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Effectiveness of Fenugreek for Lowering Hemoglobin (HbA1c) in Patients with Self-Management of Type 2 Diabetes: A Randomized Controlled Trial

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1. Introduction

The incidence of type 2 diabetes is increasing worldwide, resulting in large measure from the increasing prevalence of obesity (Yale, 2000). Diabetes mellitus is a pandemic disease and is one of the main threats to human health (Narayan, 2005). In 2003, 194 million people worldwide, ranging in age from 20 to 79 years, had diabetes. It is projected that this number will be increased by 72% to 333 million by 2025, and nearly 80% of these cases will be in the poorer industrialized countries (IDF, 2003). According to a 2005 US Government estimate, approximately 21 million people in the United States have diabetes (Gerich, 2005). In 2002, diabetes was the sixth leading cause of death and had an estimated total cost of $132 billion (Hogan et al. 2003). Type 2 diabetes is a disease characterized by a dual defect: 1) by insulin resistance which prevents cells from using insulin properly, and 2) degrees of reduced pancreatic insulin secretion.

In the local context, according to World Health Organisation (WHO, 2004), prevalence of Type 2 diabetes in Pakistan for the year 2000 was 5.2 million and for 2030 it would be around 13.8 million. A quarter of the population of Pakistan would be classified as overweight or obese with the use of Indo-Asian-specific BMI cutoff values. Jafar et al (2006) have reported that prevalence of overweight was 25% and obesity was 10% in a large population-based sample of people over the age of 15 years in Pakistan. On the age-specific prevalence of overweight and obesity, they found that more than 40% of women and 30% of men aged 35–54 years were classified as overweight or obese.

It has been suggested in a variety of observational and epidemiological studies that physical activity may play a significant role in the prevention of type 2 diabetes mellitus. The relationships between physical activity and overweight are only beginning to be understood for the adult population, sedentary behaviours, particularly watching television (TV) and videos, surfing the internet have been found to be related to higher body mass index (BMI) for adult's population (Struber, 2004). The literature linking physical activity levels with risk of overweight in adults is not consistent but physical activity is an important component of effective obesity treatments (Saelens, 2003).

The main health promotion intervention here is the public health education which highlights the importance of physical activity for the prevention of type 2 diabetes in the middle-aged population of sub-continent and particularly Pakistan, which is experiencing a rapid and substantial decline of physical activity levels as a result of poor eating habits, unhealthy food supply, expansion of television, computerization, and mechanization, more prevalent car ownership and sedentary behaviour. In parallel with decreasing levels of physical activity, the prevalence of overweight and obesity has increased significantly in Pakistan and as a consequence, diabetes mellitus has become a major public health issue.

Therefore, promoting an active lifestyle or regular exercise has become the highest public health priority in that country to overcome the onslaught of type 2 diabetes. Also, the search for dietary adjuncts along with usual medical care to treat this life altering disease has become more important and dietary supplements that can modulate glucose homeostasis and potentially improve lipid parameters would be desirable. Fenugreek (Trigonella foenum-graecum Linn) is a dietary supplement that may hold promise in this regard and is one of the oldest medicinal plants, originating in India and Northern Africa and dating back to ancient Egyptian times (Jensen, 1992).

In Pakistan and India, fenugreek is commonly consumed as a condiment (Yoshikawa et al. 1997) and used medicinally as a lactation stimulant (Patil et al. 1997). Fenugreek seeds also lower serum triglycerides, total cholesterol (TC), and low-density lipoprotein cholesterol (LDL-C) (Al-Habori and Raman, 1998). The lipid-lowering effect of fenugreek might also be attributed to its estrogenic constituent, indirectly increasing thyroid hormones (Basch, 2003). The plant protein in fenugreek is 26%, so it might exert a lipid lowering effect (Sharma, 1986). Since a high proportion of diabetic patients in sub-continent suffer from malnutrition, the use of fenugreek which is rich in protein and fiber (48%), has a distinct advantage in these patients (Sharma, 1986).

This chapter addresses the effectiveness of fenugreek for lowering hemoglobin (HbA1c) in this randomized controlled trial and determines whether the intervention of taking fenugreek in combination of usual medical care lowers HbA1c in patients with type 2 diabetes. Effectiveness trials such as this are critical in determining if the interventions are effective in the practical world in which patients live. This randomized control trial addresses the research question **"Is Fenugreek treatment with medical care for patients with type 2 diabetes more effective than usual medical care and can it help to lower the haemoglobin in patients with poorly controlled type 2 diabetes"?** and test the hypothesis in relation to type 2 diabetic patients with usual medical care and usual medical care with self-management of fenugreek supplement and evaluates the effectiveness of the fenugreek treatment in comparison with the usual medical care in clinical settings.

2. Characteristics of type 2 diabetes

Type 2 diabetes is associated with certain ethnic groups, obesity, family history of diabetes, and physical inactivity, among other factors. Diabetes is a metabolic disease characterized by elevated concentrations of blood glucose for prolonged periods of time, i.e., hyperglycemia (Gerich, 2005). Chronic, untreated hyperglycemia can lead to serious complications that include cardiovascular diseases, blindness, kidney failure, and stroke. Furthermore, very low values of blood glucose (hypoglycemia) for even a short duration can result in loss of consciousness and coma. The figure 1 shows the complications of type 2 diabetes which is a syndrome characterized by insulin deficiency, insulin resistance, and increased hepatic glucose production. These metabolic abnormalities are treated by use of various medications which are designed to correct one or more of these metabolic abnormalities (Saltiel & Olefsky, 2001).

Type 2 diabetes is most common in adults, although younger people are also developing this type of disease. It starts with a slow onset with thirst, frequent urination, weight loss developing over weeks to months. It is also considered to run in families but it may happen with a person without a family history of diabetes as well. Most of the people who get this disease are overweight and obese. The treatment for type 2 diabetes differs at various stages of the condition. In its early stages, many people with type 2 diabetes can control their blood glucose levels by losing weight, eating properly and exercising. Many may subsequently need oral medication, and some people with type 2 diabetes may eventually need insulin shots to control their diabetes and avoid the disease's serious complications (Saltiel & Olefsky, 2001).
Even though there is no cure for diabetes, proper treatment and glucose control enable people with type 2 diabetes to live normal, productive lives. A major advance for people at risk of developing type 2 diabetes - such as family members of those with the condition - occurred recently when it was shown that diet and exercise can prevent or delay type 2 diabetes. People at high risk, who already had early signs of impaired glucose tolerance, significantly reduced their risk by losing only 5-7 percent of their body weight and performing moderate physical activity for 30 minutes/day.

