



INTEGRATIVE APPROACHES IN DIABETES MANAGEMENT

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ABSTRACT

Diabetes mellitus is one of the most important non-communicable, life-style, endocrine disorders of metabolic origin, which develop due to a reduced production of insulin or resistance to its effects leading to hyperglycaemia. According to International Diabetes Federation (IDF), the number of diabetic patients is expected to rise from 366 million in 2011 to 552 million by 2030. The Indian traditional systems of medicine include Ayurveda, Yoga and Naturopathy, Unani, Siddha and Homeopathy. The use of integrated approach with the traditional medicine and modern medicine should be considered to address the multiple challenges posed by diabetes. The integrative medicine approach that combines conventional and alternative therapies with an emphasis on natural, less invasive, evidence-based option is well suited for the management of diabetes. The integrative strategy involves self-management and life-style changes and it is a new term that emphasizes the combination of both conventional and alternative approaches to address the biological, psychological, social and spiritual aspects of health and illness. When considering alternative, integrating therapeutic approaches to diabetes, all the patients must recognize the importance of careful monitoring of blood glucose levels and potential side effects, as well as frequent communication with medical care team. In the present study, the integrative approach for the management of diabetes is discussed.

KEYWORDS: Diabetes, Ayurveda, Alternative medicine, Integrative therapy.

INTRODUCTION

Diabetes mellitus is one amongst the refractory disease conditions and Ayurvedic literatures vividly describe about the etiology, pathogenesis, prognosis, complications, its management and scientifically attributed the causal relationship of dietary, lifestyle, environmental and genetic factors. Despite the recent progression in medical science, several challenges still exist in the management of diabetes that requires special attention to develop unexplored fields of medical knowledge. Ayurveda offers comprehensive, safe and effective approaches to manage such conditions of diabetes ('Madhumeha'). Designing pertinent research model is a key challenge behind the examination of safety and efficacy of Ayurvedic interventions satisfying its fundamental principles and systems approach.^[1]

Integrative medicine is a new term that emphasizes the combination of both conventional and alternative approaches to address the biological, psychological, social and spiritual aspects of health and illness. It emphasizes respect for the human capacity for healing, the importance of the relationship between the physician and the patient, a collaborative approach to patient care

among practitioners, and the practice of conventional, complementary and alternative health care that is "evidence-based."

Diabetes Mellitus is a chronic disease in which the body does not produce or properly use insulin, which affects how the body is able to use glucose for energy. The burden of diabetes mellitus lies not only in the treatment of hyperglycaemia, but more so in the associated micro- and macrovascular complications that may lead to visual impairment, amputations and renal failure. Worldwide, the number of people with diabetes mellitus has increased from 153 million in 1980 to 347 million in 2008, and is projected to increase to 552 million by 2030.

In order for cells to use glucose for energy, insulin must be present. In people with diabetes, the pancreas either produces little or no insulin (type 1), or the cells do not respond appropriately to the insulin that is produced (type 2 and gestational diabetes). Regarding the pandemic state of diabetes mellitus and the recent number of afflicted people in the world, i.e., 422 million and 1.5 million deaths per year, attributed directly to

diabetes, an integrative approach was used to treat patients suffering from the condition.^[2]

The three main types of diabetes are:

- (a) Type 1, also known as juvenile diabetes
- (b) Type 2 diabetes
- (c) Gestational diabetes (occurs in pregnant women during the pregnancy, but resolves after delivery)

The high sugar level leads to complications such as blindness, kidney failure, circulatory problems, coronary heart disease, neuropathy etc. Diabetes is treated with insulin (always in type 1 and sometimes in type 2) by monitoring blood sugar levels and oral medication (type 2). Lifestyle changes are critical in diabetes management, and they are an expected part of a conventional medical care plan. It includes:

- (a) Healthy, low-fat, high-fiber, nutritious diet, minimizing simple and processed sugars
- (b) Exercise
- (c) Weight loss (if appropriate) or maintenance of a healthy weight

Patients with type-2 diabetes mellitus are increasingly interested in integrative medical strategies, most of which involve self-management and lifestyle changes.^[3]

Treatment of diabetes: Conventional approach

Type 2 diabetes mellitus (T2DM) is linked to obesity which drives insulin resistance and an inflammatory response and a prolonged insulin resistance puts an extreme amount of stress on the pancreas. When resistance is accompanied by dysfunction of the pancreatic islet β cells that is what ultimately leads to the disease.^[4]

