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**Effect of Naturopathy on *Control of Glycemia, Insulin and Adiponectin Levels in A Randomized Control Trial in Type 2 Diabetes Mellitus Patients***

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**ABSTRACT**

**Objectives:** *Present study of randomized control trial was aimed to evaluate the effect of four months of naturopathy treatment on patients suffering from Type 2 diabetes.*

**Design:** *Randomized control trial was carried out in a total of 121 patients having Type 2 diabetes (T2D) Mellitus disease for more than ten years and fulfilling diagnostic criteria as laid down by American Diabetes Association (ADA). Control group included 61 patients taking allopathic medication. Intervention group included 60 patients taking naturopathy treatment along with allopathic medication.*

**Intervention:** *Naturopathy treatments included mudpack to abdomen, spinal cord and abdomen massage and cold hip bath. The total intervention period in study was 4 months.*

**Results:** *Parameters recorded were weight, Body Mass Index (BMI), glycaemic status (blood glucose), hormonal status (adiponectin and insulin), insulin resistance and beta cell function.*

*T- test for paired data shows that naturopathy treatment modalities resulted in a significant decrease in body weight ( $p < 0.001$ ), Body Mass Index (BMI) ( $p < 0.001$ ), blood sugar levels in Fasting ( $p < 0.001$ ), PP ( $p < 0.01$ ) in comparison to the control group. Adiponectin was significantly improved at 4<sup>th</sup> month in intervention group as compared to its baseline levels i.e. paired group ( $p < 0.001$ ). In paired control group, Insulin level increased ( $p < 0.05$ ) and insulin resistance also increased ( $p < 0.01$ ). On the other hand, in paired intervention group undergoing naturopathy, insulin level decreased ( $p < 0.05$ ) and insulin resistance also decreased significantly ( $p < 0.05$ ).*

**Conclusion:** *The study shows that naturopathy helped in control of diabetes not only by decreasing blood sugar levels and insulin resistance but also helped in increasing the levels*

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*of adiponectin which may have resulted in stimulation of glucose utilization and its uptake. Results suggest that mudpack to abdomen, abdominal and spinal massage and hip bath therapy can be considered as effective adjunct treatment modality along with allopathy medicines for T2D patients.*

**Key words-** *Type 2 Diabetes (T2D), Fasting blood glucose (FBG), Post Prandial (PP), Naturopathy, Adiponectin, insulin*

## **INTRODUCTION**

Prevalence of Type 2 diabetes (T2D) is surfacing globally at an alarming rate<sup>1</sup>. Central obesity and physical inactivity observed in the majority of patients with T2D is associated with insulin resistance, mainly at the level of adipose tissue, liver and skeletal muscle<sup>2,3</sup>. T2D is strongly associated with both micro vascular and macro vascular complications, including retinopathy, nephropathy, neuropathy, ischemic heart disease, and cerebro - vascular diseases resulting in organ and tissue damage, approximately in one third to half of people suffering from diabetes<sup>4</sup>. The number of people with T2D is estimated to double by 2030<sup>5</sup>. In India, an estimated 7.8% of the population above 18 years of age have raised blood glucose level or are on treatment for diabetes<sup>6</sup>. In developing countries like India, economic development coupled with increased consumption of high calorie diet, decreased physical activity and increased stressful situation contribute to the development and progression of diabetes.

Naturopathy modalities like massage, hydrotherapy, mud therapy, fasting etc. are found to be useful in decrease of abdominal obesity<sup>7</sup>. Also, as there is an important link between abdominal obesity and insulin resistance, so a person sticking to Naturopathy treatments may control the disease and its associated complications. Therefore, this proposed study of treatment of T2D through Naturopathy modalities may help to re-establish homeostasis resulting in normal integrity and functioning of cells and organs.

In this study, it was hypothesized that Naturopathy treatment if given to T2D patient may help to improve glucose tolerance, reduce insulin resistance by reducing weight and improving Insulin and Adiponectin levels.

## **METHOD**

**Trial design-** The study was a randomized control trial carried out in T2D patients at Babu Nature Cure Hospital and Yogashram (BNCH&Y). Institutional Ethical committee of BNCHY accorded ethical clearance for the study. The subjects were randomly divided into two groups, Control group, in which patients were given allopathy medicine and Intervention group, in which patients were subjected to Naturopathy treatment modalities in addition to allopathy medicines. Total duration of treatment was 4 months. Blood samples were taken at the start of treatment and after 4 months in both the groups. Prior written consent was obtained from participating subjects.