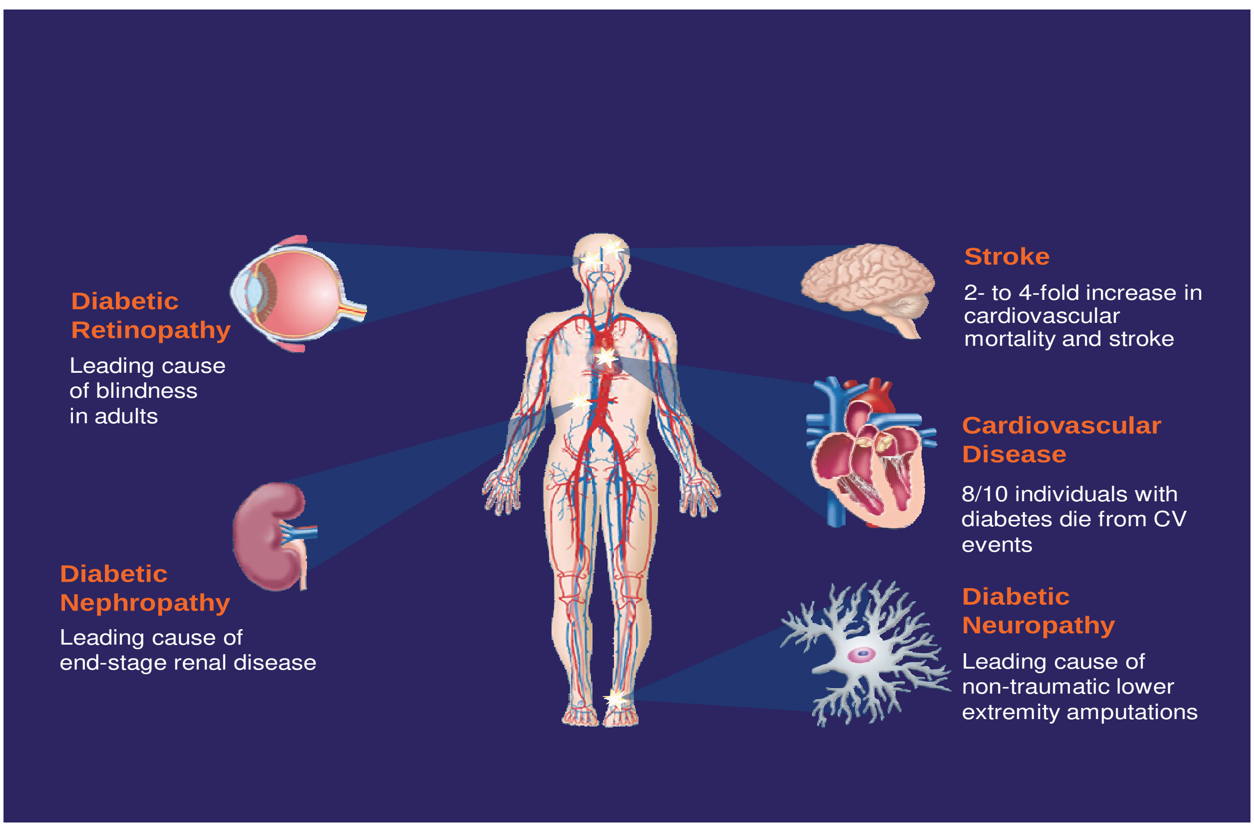


Fig. 1. Complications of type 2 diabetes – Source: Saltiel & Olefsky (2001)

The figure 1 shows the complications of type 2 diabetes from microvascular and macrovascular diseases and can have a devastating effect on quality of life and impose a heavy burden on healthcare systems.
Diabetic retinopathy *is* present in 21% of people in the world at the time type 2 diabetes is diagnosed (DSG, 1990), more than 60% have diabetes retinopathy during the first two decades of the disease and diabetic retinopathy is the leading cause of new blindness among

adults aged 20–74 years (Fong et al. 2003). Pakistan is ranked 6th among countries with the highest burden of diabetes (Wild et al. 2004), however, population-based data on the prevalence of diabetic retinopathy in Pakistan and on the visual impairment due to diabetic retinopathy is lacking and only the hospital-based data is available (Kayani et al. 2003).
Diabetic nephropathy is present in 18% of people diagnosed with diabetes (DSG, 1993) and is a leading cause of end-stage renal disease (Molitch et al. 2003)
Stroke*:* diabetes is associated with a 2- to 4-fold increase in cardiovascular mortality and stroke (Kannel et al. 1990).
Cardiovascular disease: 75% of individuals with type 2 diabetes die from cardiovascular causes (Gray & Yudkin, 1997).
Diabetic neuropathy *is* present in 12% of people at diagnosis (DSG, 1990) and diabetic neuropathy affects approximately 70% of people with diabetes and is a leading cause of non-traumatic lower extremity amputations (Mayfield et al. 2003). Therefore, early detection and treatment of diabetes is essential in order to reduce the impact of its serious complications.

2.1 Development of type 2 diabetes

Development of type 2 diabetes is the result of multifactorial influences that include lifestyle, environment and genetics. The disease arises when insulin resistance-induced compensatory insulin secretion is exhausted. A high-caloric diet coupled with a sedentary lifestyle is one of the major contributing factors in the development of the insulin resistance and pancreatic β-cell dysfunction as shown in Figure 2. However, a predisposing genetic background has long been suspected in playing a contributing role in the development of type 2 diabetes. By using whole-genome linkage analysis the entire genome of affected family members can be scanned and the family members monitored over several generations (Saltiel & Olefsky, 1996)

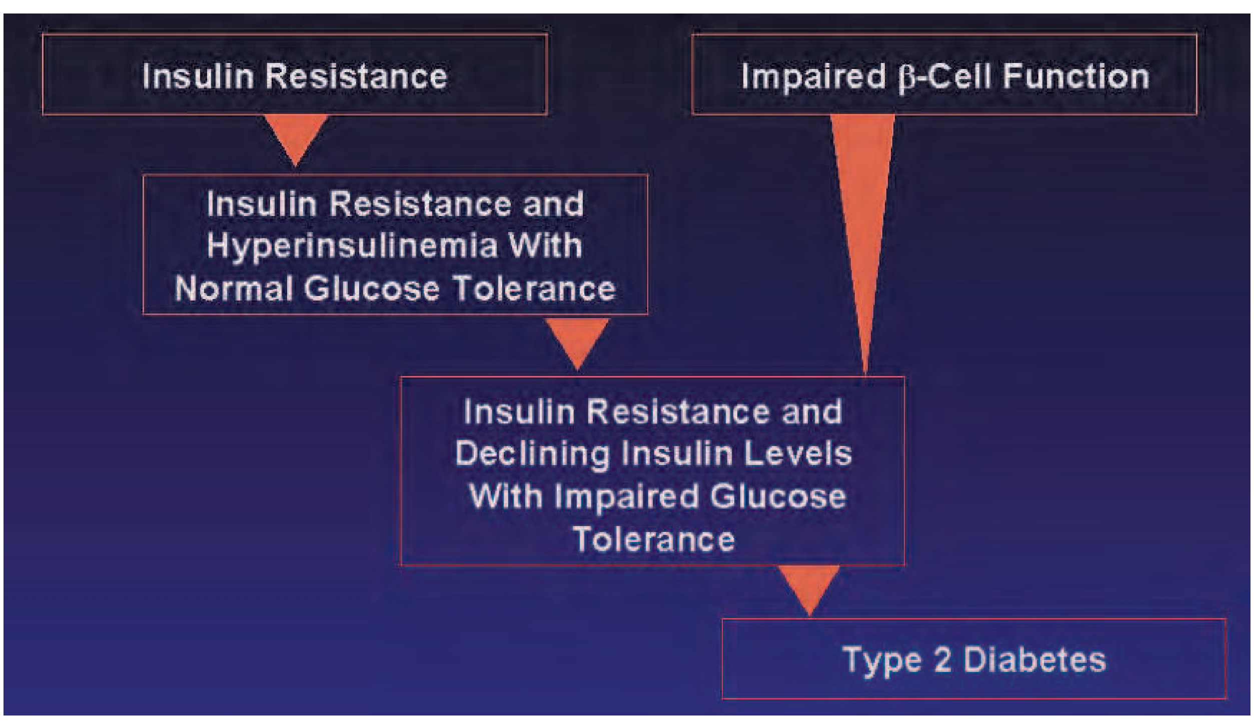


Fig. 2. Development of type 2 diabetes: Adapted from Saltiel & Olefsky (1996)

Although the metabolic syndrome is not exclusively associated with type 2 diabetes and the associated insulin resistance, the increasing prevalence of obesity and associated development of type 2 diabetes places insulin resistance as a major contributor to the syndrome. The metabolic syndrome is defined as a clustering of atherosclerotic cardiovascular disease risk factors that include visceral adiposity (obesity), insulin resistance, low levels of HDLs and a systemic proinflammatory state. There are key components to the metabolic syndrome which include in addition to insulin resistance (the hallmark feature of the syndrome), hypertension, dyslipidemia, chronic inflammation, impaired fibrinolysis, procoagulation and most telling central obesity.

3. Randomized controlled trials with fenugreek

The multiple trials in the past have shown conflicting results of the effect of fenugreek on the patients of type 2 diabetes. These studies showed some positive results on fasting serum glucose but did not examine hemoglobin (HbA1c) levels. Gupta et al (2001) reported the results of a small randomized, controlled, double-blind trial to evaluate the effects of fenugreek seeds on glycemic control. The authors reported that there were no significant differences between groups in mean glucose tolerance test values at the study's end. This study suggested that fenugreek seed extract and diet/exercise may be equally effective strategies for attaining glycemic control in type 2 diabetes. However, the trial may have been too small or brief to detect significant mean differences between groups.

Raghuram et al (1994) reported the results of a randomized, controlled, crossover trial of fenugreek seeds in 10 patients with type 2 diabetes. In the fenugreek-treated patients, statistically significant mean improvements were reported for glucose-tolerance test scores and serum-clearance rates of glucose. The absolute difference in glucose between the two groups was not mentioned. Sharma and Raghuram (1990) conducted two randomized, controlled, crossover studies in patients with type 2 diabetes. Significant mean improvements in fasting blood-glucose levels and glucose-tolerance test results were described in the fenugreek-treated patients.