Foods low on the glycemic index (GI) scale like sweet potatoes, winter squash, and beans help to stabilize blood glucose levels. The refined sugars and starches have a high GI and a very strong link to chronic disease. Clinical trials supported low GI diets and exhibited improved whole body insulin sensitivity throughout the trials with no increase in LDL cholesterol. The processed foods should be avoided and it is an important for preventing and managing diabetes.^[5]

Lifestyle modifications, nutritional planning, weight loss and diabetic education are some of the targets of diabetes treatment. However, despite efforts of diet and exercise many patients will require additional therapies. Metformin is the initial medication of choice if liver and kidney function remain stable. However, if the Haemoglobin A1C remains elevated after 3 months of therapy an additional agent may be selected. Use of Sulfonylureas, Meglitinides and Alpha-glucosidase inhibitors are less common as innovative medications such as Thiazolidinediones, DPP-IV inhibitors, GLP agonists and SGLT2 inhibitors are integrating to the market. If chronic medical conditions arise and prevent the use of certain medications, then insulin is more appropriate.

Integrative therapies for diabetes

When considering alternative integrating therapeutic approaches to diabetes, all the patients must recognize the importance of careful monitoring of blood glucose levels and potential side effects, as well as frequent communication with medical care team. The following therapies and healing practices can be used of managing type 1, and managing or eliminating type 2 diabetes (T2DM), optimizing function, and minimizing complications.

- (a) Nutrition and weight loss
- (b) Exercise
- (c) Vitamins and mineral supplements
- (d) Botanical medicines
- (e) Manual medicines
- (f) Chelation therapy
- (g) Mind/body practices

(a) Nutrition and weight loss

The patients with type 2 diabetes are advised not to take trans-fats and to limit saturated fat below 7% of total caloric intake to reduce cardiovascular disease risk factors. A moderate weight loss (5% of body weight) has been found to improve insulin action, decrease fasting blood glucose concentrations, and reduce the need for diabetes medications.^[6] It was found that there was 10% weight loss associated with a reduction in glycosylated haemoglobin (HbA1c)^[7] and weight maintenance is also an important element of diabetes management.

American Diabetes Association (ADA)^[8] suggested three types of diets for the patients with type 2 diabetes such as low glycemic index (GI) diet, a Mediterranean diet and a vegetarian diet and point out that the best diet for a particular patient is the one best suited to his or her lifestyle and dietary goals. The low glycemic index emphasizes carbohydrates and other foods with a low glycemic index, which results in a more gradual rise in glucose. It also showed a significant increase in high-density lipoprotein cholesterol (HDL) in low glycemic index diet. The Mediterranean diet which is rich in fruits, vegetables and unsaturated fats, fish and grains with a low glycemic index. It has a higher carbohydrate and fat content than a portion-controlled diet formerly recommended by the ADA. Mediterranean diet eliminates pro-inflammatory fats and restores healthy omega 3/omega 6 fatty acid balance. The vegetarian diet focuses on fruits and vegetables and foods low in saturated fat and it tends to be higher in fiber and lower in calories than other diets.^[9]

High levels of oxidative stress have been found in diabetic patients, increasing the need for antioxidant supplementation. More than 400 dietary supplements have been reported to have beneficial effects for patients with diabetes, including plant based products such as fenugreek, prickly pear, and ginseng; vitamins, and minerals. Chickpeas, beans, peas, and lentils have rich fiber content which has been shown to improve glycemic control. Gluten free diet delays or prevents the

development of T2DM due to the preservation of beta cells and vegan diets improve glycemic control. Cinnamon was found to help reduce blood sugar, LDL cholesterol and total cholesterol in people with type 2 diabetes. Omega-3 fatty acids, a type of “good” fat found in fish oil and flaxseed-oil supplements, may help reduce inflammation and insulin resistance in people with diabetes.^[10]

(b) Exercise

Regular exercise helps both weight reduction and glucose uptake and it is important in managing diabetes. Higher intensity activity did not improve glycemic control any more than moderate intensity exercise.^[11]

