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“Clinical Study on A *Unani* Formulation in Management of *Ziabetes Shakari* (Diabetes Mellitus Type 2).”

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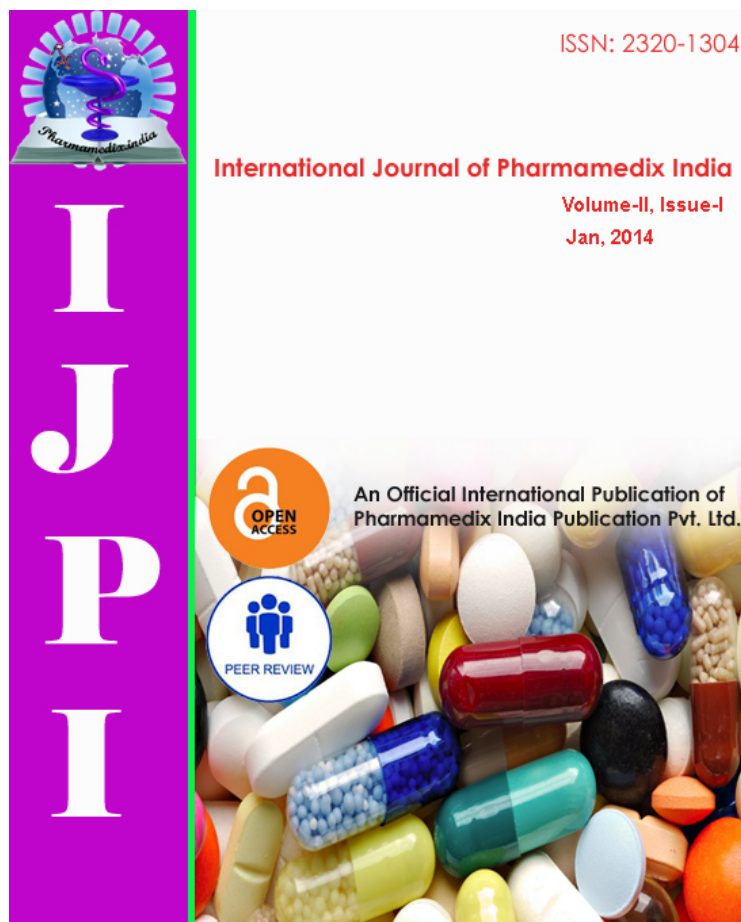
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Abstract:

A randomized single blind standard controlled study was designed to evaluate the efficacy of a *Unani* formulation, in the treatment of diabetes mellitus type 2 (DMT2). Forty diagnosed patient of DMT2 randomly allocated to Group A (Test) and Group B (Control) comprising 20 patient each. Group A was given test drug in the dose of 3 gm twice daily where as patients of Group B were given Diabecon 2 tablet orally twice daily for 45 days. The study reveals that the test drug exhibited significant effect on subjective parameters like polyuria and progressive weakness ($p < 0.05$), in polydipsia and unexplained weight loss ($p < 0.01$), and in tiredness ($p < 0.001$); while there was no effect in polyphagia ($p > 0.05$). On objective parameters there was significant effect observed on urine sugar ($p < 0.01$) and HbA_{1c} ($p < 0.05$), while there was no significant effect found on FBS and PPBS ($p > 0.05$).

Keyword: HbA_{1c}; Mizaj; Quwate Masika; Sue Mizaj; Ziabetus Shakari;