**Eligibility criteria:** Patients of either sex having age between 30-60 years, having T2D Mellitus disease for more than ten years, fulfilling diagnostic criteria as laid down by American Diabetes Association (ADA) for T2D (HbA1c 6.5%, FPG 126 mg/dl and Random Plasma Glucose  $\geq$  200 mg/dl), were enrolled for the study.

**Exclusion criteria:** Poorly controlled T2D patients on Insulin therapy or patients having past history of severe cardiac/hepatic/renal/pulmonary dysfunction/Obesity grade III/Thyroid disorder/malignancy were excluded from study.

### **STOPPING RULES FOR DISCONTINUING PATIENTS FROM STUDY**

Patients not co-operating with trial.

#### **Naturopathy treatments and its duration:**

The total intervention period of study was 4 months. Naturopathy treatments included mudpack to abdomen, massage to spinal cord and abdomen and cold hip bath were given to patients. During the first month patients were given treatment five times a week, second month thrice a week, third month twice a week and fourth month once a week.

Mud pack-Clay pack devoid of any contamination having thickness of about 1 inch was applied over the abdominal region on empty stomach for a period of 20 minutes. The size of this pack varied from patient to patient as per their abdominal circumference.

Abdominal and spinal massage therapy: Massage using til oil was given to the patients for 10 minutes each on abdomen and spinal area.

Cold Hip bath: Cold hip bath (summer: 22°C, winter: 30°C) was given to the patients for 20 minutes. On the days when patients were not given therapies in the hospital, they were advised to practice the same at their homes.

**Allopathic medicines:** Allopathic treatments were provided to both the groups. The prescribed medicines were Metformin, Glimiperide, Glibenclamide and Pioglitazone. The doses were advised in consultation with physician at the end of every month.

#### **Parameters studied**

Parameters investigated were weight, Body Mass Index (BMI), Fasting and PP plasma glucose, Adiponectin and Insulin concentration in serum. Based on the above observations, Insulin resistance and Beta cell function were calculated. The above parameters were assessed at beginning and at the end of 4<sup>th</sup> month of study.

Glucose levels were estimated using standard Roche kit on C-501 fully Auto Analyser (Roche Make). Adiponectin concentration was evaluated using the Bio Vendor Human Adiponectin kit using ELISA technique. Insulin concentration was estimated by Chemiluminescence Immunoassay (CLIA) using Roche kit. Homeostatic Model Assessment (HOMA) was used for calculation of  $\beta$ -cell function and insulin resistance from fasting glucose and insulin concentrations. The relationship between glucose and insulin in the fasting state reflects the balance between hepatic glucose output and insulin secretion.

HOMA - Insulin Resistance (HOMA-IR) =

Fasting plasma insulin  $\times$  Fasting Plasma Glucose /405

HOMA -% beta cell function (HOMA- $\beta$ ) =

$360 \times$  Fasting Plasma Insulin / Fasting Plasma Glucose -63

Insulin is calculated in mU/L and glucose in mg/dl

**Statistical methods-** Data collected during the study period was analyzed using SPSS 20.0 and STATA. The statistical significant was considered at  $p < 0.05$  levels for all the parameters and the values were expressed as mean  $\pm$  SD.

## RESULTS

The period of study was for 2 years i.e. 18-03-2015 to 17-02-2017. The study was conducted in the following three phases: -

**PHASE-I** Pre-trial preparation March, 2015 to April, 2015 (1<sup>st</sup> & 2<sup>nd</sup> month)-During this period staff was recruited and was imparted specialized training so as to meet the study requirements.

**PHASE –II** Patient recruitment & Intervention therapy May, 2015 to August, 2016 (3<sup>rd</sup>-18<sup>th</sup> month). During this period of study, patients were recruited and were given intervention therapies per study design. Patients were recruited in various batches and the first batch was recruited at the start of 3<sup>rd</sup> month of study and recruitment continued till 14<sup>th</sup> month. Each patient was given treatment for a period of 4 months. A total of 140 diabetic patients were recruited. Out of which 19 patients opted out of the study. Remaining 121 patients were divided in 2 groups i.e. Group I consisting of 61 patients (male,  $n=34$ , female,  $n=27$ ) received only Allopathic Medicine. Group II was intervention group. It consisted of 60 patients (male,  $n=30$ , female,  $n=30$ ) and received naturopathy and allopathy medicines simultaneously.