(c) Vitamins and mineral supplements

The diabetic patients at increased risk for deficiencies following very-low-calorie diets, the elderly and strict vegetarians may benefit from multi-vitamin and mineral supplements. Individuals with highest vitamin D levels have lower risk of developing diabetes.^[12] A fat-soluble antioxidant found in vegetable oil, nuts, and green leafy vegetables, vitamin E's best-studied component is alpha-tocopherol. Chromium is a trace mineral and thought to be a necessary cofactor for insulin regulation and glucose metabolism and aids glucose with transport into the cell. Chromium reduces HbA1c and fasting blood sugar levels and its deficiency induces hyperglycemia and impaired glucose tolerance. This element is present in many foods, especially brewer's yeast, liver, carrots, potatoes, broccoli and spinach. It also lowered glycosylated hemoglobin (HbA1c).^[13] Magnesium is involved in insulin secretion, binding and activity and a deficiency of magnesium is associated with decreased absorption in patients with diets high in processed food or increased elimination in those who ingest large quantities of alcohol or caffeine or take diuretics or birth control pills. Magnesium is involved with more than 300 enzymatic reactions and is vital to glucose metabolism and insulin homeostasis. Low serum and plasma levels of magnesium are associated with alterations in nerve, muscle, and cardiac conduction. This contributes to nephropathy and end stage renal disease. Increased dietary intake of magnesium improved metabolic control and reduced the risk of T2DM and dyslipidemia.^[5] Dietary sources of magnesium include whole grains, leafy green vegetables, legumes and nuts. Magnesium supplements lead to an improvement in fasting blood glucose, but did not significantly lower HbA1c in patients with type 2 diabetes.^[14] Alpha lipoic acid (ALA) is a strong antioxidant found in very small amounts in foods, has shown promise in the treatment of diabetic neuropathy. It improves glucose uptake and prevents glycosylation, a process in the body where sugars are inappropriately hooked onto proteins and fats. The essential fatty acids present in ALA can protect against the nerve and blood vessel damage from diabetes by increasing insulin secretion and lowering cholesterol levels.

The studies have found that ALA may reduce oxidative stress and improve insulin sensitivity in patients with diabetes. There was a significant decrease in fasting blood glucose and postprandial glucose after eight weeks of taking it.^[15]

(d) Botanical medicines

Numerous herbs have been recommended for the treatment of diabetes in traditional Indian medicine Ayurveda and traditional Chinese medicine and its antidiabetic effects have been reported by many researchers. These reports are confirmed by *in vitro* studies and *in vivo* models. The medicinal plants, particularly *Gymnema sylvestre*, *Momordica charantia* and *Trigonella foenum-graecum*, had clinical evidences for their antidiabetic effects. Therefore, it seems that physicians can rely on these herbs, at least as complementary therapeutics, along with current hypoglycemic drugs to improve management of diabetic patients.^[16] Vitamin C acts as strong antioxidant that improves insulin resistance and reduces free radical tissue damage. It is important for healthy immunity and wound healing. *Ginkgo biloba* also contains antioxidant compounds that stabilize beta cell membranes of the pancreas and help with peripheral circulation. Many classes of plants secondary metabolites such as alkaloids, terpenoids, phenolics, flavonoids and many others show promising antidiabetic potentials. These natural constituents may act as a promising source of delivering oral hypoglycemic effect with minimal side effect. Berberine, a compound found in golden seal, Oregon grape and barberry is effective as metformin and it reduce HbA1c, glucose and lipid levels.^[17]

Many diabetic patients in the U.S. and worldwide use complementary and alternative medicine (CAM) while receiving conventional medical therapy as a means of managing disease and improving quality of life. Herbal and natural products are the most commonly used forms of complementary and alternative medicine. Current findings suggest that CAM may help to promote an integrative, participatory model of diabetes care that relies upon provider knowledge of evidence-based therapies and patient disclosure of CAM use. Emerging evidence of positive findings with some natural products have been reported in glycemic parameters, markers of cardiovascular risk, and quality of life in individuals with type 2 diabetes.^[18]

(e) Manual medicines

There are evidences for using treatment modalities such as acupuncture, massage/energy therapy, acupressure and chiropractic and other forms, as an integrative approach for the treatment of diabetes and diabetic complications. These treatment modalities are collectively known as manual medicine. Although, acupuncture has long been reported to improve glycemic control in patients with diabetes and pre-diabetes, the evidence is limited and of poor quality. Randomized controlled trials have found that acupuncture reduced pain in patients with diabetic

peripheral neuropathy vs sham acupuncture or oral inositol.^[19] In a small 2-week randomized controlled trial, patients randomized to acupuncture vs sham acupuncture for diabetic bladder dysfunction. The study showed statistically significant improvements in both subjective symptoms and urodynamic measurements. A study comparing patients receiving electro-acupuncture in which an electric current is transmitted between two needles placed in the muscles—vs sham acupuncture found non-statistically significant improvements in symptomatic gastroparesis.^[20] Acupuncture has been shown to lower glucose levels, and has been demonstrated to improve peripheral neuropathy and neuropathic pain, one of the most common complications of type 2 diabetes.