Introduction

The word Diabetes has been derived from Greek word “*Diabanmo*” Which means “passing through” or “to run through” or “Siphon” because of excessive urination. The disease is characterized by excessive thirst, excessive urination, presence of sugar in urine, increased appetite, gradual loss of body weight etc. (Sina, n.d) (Khan, 1983). *Arab Atibba* mentioned Diabetes with the name *Ziabetus*, as a disease of kidneys. They had described *Ziabetus* by some other terms like *Moattasha*, *Atsha*, *Intesae Anmas*, *Zalaul kulliya*, *Dolab*, *Dawwarah*, *Barkar*, *Barkarya*, *Qaramees* etc. (Sina, n.d) (Majoosi, 1889) (Zohar, 1986). Buqrat (Hippocrates 460 BC)

mentioned a disease with excessive urinary flow and wasting of body. (Singh M., Kumar N., Sood S., Makkar B. & Arora V., 2010). Jalinoos (Galen 131-201 AD) defined diabetes as “*Diarrhoea Urinosa*” (diarrhoea of urine) and “*dipsakos*” (thirsty disease). He described it as a disease specific to kidneys because of weakness in their retentive ability. Ibne Sina (Ave Sina 980-1037 AD), who termed the disease “*aldulab*” (water wheel) and “*zalqul Kulliya*” (diarrhea of the kidneys) also described the complications as mental troubles, impotence, gangrene, and furunculosis. Ibne Sina was first who wrote differentiating feature of *Ziabetus* associated

with emaciation form other causes of polyuria. (Singh M., Kumar N., Sood S., Makkar B. & Arora V., 2010) (Sanders, 2005) (Qarshi, 2011).

According to the presence or absence of sugar in the urine, *Ziabetus* is divided into two types: *Ziabetus Sada* (Diabetes insipidus), which is also called *Ziabetus gair shakari*. (Qarshi, 2011). It is characterized by excessive thirst and excessive urination but there is no sugar in the urine. *Ziabetus Shakari* (DM), which is characterized by excessive thirst and urination and presence of sugar in the urine. In this disease patient has excessive thirst and takes plenty of water and passes all the water he consumed without any metabolic change. (Razi, 2002)

According to the *khiffat* and *shiddat* (intensity) of the sign and symptom it is also divided into two types: (Qarshi, 2011) (Khan, 2006)

Ziabetus Haar: Acute symptoms of the *Ziabetus* with abrupt onset occur like excessive thirst (polydipsia) and increase urination (polyuria) with other symptom and sign of *sue mizaj haar* like heat in flanks and dryness of the body, due to *sue mizaj haar sada* of kidneys.

Ziabetus Barid: In which the thirst and frequency of urine is comparatively less.

In this disease *Mizaj* of kidneys disturbed so they absorb water from blood and send to the urinary bladder immediately due to weakness in *Quwate Masika* (retentive power). It has

also been described that the kidneys attract the watery substance of blood, but the urinary bladder does not attract any thing. So kidneys attract the water from the circulation, liver, stomach and intestine because of which patient has the immoderate thirst (polydipsia). (Jurjani, 1996) (Majoosi, 1889) (Razi, 2002)

The American Diabetes Association classification scheme for DM is summarized and clinical diabetes is divided into four general subclasses: type 1, primarily caused by autoimmune pancreatic β cells destruction and characterized by absolute insulin deficiency; type 2, characterized by insulin resistance and relative insulin deficiency; other specific types of diabetes associated with identifiable clinical conditions or syndromes; and gestational diabetes mellitus. (Goldman & Dennis, 2003). In addition to these clinical categories, two forms of pre-diabetes impaired glucose tolerance and impaired fasting glucose have been defined.

The prevalence of diabetes is rapidly rising all over the globe at an alarming rate. (Huizinga & Rothman, 2006). It is estimated that 20% of global burden of DM resides in South East Asia Region, is likely to triple by 2025 increasing from present estimates of about 30 million to 80 million. (Park, 2009). The International Diabetes Federation estimates the total number of diabetic subjects to be around 40.9 million in India and this is further set to rise to 69.9 million by the year 2025. (Sicree, Shaw & Zimmet, 2006). If the

prevalence of DMT2 continues to increase at the current rate, the global burden of this disease will swell between 2000 to 2030 from 171 million to 366 million patients (Wild, Rogli, Green, Sicree & King, 2004). DM leads to complications like blindness, renal failure, coronary artery disease, gangrene and coma.

