

A simple dietary addition of fenugreek seed leads to the reduction in blood glucose levels: A parallel group, randomized single-blind trial

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Abstract

Introduction: Diabetes is prevalent in India. This study was conducted to assess the impact of ingestion of fenugreek seed on fasting blood glucose levels and glycosylated hemoglobin (HbA_{1c}) levels in patients of Type 2 diabetes mellitus controlled with diet, exercise and oral hypoglycemic agents (OHAs) or insulin. **Aims:** Assessment of impact of ingestion of *Trigonella foenum-graecum* or fenugreek seed in patients with Type 2 diabetes controlled with OHAs and insulin on fasting blood sugar levels and HbA_{1c} levels. **Settings and Design:** Prospective, randomized control trial in a single center. **Materials and Methods:** Total sixty patients of Type 2 diabetes mellitus diagnosed at least 6 months prior and on OHAs and insulin were included in the study. Patients were randomized to receive 10 gm of fenugreek seeds soaked in hot water and another group was not. Strict dietary and exercise controls were followed as per the guidelines of American Diabetic Association protocols. The parameters assessed were demographic profile on the first visits and fasting blood sugar levels and HbA_{1c} every month till 6 months. **Results:** A total of sixty patients were enrolled in the study divided into two groups each containing thirty patients. One group of patients received 10 gm of fenugreek seeds soaked in hot water every day, while the second group did not received. Statistical analysis shows that there is significant reduction in fasting blood glucose levels in the 5th month in the study group ($P = 0.0421$) while significant reduction in HbA_{1c} in the 6th month ($P = 0.0201$). **Conclusion:** A simple complementary addition of fenugreek seeds can have a synergistic effect along with diet control and exercise on fasting blood glucose and HbA_{1c} but is of delayed occurrence.

Keywords: Fasting blood glucose, fenugreek seeds, glycosylated hemoglobin (HbA_{1c}), type 2 diabetes

Introduction

Diabetes is a chronic disorder of glucose metabolism and a major cause of heart disease and end-stage renal disease (ESRD) in the Indian population. India is considered as diabetes capital of the world with total cases at around 62 million.^[1] The incidence in India is rapidly rising, as well as complications arising out of it. Various causes are ascribed to diabetes, which include genetic, environmental and lifestyle changes associated with more urbanization in India.^[2] Some interesting observation includes almost 3/4th less risk of diabetes in rural population compared to urban population^[3] and higher incidence of diabetes in the northern part of India compared to southern part. Compared with the general non-diabetic population, persons with diabetes have approximately a 7-year shorter life expectancy, an effect directly related to the major diabetic complications^[4] which

include coronary artery disease, limb amputations, ESRD and blindness.

Treatment protocols in Type 2 diabetes include in early phases, lifestyle modification, diet therapy, and at least 150 min. of exercise per week. If still hyperglycemia persists, medications are started, including biguanide, sulfonylurea, and insulin therapy in increasing order or disease severity^[5] as suggested by standards of medical care in diabetes by the American Diabetic Association (ADA) published in 2015. Although guidelines are very clear-cut in the management of Type 2 diabetes irrespective to fasting blood sugar levels and glycosylated

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Access this article online

Quick Response Code:



Website:
www.ayujournal.org

DOI:
10.4103/ayu.AYU_209_15

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How to cite this article: Ranade M, Mudgalkar N. A simple dietary addition of fenugreek seed leads to the reduction in blood glucose levels: A parallel group, randomized single-blind trial. *Ayu* 2017;38:24-7.

hemoglobin (HbA_{1c}),^[5] often it is proved that targets are not achieved and complication rates are higher worldwide.^[6]

If stricter control of diabetes is achieved, it is possible to delay or totally avoid some of the major complications of diabetes. The treatment with standard regimens is also associated with problems such as higher cost, secondary failure rates, and accompanying side effects. Furthermore, these treatments only modify secondary metabolic derangement and do not address fundamental biochemical change.^[7] In a country like India, where cost factor is major hurdle for treatment compliance as more strata are in poor socioeconomic group and health-care spending is less, there is possibility of use of herbal medicines along with the regular antidiabetics to control fasting blood glucose and HbA_{1c} levels.

Fenugreek seed also known as *Trigonella foenum-graecum* is commonly used in India in kitchens. It has been commonly used as herbal preparation for diabetes treatment. Multiple mechanisms are suggested for its efficacy in diabetes population. Soluble fibers in fenugreek including glucomannan fiber delays intestinal absorption of ingested sugars and alkaloids such as fenugrecin and trigonelline have demonstrated to possess hypoglycemic action, and 4 hydroxyisoleucine (4-OH Ile) amino acids act on pancreas to release insulin. The present study evaluated antidiabetic properties of this medication on diabetes control in tertiary care hospital based in rural India in Telangana region.

