JOURNAL OF NUTRITION FASTING AND HEALTH

A Randomized Clinical Trial Study Protocol on the Effect of Barley Savigh on Blood Glucose in Prediabetic Menopausal Women

Khadijeh Kamali[1], Fatemeh Hadizadeh-Talasaz[2], Seyed-Amir Tabatabaeizadeh[3], Nasim Khajavian[4], Narjes Bahri[5*]

1. MSc student of Midwifery, Department of Midwifery, Faculty of Medicine, Gonabad University of Medical Sciences, Gonabad, Iran.
2. Department of Midwifery, School of Nursing and Midwifery, Mashhad University of Medical Sciences, Mashhad, Iran.
3. Department of Nutrition, Varastegan Institute for Medical Sciences, Mashhad, Iran.
4. MSc of Biostatistics, Department of Epidemiology and Biostatistics, School of Health, Social Determinants of Health Research Center, Gonabad University of Medical Sciences, Gonabad, Iran.
5. Associate professor of Reproductive Health, Department of Midwifery, Faculty of Medicine, Social Determinants of Health Research Center, Gonabad University of Medical Sciences, Gonabad, Iran.

ARTICLEINFO

Article type:
Research Paper

Article History:
Received: 31 Dec 2022
Accepted: 29 Apr 2023
Published: 18 Jun 2023

Keywords:
Blood glucose
Prediabetic state
Menopause
Hordeum

ABSTRACT

Introduction: Hormonal changes during menopause may result in type 2 diabetes. Therefore, the prevention of diabetes and its complications is essential during menopause. The effects of barley (Hordeum vulgare L) in maintaining blood glucose and insulin have been previously reported. This study was designed to evaluate the impact of roasted barley flour consumption on the blood sugar level of prediabetic postmenopausal women.

Methods: This randomized controlled trial study will be conducted on 68 prediabetic postmenopausal women referring to community health centers in Gonabad, Iran. All participants will complete a demographic questionnaire, and their fasting and two-hour postprandial blood glucose levels, HbA1C, will be recorded. The intervention group will receive 60g of roasted barley flour daily (20g before each meal) for four weeks, while the control group will receive no intervention. Fasting and two-hour postprandial blood glucose will be checked by venous blood sampling at baseline, two and four weeks after intervention. All participants will complete three-day food intake record and Beck's physical activity questionnaire during the study. Data will be analyzed using the statistical package for social sciences (SPSS) software (version 16), and a p-value less than 0.05 will be considered significant.

Conclusion: This study may prove the effectiveness of roasted barley flour in reducing blood glucose. Daily consumption of this compound can be recommended for prediabetic menopausal women.

▶ Please cite this paper as:
Kamali Kh, Hadizadeh-Talasaz F, Tabatabaeizadeh SA, Khajavian N, Bahri N. A Randomized Clinical Trial Study Protocol on the Effect of Barley Savigh on Blood Glucose in Prediabetic Menopausal Women. J Nutr Fast Health. 2023; 11(2): 113-117. DOI: 10.22038/ JNFH.2023.69861.1418.

Introduction

Serum 17-beta-estradiol level, a reproductive estrogen, drops from 100-250pg/ml to less than 10pg/ml during the transition from the childbearing period to menopause (1). Decreased ovarian estrogen increases the probability of metabolic complications, including dyslipidemia, hypertension, abdominal obesity, metabolic syndrome, and type 2 diabetes (2, 3). Post-menopausal women produce more androgens due to the continued secretion of androgens from the ovary, which imparts a higher bioavailability as sex hormone-binding globulin (SHBG) decreases during the transition. These hormonal changes further increase insulin resistance (4). A reduction in estrogen to androgen ratio in the perimenopausal period results in visceral fat accumulation, abdominal obesity, insulin resistance, hyperinsulinemia, and type 2 diabetes (5).

A committee of diabetes experts in the American Diabetes Association also proposed intermediate stages, called pre-diabetes. Pre-diabetes is defined as a condition where blood glucose is higher than the normal range but has not yet reached the cut-off blood glucose for the diagnosis of diabetes. The risk of diabetes is several times higher in pre-diabetic individuals

* *Corresponding author:* Narjes Bahri, Associate professor of Reproductive Health, Department of Midwifery, Faculty of Medicine, Social Determinants of Health Research Center, Gonabad University of Medical Sciences, Gonabad, Iran. Tel: +985157225027, Email: nargesbahri@yahoo.com.

than in healthy individuals (6). Adhering to a healthy diet, increasing physical activity in a pre-diabetic state play a significant role in controlling blood glucose and preventing progression to advanced stages of diabetes (7).