The lifestyle management measures may be insufficient or patient compliance difficult, rendering conventional drug therapies necessary in many patients. These drugs should have a similar degree of efficacy without the troublesome side effects associated with these treatments. *Unani* medicines are used which are obtained mainly from plants, play important role in the management of DM, therefore a randomized single blind with standard controlled study was conducted for the purpose. The formulation consisting of *Satte Gilo* (*Tinospora cardifolia*), *Tabasheer* (*Bambusa bambos*) and *Maghze Kanwal Gatta* (*Nelumbo nucifera*) was selected as a test drug. (Firozuddin, 2009). The test group was treated with the *Unani* formulation in dose of 3 gram, whereas control group was given Diabecon 2 tablet twice a day. Total duration of study was formed of 45 days. All the patients were kept on dietary control and advised 30-40 minutes brisk walk daily. The efficacy of the test drug was compared with the standard drug Diabecon.

Methodology:

The clinical protocol was set and approved by the institutional ethical committee and written consent was taken from the patients. This study was conducted at National Institute of Unani Medicine (NIUM) Bangalore, stretched from February 2011 to January 2012.

A) Inclusion criteria: Patients of DMT2 having FBS >126mg/dl, PPBS >200mg/dl and HbA_{1c} >7% were recruited.

B) Exclusion Criteria: 1) Patients below 35 and above 65 years of age. 2) Diabetes mellitus Type 1. 3) Gestational Diabetes. 4) Malnutrition related DMT2. 5) All the complication of DMT2; Diabetic ketoacidosis, retinopathy, neuropathy, nephropathy. 6) Coronary artery disease. 7) Advanced liver, kidney, pulmonary diseases. 8) Pregnancy and lactation. 9) Patients who fail to follow up. 10) Patients who fail to give written consent.

Forty patients were randomly allocated by using simple randomization method into two groups comprising 20 patients in each of Test and Control group respectively. Some investigations were done in each and every case before and after the treatment like HbA_{1c}, Hb%, TLC, DLC, Urine routine and microscopy, AST, ALT, Blood Urea, Serum Creatinine, Serum Uric Acid and ECG. Other investigations were done on each and every follow up as: 0 day, 15th day, 30th day and 45th day like FBS, PPBS and Urine sugar. Assessment of the patients was carried out on

0 day, 15th day, 30th day and 45th day. After 45 days treatment, the value of every follow up of FBS, PPBS and urine sugar and pre and post value of HbA_{1c} were analyzed both in test and control groups. Four patients from Test group and 5 patients from Control group were lost the follow-up, leaving behind dropouts 16 patients in Test and 15 patients in Control group completed the course of treatment. Statistical analysis was done on 31 patients who completed the course of treatment.

Results:

The maximum number of patients, 16 (52.63%) were observed in age group of 35-45 years. The highest incidence of 20 (64.5%) was observed in male patients. As far as the family history of diabetes is concerned, 48.4% patients had positive family history. A maximum of 22 (71%) patients were found having *Balghami mizaj* (phlegmatic temperament).

The median scores of all subjective parameters in test group were compared statistically by using Friedman test for intra-group comparisons, showed significant deference on some subjective parameters like polyuria ($p<0.05$), polydipsia ($p<0.05$), tiredness ($p<0.001$), progressive weakness ($p<0.05$) and unexplained weight loss ($p<0.01$); while there was no effect on polyphagia ($p>0.05$) at 45th day compared with baseline.