Moosa et al (2006) conducted study to evaluate the effect of fenugreek on serum lipid profile in hypercholesteremic type 2 diabetic patients and concluded that fenugreek seeds powder significantly reduced serum total cholesterol, triglyceride and LDL-cholesterol but serum HDL-cholesterol level elevation was not significant. Neeraja and Rajyalakshmi (1996) presented a case series including six men with type 2 diabetes and six without diabetes. The cases suggested fenugreek reduced postprandial hyperglycemia primarily in subjects with diabetes, but less so in subjects without diabetes.

The results from several additional case series (Madar et al. 1988; Sharma, 1986; Sharma et al. 1996) also reported that fenugreek seeds may improve glycemic control in type 2 diabetes. The studies conducted to date have been methodologically weak, lacking adequate descriptions of blinding, randomization, baseline patient characteristics, statistical analysis, and standardization data for the therapy used. Demonstrating the efficacy of fenugreek has also been confounded by inconsistencies in the preparations, dosing regimens, and outcome measures used in the trials. Moreover, none of the investigations have been conducted over the longer period (Basch, 2003). The following table 1 gives the summary of Randomized Controlled Trials evaluating fenugreek use in diabetic patients.

Authors	Study Type	Condition	Sample size	Results
Gupta (2001)	Randomized Controlled Trials (Double-blinded)	Type 2 diabetes (hyperlipidemia)	N =25	Improved fasting glucose with fenugreek seeds and diet/exercise.
Raghuram (1994)	Randomized Controlled Trials (crossover study)	Type 2 diabetes	N =10	Improved peripheral glucose utilization with fenugreek seed supplementation
Sharma (1990)	Randomized Controlled Trials (crossover study	Type 2 diabetes	N =25	Improvement in reported diabetic symptoms
Neeraja (1996)	Case series with matched controls	Type 2 diabetes	N =12	Improvement of acute glycemic response with raw fenugreek seed powder
Moosa et al (2006)	Randomized Controlled Trials	Type 2 diabetes (hyperlipidemia)	N =30	Reduced serum total cholesterol with the use of fenugreek

Table 1. Summary of Randomized Controlled Trials evaluating the use of fenugreek in diabetes

4. Method of patient selection

The patients were recruited from the diabetic medical centre in rural area of Peshawar conducting the study of management of type 2 diabetes among the population aged 30-65 years. The patients were eligible and subjected to further screening if their records were found in the clinic database as patients with diabetes and had HbA1c >= 7.0% on a laboratory blood test during the last 6 months. Patients having coexisting liver, kidney or thyroid disorder were not included in the study. Also, the patients with allergy to fenugreek were excluded from the study.

The Word Health Organization (WHO, 2006) diabetes criteria were followed in the selection of the patients with diabetes as indicated in Table 2.

Condition	2 hour glucose	Fasting glucose
	mmol/l(mg/dl)	mmol/l(mg/dl)
Normal	<7.8 (<140)	<6.1 (<110)
Impaired fasting glycaemia	<7.8 (<140)	≥ 6.1(≥110) & <7.0(<126)
Impaired glucose tolerance	≥7.8 (≥140)	<7.0 (<126)
Diabetes mellitus	≥11.1 (≥200)	≥7.0 (≥126)

Table 2. World Health Organization (WHO, 2006). Diabetes Criteria for patients

The well known standard screening test for diabetes, the fasting plasma glucose (FPG), is also a component of diagnostic testing. The FPG test and the 75-g oral glucose tolerance test (OGTT) are both suitable tests for diabetes; however, the FPG test is preferred in clinical settings because it is easier and faster to perform, more convenient and acceptable to patients, and less expensive. This test was carried out and an FPG ≥126 mg/dl (7.0 mmol/l) considered being an indication for retesting, which was repeated on a different day to confirm a diagnosis. If the FPG is <126 mg/dl (7.0 mmol/l) and there is a high suspicion for diabetes, an OGTT was performed. A 2-h postload value in the OGTT ≥200 mg/dl (11.1 mmol/l) is a positive test for diabetes and was confirmed on an alternate day.

When it was found necessary, plasma glucose testing was also performed on individuals who have taken food or drink shortly before testing. Such tests are referred to as casual plasma glucose measurements and are given without regard to time of last meal. A casual plasma glucose level ≥200 mg/dl (11.1 mmol/l) with symptoms of diabetes is considered diagnostic of diabetes. A confirmatory FPG test or OGTT was also completed on such patients on a different day if the clinical condition of the patient permits.

Laboratory measurement of plasma glucose concentration is performed on venous samples with enzymatic assay techniques, and the above-mentioned values are based on the use of such methods. The A1C test values remain a valuable tool for monitoring glycemia, but it is not currently recommended for the screening or diagnosis of diabetes. Pencil and paper tests, such as the American Diabetes Association's risk test, may be useful for educational purposes but do not perform well as stand-alone tests. Capillary blood glucose testing using a reflectance blood glucose meter has also been used but because of the imprecision of this method, it is better used for self-monitoring rather than as a screening tool.

5. Determination of study sample size

The study sample size was determined based on the assumption of the estimation of Standard Deviation (SD). Therefore, the study design was selected to detect an effect size of 0.5 SD lowering of HbA1c. It was assumed that 15% patients might be lost to follow-up in control group over the period of three months and only 5 % patients will be lost to follow-up in intervention group. This assumption was based on the popularity of fenugreek seeds used by diabetic patients in sub-continent to manage their glycemic control. Taking into consideration all these factors, the following parameters were considered: α = Level of significance test = 0.05, Power = 0.8, m= the follow-up period 90 days (3 months), Standard Deviation (SD) = 0.5, the sample size was calculated for each group to detect an effect size of 0.5 SD. The sample size (N) for each group was =105; therefore, the total, N=210 patients were recruited to participate in both the groups.

6. Study population and randomization

Initially 325 patients with type 2 diabetes were invited to pre-randomized interview, out of which only 210 patients were included in the actual trial. Out of the 325 patients, 93 patients did not meet the inclusion criteria and 22 patients refused to participate in the trial. Finally, two hundred and ten (210) patients agreed to participate and signed informed consent documents at the clinic where they used to visit for their usual medical care for diabetes. Therefore, 102 patients were randomized to intervention group (fenugreek supplements) and 108 to the control group (usual medical care). Figure 3 shows their progress during the randomized controlled trial.