Herbal medicines are among the interventions traditionally used to reduce blood glucose and adjunctive treatment of diabetes due to their low side effects, lower cost, and effectiveness (8). Barley is among the medicinal plants that seem beneficial in reducing blood glucose. The role of barley seeds in treating diabetes is also mentioned in ancient Iranian traditional medicine texts (9, 10).

Barley and oat seeds contain alkaloids, β-carotene, steroid compounds, saturated fatty acids, starch, β-gluconase fiber, vitamins B1, B2, A, C, D, E, and zinc (11, 12). The blood glucose-lowering effects of barley are due to its low glycemic index and its high content of chromium and magnesium, and water-soluble fibers, including beta-glucan (13). Beta-glucan binds to sugars and lipids, indirectly changing the intestinal environment and thus affecting blood glucose (14).

A study reported that exercise and consumption of barley bread containing 4 grams of beta-glucan and barley bread alone significantly decreased fasting blood sugar (15). Another study also reported that consumption of breads made from oats and barley improved anthropometric and metabolic indicators; however, oat bread was found to be more effective in reducing blood glucose than barley bread (16). Another study also showed blood glucose-lowering effects for barley and sorghum bread (17). It has also been reported that whole grains and various barley foods containing at least 4g of beta-glucan and 30 to 80g of available carbohydrates can significantly reduce postprandial blood glucose (9).

Although many studies have shown good blood glucose-lowering effects for barley and oat bread, to our knowledge, no study has yet evaluated the impact of consuming roasted barley flour on blood glucose. The present study was designed to investigate the effect of roasted barley flour consumption on blood glucose levels among prediabetic postmenopausal women.

