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CLINICAL STUDY TO EVALUATE THE EFFICACY AND SAFETY OF HFDM01 TABLETS IN DIABETES MELLITUS AND RELATED SYMPTOMS: A CLINICAL OUTCOME BASED EVIDENCE

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ABSTRACT

Diabetes Mellitus is a metabolic condition, to be precise. It has to do with the precise process through which Bets cells in the pancreas produce insulin. Glucose is released throughout the digestive process as a result of meal absorption in the intestine. Insulin facilitates the entry of glucose into body cells as a source of energy. According to Ayurveda, this is due to a Kapha imbalance, which causes Kapha to accumulate and spread throughout the body's tissues. All the contents of HFDM01 help in balancing this Kapha as well as The Earth matter i.e. Prithvi Mahabhoot by its Tikta, Katu and Kashay Rasa. Rukha Guna helps in absorption of excess Parthivtva from Mootra. During the trial, no adverse effects were reported by any of the patients. The patients' adherence to the drug was excellent, implying a high level of tolerability and, most likely, a favorable safety profile over the course of the study. Patients demanded the study medicine long after the experiment ended since it provided them with symptomatic alleviation. However, the results of the biochemical study show no substantial improvement in blood sugar levels or HbA1C. In consideration of the study's overall findings, we believe that this formulation should be investigated further for its therapeutic effects employing cutting-edge approaches.

KEYWORDS: Diabetes, Kapha, Ayurved, HbA1c.

INTRODUCTION

In the definition of term 'Swasthya' in Ayurved, utmost importance has always been given to the healthy state of mind. This aspect of Ayurved is widely accepted by the whole world. However, stressful lifestyle and faulty food habits have resulted into an increasing number of mortality and morbidity across the globe.[1] Globally, as of 2010, an estimated 285 million people had diabetes, with type 2 making up about 90% of the cases. In 2013, according to International Diabetes Federation, an estimated 381 million people had diabetes. Its prevalence is increasing rapidly, and by 2030, this number is estimated to almost double. Diabetes mellitus occurs throughout the world, but is more common (especially type 2) in the more developed countries. The greatest increase in prevalence is, however, expected to occur in Asia and Africa, where most patients will probably be found by 2030. The increase in incidence in developing countries follows the trend of urbanization and lifestyle changes, perhaps most importantly a "Western-style" diet.

Diabetes has emerged as a major healthcare problem in India. It is estimated that every fifth diabetic person will be an Indian.[2] Due to these sheer numbers, the economic burden due to diabetes in India is amongst the highest in the world. Due to the anthropometric, genetic and biochemical peculiarities, Indian population is one of the most vulnerable groups for metabolic disorders, including type 2 diabetes mellitus. The pathology of T2DM progresses through a reversible "window-of- opportunity" where there is a significant possibility of reverting back to normal glucose metabolism. More than 80 % of Diabetic deaths occur in low and middle income countries. Thus Diabetes has a devastating effect from human, social and economic standpoint. It is chronic in nature leading to long term complications in cardiovascular, neurological, ocular, renal and psychological death.[3]

Unfortunately for now there appears no concrete solution to the reversal of such a dreadful silent killer that to maintain the blood sugars through modern medicine. On the contrary, the role of Ayurveda in its purest form can provide a better solution to this problem through Panchakarma, Lifestyle modulations and Herbal supplementation. This role of Ayurveda treatments remains underexplored. To manage the overall effects of increasing blood glucose, maintain the glycemic control and prevention of diabetic complications can be one of the possible areas for Ayurveda medicines to look for.

The present study is hence focused to explore the possible adjuvant beneficial effect of HFDM01 tablet in the cases of T2DM.

AIM

To evaluate the efficacy and safety of HFDM01 tablet in patients suffering from Type 2 Diabetes Mellitus.

Formulation

HFDM01 consist of ingredients such as Neem (*Azadiracta Indica*), Chiraita (*Swertia Chiraita*), Gudmar (Ext) (*Gymnema Silvestre*), Karela (Ext) (*Momordica Charantia*), Methi (*Trigonella Foenum/Graecum*), Dalchini (*Cinamomum Zeylanicum*), Jamun Beej (*Syzigium Cumini*), Saptarangi Ext. (*Salacia Oblonga*).

OBJECTIVES

The primary goal of the study is to evaluate the efficacy of HFDM01 tablet adjuvant treatment in patients with T2DM using efficacy variables at 90 days of treatment to see if clinical symptomatology has improved or not together with any change in glycosylated hemoglobin.

MATERIALS AND METHODS

It is an open label, non-comparative safety and efficacy trial.