Materials and Methods

This is prospective, randomized, parallel group single-center study carried out between July 2015 and December 2015. The study is conducted in a tertiary care hospital, based in rural India. All patients received ADA^[5] protocol-based therapy. Type 2 diabetes was diagnosed with HbA_{1c} levels of 6.5 and above equal to or more than or fasting blood glucose of 126 mg/dl or oral glucose tolerance test 2nd h glucose level of 200 mg/dl. After initial diagnosis, comprehensive diabetes evaluation was done by a diabetologist or physician. Patients were enrolled in the study after consecutive 6 months of antidiabetic treatment. Nutrition therapy was started after patients diagnosed with diabetes. In the diet planning, there was no specific percentage of calories from carbohydrates, proteins and fats and macronutrient distribution was based on their current diet patterns as suggested by the ADA. In the exercise part, patients were advised to perform at least 150 min/week of moderate-intensity aerobic physical activity (50%–70% of maximum heart rate), spread over at least 3 days/week with no >2 consecutive days without exercise. Patients were asked to keep diary of their daily diet and exercise patterns. Patients were counseled and written informed consent was taken to participate in the study. Ethical committee approval IEC/PIMS/02/15 was taken from the local institutional review board before participation. A total of sixty patients were included in the study, thirty in each group. After obtaining written valid and informed consent, baseline demographic data were collected.

Inclusion criteria

Patients diagnosed to have Type 2 diabetes above the age of 18 years of either sex and noninsulin-dependent diabetes minimum of 6 months before the study enrollment were included. Diabetes was diagnosed with the criteria defined by the ADA.^[5] Inclusion criterion included patients with diabetes and on any antidiabetic medication (oral hypoglycemic agent, insulin).

Exclusion criteria

Patients with other comorbid conditions (cardiac, renal, macrovascular and microvascular complication) were omitted. Patients not adhering to ADA^[5] guidelines in diet control and exercise as taught to them by primary investigator were also excluded. Patients were also excluded if there is any change in medication or dose of medication he/she is receiving from the first visit.

Grouping and posology

Patients were randomized to receive fenugreek seed soaked in hot water 10 gm/day, along with their routine antidiabetic medication 30 min before meal, while patients in another group continued to receive only antidiabetic medication.

Randomization was done with Stat Trek's Random Number Generator using a statistical algorithm to produce random numbers. Patients were not blinded for the study because of difficulty in achieving blinding, while the primary investigator was blinded and data collection was done by an independent investigator. The independent investigator who collected the data was not associated with statistical analysis.

Primary outcome measures

Patients were serially followed up every month for the next 6 months. During each visit, anthropometric parameters, fasting blood glucose and HbA_{1c} levels were assessed.

Statistical analysis

The statistical analysis was carried out using Statistical Package for the Social Sciences (SPSS Inc., Chicago, IL, USA, version 15.0 for Windows). All quantitative variables were estimated using measures of central location (mean, median) and dispersion (standard deviation). Unpaired *t*-test with two-tailed distribution was used to calculate the *P* value. Statistical tests were two-sided and performed at a significance level of $\alpha = 0.05$.

Results

A total of sixty cases were registered in the study, comprised 30 in each groups. Baseline demographic characteristics are presented in Table 1. There was no significant change in baseline demographic characteristics which included age, sex, and body mass index.

Baseline fasting blood glucose level in the study group was 154.22 ± 30.11 while in control group was 160.11 ± 28.11 , which showed no significant *P* values (0.231) at the time of enrolment in the study. A similar trend was observed with HbA_{1c} values with nonsignificant *P* value (0.441) at the time of enrolment in the study.

During the study period, when monthly fasting blood glucose levels and HbA_{1c} levels were assessed, the study group showed reduction in trend of sugar levels, though statistically, it was not significant till 4th month ($P = 0.821, 0.112, 0.188$ and 0.432 , respectively). At 5th month, the fasting sugar in the study group was 146 ± 25.80 while it was 155.65 ± 24.84 in control group. Here, first-time statistically significant difference between two groups was observed with $P = 0.0421$. However, this did not culminate in values of HbA_{1c}, which were 6.9 ± 1.95 and 7.03 ± 2.08 in the study group and control group, respectively showing no significant change ($P = 0.52$) in P value of HbA_{1c}. Upon comparison of data at 6th month, there is statistically significant difference in both fasting blood glucose values and HbA_{1c} values, showing difference in absolute values also as well as in P values. Statistical values showed fasting blood sugar of 143 ± 23.25 in the study group and of 153.59 ± 23.37 in the control group with $P = 0.0351$. HbA_{1c} levels also showed similar trend in the 6th month where HbA_{1c} of the study group is 5.78 ± 1.56 and that of the control group is 6.96 ± 2.02 showing $P = 0.0201$ [Table 2].

Discussion

Trigonella foenum-graecum is widely used in the Indian subcontinent as dietary supplement. It is known that it since long possess antidiabetic properties. The various mechanisms are already described and well studied in various studies.

