EFFECTS OF SELECTED HERBAL SUPPLEMENTS IN PERSONS WITH TYPE 2 DIABETES

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ABSTRACT

Diabetes mellitus is a metabolic abnormality leading to an increase in the plasma concentration of glucose and is a major cause of stroke and peripheral circulatory disorders. *Momordica charantia* (MC), commonly known as bitter gourd/*Karela*, and Trigonella foenum-graecum (TFG) (fenugreek/*Methi*) have several medicinal values like anti-diabetic, lipid-lowering property, anti-oxidant activity, anti-inflammatory, and anti-mutagenic activity. This is an open-label, four-parallel-group, prospective interventional clinical trial with a total number of 48 patients enrolled in the study and divided into four equal groups (12 in each group) viz; Group I (allopathic drug), Group II (allopathic drug and *Karela* (MC), Group III (allopathic drug and *Methi* (TFG) and Group IV (allopathic drug, methi, and karela). Blood sugar and lipid profile were measured at day 0 and day 90. One way ANOVA test was applied to find the significant difference between the groups and Tukey HSD post hoc test was applied for multiple comparisons among the four groups with probability p-value 0.05%. Multiple comparisons by post-hoc analysis between groups on day 90 showed a significant reduction of fasting blood sugar by 19.0% (p = 0.021), postprandial blood sugar by 35.0% (p= 0.001), total serum cholesterol by 14.0% (p= 0.000), serum triglyceride by 21.0% (p=0.000), and serum LDL cholesterol by 17.0% (p= 0.000)ingroup receiving *Karela* and fenugreek seeds supplementation. Whereas serum HDL cholesterol on the 90th day was higher in the group by 10.0% (p=0.015) receiving only fenugreek seeds as a supplementation. Fenugreek and karela, when given as a supplement, have a beneficial effect on blood sugar and lipid profile.

KEYWORDS

Blood sugar, fenugreek, lipid profile, *Momordica charantia,* Nepal

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INTRODUCTION

Diabetes mellitus (DM), one of the major global health problems, has been rising rapidly in low-middle-income countries than in high-income countries.[1] WHO estimated DM as the seventh leading cause of death in 2016.[1] It is a complex disease, a leading cause of morbidity and mortality, resulting in stroke and peripheral circulatory disorders.[2]

Momordica charantia (*MC*) (Bitter gourd or bitter melon or *Karela*) has been found to increase cellular glucose uptake by enhancing cellular insulin signaling pathways through the up regulation of GLUT4, PI3K and PPAR gamma.[3] The active compound of *MC* is believed to be charantin, vicine and polypeptide, and the extracts are known to bear structural similarities to animal insulin.[4]

*Trigonella foenum-graecum (TFG) (*fenugreek), stimulates the tyrosine phosphorylation of insulin receptor and enhances glucose uptake into cells.[5] The leaves, chemical extracts and shoots of *TFG* have shown anti-oxidant, anti-diabetic and hypocholesterolemic properties.[6]

This study was undertaken with the purpose of evaluating the effects of *MC* and *TFG* on blood sugar and lipid control of diabetic patients.

MATERIALS AND METHODS

This open label, four-parallel-group, prospective interventional clinical trial was conducted in BPKIHS, Dharan, Nepal from July 2015 to May 2016.Ethical approval was taken from Ethical Review Board, BPKIHS.

Sample size was calculated using the following formula:

$n = 2SD^2 (Z\alpha/_2 + Z_\beta)^2/d^2$
$= 2 (17.6)^2 (1.96 + 01.65)^2/ (27)$
$=11.07$
$= \sim 12$
Where,
n = sample size
SD = standard deviation of 17.6[2]
$Z\alpha/_2 = 1.96$ for 0.05 significance level
$Z_\beta = 1.65$ for95% power
d= difference between mean values[7]

After calculating the sample size, the total no. of subjects was 48 (12 in each group). Patients above 30 years with independent consciousness and behavior, who were diagnosed with DM type 2 by qualified physicians and taking anti-diabetic drugs prescribed by physicians, were included in the study. The *MC* used in this study was *MC* juice, which was prepared by crushing one medium-sized *MC* fruit with water in a mixer grinder and filtering through a tea filter. Participants were advised to take 200 ml of *MC* juice in the morning on an empty stomach. The *TFG* extract used was 6-7 gm of *TFG* seeds (one teaspoonful). The seeds were chewed and swallowed on an empty stomach once a day. MC+TFG extracts were 200ml of the MC juice and 6-7gm of the TFG seeds taken in a gap of half an hour on an empty stomach once a day. After enrolling 48 patients in the study, they were divided equally into four groups, twelve participants in each. All the participants were taking the same allopathic drug, metformin hydrochloride, so comparable in all groups. viz: group I (metformin hydrochloride only), group II (metformin hydrochloride and *MC*), group III (metformin hydrochloride and *TFG*), and group IV (metformin hydrochloride, *MC*, and *TFG*).

