ORIGINAL ARTICLE

Myoinositol Potential against Polycystic Ovary Syndrome (PCOS) in Diabetic Patients

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ABSTRACT

Objective: To find the potential of myoinositol extract from beans against PCOS in obese diabetic females.

Methods: This experimental research work was performed during October 2017 to March 2018, in industrial biotechnology research lab of biochemistry in Government College University Faisalabad, 30 obese diagnosed females of type-2 diabetes mellitus (T2DM) with PCOS, having age ≥30 years and BMI>1.18 kg/m^{2}were selected in accordance to convenient sampling technique from Independent University Hospital Faisalabad. A physical examination, medical history and informed consent were recorded. The subjects were divided into 2 groups, one treatment group (15 subjects, taking myoinositol extract dose 2g/twice a day) and other placebo group (15 subjects).

Results: Thirty diabetic PCOS subjects with mean age 35.96±2.13 years and BMI 25.84± 1.81kg/m^2 were included., fasting blood glucose level (123±3.17mg/dl) and HbA_1C level (6±0.41%) significantly reduce ($p<0.05$) as compared to control. No significant difference was observed in CBC and BMI ($p>0.05$). Moreover, MI dosage (2g/day) indicated no side effects.

Conclusion: HbA_1C and fasting blood glucose level was significantly decrease in diabetic PCOS subjects when treated with MI for three months. MI dosage 2g/twice a day indicated no side effect e.g diarrhea, nausea, and flatus

Key Words: Type 2 Diabetes Mallitus, Polycystic Ovary Syndrome, Obesity, Myoinositol

Article Citation: Hamid M, Meraj M, Khaskheli MS, Irfan R, Langah AI, Kamal S, Sarfarz M. Myoinositol Potential against Polycystic Ovary Syndrome (PCOS) in Diabetic Patients. J Peoples Uni Med Health Sci. 2018;8(2):98-103.

INTRODUCTION:

Polycystic ovary syndrome (PCOS) is one of the main reasons in disturbance in chronic ovulation. It is one of most common endocrine disease[1]. The PCOS's patients seek clinical treatment for hirsutism andinfertility. PCOS with obesity is worsened by insulin resistance. Obese females with PCOS have high concentration of testosterone and low concentration of luteinizing hormone[2].

According to WHO, in 2012 approximately 116 million females worldwide affected by PCOS[3]. Worldwide occurrence of PCOS are significantly vary from 2.2% - 26%. In India 36% females are suffering from PCOS[1]. According to WHO, in Pakistan 26% females are obese in pregnancy having PCOS. Worldwide the prevalence of PCOS is 7% to 10%. The females with PCOS are at high risk of fatty liver disease, irregular menstrual cycle, excess facial hair, cardiovascular disease and abortion[1,3,4].

Myo-inositol (MI) chemical name hexane-hexadiole act as a precursor of second messenger

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(inositol triphosphate) which regulates many hormones e.g insulin, TSH and FSH. Follicular fluid plays very important role in maturity of follicles and gives good quality oocytes[5]. Currently, administration of Myoinositol (MI) in problem of infertility associated with PCOS, has been proved good insulin sensitizer. MI could be recommended as replacement of metformin because of neglible side effect on insulin target cells and also helpful to potentiate insulin effects [6]. Several studies have demonstrated that MI therapy proved helpful in lowering the metabolic, oxidative and hormonal abnormalities associated with PCOS in patients by improving the insulin resistance[1,5,7].

PCOS adversely affect the health by causing stress, anxiety, weight gaining, infertility and hirsutism[8,9]. This project was planned to use bean MI extract for obese diabetic PCOS females. In our body mayoinositol is naturally occurring, so it shows no side effect as compare to other market available synthetic drugs. MI extracted from beans and given to obese PCOS females and then checked its efficacy.

METHODS:

This experimental study was performed in Industrial Biotechnology Research Lab of Biochemistry Department in GC University Faisalabad, during October 2017 to March 2018, on 30 diagnosed obese type-2 diabetic patients with PCOS, which were collected from Independent University Hospital, Faisalabad. The inclusion criteria was obese females with diagnosis of T2DM with PCOS, age ≥30 years and BMI>1.18 kg/m^2, while females with pregnancy, physical or mental disability were excluded in this study. All the biochemical parameters were performed in pathology lab under the supervision of medical officer. The work started after the endorsement of ethical committee GCU Faisalabad. The subjects were informed in detail about all phases of the study and only voluntaries were included in this study.

Collection of beans: Beans were collected from the Ayoub research Faisalabad, washed and air dried. Then subjected to grind with particle size 500-600 µm. This bean powder was stored at 15°C in plastic jars at dry and dark place[10].