**PHASE-III** -Analysis of data and preparation of report September, 2016 to February, 2017 (19<sup>th</sup> to 24<sup>th</sup> month) - After completion of Phase II of study, data collected during the study was analysed.

TABLE1: Effect of Naturopathy on Weight and Body Mass Index of Type 2 Diabetic patients.

Parameter	Group	Baseline result	4 <sup>th</sup> month result	P value(paired data)
Weight(Kg)	Control	67.87 $\pm$ 12.35	67.89 $\pm$ 11.85	0.947
	Intervention	74.78 $\pm$ 13.74	73.53 $\pm$ 14.17	0.000***
	P value(unpaired data)	0.004**	0.019*	
BMI (Kg/m <sup>2</sup> )	Control	26.93 $\pm$ 5.08	26.92 $\pm$ 4.76	0.975
	Intervention	29.23 $\pm$ 4.51	28.76 $\pm$ 4.73	0.000***
	P value(unpaired data)	0.009**	0.035*	

TABLE 2: Effect of Naturopathy on plasma glucose levels (F, PP) in Type 2 Diabetic patients.

Parameter	Group	Baseline result	4 <sup>th</sup> month result	P value(paired data)
Blood Glucose F (mg %)	Control	139.82±49.34	155.39±48.82	0.065
	Intervention	149.95±42.27	132.82±29.48	0.006**
	P value(unpaired data)	0.228	0.003**	
Blood Glucose PP (mg %)	Control	232.54±52.48	233.54±67.23	1.000
	Intervention	239.37±59.34	204.73±50.29	0.000***
	P value(unpaired data)	0.504	0.009**	

TABLE 3: Effect of Naturopathy on Hormonal status in Type 2 Diabetic patients.

Parameter	Group	Baseline result	4 <sup>th</sup> month result	P value(paired data)
Adiponectin (µg/ml)	Control	7.76±5.33	8.18±6.68	0.504
	Intervention	6.6±4.96	9.37±7.19	0.001**
	P value(unpaired data)	0.219	0.350	
Insulin(mIU/L)	Control	11.7±6.27	13.68±7.67	0.028*
	Intervention	13.08±6.31	11.76±4.93	0.027*
	P value(unpaired data)	0.229	-1.637	
Insulin resistance (HOMA-IR)	Control	1.68±0.88	2.07±1.19	0.007**
	Intervention	1.99±1.00	1.73±0.75	0.022*
	P value(unpaired data)	0.079	0.063	
Beta Cell function (HOMAβ%)	Control	69.25±54.9	58.57±40.19	0.126
	Intervention	57.12±45.48	64.00±34.99	0.184
	P value(unpaired data)	0.189	0.430	

\*(p<0.05), \*\* (p<0.01) and \*\*\* (p<0.001)

For weight and BMI (Table 1), Paired t test mean comparison for control group showed that there was no significant change in weight after 4 months but in case of intervention group a significant decrease in weight from its baseline value was observed ( $p=0.001$ ). However, difference in weight and BMI between both groups at 0 month ( $p<0.01$ ) and 4 months ( $p<0.05$ ) was statistically significant showing that whatever difference in weight was there at the start of treatment, the same existed after 4 months also.

In glycaemic status (Table 2), Fasting Blood Glucose was significantly reduced ( $p < 0.01$ ) at 4<sup>th</sup> month in intervention group as compared to control group (unpaired) and also as compared to the base line levels of intervention group (Paired group). Post prandial blood glucose was also found to be statistically reduced ( $p < 0.001$ ) at 4<sup>th</sup> month in intervention group as compared to control group (unpaired) ( $P<0.01$ ) and also as compared to the base line levels of intervention group (Paired group) ( $P<0.001$ ).

In case of glycated Haemoglobin there was no significant improvement as compared to control group (unpaired data) but as compared to the baseline levels of intervention group (Paired data), the level was significantly reduced ( $P<0.001$ ).