Blood sugar and lipid profile was measured on days 0 and 90. Adverse events were closely monitored and participants were encouraged to report potential adverse events during the study via phone calls or follow-up.

Each patient was contacted via telephone at the end of the month to ensure medication compliance throughout the three months. Fasting and postprandial blood sugar, and fasting lipid profile (investigations done at Central Laboratory Services, BPKIHS) were done upon enrollment, on days 0, and 90. Descriptive statistics such as mean, standard deviation, and percent were calculated; comparative statistical analysis was done using one-way ANOVA followed by Tukey HSD post hoc test for multiple comparisons, using SPSS version19 with a probability of significance set at 5%.

RESULTS

A total of 48 uncomplicated type-2 DM patients participated in the study, of whom 42 completed the study. Six patients withdrew from the study; two each from groups II, III and IV as they were not willing to continue the treatment. Among 42 patients who completed the study, 18 were males and 24 females. The mean age of the patients was 56.6±1.5 years and mean BMI was 25.7±0.5 kg/m^2 (Table 1).

Add on treatment for 90 days with 200 ml/day of *MC* in Group II, 6-7 gm/day of TFG in Group III, and both 200 ml/day of *MC* and 6-7 gm/day of *TFG* in Group IV significantly reduced the serum FBS, PPBS, and total cholesterol in all the groups. There was significant reduction of fasting blood sugar by 19% (p = 0.021),

Table 1: Baseline characteristics of the study population at day 0

Variables	Group I (allopathic drugs only) (N=12)	Group II (allopathic drugs + Bitter gourd juice) (N=10)	Group III (allopathic drugs + Fenugreek seeds) (N=10)	Group IV (allopathic drugs + Bittter gourd juice + Fenugreek seeds) (N=10)
Age(years)	61.9±3.1	57.7±2.9	47.6±2.5	58.5±2.1
Weight (kg)	63.5±3.6	58.7±2.3	61.9±2.6	68.0±3.9
Height (meter)	1.5±0.02	1.60±0.02	1.57±0.02	1.63±0.02
BMI (m/Kg^2)	25.61±0.9	22.75±0.7	24.91±0.8	25.48±1.2
Fasting blood sugar (mg/dl)	177.08±19.9	156.9±15.4	136.2±8.3	188.7±21.1
Postprandial blood sugar (mg/dl)	236.2±24.9	227.5±33.3	240.7±27.7	372.4±38.7
Total serum cholesterol (mg/dl)	201.08±4.7	197.6±19.3	216.6±10.5	209.7±17.9
Serum Triglycerides (mg/dl)	159.0±10.04	212.7±22.5	194.8±8.4	248.7±45.8
Serum LDL-cholesterol (mg/dl)	114.6±7.09	101.10±12.4	115.7±3.5	125.2±11.4
Serum HDL-Cholesterol (mg/dl)	40.1±2.6	41.1±2.8	40.2±1.9	43.0±2.8

postprandial blood sugar by 35.0% (p= 0.001), total serum cholesterol by 14.0% (p= 0.000), serum triglyceride by 21.0% (p=0.000), and serum LDL cholesterol by 17.0% (p= 0.000) in a group receiving *karela* and fenugreek seeds supplementation. Whereas serum HDL cholesterol on the 90th day was higher in a group by 10% (p=0.015) receiving only fenugreek seeds as supplementation (Table 2).

Multiple comparison by Tukey HSD post-hoc analysis of serum FBS, PPBS, and total cholesterol, serum triglyceride, serum LDL-cholesterol and serum HDL-cholesterol on 90th dayrevealed that Group D receiving *TFG* + *MC* seeds supplementation has significant reduction in serum FBS (p = 0.021), PPBS (p =0.001), total serum cholesterol (p = 0.000*), serum triglyceride(p =0.000), serum LDL-cholesterol(0.000). Multiple comparison by Tukey HSD post-hoc analysis of total cholesterol,serum triglyceride, serum LDL-cholesterol and serum HDL-cholesterol on 90thdayrevealed that Group C receiving TFG supplementation also revealed significant reduction in total serum cholesterol (p =0.000), serum triglyceride (p =0.000), serum LDL-cholesterol (p =0.000), and significant increase in serum HDL-cholesterol (p= 0.015) (Table 2).