Sample size

An adequate number of patients of either sex will be screened so that a total of 30 patients will complete the study. This being an exploratory trial, the sample size is just to get statistically significant results and not intended to represent the population.

Inclusion criteria

Known diabetic subjects having a fasting blood sugar level of more than 126 mg/dl and patients willing to comply with research procedures and conditions are eligible to participate in the trial.

Exclusion Criteria

The subjects should not present any of the severe cardiac, renal and hepatic disease, the study did not involve pregnant or lactating woman. Patients who participated in any clinical study within 30 days before enrolment into the study were not selected.

Site of the study

The study has been conducted at Vishwanand Kendra – Center for Integrative Medicine and Research 101, Pramod Vihar, Walvekar Nagar, Pune Satara Road, Pune 411009.

Study Medication

The medication used in the Study is Tab HFDM01 –500 mg tablets which is manufactured by Siddhayu Ayurveda Research Foundation, Nagpur.

Treatment schedule

It is adviced to patients to take 1 Tablet one hour before meals with water twice daily for a period of 3 months.

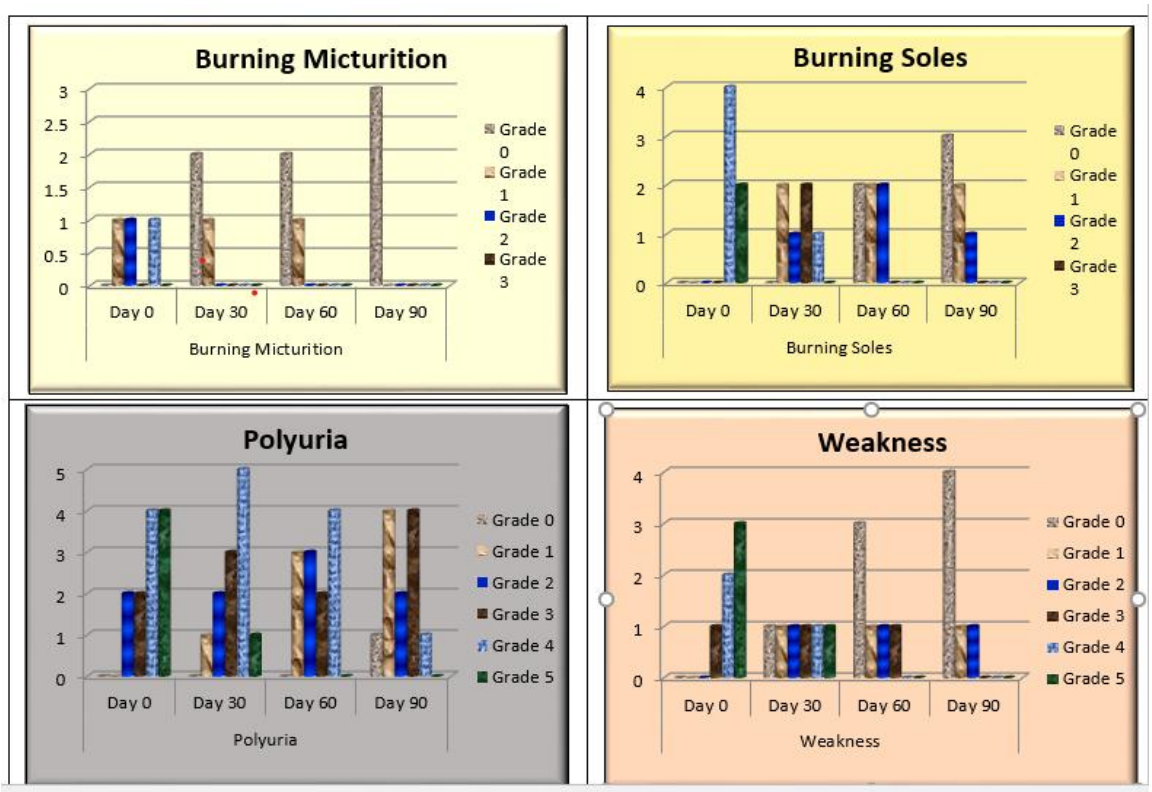
Clinical Assessment

The patients are clinically assess during every visit i.e Day 0, 30, 60 and 90.