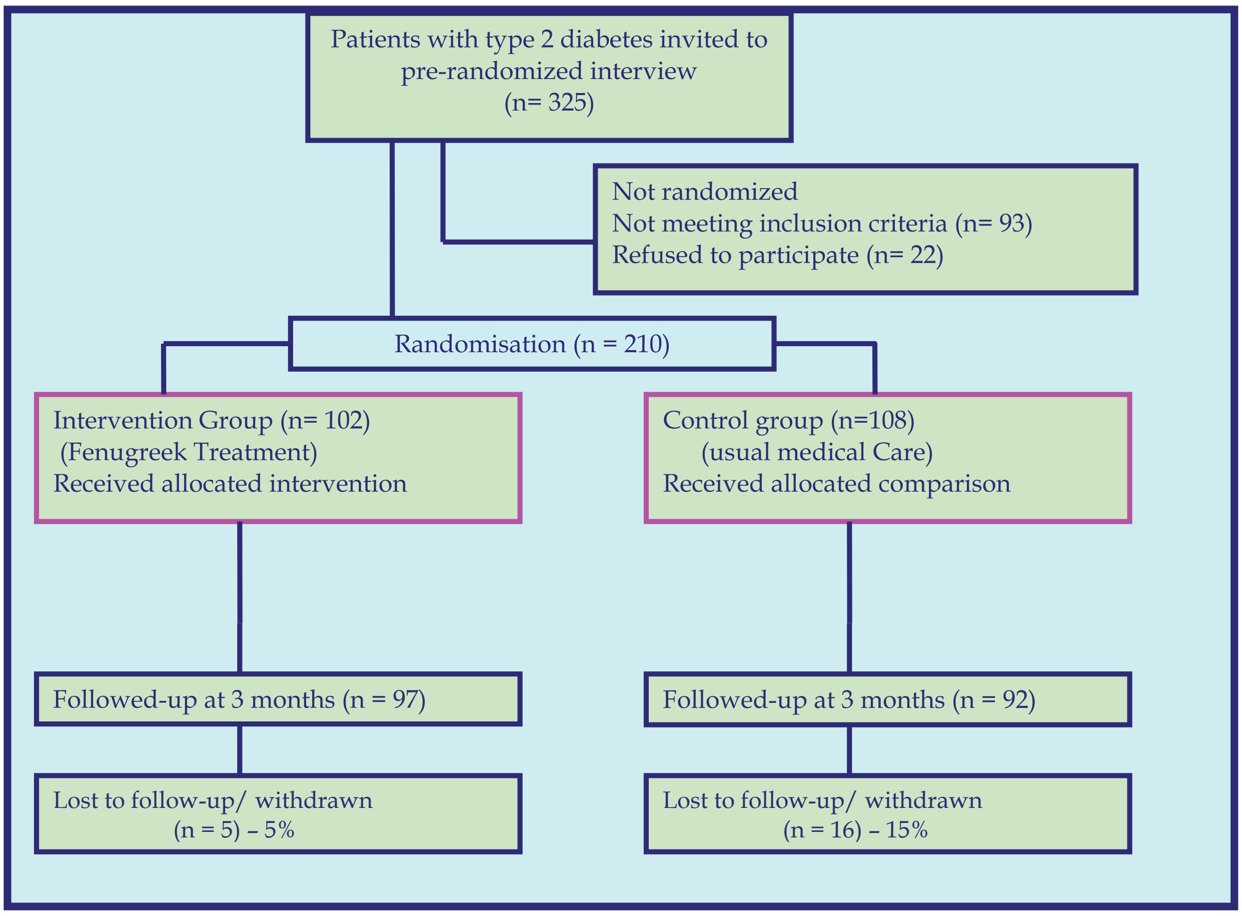


Fig. 3. Flow chart describing Randomized Controlled Trial of fenugreek treatment:

The sequence of allocation to treatments (a randomized list) was generated using the random number function in Excel worksheet. The baseline assessment was carried out prior to group allocation by an investigator/coordinator blind to the allocation sequence. The participants were issued a sealed envelope containing their group allocation. The randomization code was developed using a computer random number generator in a block size of eight patients. That helped to allocate patients to the intervention and control groups equally in each block – that is each patient would have an equal chance of allocation to either group. Once the randomization phase was completed, all patients were instructed to follow-up the usual medical care for their diabetes for the duration of the 90 days trial. The patients were allowed to adjust their usual medications as recommended by their doctors. In addition, each patient was asked to go for blood test for HbA1c on day 1 and then return to give blood sample after 90 days. In addition, participants were advised not to take any other new treatments for the management of type 2 diabetes during the trial periods.

The control group in randomized controlled trial received medical care from a physician-coordinated team. This team included physicians, nurses, dietitians, and mental health professionals with expertise and a special interest in diabetes. It is essential in this collaborative and integrated team approach that individuals with diabetes assume an active role in their care. The management plan in that group was based on individualized therapeutic alliance among the patient and family, the physician, and other members of the health care team. This plan has recognized diabetes self-management education as an integral component of care and in developing the plan, consideration was given to the patient's age, work schedule and conditions, physical activity, eating patterns, social situation and personality, cultural factors, and presence of complications of diabetes or other medical conditions. Treatment goals were set together with the patient, family, and health care team. Patient self-management was emphasized, and the plan emphasized the involvement of the patient in problem-solving as much as possible. A variety of strategies and techniques were employed to provide adequate education and development of problem-solving skills in the various aspects of diabetes management. During the implementation of the management plan it was assured that each aspect of diabetes management was understood and agreed on by the patient and the care providers and that the goals and treatment plan were reasonable.

Those patients randomized to take fenugreek (intervention group) received 100 gms fenugreek seeds powder from the pharmacy in the clinic. They were instructed to take 50 gms doses twice a day at lunch and dinner time in addition to their normal medications for diabetes. Those patients randomized to usual medical care (control group) were instructed to take their normal medicines and follow-up with their doctor as per their normal schedule. All participants were contacted again after 90 days (3-months) to give their blood sample for HbA1c testing. At that time, a questionnaire was sent via e-mail to participants in both intervention and control groups to assess the progress of the fenugreek treatment and clinical care without fenugreek.

The clinical and demographic characteristics of the patients in the two groups were well balanced at randomization. A demographic measure included age, gender, weight, ethnicity, religion, marital status, previous episodes of glycemic control, previous and current treatments of type 2 diabetes. The table 3 gives baseline characteristics of intervention and control groups in RCT trial.

Characteristics	**Intervention Group (n = 97)**	**Control Group (n = 92)**	**P-value**
Age (years)	Mean (62.5) ± SD (10.5)	Mean (59.5) ± SD (8.5)	0.78
Sex Male Female	 56% (n = 54) 44% (n = 43)	 58% (n = 53) 42% (n = 39)	
Body Mass Index (Kg/m2)	Mean (30.8) ± SD (6.5)	Mean (31.6) ± SD (6.5)	0.40
Fenugreek Intake Normal High	 98% (n=95) 2% (n = 2)	 - -	
Baseline Hemoglobin (HbA1c) %	Mean (8.5) ± SD (1.6)	Mean (8.4) ± SD (1.5)	0.59
Diabetes Medications	Mean (1.75) ± SD (0.8)	Mean (1.82) ± SD (0.8)	0.15

Table 3. Baseline characteristics of intervention and control groups in RCT trial

7. Type 2 diabetes treatments

7.1 Diabetes treatment with medications

The treatment options of type 2 diabetes is shown in figure 4 suggesting the specific areas of actions using medications which influence the various organs of the body to correct the metabolic abnormalities such as reducing the liver glucose production, slowing down absorption of sugars from the gut and reducing the insulin resistance. There are currently six distinct classes of hypoglycemic agents available to treat type 2 diabetes. These agents are Sulfonylurea (gliclazide, glipizide etc) – increase insulin secretion; Meglitinide (repaglinide) – increase insulin secretion; Biguanides (metformin) – reduce glucose production; Alpha-glycosidase (acrobase) – slow down absorption of sugar from the gut; Thiazolidendiones (pioglitazone) – reduce insulin resistance and Incretins – increase insulin secretion.

The patients in both the groups in RCT trials received medications recommended by their physicians. The most common combinations among both the groups were Meglitinide (repaglinide) with Thiazolidendiones and Sulfonylurea with Biguanides. However, the intervention group was given fenugreek as an additional supplement. The table 4 shows the hypoglycemic medications used by the patients during fenugreek RCT trial for 90 days.

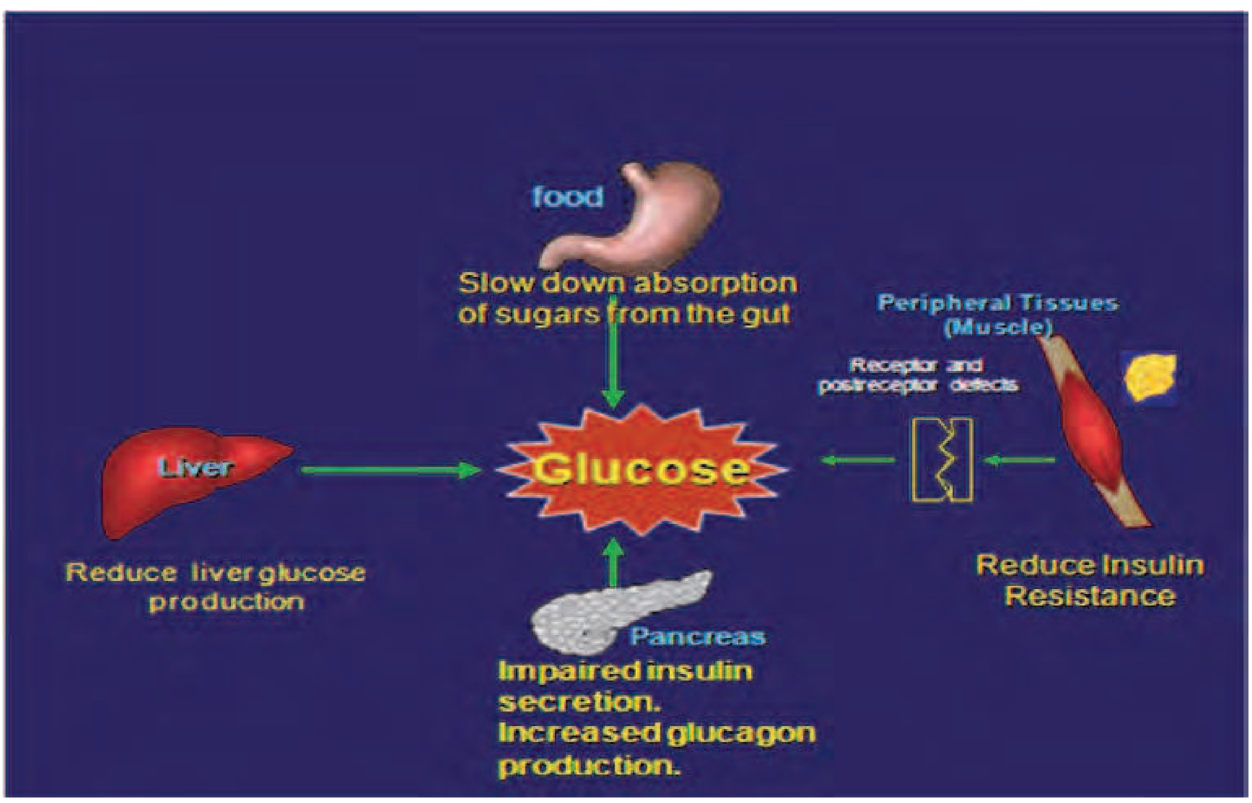


Fig. 4. Treatment options for type 2 diabetes – Source: Saltiel & Olefsky (2001)

