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Antihyperlipidemic Effect of Seeds of *Jamun (Eugenia jambolana)* in Subjects of Intermediate Hyperglycemia: A Pilot Study

Shagufta Parveen[1]*, Asim Ali Khan[1], Qamar Alam Khan[2]

[1]*Central Council for Research in Unani Medicine, Ministry of AYUSH, New Delhi, India*
[2]*Clinical Registrar, Majeedia Unani Hospital, Jamia Hamdard, India*

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Abstract

Intermediate hyperglycemia (Prediabetes) is a type of metabolic disorder with slight increase in the blood glucose levels from the normal but not reaching up to the level of diabetes. It is associated with many micro-vascular as well as macro-vascular complications. Abundance of Unani medicines are known for anti-hyperlipidemic activity, among them is *Maghz-e-Jamun (Eugenia jambolana)*. The present study was to evaluate the anti-hyperlipidemic effect of *Maghz-e-Jamun (Eugenia jambolana)* in intermediate hyperglycemia. Patients diagnosed with prediabetes as per ADA criteria were randomly divided in two groups- group A was supplemented with 4.5g powder /day jamun seed powder in the form of capsules and group B was given placebo capsules. Lipid profile assessment was done at baseline and end of the treatment i.e., 84th day. There is considerable improvement in the lipid profile of the prediabetic subjects enrolled in the study especially significant improvement in total cholesterol level (from 266.47 ± 62.92 to 216.058 ± 40.14 with p value of 0.008**) and LDL (from 189.23 ± 55.07 to 138.58 ± 34.86 with p value of 0.003**). -*Maghz-e-Jamun (Eugenia jambolana)* show substantial effect on dyslipidemia in the patients of intermediate hyperglycemia.

Keywords: *Maghz-e-Jamun (Eugenia jambolana)*; Antihyperlipidemic; Unani; Prediabetes; Intermediate hyperglycemia

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*Corresponding Author: Shagufta Parveen
Central Council for Research in Unani Medicine, Ministry of AYUSH, New Delhi, India
Email: shaguf.ccrum@gmail.com

Introduction

It is estimated that worldwide 6.7% of the adult population, which is approximately equivalent to 318 million persons have prediabetes. The prevalence of prediabetes is increasing worldwide and it is anticipated that more than 470 million people will have prediabetes in 2030. [1]

Prediabetes is condition of abnormal glucose homeostasis characterized by Impaired Fasting Glucose (IFG), Impaired Glucose Tolerance (IGT), or both [2]. Effects of the disease can be macrovascular, as seen in the cardiovascular system, or microvascular, as seen with retinopathy, nephropathy, and neuropathy. IFG sometimes progresses to type 2 diabetes. The dyslipidemia is characterized by elevated triglycerides (TG), reduced high density lipoprotein (HDL) cholesterol, and predominant presence of small dense low-density lipoprotein (LDL) particles. Condition of dyslipidemia play a central role in acceleration of macrovascular atherosclerosis and contribute to the excess risk of CVD [2]. Prediabetic condition also has been found to be associated with an increased risk for cardiovascular disease. Lipid abnormalities are common in people with type 2 diabetes as well prediabetes, but the pattern of the different lipids may vary individually [2]. The lack of prediabetes guidance/ consensus and the screening on diabetes creates the condition that makes prediabetes goes unknown and unwatched [3].

Management of diabetic and prediabetic condition without side effects ischallenge that appeals researchers toward plant based new products. Many scientific studies as well classical literature advocated anti-diabetic and antihyperlipidemic properties of seeds of Maghz-e-Jamun *(Syzygium cumini)*. So, it should

be further explored for its benefits especially in management of dyslipidemia in prediabetic patients. This paper aim to assess the incidence of dyslipidemia in prediabetic subject and to evaluate the effect of *Maghz-e-Jamun (Eugenia jambolana) as* antihyperlipdemic agent.