Adiponectin levels in paired data (Table 3) were significantly increased at 4<sup>th</sup> month in intervention group as compared to the baseline levels ( $p < 0.001$ ) but no significant change was observed in unpaired group i.e. as compared to control group.

Paired data for control group showed that insulin level (Table 3), increased ( $p< 0.05$ ) and insulin resistance also increased ( $p< 0.01$ ) after 4 months. On the other hand, in paired data for intervention group insulin level decreased ( $p< 0.05$ ) and insulin resistance also decreased ( $p< 0.05$ ).

Paired and unpaired group t- test mean comparison for control group and intervention group showed non-significant changes in beta cell function (Table 3).

## **DISCUSSION**

In our study, naturopathy treatments given to T2D patients consisted of mud therapy, massage therapy and hydrotherapy for a period of four months. Mud therapy has various therapeutic properties which are highly useful in the treatment of various diseases<sup>8</sup>. The intent of mud therapy was to improve blood circulation in the abdominal and pelvic regions so as to remove heat and congestion, absorb toxic substances, and tone up the tissues and organs which enhances the functional capacity of body<sup>9-11</sup>. Cold Hip bath excites contraction of the muscular structures of viscera and thus helps to stimulate the functions of abdominal and pelvic organs including pancreas, liver and bladder and it also decreases tissue blood flow by causing vasoconstriction, thus reduces tissue metabolism, inflammation and muscle spasm<sup>12</sup>. Massage therapy is beneficial in increasing the circulatory activities of muscle, lymphatic and nervous system which helps in expelling the impurities through sweat or urine<sup>13</sup>. It reduces the tension in muscles and gives relaxation by reducing stress. The stress reducing effect of massage might be attributed to control of counter regulatory stress hormones permitting the body to use insulin more effectively<sup>14</sup>. Diabetic patients were given above mentioned therapies of naturopathy because of their expected stress reducing outcome and consequential better glycaemic control.

The hypothesis of our study was to arrest diabetes by reduction in weight so as to up regulate insulin receptors, stimulation of abdominal organs so as to decrease insulin resistance and to stimulate adipose tissue, an important source of adipocytokine, having insulin sensitizing properties.

In intervention group, after treatment a significant decrease in weight and BMI was observed as compared to its own baseline level, whereas comparison between control and intervention groups was found to be as significant as at the beginning and so holds no value. This highlights the fact that paired group comparison (where group of patients receiving intervention therapy are acting as their own control) is far more important than comparison with a control group. The increased prevalence of T2D is strongly related to the modern global lifestyle i.e. over nutrition, changes in the food environment and a sedentary lifestyle, which has resulted in increased rate of overweight individuals and obesity<sup>15</sup>. It is also estimated that for every 1 kg increase in body weight there is a 4.5% higher risk of developing T2D<sup>16</sup>.

In our study, FBG and PPBG decreased significantly in intervention group as compared to control group and as well to its own baseline levels. Levels of glycated Hb were significantly reduced in intervention paired group. Also, insulin level and insulin resistance increased in paired control group whereas it decreased significantly in paired intervention group. This shows that control group maintained the same levels of F and PP as before their participation in the study. This is expected as most patients are assumed to be already on allopathy medicines before taking part in the study. However, in control group insulin and insulin resistance showed a significant increase. Naturopathy on the other hand helped diabetic patients in better glycaemic control. These effects might have been possibly through reduction in weight and improvement of BMI by different types of naturopathy treatments. Literature report also show that both obesity and physical inactivity underlie the development of insulin resistance observed in approximately 90% of patients with T2D and in 66% of individuals with impaired glucose tolerance (IGT). Insulin resistance together with  $\beta$ -cell dysfunction and apoptosis are the two fundamental mechanisms for the development of T2D<sup>3,17</sup>. Elevated body weight along with associated increase in FBG, PPBG, blood pressure and lipid profile are the major characteristics of metabolic syndrome<sup>18</sup>. On the other hand, weight reduction along with improvement in insulin sensitivity is often accompanied by favourable modifications in components of metabolic syndrome and elevated levels of insulin have been reported to contribute to its pathogenesis of metabolic syndrome<sup>19</sup>. Weight gain has been reported to be one of the most common side effects of insulin<sup>14</sup>. In our study also weight reduction, improvement of Glycaemic status, reduction in insulin and insulin resistance has been observed. By administering naturopathy treatments, body may be losing fat resulting in more number of receptors in muscle and adipose tissue due to reduction in weight. A literature report also emphasizes the need for therapeutic strategies in order to achieve weight reduction in obese patients with T2D<sup>20</sup>