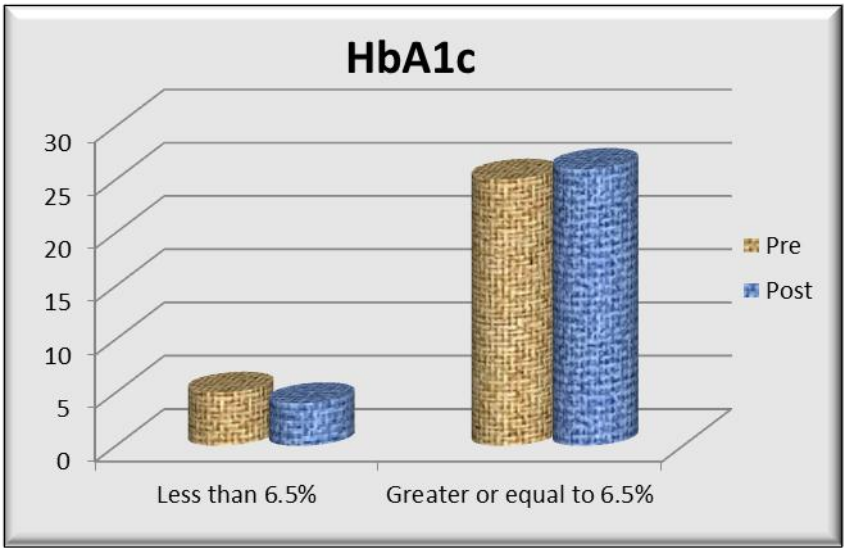
RESULTS AND DISCUSSION

The word Diabetes, originally a Latin word, means 'a passer through' which in turn was used with the intend of meaning 'excessive discharge of urine' as the name of disease. In Ayurved it is described as, 'प्रकर्षेण मेहति इति मेह'|: When the urine of Diabetic had been observed sweet in taste, the latin word 'mellitus' was added to the word Diabetes, which means sweetness. The earliest description of Diabetes is found in Atharv Veda from 1500 to 1000 BC and is known as 'Madhumeha' – 'madhu' meaning 'sweet' and 'meha' meaning 'excessive urination'. Diabetes Mellitus occurs throughout the world but is more common in more developed countries due to urbanization and lifestyle changes including a 'western style diet'. The greatest increase in rates is expected to occur in Asia and Africa. As of 2013, 382 million people have Diabetes worldwide. Type II makes up about 90 % of the cases. This is equal to 8.3% of the adult population with equal rates in both men and women. The patient symptoms at the start of the treatment and at the time of follow up visits were noted. They were graded as per the patient verbatim. The patients were asked to rate their symptoms at day 0 and at every follow up visits. Change in the gradation of symptoms here serves as a measure of efficacy of the formulation.

The frequency distribution of groups according symptoms of the patients. (Fig 1) & (Fig 2)



(Fig 1)



(Fig 2)

There are considerable variations in follow up readings on an average if factors Burning Micturition (Score), Burning soles, Polyuria, Weakness and HbA1 care considered. Following are the ingredients of the formulation. Following are the possible actions which are studied before may contribute to their potential role in managing diabetes and related symptoms.

Neem (*Azadiracta indica*)

The nutrients located in Neem's bark and seed oil are valuable; the most beneficial part of the tree comes from its leaves. It works as Antihyperglycemic by increasing peripheral utilization of Glucose. Neem helps to control high blood glucose levels by stimulating insulin production in the Beta cells. It helps the pancreas to distribute sugar throughout the body to provide energy. The Neem leaf can improve poor circulation by making it easier for blood to travel through your system.[4]

Chiraita (*Swertia chiraita*)

The plant contains glycoside chiratin which yields on hydrolysis. The ophitic acid in the plant is hydroscopic substance which is useful to absorb excess accumulated Kapha and in turn excess sugar in the blood and urine of Diabetic patients. It corrects nutrition disorders thereby helps in proper breakdown of glucose in digestion process. The herb is used widely to stimulate the appetite of people suffering from anorexia and other such problems. It helps in relieving acidity, nausea and biliousness. It has blood purifying properties.[5]

Gudmar (*Gymnema sylvestre*)

The literal translation of "Gudmar" plant name is "sugar killer" or "destroyer of sugar" as it neutralizes the excess sugar present in the body. It accelerates the function of insulin-secreting beta cells in the pancreas and also helpful in regeneration of beta cells therefore blood sugar level returns to the normal. It increases the activity of enzymes responsible for glucose uptake and utilization. It is helpful in correcting metabolic liver dysfunction. The key component of Gudmar leaves is gymnemic acid, which helps in neutralizing the excess sugar present in the body in diabetes mellitus by promoting repair or regeneration of the residual beta cells in the islets of Langerhans, thus body is triggered to produce its own insulin. It also activates pancreas to increase the quantity of insulin secretion so that extra glucose gets converted into glycogen and assists in the production of insulin in Type 2 diabetes. It inhibits the absorption of glucose from intestine and increases the activities of enzymes responsible for utilization of glucose by insulin-dependent pathways.[6]

Karela (*Momordia charantia*)