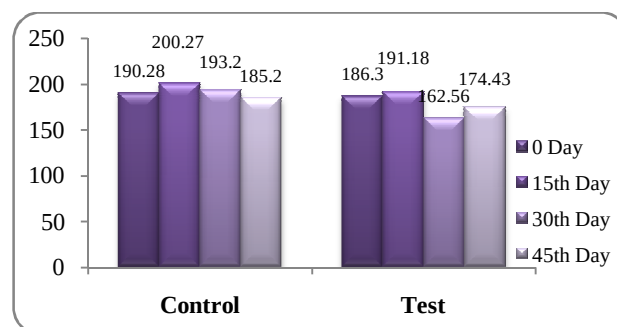


Figure No. 1: Effect of drugs on FBS

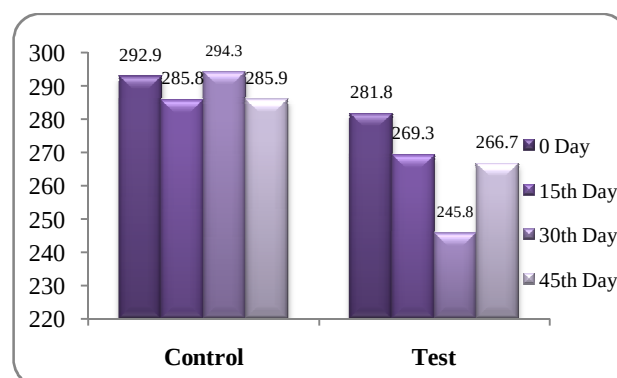


Figure No. 2: Effect of drugs on PPBS

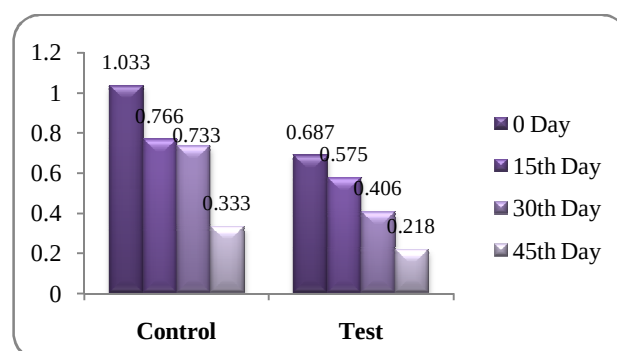


Figure No. 3: Effect of drugs on Urine Sugar

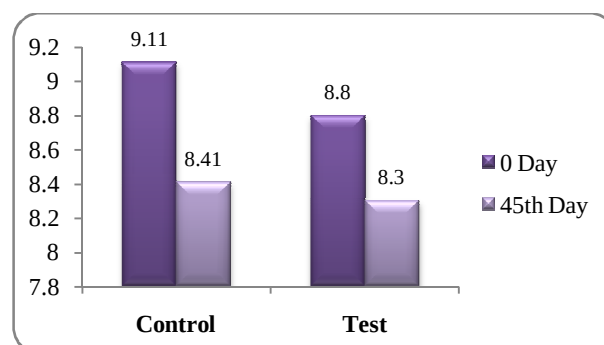


Figure No. 4: Effect of drugs on HbA_{1c}

Table 1 – Effect of the therapy on objective parameters in group A, N=16

Parameters	0 Day	15 th Day	30 th Day	45 th Day
FBS	186.31±12.14	191.18±19.86	162.56±12.32	174.43±14.92
PPBS	281.8±19.11	269.3±20.82	245.8±15.53	266.7±18.23
Urine Sugar	0.687±0.18	0.575±0.19	0.406±0.18	0.218±0.10
HbA _{1c}	8.818±0.25	#	#	8.3±0.28

HbA_{1c} done on 0 day and 45th day only

Table 2 – Effect of the therapy on objective parameters in group B, N=15

Parameters	0 Day	15 th Day	30 th Day	45 th Day
FBS	190.28±13.27	200.27±19.569	193.2±123.88	185.2±15.23
PPBS	292.9±10.65	285.8±25.08	294.3±25.98	285.9±21.45
Urine Sugar	1.033±0.22	0.766±0.23	0.733±0.22	0.333±0.15
HbA _{1c}	9.11±0.35	#	#	8.41±0.30