Myoinositol extract preparation: Myoinositol extract was prepared by dissolving 15g beans powder in 150 ml of 80% ethanol. The sample was subjected to magnetic stirrer for 60 minutes then sonicated through ultrasonicator at 35°C for twenty minutes. The resulted solution was again stirred for three hrs. This solution was filtered by using whatmann filter paper No-2. The extract was dried in rotary evaporator at 45 °C for three hours and finally get a semi thick liquid[10].

Confirmation of myoinositol: FT-IR spectroscopy was used to confirm the presence of myoinositole in semi thick liquid. The spectra were collected in the range of 4000-650cm^{-1} at a resolution of 4cm^{-1}.

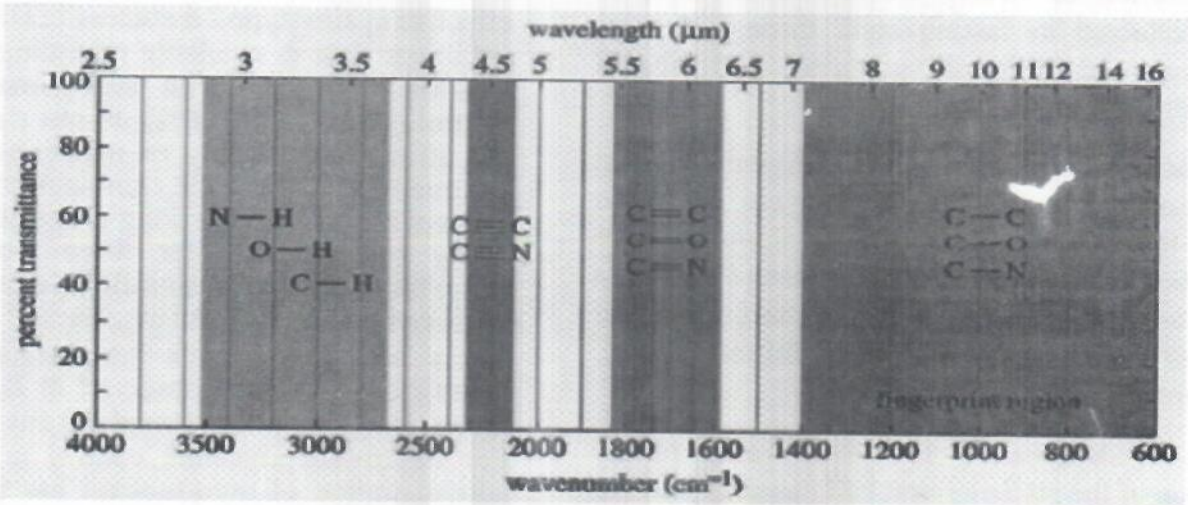

Figure I. FTIR Spectra Exhibits Functional Group at Various Wavelength

This figure exhibits the functional group at various wavelengths revealing that MI belongs to alcoholic family.

Experimental design: Obese diabetic female patients with age more than 30 years were included in this study. The patients were selected in accordance to convenient sampling technique. A physical examination medical history and informed consent were recorded. Female patients were divided into two groups, one treatment group (15 females, taking selected MI extract dose) and other placebo group (15 females). Total thirty female patients were selected in this study. Intervention for research was performed for 12 weeks between Jan-April 2018.

Optimum dose: The dose was optimized for treatment group throughout the research experiment by adopting the method of Croze & Soulage. 2013[5]. The dose of myoinsitol powder (two times per day) of 2g was given to volunteer obese diabetic females with water, one hour before breakfast and other dose one hour before dinner for twelve weeks.

Physical examination: All the volunteers were physically examined for demographic data including age, BMI, height, body weight, blood pressure and oral temperature was measured before start of the study[10]. Blood sample from experimental group was collected before and after the administration of dose (MI powder) for the duration of twelve weeks. Blood samples was collected in fasting state through venous puncture with help of vacutainer and labeled carefully.

Ethical consideration: Informed written consent was signed by all patients and were explained about the purpose of study. All volunteers were informed about the procedure and each step of this research. The research work was started after the consent of ethical review committee of GC University Faisalabad.

SPSS (version 17 USA) was used for analysis of the statistics and LSD used to find the difference between means.

RESULTS:

The study included thirty patients with diabetic PCOS. The demographic and clinical features of the all the subjects are explained in table-I. After the completion of treatment duration (3 months), HbA_1C level and fasting blood glucose levels were significantly decreased as compare to baseline but there was no significant difference in CBC and BMI values.

It was observed at the end of this study that a non-significant reduction in BMI for treatment as compared to control group was observed.