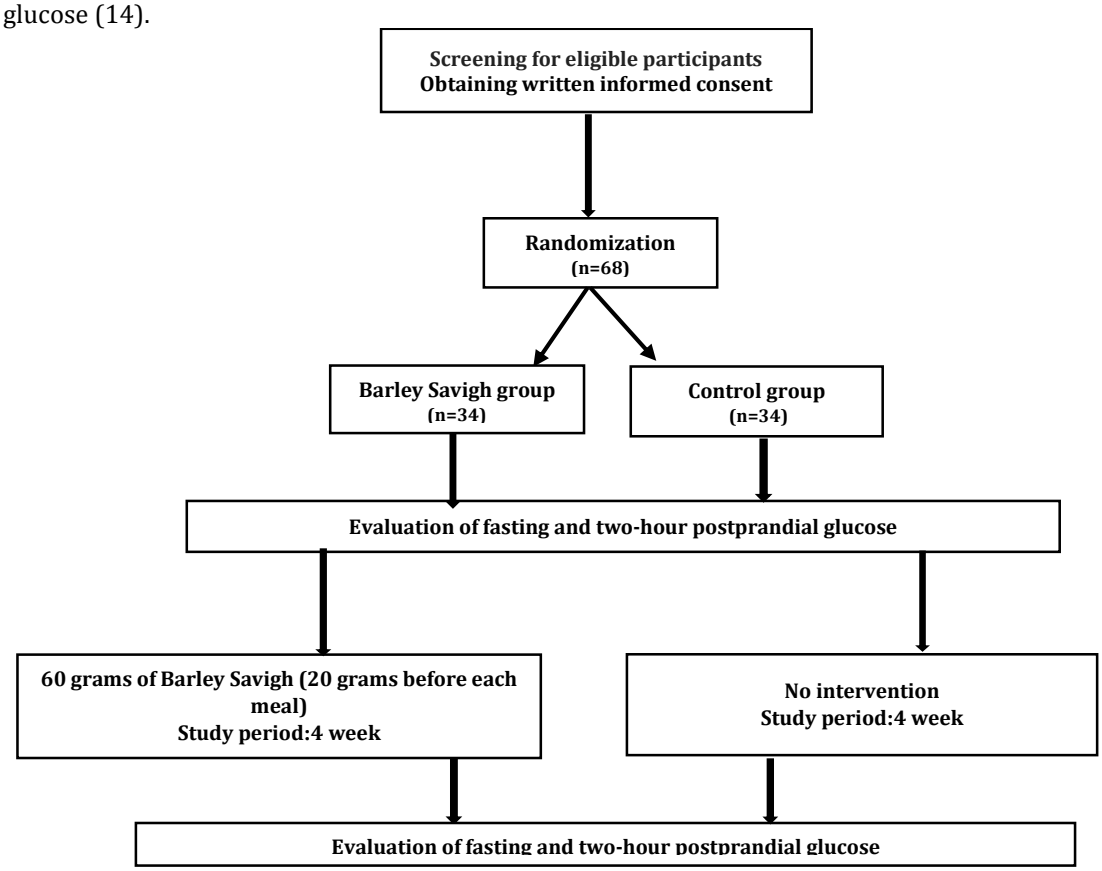

Figure 1. Flowchart of the study

Materials and Methods

Study design and setting

This single-blind, two-group, randomized clinical trial protocol was prepared based on the Standard Protocol Items Recommendations for Interventional Trials (SPIRIT) checklist (18). This study will be conducted in the Comprehensive Health Centers of Gonabad City, Iran.

The study hypothesis was that roasted barley flour could significantly reduce mean blood glucose levels compared to the control group. Figure 1 shows the flowchart of the study. A summary of the study enrolment schedules, interventions, and evaluations is shown in Table 1.

Table 1. Summary of enrolment, intervention and evaluations in the study

	Enrolment	Allocation	Post-allocation	
TIMEPOINT**	***-w***	**w0**	***W2***	***w4***
ENROLMENT:				
Eligibility screen	X			
Informed consent	X			
Allocation	X			
INTERVENTIONS:				
Measuring fasting blood sugar		X	X	X
Measuring blood sugar two hours after a meal		X	X	X

This study has been approved by the Research Ethics Committee of Gonabad University of Medical Sciences (Code: IR.GMU.REC.1399.070). This study protocol has been registered in the Iranian Registry of Clinical Trials (Code IRCT20200929048880N1).

Randomization

Eligible participants will be identified by referring to Comprehensive Health Centers. A convenience sampling method will be used to select participants after identifying eligible participants based on inclusion and exclusion criteria. Participants will be briefed about the study and its objectives, and written informed consent will be obtained from willing participants. In addition, participants will be assigned to either the intervention or control group using the quadruple permutated block allocation method.

Sample size

The sample size was calculated based on the findings of a previous study (19) using the sample size equation for mean differences as follows:

$$\frac{(z_{1-\frac{a}{2}} + z_{1-B)}{}^{2} \times (s_1^2 + s_2^2)}{(\mu_1 - \mu_2)^2} = \frac{(1.96 + 0.84) \times (29.1^{\,2} \times 60.9^2)}{(175.7 - 140.5)^2} = 31$$

The calculated sample size was increased to 34 participants in each group (N= 68), considering a 10% dropout rate.

Eligibility criteria

The inclusion criteria were natural menopause (no menstruation for at least 12 months), age between 45 and 65 years, fasting plasma glucose level between 100 and 125mg/dl or two-hour postprandial plasma glucose level between 140 and 199mg/dl, or glycosylated hemoglobin (HbA1C) between 5.7 and 6.4%, no documented diabetes diagnosis, not consuming blood glucose-lowering medications, no history for documented cardiovascular disease or other systemic diseases (renal or liver diseases, hypertension or thyroid disorders), no history for a cigarette, alcohol consumption or drug abuse, ability to read and write, body mass index (BMI) between 19.8 and 29kg/m^2, no allergy to cereals, and no history for celiac disease. The exclusion criteria were diagnosis of type 2 diabetes, need for initiation of glucose-lowering medications, exposure to stressful situations (e.g., death of close relatives), not consuming barley Savigh as recommended, presence of side effects (e.g., dermatitis, flatulence, diarrhea), being hospitalized during the study period, lack of cooperation in filling the study questionnaires, the experience of hypoglycemia, defined as plasma glucose less than 45mg/dl along with clinical presentations of hypoglycemia including noradrenergic symptoms (fatigue, perspiration, hunger, visual impairment, and palpitation) or neuroglycopenic symptoms (headache, diplopia, memory or concentration impairment; drowsiness, seizures, and coma) (19).

