.6	49.2±18.1
Total fat (g)	60.5±24.2	55.0±20.0	65.1±31.6	59.1±28.7
Fiber (g)	15.4±5.5	14.0±5.6	14.9±5.4	13.6±6.1
K (mg)	1677.9±511.7	1568.8±489.5	1573.1±463.0	1472.6±433.0
Na (mg)	1492.1±587.0	1506.7±586.6	1400.1±512.0	1430.0±562.4
Cr (μg)	2.5±2.0	2.0±1.7	2.2±1.6	1.9±1.3

K=Potassium, Na=Sodium, Cr=Chromium, †Data are expressed as mean±standard deviation

of study after removing the effects of baseline values [$P < 0.001$, Table 3]. The percent of changes in QUICKI was significantly different between the two groups [$P = 0.02$, Figure 2]. After removing the effects of baseline value, significant difference was shown between the two groups in QUICKI at the end of the project [$P = 0.02$, Table 3]. QUICKI significantly decreased in the brewer's yeast group after 12 weeks of supplementation ($P = 0.01$). HOMA-IR decreased in brewer's yeast group, but the reduction was not statistically significant (from 5.22 to 4.36). Meanwhile, it increased slightly and nonsignificantly in the placebo group (from 4.63 to 4.68), although there was a tendency for a decrease in HOMA-IR values (from 5.2 ± 2.7 (μIu/mL) to 4.3 ± 3.1 (μIu/mL) in the brewer's yeast group compared with the placebo group which did not show any change [Table 3].

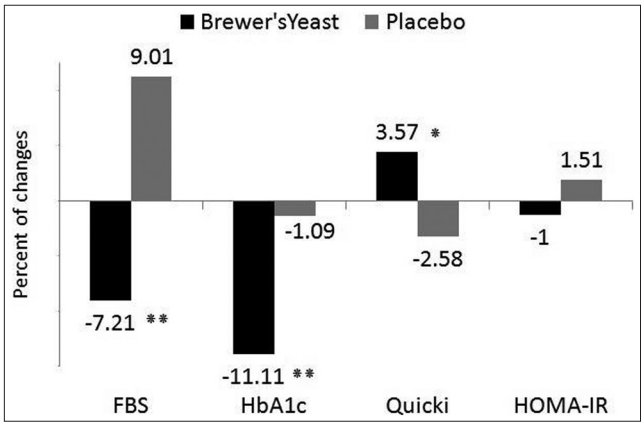

Figure 2: Percent of changes in glycemic indices in study groups after 12 weeks intervention
(Significant difference of the percent of changes during the study between the Brewer's yeast group and the placebo group (Independent *t*-test): $\frac{(12\,\text{week value} - \text{baseline value})}{\text{Baseline value}} \times 100$
$^{*}P < 0.05$; $^{**}P < 0.001$)

DISCUSSION

The results of this study showed that daily consumption of six tablets of brewer's yeast for 12 weeks in type 2 diabetic patients can reduce HbA1c and FBS levels and increase insulin sensitivity. The findings are consistent with those of previous reports in the literature.[8,14,21] While the investigations carried out by Grant[17] and Robinowitz[24] showed no significant change for FBS. It seems it would be due to fewer samples and shorter duration of intervention. Chromium is part of the GTF structure in brewer's yeast. The absorption of brewer's yeast is more efficient in an individual with a poor chromium status. As a result, the body chromium pool in diabetics with chromium deficiency is saturated faster and finally the surplus of that is excreted through urine.[25] This supports the theory that type 2 diabetes patients may have a low level of chromium and an effective source for chromium repletion such as brewer's yeast may improve their carbohydrate tolerance. Therefore, patient selection may be an essential part in determining clinical response, as it was concluded that a clinical response (i.e., decreased glucose and improved insulin sensitivity) may be more likely in insulin-resistant individuals with type 2 diabetes.[9,26] Wang *et al.*,[13] supplemented healthy individuals with brewer's yeast and torula yeast for 12 weeks. No significant change was observed in insulin sensitivity of either group which was in contrast with our results. Two reasons could explain this discrepancy: First,

Table 3: Comparison of BMI and glycemic indices at the beginning and at the end of the study between the two treatment groups

¶Variables	Brewer's yeast		Placebo	
	Baseline	12w	Baseline	12w
FBS (mg/dL)	176.0±61.1	163.3±53.3*‡	153.1±40.9	166.9±44.6
HbA1c (%)	9.0±1.5	8.0±1.6***‡	9.1±1.6	9.0±1.8
QUICKI	0.308±0.023	0.319±0.026**†	0.310±0.020	0.302±0.021
HOMA-IR	5.2±2.7	4.3±3.1	4.6±2.0	4.6±1.7
BMI (Kg/m^2)	30.0±4.4	29.8±4.4	29.9±4.7	30.1±4.6