Table-I: Clinical & Biochemical Characteristics of Diabetes Subjects (n=30)

Variables	Baseline
Age	35.96±2.13
BMI (kg/m2)	25.84± 1.81
HBA1C	7±4.76%
WBC count (/µl)	6.55±1.74
MCV (fl)	80.59±6.93
MPV (fl)	8.95±1.05
RDW (%)	12.14±1.34
Platelet count (/µl)	254.75±60.80

Placebo treated uncontrolled glycaemia ($HbA1_c$ >7%), patients treated with myoinositol good control ($HbA1_c \leq 7\%$)

Inositol has been used for treatment of various pathological conditions like PCOS, gestational diabetes band metabolic syndrome. It was observed that use of Myo-inositol is also effective against type 2 diabetes (T2DM), while no sufficient data is available regarding the use of inositol in T2DM with suboptimal glycemic control (HbA_1C 7.010.0%). In our study we find the efficacy and safety of myo-inositol for the treatment in T2DM. The combination of MI (2g) along with glucose lowering drugs administrated orally twice a day for three months. After completion of the trial significant decreased were observed in fasting blood glucose and glycated Hb levels as compared to the baseline, but no significant difference observed in B.P and BMI levels. No participant's complaint any side effects. For improving glycemic control in T2DM the administration of myo-inositol has been proved safe and valuable therapy.

After MI powder consumption, this group was assessed for safety test including liver function test (LFT), alanine aminotransferase (ALT) and aspartate aminotransferase (AST), gastrointestinal symptoms e.g nausea, vomit, flatus, diarrhea etc in patients showed significant results.

Table-II: CBC Indices in Diabetic Subjects after 12 weeks.

Variables	Treated with Placebo (n=15)	Treated with MI (n=15)	P-value
Fasting blood glucose (mg/dl)	133±8.46	123±3.17	0.000
HBA1c (%)	7±4.76	6±0.41	0.002
WBC count (/µl)	6.55±1.74	7.87±1.45	0.095
MCV (fl)	80.59±6.93	90.49±6.78	0.016
MPV (fl)	8.95±1.05	9.03±0.965	0.524
RDW (%)	12.14±1.34	15.09±1.87	0.035
Platelet count (/µl)	254.75±60.80	257.69±65.65	0.706
TG	1.97±0.79	1.00±0.80	0.666
LDL	2.81±0.93	2.55±0.92	0.079
HDL	1.1±0.49	1.08±0.31	0.587

Table-III: Safety Data of Diabetic Females (n=30)

Variables	Baseline (Meain±SD)	Treatment with MI (Meain±SD)
ALT (IU/L)	22.87 ± 20	22.16 ± 20.44*
AST (IU/L)	12.97 ± 13.03	12.50 ± 10.69?
Nausea, vomit	--	None
Flatus	--	None
Diarrhea	--	None
Insomnia	--	None
Headache	--	None
Dizziness	--	None

p value 0.764*, 0.790* non-significant differences between baseline and treatment with MI

DISCUSSION:

In this study significant difference has been observed after the treatment of PCOS in patients over a period of three months. Several earlier studies have evaluated the effect of MI for 1-12 months at dosage range 4-30 g/day in polycystic syndrome[5,6,10]. These results corroborate with our findings revealing significant difference in fasting blood sugar and HbAIC. In our study elevated RDW was observed in diabetic patients as compare to healthy persons (p= 0.035) showing the presence of anisocytosis which is associated with the damage of erythropoiesis and degeneration of erythrocytes breakage or aggregation[11,12]. This takes place in presence of severe swelling and elevated level of oxidative stress[13]. Hyperglycemia has diverse effect on RBCs, in addition to the formation of glycated Hb, it alleviates deformability, alterations in mechanical traits of RBCs, enhanced adhesion and excessive osmotic fragility, causing changes in erythrocyte structure and hemodynamic traits[4,7,11].

Our results reported here are in accord with those of other studies conducted elsewhere 12. Very high correlation observed between RDW and BMI. A low grade inflammatory process in the white adipose tissues is the cause of obesity, so its association with RDW is sensible[12]. In the present study non-existence of a good correlation between HBA1c and MPV confirm with the results reported by Arivarasan et al[12]. Likewise, Nanda et al did not find any association between HBA1c and MPV, patient age, length of time of diabetes or blood pressure 31. This confirms our report and others[13]. In accordance with Kodiatte et al we observed negligible difference in MPV in patients having HbA1c $\leq$ 7% or > 7% and there was little association with BMI[14].

Earlier studies indicated that MI dosage 4mg/day has no side effects whereas dosage above 12-30mg/day had some side effects i.e diarrhea, nausea, abdominal pain and flatus[15,16].

CONCLUSION:

In diabetic PCOS subjects, HbA1c and fasting blood glucose level was significantly decreased when treated with MI for three months. MI dosage 2g/twice a day indicated no side effect e.g liver function, nausea, loos stool, diarrhea and flatus.

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