HbA_{1c} done on 0 day and 45th day only

The Mean±SEM score of objective parameters were compared. When Mean±SEM score of FBS in both Groups, Test and Control, were compared statistically by using Friedman test for intra-group comparison and Kruskal-Wallis test for inter-group comparison there was no significant difference ($p>0.05$) found in Test and Control groups at 45th day with comparison to baseline (Fig No. 1). When Mean±SEM score of PPBS in both Groups, Test and Control, were compared statistically by using Repeated measures ANOVA in Control group and Friedman test in Test group for intra-group comparison and Kruskal-Wallis test for inter-group comparison, there was no significant difference ($p>0.05$) found in Test and Control groups at 45th day with comparison to baseline (Fig No. 2). When the Mean±SEM score of urine sugar in both groups were

compared statistically by using Friedman test for intra-group comparison and Kruskal-Wallis test for inter-group comparison, the difference between the mean scores of Control group at 45th day with baseline was significant ($p<0.05$), while in Test group on 45th day compared with baseline was very significant ($p<0.01$). Inter-group comparison was also not significant at 45th day ($p>0.05$) (Fig No. 3). When Mean±SEM score of HbA_{1c} in both Groups, Test and Control, were compared statistically by using Wilcoxon matched pair test for intra-group comparison and Kruskal-Wallis test for inter-group comparison the difference between the Mean±SEM score of Test and Control groups at 45th day compared with baseline was significant ($p<0.05$) (Fig No. 4).

Discussion:

The patients treated with *Unani* formulation and Control drug both showed statistically significant difference on some subjective parameters like polyuria, polydipsia, tiredness, progressive weakness and unexplained weight loss; while there was no effect on polyphagia. The objective parameters were also assessed and analyzed in both groups. There was no significant difference ($p>0.05$) in FBS and PPBS but significant difference ($p<0.05$) was observed on Urine Sugar in both groups. The significant difference ($p<0.05$) was observed in HbA_{1c} in both groups equally, it means that both test and control drug maintain average glycaemia round the clock in diabetics. HbA_{1c} provide mean value of blood glucose level and useful index of average glycaemia over the preceding 6–8 weeks, considered most effective method for monitoring the effectiveness of diabetes treatment. The safety markers i.e. Haemogram, AST, ALT, Blood Urea, Serum Creatinine and ECG remained within normal limit during the study. On the basis of observations and results it can be understood that the test drug is effective in reducing the symptoms of *Ziabetus Shakari* (DMT2), and control the Urine Sugar and reduce the HbA_{1c} levels. Further, no obnoxious side effect was observed in Test group during and after the study and overall compliance to the treatment was good. The study also revealed that the disease is more

prevalent in *Balghami mizaj* patients, which may open the new window in the management of DMT2 because knowing the temperament of the disease and individual will give a way to the understanding and management of the disease especially in the *Unani* system of medicine.

The patients of establish diabetes, who are not taking any pharmacological treatment and not following control diet and regular exercise, almost always develop hyperglycemia and its complication after few days or months. In this study we observed that the treatments which were given in Test group and Control group both managed the blood sugar level and reduced it upto some extent and prevents further hyperglycemia. So we can conclude that the test drug have antidiabetic effect. It is supported by several experimental studies, demonstrating the hypoglycemic activity of *Gilo*. (Sivakumar & Dhana, 2011) (Stanely, Prince & Menon, 2000) (Stanely, Prince, Menon & Gunasekaran, 1999) (Dinesh, Vaneeta, Sunil & Kumar, 2011). Further more *Kanwal Gatta* have antioxidative property. (Wang, Yen, Liang & Wu 2003). DM is characterized by oxidative stress, which in turn determines endothelial dysfunction. It has been reported that anti-oxidative property of the drug potentially protects the vasculature through improvements in plasma lipid levels and platelet function. (Sena, Louro, Matafome, Nunes, Monteiro & Seica, 2009)

Conclusion:

The study revealed that the test drug exhibits good response on most of subjective parameters such as polyuria, polydipsia, tiredness, progressive weakness and unexplained weight loss; and on objective parameters such as urine sugar, and HbA_{1c}. Furthermore, no adverse effect was observed and safety parameters remained within normal limits in both groups. Therefore, it may be concluded that the test drug formulation is safe and effective in relieving the symptoms and maintaining glycaemic index in the patient of DMT2 and can be used for the management. However, long term study on larger population is required to elicit hidden potential and other pharmacological action of Test drug.

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