Table 1: Demographic profile of the patients

Baseline parameters	Group A (FG)	Group B
Age	48±16.25	46.22±12.25
Male sex	21	24
BMI	25.23±4.2	26.02±3.9
Dyslipidemia	28	29

FG: Fenugreek seed group, BMI: Body mass index

Table 2: Blood sugar levels in both the groups with P value

Study parameters	Group A	Group B	P
FBS0	154.22±30.11	160.11±28.11	0.231
HbA1c0	7.2±3.11	7.9±3.11	0.441
FBS1	156±29.23	160.05±28.02	0.821
HbA1c1	7.4±3.07	7.8±3.08	0.233
FBS2	151.08±28.88	158.57±27.46	0.112
HbA1c2	6.94±2.94	7.4±2.69	0.149
FBS3	150.06±27.32	156.11±26.72	0.188
HbA1c3	6.58±2.67	6.9±2.48	0.87
FBS4	152.43±26.96	156.76±25.22	0.432
HbA1c4	6.75±2.04	7.24±2.39	0.974
FBS5	128±25.80	155.65±24.84	0.0421
HbA1c5	6.9±1.95	7.03±2.08	0.52
FBS6	122.21±23.25	153.59±23.37	0.0351
HbA1c6	5.78±1.56	6.96±2.02	0.0201

FBS: Fasting blood sugar level, HbA_{1c}: Glycosylated hemoglobin level, Abbreviation after HbA1C and FBS: month of checking

Scientists have demonstrated that the amino acid 4-OH Ile in fenugreek seeds increases glucose-induced insulin release *in vitro* in human and rat pancreatic islet cells,^[8] while others showed that fenugreek seed extract phosphorylates a number of proteins, including the insulin receptor, insulin receptor substrate 1 and p85 subunit of PI3-K, in both 3T3-L1 adipocytes and human hepatoma cells, HepG2.^[9] Unique major free amino acid, 4-OH Ile, has also been characterized as one of the active ingredients for blood glucose control.^[10]

Various authors tried to assess impact of fenugreek on blood glucose control, and majority of them showed significant improvement in diabetes control when assessed in terms of fasting blood sugar levels.^[11,12]

The dose of fenugreek seeds given also affect the blood sugar levels and higher dosages do show more hypoglycemic effect as shown in the previous trials. The dose range was wide ranging from 2 to 25 g/day.^[13] The authors did a small initial pilot study in which tolerability of fenugreek seeds was assessed on 20 patients. The maximum percentage of tolerability and compliance was found to be with dose of 10 gm and hence, the dose is selected.

Whole fenugreek raw seeds, extracted seed powder, cooked seeds (25 g) and gum isolate of seeds (5 g) decreased postprandial glucose levels, whereas degummed seeds (25 g) showed little effect as suggested in the review article.^[14] The authors concluded that the hypoglycemic effects of the drug are secondary to fiber fraction of the drug. In the present study, it was found out delayed occurrence of hypoglycemic effect compared to acute effects seen in various other studies. If hypoglycemia actions are because of fiber fraction only, the effects should be early and not delayed. This might suggest other mechanisms of action for the drug other than fiber action.

The initial references of *Madhumeha* found in classical text of Ayurveda as *Charak Samhita*, *Sushrut Samhita* and *Madhav Nidan* though they do not seem exactly as modern medicine thinks. The primary symptom in *Prameha* disorder is polyuria and all types of *Prameha* are distinguished by the different types of urine. *Madhumeha* is one type where urine tastes sweet. The etiology matches with modern medicine where sedentary lifestyle, improper dietary habits and genetic factors are described as causative factors in *Charak Samhita*.

While coming back to the treatment of *Prameha* disorder, *Methika Beeja* is a modern addition in Ayurveda, first being mentioned in *Dhanvantari Nighantu* which is supposed to be written in the 10th century.

The lacunae of previous studies might be, because changes in diet pattern and exercise do affect blood sugars levels, it is difficult to say that only study drug has caused the reduction in blood sugar levels, as these factors are not controlled and can lead to bias. The present study scores over other studies in this parameter. The investigators could strictly control diet patterns and exercise patterns of the patient as now specific guidelines

are there in the form of ADA^[5] and hence can suggest that changes in sugar and HbA_{1c} levels are secondary to study drug.

Fenugreek is widely available in India and cost effective product. This study statistically proves that hypoglycemic effects of fenugreek are over and above the diet control and exercise. In a country like India, this can be promising complimentary option for diabetes controls in addition to diet, exercise and drug therapy. It may reduce requirement of drugs and can give better blood glucose control and can be helpful in preventing long-term morbidity.

This study has got certain limitations. It lacks adequate strength because of less number of participants enrolled in the study. Secondly, long-term results in sugar control were not assessed in the study and also delayed reduction in sugar and HbA_{1c} levels were also could not be satisfactorily explained as it does not correlate with other studies where sugar reduction is more sharp. The strength of the study is that this is the first study in which diet and exercise factors are controlled and gives statistically significant result on assessed parameters; this study paves a way to do further randomized control trials in this regard with more number of patients to increase the strength.

Conclusion

A simple complementary addition of fenugreek seeds 10 gm/day can have a synergistic effect along with diet control and exercise on fasting blood glucose and HbA_{1c} within 6 months of treatment.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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