Evaluations

Participants will be allocated to intervention and control groups and undergo blood glucose tests at fasting and two-hour postprandial states. Fasting blood glucose will be evaluated by drawing 5cc of venous blood after fasting (8 to 10 hours). Two-hour post-prandial plasma glucose will be assessed by drawing 5cc of venous blood two hours after eating a standard breakfast of bread, cheese, and tea. All participants will be referred to a single laboratory to prevent laboratory errors. In the laboratory, the serum will be obtained using a blood sample centrifuge, and then the serum will be used to determine fasting blood glucose using the Mindray BS600 biochemistry autoanalyzer.

At the beginning of the study, all participants will complete a demographic questionnaire, and their fasting and two-hour postprandial blood glucose levels; and HbA1C will be recorded. Participants will also complete a three-day food intake record and Beck's physical activity questionnaire.

In both groups, fasting and two-hour postprandial blood glucose levels and HbA1C will be measured at baseline and the end of the second and fourth week after starting the intervention. Furthermore, all the participants will complete the nutritional and physical activity evaluation questionnaires in the second and fourth weeks.

Intervention

Barley was bought from Gonabad Agricultural and Natural Resources Research and Training Station to prepare roasted barley flour (barley Savigh). Barley will then be ground to separate the mill from the bran. The flour and bran will be roasted separately. The roasted bran will be ground again and mixed with roasted flour.

Participants in the intervention (barley Savigh) group will be asked to consume 60g of barley Savigh, which contains 40g of carbohydrates (20g before each main meal), preferably in dry form, for four weeks. No intervention will be provided to the control group. In addition, all participants in both groups will be given similar verbally advises about the type of diet, the substances that increase blood glucose, and avoiding these substances, as well as the number of appropriate meals and snacks to control the effect of confounding factors. Participants are requested not to change their physical activities during the study period.

Ethical considerations

This protocol will be approved by the Ethics Committee of Gonabad University of Medical Sciences (Code: IR.GMU.REC.1399.070). All participants will provide written informed consent for participation in the study.

Discussion

This study is expected to provide reliable findings considering the appropriate sample size and random allocation using quadruple permutation blocks.

Individual differences and unknown and unpredictable neurological factors may also affect blood glucose. Comprehensive control of these factors will be impossible; therefore, these factors can be considered limitations of this study.

A review of previous studies showed that barley has blood glucose-lowering effects due to its low glycemic index, high chromium and magnesium content, and water-soluble fibers, including beta-glucan (2). A study showed that whole grain oats, barley, and β-glucans reduce the risk of coronary heart disease, type 2 diabetes, and other noncommunicable chronic conditions. The mechanisms of this effect have been explained by the role of soluble dietary fibers and smaller bioactive compounds, such as phenolic compounds, in oats and barley. These help reduce serum low-density lipoprotein cholesterol, decreasing postprandial blood glucose and modulating gut microbiota (21).

These results will provide evidence regarding the glucose-lowering effects of roasted barley flour in prediabetic post-menopausal individuals and accurate scientific evidence for using barley Savigh to reduce blood glucose.

Availability of Data and Materials

The study data will be available through approval from the Research Council of the Gonabad University of Medical Sciences upon request.

Conflicts of Interest

None to declare.

Funding

This study will be funded by the Research Council of the Gonabad University of Medical Sciences.

Author Contributions

K. K, N.B, F. H, A. T, and N. Kh were involved in creating and designing the protocol.

K. K and N. B compiled and revised the study protocol in terms of content.

N. Kh reviewed statistical methods and calculations.
K. K, N. B, F. H, A. T, and N. Kh approved the final version of the manuscript.

Acknowledgment

The authors would like to thank the Research Council of Gonabad University of Medical Sciences for funding this project.