Besides measuring glycaemic status and insulin levels we estimated Adiponectin levels also. In the last decade, adipose tissue was recognized as an active endocrine organ that can affect the function of other organs as it is an important source of several hormones: cytokines, chemokines, growth factors and complement proteins called ‘adipokines’ or ‘adipocytokines’. Adiponectin has anti-atherogenic, anti-inflammatory and insulin sensitizing properties<sup>21</sup>. It is involved in the homeostatic control of circulating glucose and lipid

levels<sup>22</sup> and is linked to cardiovascular disease, T2D and obesity<sup>23-24</sup>.

Our results shows significantly increased Adiponectin levels after intervention therapy as compared to its own baseline levels. As per our knowledge this is study of its own kind where effect of naturopathy on Adiponectin has been carried out. Numerous reports<sup>25-27</sup>, confirm plasma Adiponectin levels to be inversely related to insulin resistance. In a study effects of exercise intervention were seen on Adiponectin levels in overweight males and it was observed that the short-term exercise training increased circulating Adiponectin levels with accompanied improved insulin sensitivity<sup>28</sup>.

In our study, we have observed that with reduction in weight, levels of Adiponectin have increased. Literature report also shows that Weight loss increases Adiponectin levels<sup>29</sup>. Similarly, Plasma Adiponectin levels are decreased in obesity. This is because fat accumulation in obesity results in an altered expression of several hormones, growth factors, and adipokines<sup>30</sup>. High Adiponectin levels are associated with reduced risk for T2D<sup>31</sup>. Low plasma Adiponectin concentration is an independent risk predictor for development of insulin resistance and T2D mellitus<sup>32</sup>. Experimental studies have shown that Adiponectin facilitates glucose uptake, through increase in glucose transport 4 expressions and its translocation, stimulates glucose utilization, fatty acid oxidation and suppresses gluconeogenesis in skeletal muscle and in liver<sup>33</sup>. In metabolic syndrome the Adiponectin, which enhances insulin sensitivity is reduced, and serum lipids are increased<sup>(18)</sup>. Methods to improve Adiponectin levels include lifestyle modification, medical therapy and gastric reduction surgery<sup>21</sup>. Yoga has been reported to improve Adiponectin, serum lipids and metabolic syndrome risk factors which helps to reduce insulin resistance and its associated conditions<sup>34,35</sup>. Naturopathy, in our study resulted in improved Adiponectin activity which might be the reason for decreased insulin resistance. Weight loss as found in our study may have resulted in raised levels of Adiponectin which further are found to be inversely related to low insulin resistance and improved glycaemia.

Results of one case report<sup>36</sup> showed that in a patient receiving integrative naturopathy and yoga therapies (INYT) for three weeks showed better reduction in all variables along with reduction in insulin intake. Changes in lifestyle and some drug treatments have shown significant effect to increase Adiponectin levels, and simultaneously decrease in insulin resistance and endothelial dysfunction<sup>37</sup>. Our study having larger number of patients receiving naturopathy for a longer duration of four months has also validated the earlier findings where life style improvement had resulted in better glycaemic control. This study will be helpful in understanding that ultimately altered lifestyle due to modernization, westernization is becoming more responsible for the generation of diabetes as compared to genetic predisposition. Naturopathy regime so developed if adopted by T2D patients can result in better control of the diabetes which is slowly becoming an epidemic

**Trial limitations-** There is need to conduct scientifically larger clinical trials so as to evaluate the effectiveness of naturopathic care for this prevalent health problem of T2D patient.

## CONCLUSION

It is concluded that naturopathy not only helped in control of diabetes by decreasing weight, FBG, insulin resistance but also increased levels of Adiponectin which stimulates glucose



utilization and uptake. This study helped us to develop a natural regime for the treatment and management of diabetes. So, naturopathy therapies may be helpful for controlling diabetic conditions and reversing to normal physical and mental health with the prevention of disability, morbidity and mortality due to epidemic of T2D.

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