DISCUSSION

Majority of the complication of diabetes mellitus can be prevented with adequate glycemic and lipid control. In spite of vigorous allopathic drug used in the prevention of these complications, it remains a challenge. Significant number of medicinal plants have hypoglycemic and hypolipidemic activity in experimental and clinical anti-diabetic models.

This open-label, four-parallel group, prospective interventional clinical trial on the effects of *M. charantia* and *T. foenum-graecum* supplements in type 2 diabetics taking allopathic drug shows significant improvement in fasting blood sugar, post-prandial blood sugar, and lipid profile compared to its respective baseline.

This study found that FBS and PPBS are significantly reduced with add on therapy with both *MC* and *TFG* which is in consistent with the beneficial effects of *MC* and *TFG* in other studies.[6, 8-11] It has been proposed that fenugreek seeds in humans and animals attenuate glucose tolerance and improvement in glucose-induced insulin response, thereby ratifying the potential hypoglycemic activity of fenugreek seeds.[10] Studies reveal the hypoglycemic effect of MC is

Table 2: Primary outcome following allopathic medication and MC and TFG (N=42)

Variables (Mean)	Groups	Baseline	7 days	15 days	30 days	90 days	P -value
Fasting blood sugar (mg/dl)	I	177.1	169.0	159.7	157.4	147.5	0.126
	II	156.9	134.7	137.0	124.8	108.7	0.106
	III	136.2	132.3	125.9	122.6	115.4	0.992
	IV	188.7	173.4	152.2	139.8	122.2	0.021*
Post prandial blood sugar (mg/dl)	I	236.3	224.5	216.9	205.9	197.7	0.712
	II	227.5	208.1	205.2	184.0	154.51	0.608
	III	240.7	230.4	211.2	200.7	184.3	0.830
	IV	372.4	296.6	149.6	216.0	176.3	0.001*
Total cholesterol (mg/dl)	I	201.1	200.0	200.9	200.0	197.9	0.924
	II	197.6	196.3	193.1	188.5	184.5	0.322
	III	216.6	210.3	201.1	191.6	176.5	0.000*
	IV	209.7	206.1	200.8	192.7	172.4	0.000*
Serum Triglyceride (mg/dl)	I	159.0	159.3	158.2	157.2	157.8	0.906
	II	212.7	210.9	208.9	202.7	198.9	0.520
	III	194.8	191.0	187.4	178.3	162.4	0.000*
	IV	248.7	245.5	228.9	220.8	176.0	0.000*
Serum LDL – Cholesterol (mg/dl)	I	114.6	114.0	114.8	116.5	114.3	
	II	101.10	99.5	97.4	96.4	93.5	0.113
	III	115.7	112.0	108.7	104.6	94.5	0.000*
	IV	125.2	121.8	118.5	115.0	101.6	0.000*
Serum HDL-Cholesterol (mg/dl)	I	40.2	40.3	41.1	40.6	40.9	0.978
	II	41.1	41.1	41.0	41.8	41.8	1.000
	III	40.2	40.5	42.8	43.3	44.4	0.015*
	IV	43.0	43.1	43.9	44.5	45.6	0.367