Methods

Ethics statement

The protocol was approved by the Institutional Ethics Committee of Jamia Hamdard on 31/ March/2016and was implemented in accordance with provisions of the Declaration of Helsinki and Good Clinical Practice (GCP) guidelines.

Study design

The study was designed as a pilot study with objective to evaluate the effect of powder of *Eugenia jambolana (Maghz-e-Jamun)* on the lipid profile of prediabetic patients. Study was conducted over a period of one year in Majeedia Unani Hospital, Jamia Hamdard, New Delhi.

Participant's eligibility, recruitment and informed consent

Screening of patients who attended IPDs and OPDs of Majeedia Unani hospital and HAHC hospital was done for prediabetes. Also, the patients who were accidentally diagnosed with prediabetes were screened for the enrolment in study. Among screened patients, further investigations i.e., FBS, BSPP and HbA1c were done to confirm the prediabetes. Afterwards, the prediabetic male and female of age between 18

years to 65years diagnosed as per ADA Criteria i.e., Fasting Blood Sugar range100-125 mg/dl or 2h plasma glucose level range140-199 mg/dl (after 75g glucose load on OGTT) or HbA1c in the range of 5.7%-6.4%were enrolled in study. Pre-diabetics suffering from any severe complications, patients with deranged kidney and liver profiles, pregnant &lactating females were excluded. Mentally retarted patients and the patients who fail to give consent, and unable to follow up were also excluded from the study. Those fulfilling the inclusion and exclusion criteria's were given the patient information sheet attached with Case Record Form (CRF) regarding the nature of the study, the drugs to be used and the study procedure. Afterwards patients were randomly allocated into one of the two groups Test group and Control group by computer generated randomization sequence. Patients were given the opportunity to ask any question and if he/she agreed to participate in the study, he/she was asked to sign the informed consent form. The benefits and possible risks of participating in the study were carefully explained, patient confidentiality guaranteed. Written informed consent was taken from the patients in their known languages and signed by them.

Intervention

Seeds of Jamun (Eugenia jambolana) were procured from the local market at Khari Baoli, Old Delhi, India were authenticated by Department of Botany, Faculty of Life Science, AMU, Aligarh, India. Standardization of powder of the seeds of Eugenia jambolana was done at physic-chemical as well phyto-chemical parameters for good quality of drug. After standardization of test drug, powder was filled in capsules, (each capsule containing 0.75g powder). This preparation and storage of drug was done in pharmacology lab, Department of Moalajat, Jamia Hamdard, New Delhi. In test group, 4.5 g powder of Eugenia jambolana (3 capsules, each capsule containing 0.75g powder twice a day) were given orally for 12 weeks. Whereas, in control group, placebo prepared with starch was given in the same form and dosage as in test group for the same duration. During the protocol therapy, patient in both the groups were asked to follow the prescribed diet as provided by dietician. In prescribed diet carbohydrate and mono-saturated fats together were contributing 60-70% of total caloric intake. Protein covering 15-20% of caloric intake and saturated fats should accounts for less than 7%. Cholesterol levels were limited more than equal to 200mg/dl [4,5].

Follow up was done at baseline (0th day), 4th week (28th day), 8th week (56th day) and 12th week (84th day). Assessment of sign and symptoms was done at every follow up. Lipid profile (S. cholesterol, S. triglycerides, S. HDL and S. LDL) assessment of the patients were done before and after the intervention therapy alongwith other investigations associated with safety and efficacy of the drug.

Statistical Analysis

Student t test (two tailed, dependent) has been used to find the significance of study parameters on continuous scale within each group. Chi-square/ Fisher Exact test has been used to

find the significance of study parameters on categorical scale between two or more group, non-parametric setting for Qualitative data analysis [6,7,8].

The Statistical software namely SPSS 18.0, and Renvironment ver.3.2.2 were used for the analysis of the data and Microsoft word and Excel ver.2011 have been used to generate graphs, tables etc.