Medication	Doses	Action
Sulfonylurea (Gliclazide)	30-120 mg/day	Increase insulin secretion
Meglitinide (Repaglinide)	0.5-4 mg/meal	Increase insulin secretion
Biguanides (Metformin)	25-3000 mg/day	Decrease hepatic glucose secretion
Thiazolidendione (Glitazone)	15-30 mg/day	Increase the insulin receptor number
Fenugreek (only for patients in intervention group)	100 gm/day	Help to lower HbA1c

Table 4. Hypoglycemic medications used by patients in fenugreek RCT trial

7.1.1 Details of hypoglycaemic medications used in RCT trial

The diabetes medications mentioned in table 4 work in different ways but the main function of all these medications include lowering blood sugar levels; help improve the body's use of glucose, decrease the symptoms of high blood sugar, help keeping patients with diabetes functioning normally and may prevent the complications, organ-damaging effects and premature deaths diabetes can cause. Since the drugs work in different ways, these are sometimes used in combination to enhance the effectiveness of treatment. In this RCT trial Sulfonylurea was used in combination with Biguanide (metformin) and Meglitinide was used in combination with Thiazolidinedione. However, fenugreek supplementation was only given to the patients in intervention group. The advantages and disadvantages of these medications used in RCT trial are given in Table 5 and the details of their mode of actions are summarized as follows:

Sulfonylurea: The sulfonylurea (Gliclazide) is an oral hypoglycemic drug and referred to as endogenous insulin secretagogues because the drug induces the pancreatic release of endogenous insulin. The fact that this drug induces pronounced hypoglycemia, treatment is initiated with the lowest possible dose and carefully monitored until the dose is found to control glucose level at 110-140mg/dL. The main function of Sulfonylurea is to bind and inhibit the pancreatic ATP-dependent potassium channel that is normally involved in glucose-mediated insulin secretion. Sulfonylurea has no significant effects on circulating triglycerides, lipoproteins or cholesterol.

Meglitinide: The meglitinide (repaglinide) is a non-sulfonylurea insulin secretagogues that is both fast acting and of short duration. Like the sulfonylurea, meglitinide therapy results in significant reduction in fasting glucose as well as HbA1c. The mechanism of action of the meglitinide is initiated by binding to a receptor on the pancreatic β-cell that is distinct from the receptors for the sulfonylurea. However, meglitinide do exerts effects on potassium conductance. Like the sulfonylurea, the meglitinide have no direct effects on the circulating levels of plasma lipids.

Biguanide: The biguanide (metformin) is a class of drugs that function to lower serum glucose levels by enhancing insulin-mediated suppression of hepatic glucose production and enhancing insulin-stimulated glucose uptake by skeletal muscle. Metformin is a member of this class and is currently the most widely prescribed insulin-sensitizing drug in current clinical use. Metformin administration does not lead to increased insulin release from the pancreas and as such the risk of hypoglycemia is minimal. Because the major site of action for metformin is the liver its use can be contraindicated in patients with liver dysfunction. The drug is ideal for obese patients and for younger type 2 diabetics.

Thiazolidinedione: The thiazolidinedione (pioglitazone) has proven useful in treating the hyperglycemia associated with insulin-resistance in both type 2 diabetes and non-diabetic conditions. The net effect of the thiazolidinedione is a potentiation of the actions of insulin in liver, adipose tissue and skeletal muscle, increased peripheral glucose disposal and a decrease in glucose output by the liver.

Medications	Advantages	Disadvantages
Sulfonylurea (Gliclazide)	Fast onset of action No effect on blood pressure No effect on LDL cholesterol Convenient dosing Low cost	Weight gain reported Risk of hypoglycemia
Meglitinide (Repaglinide)	No bad effect on cholesterol Rapid onset of action	Risk of hypoglycemia Weight gain reported Inconvenient dosing High cost
Biguanides (Metformin)	Low risk of hypoglycemia Not linked to weight gain Good effect on LDL cholesterol No ill effect on blood pressure Low cost	High risk of GI side effects (nausea and diarrhea) Risk of lactic acid build-up Less convenient dosing
Thiazolidendione (Glitazone)	Low risk of hypoglycemia Increase in HDL cholesterol Linked to decreased triglycerides Convenient dosing	Higher risk of heart failure Linked to weight gain Linked to risk of edema Linked to risk of anemia Slower onset of action Increase in LDL cholesterol

Table 5. Advantages and disadvantages of medications used by patients in fenugreek RCT trial

7.2 Diabetes treatment with diet and exercise

The normal diabetes treatment addresses the issues related to unhealthy lifestyles, such as lack of physical activity and excessive eating, which are the main causes to initiate and propagate the majority of type 2 diabetes (Michael, 2007). Studies have demonstrated strong relationship between excess weight and the risk of developing type 2 diabetes, hypertension, and hyperlipidemia. Therefore, the objective of physicians is to motivate patients to lose weight and exercise to improve the control of diabetes and slow down or even reverse the natural course of the disease (Michael, 2007).

However, it is difficult to overstate the importance of the relationship between lifestyle and the risk of developing type 2 diabetes. It has been demonstrated in recent studies that both women and men who have a BMI >35 kg/m² had a 20-fold increase in their risk of developing diabetes compared to people with a BMI of 18.5 – 24.9 kg/m² (Mokdad et al. 2001; Field et al. 2001). There are prospective studies which have demonstrated that lifestyle modification in the form of diet and regular moderate exercise sharply decrease the likelihood of developing type 2 diabetes in high-risk individuals who have impaired glucose tolerance or impaired fasting glucose. The effectiveness of this intervention superseded that of metformin therapy (Knowler et al. 2002). In this RCT trial, physicians compiled the flow scheme shown in Figure 5 which represents the method of treatment of type 2 diabetes by the combination of diet, exercise and medication for diabetes monitoring and control. It has been divided into two segments: for obese and normal weight patients and the combination of medication for both the groups of patients. The supplement of fenugreek was given to the patients belonging to intervention group.