It is known to be highly beneficial for diabetics due to its two very essential compounds called charatin and momordicin. It is also filled with anti-oxidants that helps the body fight off the associated complications commonly seen in diabetics by removing free radicals from body. The seeds of the plant are packed with plant insulin called Polypeptide-P whose action

is similar to that of insulin in reduction of blood glucose level. It creates hypoglycemic effect after its consumption. It decreases plasma cholesterol and triglycerides. It improves glucose utilization in tissues and also glucose regulation by enhancing liver function.[7]

Methi (*Trigonella foenum-graceum*)

The seeds of this plant contain an alkaloid trigonelline and another compound known as choline. Seeds are high in soluble fiber, which helps lower blood sugar by slowing down digestion and absorption of carbohydrates. It works as hypoglycemic agent by reducing insulin resistance of body cells and tissues. Therefore, glucose utilization of tissues is improved. It reduces harmful proteins associated with renal injury.[8]

Dalchini (*Cinnamomum zeylanicum*)

It activates insulin receptors for transportation of the glucose from blood circulation into the body cells. It regulates carbohydrate metabolism by stimulating the action of an enzyme that plays a key role in lowering blood glucose levels. It acts as a potent vasodilator that helps in reducing the risk associated with cardiovascular diseases which is a common condition normally seen in diabetics. It helps in significant reduction in LDL and VLDL components of cholesterol. It plays antioxidant role by reducing accumulation of advanced glycation end products.[9]

Jamun Beeja (*Eugenia jumbolana*)

This fruit is of low glycemic index which keeps blood sugar level under check as well as cures common diabetes symptoms and complications like excess thirst, urination and etc. Its seeds contain Glucoside, Jamboline and Ellagic acid which have the ability to check the conversion of starch into sugar in case of excess production of glucose. It increases level of pancreatic insulin with protective and restorative effect on Beta cells of pancreas.[10]

Saptarangi (*Salacia oblonga*)

It contains Glucosidase inhibitors – Salacinol and Kotalanol 9. It binds to intestinal enzymes that break down carbohydrates in the body. These enzymes turn carbohydrates into glucose. If the enzyme binds to the herbal extract rather than to a carbohydrate, then less glucose gets into the blood stream, resulting in lowered blood glucose and insulin levels. Lowering blood glucose levels lowers the risk of disease related complications in people with diabetes.[11]

CONCLUSION

Diabetes Mellitus is precisely a metabolic disorder. It involves the specific mechanism of production of insulin by Bets cells of Pancreas. Intestinal absorption of food leads to release of Glucose during digestion process. Insulin helps this glucose to enter into the body cells as a source of energy. Reduction in production of specific amount of Insulin by Bets cells affects glucose transport. Also this metabolic procedure is relatively dependent on the physical as well as mental stress of an individual. This is the primary cause of onset of Diabetes. According to Ayurveda this is basically a Kapha imbalance leading to accumulation and dissemination of this Kapha through body tissues.

All the contents of this medicine help in balancing this Kapha as well as The Earth matter i.e. Prithvi Mahabhoot by its Tikta, Katu and Kashay Rasa. Rukha Guna helps in absorption of excess Parthivtva from Mootra.

These contents correct nutrition disorder which helps in proper digestion of glucose. They stimulate insulin production by Beta cells. Along with it these are helpful in repair and regeneration of beta cells in Islets oh Langerhans. It is also helpful in correcting metabolic liver dysfunction which regulates glucose transport.

Thus if the onset of Diabetes is mainly due to the improper metabolic digestion, the drug proves to be effective as compared to stress induced Diabetes.

There is significant difference in follow up readings on an average if factors Dribbling Micturition (Score), Burning soles, Acidity, Bowel Discomfort, Dryness in Eyes, Polyuria, Gases, Weakness, Headache, Giddiness are considered.

It was observed during the trial that none of the patients complained about any adverse reactions. The patients' compliance to the medication was very good suggesting a very good tolerability and probably a good safety profile during the study duration. The patients even after the trial continued demanding the study medication as it was giving them a symptomatically better relief. The data from the biochemical analysis however does not suggest any significant efficacy in the blood sugar levels and HbA1C. This conflict in the patient response and blood biochemistry suggest a probable another mode of action of the formulation. Based on the patient responses we can hypothesize that the formulation could be acting by reducing the variability in the blood sugar levels which is in fact a more beneficial

mode of action. Recent researches have shown that more variability in the blood glucose levels is one of the major causative factors for Diabetic complications like cardiovascular disorders, renal impairment etc.

However, in the present scope of study was unable to elucidate this mechanism. Considering the overall results of the study we suggest this formulation can be explored further for its beneficial effects using latest advanced techniques.

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