Statistical analysis was done twice; primarily on the lipid profile of all prediabetic patients and secondly only on those patients who were having deranged lipid profile. Tables of both assessments are mentioned separately.

Observation and Results

Out of total 75 screened patients, 68 patients who fulfilled inclusion criteria were enrolled in the study. Among screened patients, 5 patients did not meet eligibility criteria and 2 patients refused to sign informed consent form. 64 patients included in the study were equally distributed among both the groups. After period of 12 weeks (84 days) only 52 patients completed the trial with 30 patients in test group while 22 patients in controlled group. Lipid profile assessment of all enrolled prediabetic patients was done before and after of intervention therapy. Among 52 enrolled patients, 23 patients from both test as well control group were having deranged lipid profile. Among these patients, 17 were from test group while only 6 patients were under control group.

Table 1: change in lipid profile of all prediabetics

Effect on Cholesterol Total (mg/dl)				
Study Group	**Follow-up**	**Mean ± SD**	**p value**	**% change**
Test Group (n=30)	0^{th} day	219.23±12.2	0.12	7.7
	84^{th} day	202.63±7.07		
Control Group (n=22)	0^{th} day	195.18±6.93	0.12	3.5
	84^{th} day	188.23±4.61		
Effect on Triglyceride (mg/dl)				
Test Group (n=30)	0^{th} day	175.67±10.28	0.10	4.5
	84^{th} day	167.83±8.72		
Control Group (n=22)	0^{th} day	152.32±8.37	0.27	0.6
	84^{th} day	153.32±9.72		
Effect on HDL (mg/dl)				
Test Group (n=30)	0^{th} day	39.40±0.94	0.11	3.0
	84^{th} day	40.60±0.84		
Control Group (n=22)	0^{th} day	41.36±0.66	0.46	4.2
	84^{th} day	39.59±1.10		

Effect on LDL (mg/dl)				
Test Group (n=30)	0th day	147.23±11.49	0.08	15.01
	84th day	125.13±6.00		
Control Group (n=22)	0th day	120.86±7.50	0.26	4.50
	84th day	115.41±5.77		
Effect on VLDL (mg/dl)				
Test Group (n=30)	0th day	35.30±2.04	0.43	No change
	84th day	35.30±2.04		
Control Group (n=22)	0th day	32.55±2.99	0.74	Slight increase
	84th day	33.55±4.12		

Table 2: Change in Lipid of Prediabetics having deranged Lipids Profile

Effect on Cholesterol Total (mg/dl)				
Study Group	**Follow-up**	**Mean ± SD**	**p value**	**% change**
Test Group (n=17)	0th day	266.47±62.92	$p=0.008^{**}$	18.9
	84th day	216.058±40.14		
Control Group (n=06)	0th day	236.00±29.88	$p=0.03^{*}$	16.5
	84th day	196.83±23.88		
Effect on Triglyceride (mg/dl)				
Test Group (n=17)	0th day	194.47±60.36	$p=0.34^{ns}$	9.6
	84th day	175.70±53.51		
Control Group (n=06)	0th day	161.16±33.84	$p=0.5^{ns}$	8.5
	84th day	146.83±37.63		
Effect on HDL (mg/dl)				
Test Group (n=17)	0th day	37.17±5.94	$p=0.6^{ns}$	2.69
	84th day	38.17±5.45		
Control Group (n=06)	0th day	42.33±2.94	$p=0.19^{ns}$	-10.6
	84th day	37.83±7.36		
Effect on LDL (mg/dl)				
Test Group (n=17)	0th day	189.23±55.07	$p=0.003^{**}$	26.7
	84th day	138.58±34.86		
Control Group (n=06)	0th day	161.15±28.82	$p=0.06^{*}$	20.7
	84th day	127.66±27.07		