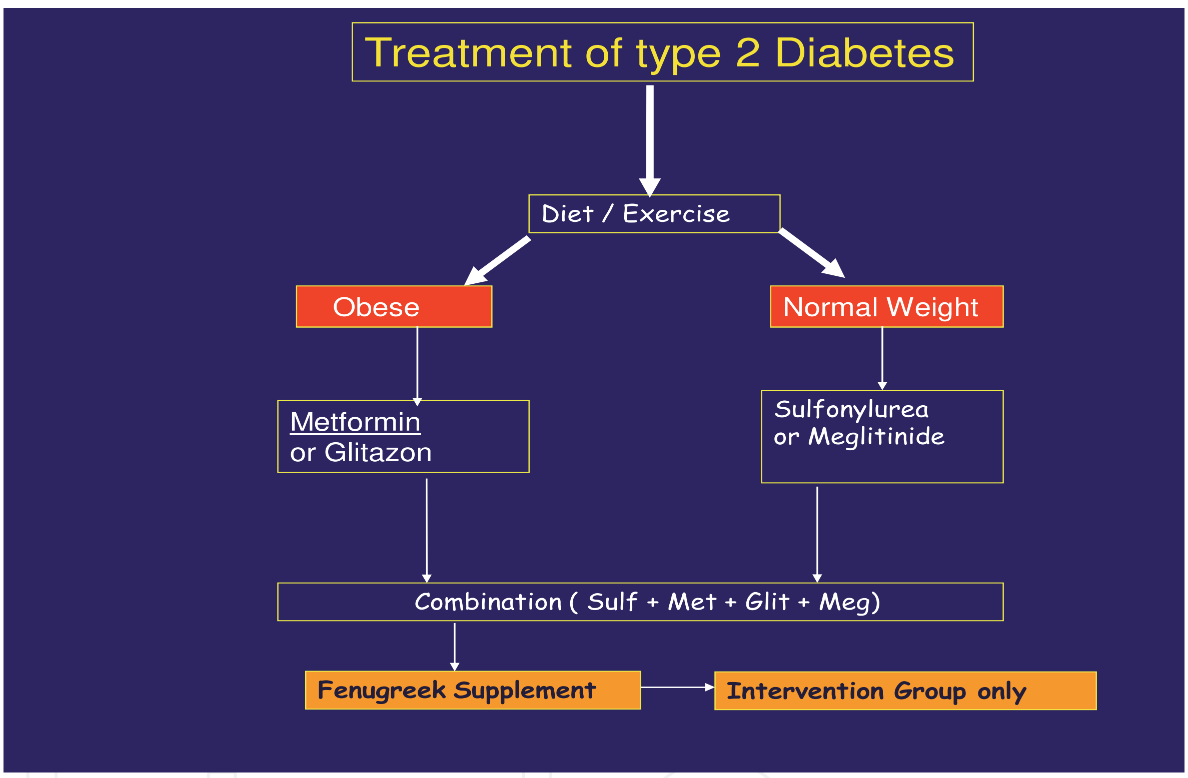


Fig. 5. Treatment of type 2 diabetes with the combination of diet, exercise and medications.

7.2.1 Dietary consideration for patients (intervention and control group)

It has been recommended that carbohydrate and monosaturated fat consumption for the patients with type 2 diabetes should comprise 60-70% of total calories. However, there is some concern that increased unsaturated fat consumption may promote weight gain in obese patients with type 2 diabetes and therefore may cause in reduction of insulin sensitivity (Bantle et al. 1993). The "glycemic index" is an attempt to compare the glycemic effects of various foods to a standard, such as white bread. Although several authors have proposed its clinical usefulness in controlling postprandial hyperglycemia, prospective studies have not demonstrated a clear improvement in hemoglobin (HbA1c) in patients using low-glycemic index diets (Michael, 2007).
The physicians in this trial have recommended the best mix of carbohydrate, protein, and fat that was adjusted to meet the metabolic goals and individual preference of the patients with

diabetes in both the intervention and control groups. It has been recommended for individuals with diabetes, that the use of the glycemic index and glycemic load may provide a modest additional benefit for glycemic control over that observed when total carbohydrate is considered alone (ADA, 2011). Monitoring carbohydrate, whether by carbohydrate counting, choices, or experience-based estimation, remain a key strategy in achieving glycemic control. In addition, saturated fat intake should be less than 7% of total calories and the intake of trans fat should also be minimized.

7.2.2 Physical activity consideration for patients (intervention and control group)

Physical activity is a key component of lifestyle modification that can help individuals prevent or control type 2 diabetes. It is considered that diet is probably more important in the initial phases of weight loss, incorporating exercise as part of a weight loss regimen helps maintain weight and prevent weight regain (Klein et al. 2004). In this trial, the message was given to both the groups that as little as 30 minutes of moderate physical activity daily may offer greater benefits to these patients in managing their diabetes. It has also been reported that in patients with type 2 diabetes, structured regimens of physical activity for 8 weeks or longer improved HbA1c independent of changes in body mass (Sigal et al. 2006).

The evidence supports the contention that controlling blood glucose through modification of diet and lifestyle should be mainstay of diabetes therapy. It was found in this RCT that despite being one of the most time-consuming discussions with the patients in both the groups, this is probably the most important patient-physician discussion in regard to diabetes control and prevention of disease progression and complications.

8. Statistical analysis

We analysed the primary outcome by an un-paired sample t-test (mean difference between baseline and final HbA1c). The statistical analysis was carried out on an intention to treat basis and that was subject to the availability of data at follow up as well as at entry level for individual patients. The differences between mean changes were tested by unpaired t tests, and χ^2 tests (chi-squared test) were used to test for differences in proportions between the fenugreek treatment and clinical based treatment groups. For the χ^2 tests, the following formula was used.

$$\chi^2 = \Sigma \frac{(\text{observed} - \text{expected})^2}{\text{expected}}$$

In this study for example (using the data from Figure 3) – it shows that number of patients at three months follow-up who were allocated to intervention group to help lowering their glycemic control were 95 % as compared the patients in clinical care (85 %), so $\chi^2 = 5.73$, P=0.02). The association between the groups and outcome is considered statistically significant.

All the patients in intervention and control groups were provided glucometers to check their blood sugar three times in a day (Fasting sugar in the morning, at bed time and 2-hrs after meal) and record that on XL-worksheet prepared for them to enter the data. Then linear regression analysis was performed after three months between HbA1c and on the blood glucose results. The HbA1c and the self-glucose monitoring via a glucometer demonstrated a significant relationship (R = .90, P < 0.0001).

These findings are in agreement with the findings of Nathan et al. (2008) who reported that the linear regression analysis carried out by these authors between the HbA1c and blood glucose (BG) values provided the tightest correlations ($BG = 28.7 \times A1C - 46.7$, $R^2 = 0.84$, $P < 0.0001$), allowing calculation of an estimated average glucose for HbA1C values. The linear regression equations did not differ significantly across subgroups based on age, sex, diabetes type, race/ethnicity, or smoking status.

9. Results and discussions

The results of this randomized controlled trial support the hypothesis and research question that fenugreek supplement with usual medical care for type 2 diabetes is more effective than the usual medical care alone. The changes in HbA1c from baseline values in intervention and control groups after 3 months were calculated by unpaired sample t-test, the results are given in Table 6. At 3 months follow-up, the intervention group (fenugreek treatment) has shown significantly greater improvement and lowered HbA1c by 0.92% (95% CI, 0.34-1.50), $p < 0.001$ as compared with usual medical care alone lowering HbA1c by 0.42% (95% CI, 0.11-0.94), $p = 0.12$ in patents with poorly controlled diabetes.

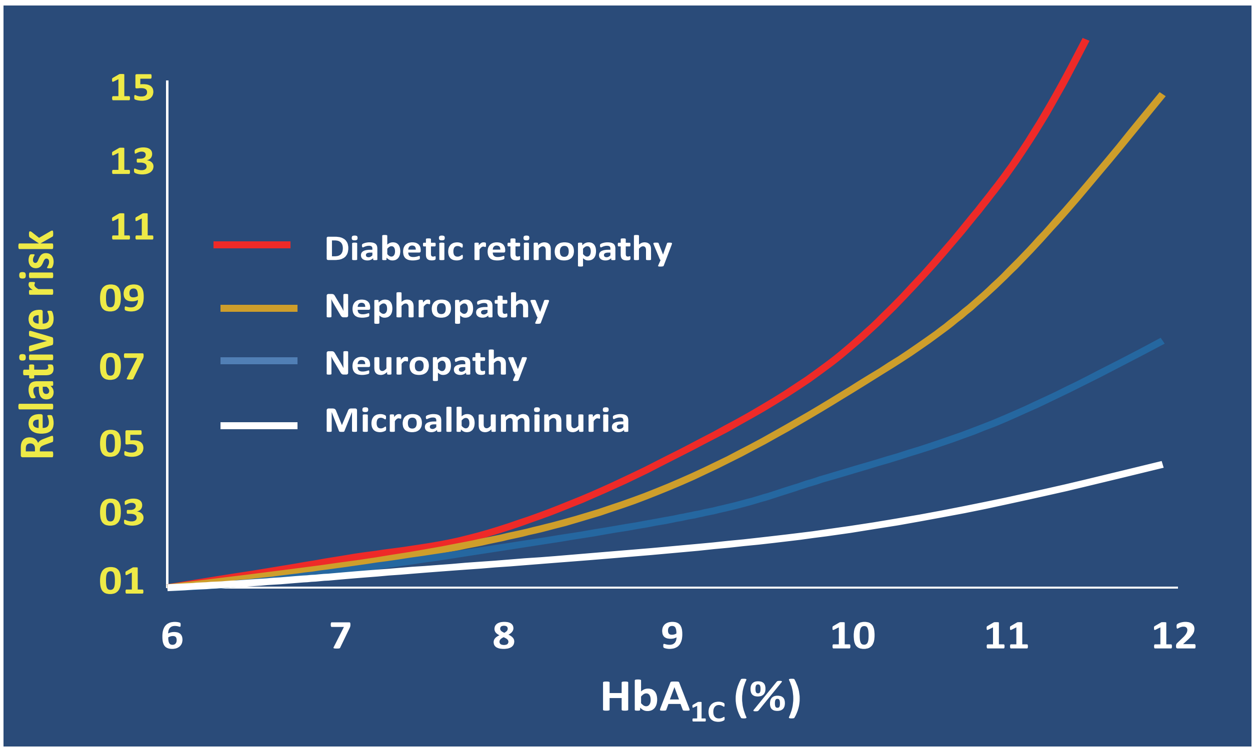
The higher % age of lost to follow up throughout this trial (Figure 3) in those patients with usual medical care (15%) than in those treated by fenugreek (5%) suggests greater satisfaction with fenugreek supplement. The difference at 3 months follow up is the mean change for the intervention group minus the mean change for the control group. Therefore, the positive differences reflect more improvement in those treated by fenugreek supplement than in medical care alone.