FBS=Fasting blood sugar, HbA1c=Glycated hemoglobin (whole blood), QUICKI=Quantitative insulin sensitivity check index, HOMA-IR=Homeostasis model assessment of insulin resistance, BMI=Body mass index, ¶Data are fasting values, expressed as mean±standard deviation; Significant difference when compared with the baseline values (Paired *t*-test): *P<0.05; **P<0.01; ***P<0.001; Significant difference at the end of study between two groups after removing the effects of baseline values (ANCOVA): †P<0.05; ‡P<0.001

the methods of measurement and assessment of insulin sensitivity in these studies were not the same, such that in each study a different method for measurement of fasting glucose and 2-h insulin was used, based on insulin glucose ratio or assessment of homeostasis model.[27] Second, in the Wang study, all subjects were healthy, which might have affected the results. It has been claimed that some persons cannot convert non-biological forms of chromium into its biologically active form.[8] On the contrary, subject phenotype seems to be very important when assessing the clinical response to brewer's yeast, because baseline insulin sensitivity was found to cause nearly 40% of the variance in the clinical response.[25] It is not certain whether the beneficial effect of the brewer's yeast in Cr-depleted individuals is due to a natural physiological feedback of the body leading to improved utilization of the Cr-contained in the brewer's yeast. It is notable that brewer's yeast had similar effects as other chromium forms despite substantially lower doses of chromium, suggesting that possibly the organically complex chromium in yeast is metabolically advantageous and another component in brewer's yeast may enhance the effect of chromium on insulin sensitivity.[14,28] The findings of the current investigation on insulin resistance were similar to those of a study which treated two groups of aged healthy individuals with 5 g brewer's yeast pills and 200 μg chromium chloride capsules.[10] Also, our results are consistent with Racek *et al.*,[14] findings whose work on type 2 diabetics aged 61 years supplemented with four brewer's yeast tablets supplying 100 μg of chromium daily. Hyperinsulinemia in type 2 diabetes leads to reduced insulin effects. This can bring about gradual destruction of beta cells in pancreas. Therefore, supplementing these patients may produce the desired insulin sensitivity via the effect on insulin function and prevention of the loss of beta cells.[8,14] Conclusions of Li *et al.*,[16] disagreed with current study. In clinical trial on Chinese adult with mean age 51 years who supplemented by 10 g brewer's yeast capsules, a significant decrease in serum insulin was seen. To survey causes of these differences, Althuis *et al.,*[29] conducted a systematic review of randomized clinical trials assessing the effect of dietary chromium supplements on glycemic control in healthy, glucose intolerant, and type 2 diabetes subjects. As Althuis mentioned the Li's study had not adequate standards to generalize its results due to its brewer's yeast formulation and dose, at-risk population, and level of exercise. Also, the subjects enrolled in that trial had low BMIs of 20-21, which may this indicate poor nutritional status of the population at baseline and hence poor chromium status. Therefore, it seems poor chromium status could affect insulin secretion and its sensitivity. Bahijiri *et al*.[8] implied a direct correlation between brewer's yeast and insulin activity. It meant that in attendance of GTF, lower insulin concentrations were needed. This was justified as a part of our finding about insulin activity that could be related to the insulin circulation in the body. Also, in the current study because BMI was not significantly different between two groups, the reduction of insulin resistance was probably related to consumption of brewer's yeast. HbA1c results of our research contradict with some of the previous studies which can be explained by following reasons: The method of measuring HbA1c in this study was different from former researches. Furthermore, according to the half-life of the HbA1c, it is noticeable that supplementations which were lower than 12w may not be sufficient and in studies which supplementation continued for a long period, reduction of HbA1c concentration perhaps has been more prominent. Last, in a study by Racek *et al*.[14] unlike our patients, most of the subjects had type 2 diabetes that was generally well controlled via diet alone and small number of them used antidiabetic drugs. In meta-analysis of brewer's yeast,[27] across the studies were statistically heterogeneous, doses of brewer's yeast with 10 μg/day chromium had larger net decreases in fasting glucose than lower doses. Rabinowitz *et al*.[24] found no significant difference in fasting glucose among participants taking two relatively low doses of chromium (6 and 8 μg/day). The greater effects which were seen in present study and some other studies might be due to the higher doses of chromium.[30]

In spite of the similarities in socioeconomic status, ethnicity and age, the participants of the current study commonly consumed the foods thought less likely to provide adequate chromium.

The National Academy of Science (USA) has set the adequate intake of Cr for adult as 30 μg/day.[14] Based on our evaluation from our subjects' diet

records, we observed an inadequate chromium intake that was almost 2 μg/day for each patient. In contrast, the volunteers of one study represent a select socioeconomic segment of the healthy elderly population who were better educated and more affluent. Thereupon, they were well-nourished and had sufficient daily chromium intake. Perhaps these dietary divergences have accounted for the different responses to supplementation of the yeast tablets.[10] In meta-analysis that was conducted in 2009 by Nahas and Moher,[18] therapeutic effects of brewer's yeast supplementation on type 2 diabetes in clinical trials doing from 1996 to 2008 was investigated. Data demonstrated that the major limitations in most of these studies including small sample size, short period of intervention, nonrandomized design, and diverse dose of supplement may cause various conclusions.

CONCLUSIONS

On the basis of the findings of this study, it can be concluded that brewer's yeast supplementation has a modest beneficial effect on glycemic indices in type 2 diabetic patients. More investigations are required to find the best dose of brewer's yeast. Further studies would throw light on other possible effects of brewer's yeast in diabetes, for example, oxidative stress markers.

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