Effect on VLDL (mg/dl)				
Test Group (n=17)	0th day	39.11±12.33	p=0.7ns	3.14
	84th day	37.88±15.36		
Control Group (n=06)	0th day	32.00±6.78	p=0.43ns	10.4
	84th day	28.66±7.25		

** highly significant* significant ns not significant

Discussion

Lipid profile assessment of all enrolled patients of prediabetes was done before and after the treatment in both test and control group. Assessment of changes in lipid profile (S. cholesterol, S. triglycerides, S. HDL and S. LDL) revealed that there was statistically insignificant difference in S. cholesterol, S. triglycerides; S. HDL in both groups, only significant change (p = 0.018) of LDL in test group was noticed. Intergroup comparison was not significant for all parameters of lipid profile (p > 0.05). This finding is in conformity with clinical trial conducted by Sidana et al. a significant overall effect of *Eugenia jambolana* supplementation was found in improvement of lipid profile in type 2 diabetes subjects [9].

While taking in consideration the prediabetics having deranged lipid profile, it was revealed that around 50% of enrolled prediabetics were dyslipidemic. This finding is with consonance to study conducted by Srivastava et al which showed that prevalence of dyslipidemia is more significant in pre-diabetic subject.[10] As far as change in lipid profile is concern, when total cholesterol is assessed before and after the treatment among both groups, results are statistically significant. But in test group this result is highly significant. Significant changes in total cholesterol in placebo group may be due to dietary and exercise intervention. Percentage reduction in cholesterol level in test group is 18.9 while in placebo group this reduction is 16.5.

Assessment of changes in triglyceride level revealed statistically insignificant difference (p > 0.05) in both groups; though percentage reduction is 9.6 and 8.5 simultaneously in test and placebo group.

LDL was assessed on 0th and 84th day of protocol therapy. Mean LDL was (189.23 ± 55.07) in test group on 0 day before starting the therapy and declined to (138.58 ± 34.86) with (p = 0.003**) that is statistically highly significant at the end of treatment. While in placebo group, it was noticed that LDL level declined to 127.66 ± 27.07 from 161.15 ± 28.82 with (p = 0.06*) after completion of treatment. This finding is in conformity with clinical trial conducted by Sidana et al. a significant overall effect of Eugenia jambolana supplementation was found in improvement of lipid profile in type 2 diabetes subjects [9].

As far as level of HDL is concerned, mean value was 37.17 ± 5.94 at the time of enrolment which get improved and rose to 38.17 ± 5.45 with statistically non-significant value and percentage change of 2.69 while in control/ placebo group HDL get 10.6% worse to 37.83 ± 7.36 from 42.33 ± 2.94. There are no significant changes

revealed in VLDL when assessed after intervention therapy in both groups.

Above results are in consonance to pre-clinical studies advocated the antihyperlipidemic effect of seeds of Eugenia jambolana which show significant improvement in serum total cholesterol, triglycerides, high-density lipoprotein cholesterol, and the total cholesterol/high-density lipoprotein cholesterol ratio after administration of active principle isolated from seed of Eugenia jambolana. [10,11]. Findings are also in cohesion with previous study conducted by Kasiappan et al to elaborate the anti hyperlipidemic effect of seeds of Eugenia jambolana [12]. The improvement in the test group can be attributed to anti hyperlipidemic action of Eugenia jambolana while in placebo group change may be due to exercise and modified diet, as lifestyle modification play key role in the management of lipid profile.

Conclusion

In the light of observations of the above and previously conducted studies, it may be concluded that there is association of dyslipidemia with glucose metabolism. Further, it could be inferred that the test drug *Maghz-e-Jamun (Eugenia jambolana)* plays substantial effect on the improvement of lipid profile of the patients diagnosed with intermediate hyperglycemia. Further clinical trial on large sample size with more duration of follow up may explore the antihyperlipidemic effect of seeds of Eugenia jambolana.

Conflict of Interests

None.

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