RCT (Groups)	Baseline (HbA1c)	Final (HbA1c)	Difference	P-value
Treatment (n=97)	9.32 ± 2.2	8.4 ± 1.9	- 0.92 (95% CI, 0.34-1.50)	< .001
Control (n= 92)	9.10 ± 2.1	8.68 ± 1.6	- 0.42 (95% CI, 0.11- 0.94)	0.12

Table 6. Effect of Fenugreek on Hemoglobin (HbA1c) in type 2 diabetes

In patients with type 2 diabetes previous studies have shown an association between the degree of hyperglycemia and increased risk of microvascular complications (Klein, 1995), sensory neuropathy (Alder et al 1997), myocardial infarction (Klein, 1995; UKPDS,1998), stroke (Lehto et al. 1996), macrovascular mortality (Groeneveld et al. 1999) and all cause mortality (Wei et al. 1998; Knuiman et al. 1992). Generally, these studies measured glycemia as being high or low or assessed glycemia on a single occasion, whereas repeated measurements of glycemia over several moths or year would be more informative.

The existence of thresholds of glycemia—that is, concentrations above which the risk of complications markedly increases was studied in patients with type 2 diabetes by Stratton et al. (2000). The relative risk for myocardial infarction seems to increase with any increase in glycemia above the normal range (Fuller et al. 1983) as shown in figure 6 whereas the risk for microvascular disease is thought to occur only with more extreme concentrations of glycemia (Krolewski et al. 1995). The diabetes control and complications trial (DCCT) research group showed an association between glycemia and the progression of microvascular complications in patients with diabetes for hemoglobin HbA1C over the range of 6-11% after a mean of six years of follow up (DCCT, 1996).



Source: Diabetic Control and Complications Trials (DCCT, 1996; Stratton et al. 2000)

Fig. 6. Relative risk of progression of diabetic complications by mean HbA1c

It has been reported by Stratton et al (2000) that the incidence of clinical complications was significantly associated with glycemia. That is each 1% reduction in updated mean HbA1c was associated with reductions in risk of 21% for any end point related to diabetes (95% confidence interval 17% to 24%, P<0.0001), 21% for deaths related to diabetes (15% to 27%, P<0.0001), 14% for myocardial infarction (8% to 21%, P<0.0001), and 37% for microvascular complications (33% to 41%, P<0.0001). The current fenugreek trial has demonstrated that there is a significant improvement after 3 months follow-up in the intervention group (fenugreek treatment) which has lowered HbA1c by 0.92% (95% CI, 0.34-1.50), p < 0.001 as compared to medical care alone lowering HbA1c by 0.42% (95% CI, 0.11-0.94), p = 0.12 in patents with poorly controlled diabetes. These finding are in agreement with the studies by Stratton et al (2000) that any reduction in HbA1c is likely to reduce the risk of complications, with the lowest risk being in those with HbA1c values in the normal range (< 6.0%).

10. Strength and weakness of the study

The strength of this trial is that it was an effectiveness trial that addressed the community clinical practice specific to the population in sub-continent and it has measured outcomes that are most significant to diabetes care providers. Previous trials have shown conflicting results about the efficacy of fenugreek to treat diabetes as summarized in Table 1 and none of the trials measured HbA1c as an outcome in their studies. There are several reasons of the success of this trial as compared to previous trials. The first reason is that this is the largest randomized fenugreek trial (n =210) to date in type 2 diabetes. The other reason is that we studied only patients with poorly controlled type 2 diabetes and finally, diabetics in sub-

continent may have different characteristics than those in other western countries due to their eating of different foods and drinking habits.
It is possible that the outcome measures associated with fenugreek treatment are subject to bias particularly when treatment was in progress or just afterwards. The main difference between usual medical care alone for the patients and usual medical care with fenugreek treatment occurred after 3 months period of trial. In order to reduce the bias, the questionnaire was sent to patients at home or via e-mail to minimize any chance that their answers might be affected by actual or perceived influence by medical practitioners at clinic. Also, the doctors did not know about those patients who were using fenugreek supplement and were blinded to the treatment allocation.

11. Contribution of the trial to public health

The main contribution of this study is to provide health professionals (diabetes care providers) and patients with type 2 diabetes an easily available, safe and cheap alternative (fenugreek seeds powder) to help them in the self-management and treatment of type 2 diabetes. The United Kingdom Prospective Diabetes Study (UKPDS) reported that a reduction of HbA1c from 7.9% to 7% lowers the risk of macro-vascular disease by 16%, retinopathy by 17% to 21% and nephropathy by 24% to 33% (UKPDS, 1998). Therefore, the results of this trial which have shown improvement in patients of diabetes by lowering HbA1c by 0.92% (95% CI, 0.34-1.50) might be expected to provide similar reductions in morbidity.

12. Future research

The use of fenugreek as a dietary supplement hold promise in future to be used in patients who manifest abnormalities of glucose monitoring and could benefit from a low-risk, inexpensive, food-based intervention aimed at normalizing their blood sugar levels and more specifically the HbA1c targets. However, the data collected to date on the benefits of fenugreek are sparse but may be used in future research for the development of well-designed, adequately powered, large scale randomized clinical trials for evaluating the effect of fenugreek seed powder on measures of insulin resistance, insulin secretion and better glucose control among the patients with type 2 diabetes.

13. Conclusion

In this randomized controlled trial, it has been shown that the levels of HbA1c reduced in the patients of poorly controlled type 2 diabetes who were taking 50 gms doses of fenugreek twice a day in addition to their normal medications for diabetes. These results of RCT support the hypothesis and the research question that fenugreek supplement with usual medical care for type 2 diabetes is more effective than the usual medical care alone. Therefore, it is recommended that fenugreek supplementation is safe and may be considered in patients with HBA1c > 7% as a potential means to lower the high levels of HbA1c.

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15. References

Adler AI, Boyko EJ, Ahroni AJ (1997), Risk factors for diabetic peripheral sensory neuropathy. Results of the Seattle prospective diabetic foot study. Diabetes Care; 20:1162-1167.

Al-Habori M, Raman A (1998). Antidiabetic and hypocholesterolaemic effects of fenugreek. Phytother Res; 12:233-242.

American Diabetes Association (2011). Standard of Medical care in Diabetes. Diabetes care, vol 34, Supplement 1 (S11-S61).

Bantle JP, Swanson JE, Thomas W et al (1993). Metabolic effects of dietary sucrose in type II diabetic subjects. *Diabetes Care* 16:1301–1305.

Basch, E, Ulbricht, C, Kuo, G et al (2003). Therapeutic applications of fenugreek. Alter Med rev; 8: 20-7.

DCCT Research Group (1996). The absence of a glycemic threshold for the development of long-term complications: the perspective of the diabetes control and complications trial. Diabetes; 45:1289-1298.

Diabetes Study Group (1990). UK Prospective Diabetes Studies, Diabetes Res; 13:1-11.

Diabetes study group (1993). Hypertension in Diabetes, J Hypertens; 11: 309-317.

Field AE, Coakley EH, Must A et al (2001). Impact of overweight on the risk of developing common chronic diseases during a 10-year period. *Arch Intern Med* 161:1581–1586.

Fong, DS, Aiello, L, Gardner, TW et al (2003). Diabetic Retinopathy, Diabetes Care; 26 (Suppl. 1): S99-S102.

Fuller JH, Shipley MJ, Rose G (1983). Mortality from coronary heart disease and stroke in relation to degree of glycaemia: the Whitehall study. BMJ; 287:867-870.

Gerich JE (2005). The importance of tight glycemic control. *Am J Med.* pp. 7–11.

Gray RP & Yudkin JS (1997). Cardiovascular disease in diabetes. In *Textbook of Diabetes* 2nd Edition, Blackwell Sciences.