References

1. Sayahi M, Zakerkish M, Haghighizadeh M H, ziagham S. Relationship between menopausal symptoms, age, body mass index and metabolic syndrome in postmenopausal women in a number of health centers in Ahvaz in 2013. J Arak Uni Med Sci. 2015; 17 (10):50-7
2. Mehdizadeh R. The effect of core stability training on body composition and lipoprotein in menopausal older women. Salmand. Iranian Journal of Ageing. 2015; 10(2):153-63
3. Shabani R. The Effect of Concurrent Aerobic–Resistance Exercise Training on Estrogen Level and Glucose Homeostasis of Menopausal Females with Blood Glucose Impairment. Iranian Journal of Rehabilitation Research. 2017:3(3):1-10.
4. Slopien R, Wender-Ozegowska E, Rogowicz-Frontczak A, Meczekalski B, Zozulinska-Ziolkiewicz D, Jaremek JD, et al. Menopause and diabetes: EMAS clinical guide. Maturitas. 2018; 117:6-10
5. Ziaei S, Ziagham S, Sayahi M. Relationship between menopausal age and metabolic syndrome in non-obese postmenopausal women. J Arak Uni Med Sci. 2013; 16(5):41-8.
6. Bakhtiari MR. a review on the latest criteria for laboratory diagnosis of diabetes mellitus, pre-diabetes and gestational diabetes. Journal of laboratory and diagnosis. 2014; 6(24):4-8.
7. Yazdani A, M, Marjan, F, Elham, Zareh M, A, Masoud. The effects of macronutrient intake on the risk of pre-diabetes in first degree relatives of patients with type 2 diabetes. Journal of Isfahan Medical School. 2014; 32:301.
8. Bathaie S, Mokarizade N, Shirali S. An overview of the mechanisms of plant ingredients in the treatment of diabetes mellitus. J Med Plants. 2012; 11 (44):1-24.
9. Tosh SM. Review of human studies investigating the post-prandial blood-glucose lowering ability of oat and barley food products. European Journal of Clinical Nutrition. 2013; 67(4):310.
10. Arbai F, Minae zangi B, Sadooghi M. The effect of hordeum vulgare L. on the development of lung tissues in the embryo of diabetic albino rats. Comparative Pathobiology, Science-Research. 2014; 11(4(47)):1429-36
11. Mohsenzadeh A, Javadi T, Yari F, Shah K. Effect of barley flour on neonatal jaundice reduction. Yafte. 2013; 2(3):17-22.
12. Nazari H, Jahanjo N, Safarieh M, Taherian M, Khaleghian A, Vafaei A. The effect of avena sativa alcoholic and aqueous extract on the wound healing and skin inflammation. J Urmia Univ Med Sci. 2011; 22(5):467-73.
13. Kamrani Moghadam L, Sadoughi, Zangi M, Farmani M, Ramazani, Najd F. The effects of barley grain (Hordeum Vulgare L.) during pregnancy on development and heart histopathological changes of embryos of diabetic rats. Razi Journal of Medical Sciences. 2015; 22(133):80-8.
14. Goto Y, Nishimoto Y, Murakami S, Nomaguchi T, Mori Y, Ito M, Nakaguro R, Kudo T, Matsuoka T, Yamada T, Kobayashi T, Fukuda S. Metabologenomic approach reveals intestinal environmental features associated with barley-induced glucose tolerance improvements in Japanese: A Randomized Controlled Trial. Nutrients. 2022; 14(17):3468.
15. Mokhtari F, Esfarjani F, Kargar Fard M. The effect of combined aerobic exercise and barley B-glucan on lipid profile and glucose blood of women with diabetes type two .Journal of Diabetes and Metabolism of Iran. 2014; 13(4):340-51.
16. Najjar safari S, Rezvani SV, Haji Faraji M, Rashidkhani B. The effect of "real oat bread" compared with "barley bread offered in Tehran" on serum glucose and lipid profiles in dyslipidemia and type 2 diabetic subjects. Iranian Journal of Endocrinology and Metabolism. 2011; 13(3):233-42.
17. Montazeri Far F, Karaji Bani M, Ali Kikhuaei M, Dashipour A, Amiyar M, Nikoei G. Effect of breads in Iran on blood glucose level in patients with type 2 diabetes. Yafteh. 2016; 18(2):67-75.
18. Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT). Available at: https://www.spirit-statement.org/. [Site access: 25 Dec 2022].
19. Mokhtari F, Esfarjani F, Kargar Fard M. The effect of combined aerobic exercise and barley B-glucan on lipid profile and glucose blood of women with diabetes type two .Journal of Diabetes and Metabolism of Iran. 2014; 13(4):340-51.
20. Sarvghadi F, Yasari F, Yavari P. Causes and clinical presentations of hypoglycemia in patients with low blood glucose admitted to the emergency ward. Iranian Journal of Endocrinology and Metabolism. 2006; 8(1):57-62.
21. Tosh SM, Bordenave N. Emerging science on benefits of whole grain oat and barley and their soluble dietary fibers for heart health, glycemic response, and gut microbiota. Nutr Rev. 2020; 78(Suppl 1):13-20.