** P value (<0.05) was statistically significant (One –Way ANOVA test and Turkey HSD post hoc test)*

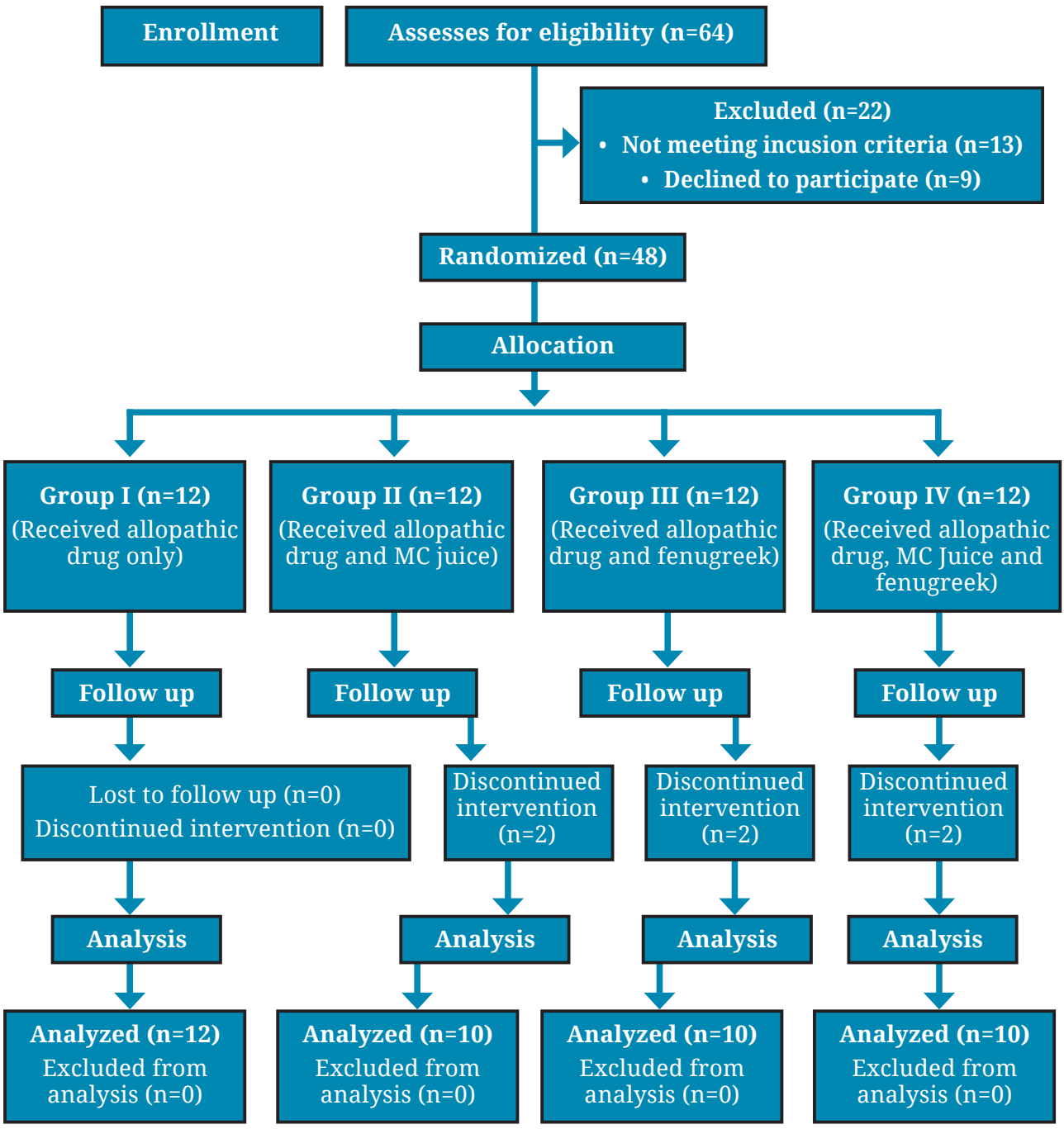
due to its ability to maintain structural integrity of pancreatic islets and release of hormones and the presence of charantine, vicine, and polypeptide like active components that have structural similarity with human insulin.[8,12]

The lipid lowering effect of *TFG* and *MC* has been extensively studied in animal models but only few clinical trials have been conducted. This study reveals significant improvement in lipid profile with *MC* and *TFG* when used as an adjuvant to anti diabetic drugs. This is in accordance with the other clinical trials.[13, 14]A gel like soluble fiber present in fenugreek seeds combine with bile acids and lower the triglyceride levels and the amino acids present in the seeds boost insulin sensitization and glycogen synthesis. The hypoglycemic activity is enhanced by the dietary fibers and the saponins present in the fenugreek seeds.[15]

It has beenfound that *MC* and *TFG* preparation were highly tolerable in all the trials and were associated with minimal or no side effects and can be considered as an add on therapy option with safety profile along with conventional cholesterol and sugar lowering agents. On the other hand *MC* and *TFG* also significantly increased the HDL cholesterol level in this study which is in accordance with other studies.[7,16,17]

Patients enrolled in his study self-administered the extracts of *MC* and *TFG*. Thus, the relationship between various confounding

Fig. 1: Consort Flow Diagram



factors and the glycemic and lipid control in these patients cannot be overruled. This study further recommends the need of clinical trial exploring more of association of glycemic control, lipid profile control and various confounding factors with a larger sample size.

In conclusion, this study showed the significant improvement in the blood sugar and lipid profile after short term (90 days) treatment with add on therapy with oral supplementation of *MC* and *TFG* in patients with type 2 Diabetes Mellitus.

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