Groeneveld Y, Petri H, Hermans J et al (1999). Relationship between blood glucose level and mortality in type 2 diabetes mellitus: a systematic review. Diabet Med; 116:2-13.

Gupta A, Gupta R, Lal B (2001). Effect of Trigonella foenum-graecum (fenugreek) seeds on glycaemic control and insulin resistance in type 2 diabetes mellitus: a double blind placebo controlled study. J Assoc Physicians India; 49:1057-1061.

Hogan P, Dall T, Nikolov P (2003). Economic costs of diabetes in the US in 2002. *Diabetes Care.* 26(3):917–932.

International Diabetes Federation (2003): Diabetes Atlas, 2nd ed. Brussels, IDF.

Jafar TH, Chaturvedi N, Pappas G (2006). Prevalence of overweight and obesity and their association with hypertension and diabetes mellitus in an Indo-Asian population. *CMAJ*; 175(9):1071-7.

Jensen, R (1992). Fenugreek overlooked but not forgotten. UCLA Lactation Alumni Newsletter; 1: 2-3.

Kannel WB, D'Agostino RB, Wilson PWF et al (1990. Diabetes, fibrinogen, and risk of cardiovascular disease: the Framingham experience. *Am Heart J.* 120:672–676.

Kayani, H, Rehan, N, Ullah, N (2003). Frequency of retinopathy among diabetes admitted in a teaching hospital of Lahore. J Ayub Med Coll, Abbottabad; 15(4): 53-6.

Klein R (1995) Hyperglycemia and microvascular and macrovascular disease in diabetes. Diabetes Care; 18:258-268.

Klein S, Sheard NF, Pi-Sunyer X et al (2004). Weight management through lifestyle modification for the prevention and management of type 2 diabetes: *Diabetes Care* 27:2067–2073.

Knowler WC, Barrett-Connor E, Fowler SE, et al (2002). Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. N Engl J Med; 346:393–403.

Knuiman MW, Welborn TA, Whittall DE (1992). An analysis of excess mortality rates for persons with non-insulin-dependent diabetes mellitus in Western Australia using the Cox proportional hazards regression model. Am J Epidemiol; 135:638-648.

Krolewski AS, Laffel LM, Krolewski M et al (1995). Glycosylated hemoglobin and the risk of microalbuminuria in patients with insulin-dependent diabetes mellitus. N Engl J Med; 332:1251-1255.

Lehto S, Ronnemaa T, Pyörälä K (1996). Predictors of stroke in middle-aged patients with non-insulin-dependent diabetes. Stroke, 6; 27:63-68

Madar Z, Abel R, Samish S, Arad I (1988). Glucose-lowering effect of fenugreek in non-insulin dependent diabetics. Ear J Clin Nutr; 42:51-54.

Mayfield JA, Reiber, GE, Sanders, LJ et al *(2003).* Preventive Foot Care in people with Diabetes. *Diabetes Care* 2003; 26 (Suppl.1):S78–S79.

Michael, JE (2007). Diabetes Treatment: Diet and Exercise. Clinical Diabetes, vol. 25(3), 105-109.

Mokdad AH, Ford ES, Bowman BA et al (2003). Prevalence of obesity, diabetes, and obesity-related health risk factors, *JAMA* 289:76–79.

Molitch ME, de Fronze, RA, Franz, MJ et al (2003). Diabetic Nephropathy, *Diabetes Care*; 26 (Suppl. 1): S94–S98.

Moosa, ASM, Mamun, R, Asadi, AZS et al (2006). Hypolipidemic effects of fenugreek seed powder, Bangladesh J of Pharmacology, 1:64-67.

Narayan, K.M.V. (2005). The Diabetes Pandemic: Looking for the silver lining: Clinical diabetes. Volume 23, 2, p: 51-52.

Nathan D, Kuenen J, Borg R, et al (2008). Translating the A1c assay into estimated average glucose values. *Diabetes Care*: 31(8): 1473-1478

Neeraja A, Rajyalakshmi P (1996). Hypoglycemic effect of processed fenugreek seeds in humans. J Food Sci Technol; 33:427-430.

Patil SP, Niphadkar PV, Bapat MM (1997). Allergy to fenugreek (Trigonella foenum graecum). Ann Allergy Asthma Immunol; 78:297-300.

Raghuram TC, Sharma RD, Sivakumar B, et al (1994). Effect of fenugreek seeds on intravenous glucose disposition in non-insulin dependent diabetic patients. Phytother Res; 8:83-86.

Saelens, BE (2003). Helping individuals reduce sedentary behavior. In: Andersen RE, ed. *Obesity: Etiology, Assessment, Treatment, and Prevention*. Champaign, IL: Human Kinetics; 217 –238.

Saltiel, AR, Olefsky, JM (2001). Diabetes. Am Fam Physician; 63: 1747-56.

Sharma RD (1986). Effect of fenugreek seeds and leaves on blood glucose and serum insulin response in human subjects. Nutr Res; 6:1353-64.

Sharma RD (1986). Effect of fenugreek seeds and leaves on blood glucose and serum insulin responses in human subjects. Nutr Res; 6:1353-1364.

Sharma RD, Raghuram TC (1990). Hypoglycaemic effect of fenugreek seeds in non-insulin dependent diabetic subjects. Nutr Res; 10:731-739.

Sharma RD, Sarkar A, Hazra DK, et al (1996). Use of fenugreek seed powder in the management of non-insulin dependent diabetes mellitus. Nutr Res; 16:1331-1339.

Sigal RJ, Kenny GP, Wasserman DH et al (2006). Physical activity/exercise and type 2 diabetes: a consensus statement from the American Diabetes Association. *Diabetes Care* 29:1433–1438.

Stratton, IM, Adler, AI, Neil, HAW et al (2000). Association of glycemic with macrovascular and microvascular complications of type 2 diabetes: Prospective observational studies. BMJ 321: 405-412.

Struber, J (2004). Considering physical inactivity in relation to obesity. The Internet Journal of Allied Health Sciences and Practice; January, Vol 2 Nr 1.

UKPDS (1998). Intensive blood glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes. UK Prospective diabetes study (UKPDS) Group. Lancet; 352: 837-53.

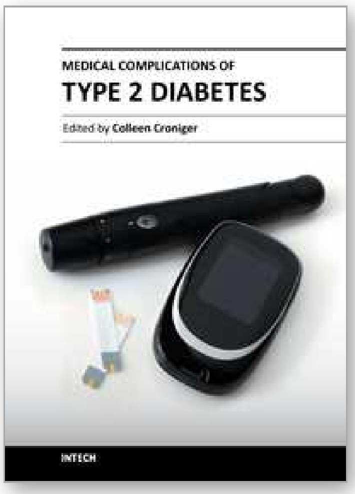
Wei M, Gaskill SP, Haffner SM (1998). Effects of diabetes and level of glycaemia on all-cause and cardiovascular mortality. Diabetes Care; 21:1167-1172

WHO (2004). Expert Consultation: Appropriate body-mass index for Asian populations and its implications for policy and intervention. *Lancet*; 363:157-63.

Wild, S, Roglic, G, Green, A et al (2004). Global prevalence of diabetes: estimates for the year 2000 and projections for 2030. Diabetes care; 27(5):1047-53.

Yale JF (2000). Prevention of type 2 diabetes. Int J Clin Pract Suppl; 113:35-39.

Yoshikawa M, Murakami T, Komatsu H, et al (1997). Medicinal foodstuffs. IV. Fenugreek seed. (1): structures of trigoneosides Ia, Ib, IIa, IIb, IIIa, and IIIb, new furostanol saponins from the seeds of Indian Trigonella foenum-graecum L. Chem Pharm Bull (Tokyo); 45:81-87.



Medical Complications of Type 2 Diabetes

Edited by Dr. Colleen Croniger

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Obesity and type 2 diabetes are increasing worldwide problems. In this book we reviewed insulin secretion in both healthy individuals and in patients with type 2 diabetes. Because of the risk associated with progression from insulin resistance to diabetes and cardiovascular complications increases along a continuum, we included several chapters on the damage of endothelial cells in type 2 diabetes and genetic influences on endothelial cell dysfunction. Cardiovascular complications occur at a much lower glucose levels, thus a review on the oral glucose tolerance test compared to other methods was included. The medical conditions associated with type 2 diabetes such as pancreatic cancer, sarcopenia and sleep disordered breathing with diabetes were also discussed. The book concludes with several chapters on the treatments for this disease offering us hope in prevention and successful alleviation of the co-morbidities associated with obesity and type 2 diabetes.

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