In massage/energy therapy, massage has been shown in several studies to reduce glucose levels. Connective tissue reflex massage led to improved lower limb blood flow in patients with diabetes and peripheral artery disease in another study, but the clinical significance is uncertain. Studies of reflexology and acupressure are similarly limited to small experimental and observational studies.^[21]

(f) Chelation therapy

Trial to Assess Chelation Therapy (TACT) is one of the most promising advances for the treatment of diabetes. TACT was designed to determine if future cardiac events could be reduced for patients at least 50 years of age who had already suffered at least one heart attack and it reduced future cardiac events by lowering the death rate of diabetic patients who had a previous myocardial infarction. It was a randomized, double-blind, clinical trial of 1708 patients, who were given more than 55,000 intravenous treatments and half of the patients were given high dose vitamins. The benefit of EDTA chelation was shown to be statistically significant. All of the cardiac events (death, re-infarction, stroke, coronary artery revascularization, and hospitalization for severe angina) were less in the EDTA groups than in the groups that received IV placebos. The removal of toxic heavy metals such as lead, cadmium, arsenic and mercury is the major action of EDTA chelation. There was a significant improvement in diabetic control with the use of the iron chelator, desferoxamine, in diabetic patients who also had high ferritin levels.^[22]

(g) Mind/body practices

Chronic stress increases the release of glucose from the liver and decreases insulin receptor sensitivity, making insulin work less effectively. Stress management helps individuals more effectively regulate their diet and exercise, which are both important in managing diabetes. Yoga and Meditation, the Relaxation Response, Mindfulness-Based Stress Reduction (MBSR), and Biofeedback are just a few of the practices that have been used to manage stress, and have positive impacts on the diabetic patient. The other treatment modalities include Qigong.

Biofeedback is a mind-body relaxation therapy, in which the patient hooked up to electric sensors that monitor blood pressure, muscle tension, heart rate, brain waves and other physiological functions, was found to improve blood sugar when used in combination with standard diabetes treatment. It can produce clinically significant toe temperature elevations. In patients with type 2 diabetes, volitional warming has been associated with increased circulation, improvement or elimination of intermittent claudication pain, more rapid healing of diabetic ulcers, and improved functional status.^[23]

Yoga is likely to benefit patients with type 2 diabetes (T2DM) leading to lower blood sugar, LDL levels, triglycerides, body weight, waist-to hip ratio, HbA1c and higher HDL. Yoga appears to have a beneficial effect on the blood pressure, heart rate, oxidative stress, sympathetic activation, catecholamine levels, coronary stenosis, coagulation profiles, and pulmonary function of patients with T2DM, and is associated with reductions in the amount of medication needed and in psycho-social risk factors.^[24] The regular practice of transcendental meditation is associated with a reduction of catecholamine levels. A study examining the relationship between depression and diabetes found compelling evidence of an association between mental stress and hypothalamic pituitary- adrenal axis hyperactivity and another comparing mediators' with controls found the regular practice of TM to be associated with a reduction in catecholamine levels. As increased catecholamine levels affect glucose transport and insulin resistance, this finding suggests that reducing stress levels through meditation might lead to improved glycemic control.^[25]

Mechanistic explanations for yoga's mental and physical health benefits have highlighted reductions in sympathetic tone and increases in parasympathetic activity. Many “restorative” yoga practices claim to improve immune function and decrease inflammation.

The effectiveness of Qigong systems such as Tai Chi—which integrate physical postures, breathing techniques and focused attention is difficult to determine because of methodological challenges in design and variability in practice. A study of Qigong for T2DM reported some improvement in glucose control.^[26]

Ayurvedic Translational approach in diabetes

About hundreds of Ayurvedic herbs, different herbal preparations are used in Ayurveda against diabetes. The herbo-mineral preparations and mineral formulations have been practiced to manage ‘Madhumeha’ or diabetes for ages. There is a lack of clinical evidence to prove efficacy and safety. This has been hindered by a lack of appropriate methodology and approaches to evaluate and conduct research. Translational research in medicine is a two-way street and aims at breaking down barriers between clinical and basic medical sciences to promote rapid transfer of knowledge from bench to bedside and vice versa.^[27] Herbal drugs are emerging as viable

alternatives for complex disease states and modern scientific methodology are being adopted to validate the effects of such agents used in the traditional systems of medicine.

Recent bedside to bench effort elucidates the role of innate immunity in the response to environmental pathogens in clinical diabetes which in future may reveal new therapies and strategies to prevent type 1A diabetes.^[28] A two-pronged effort encompassing bedside to bench and reverse pharmacology should be initiated in Ayurvedic drug research to develop novel therapies in chronic ailments like diabetes. The first approach bedside to bench is mainly directed towards herbo-epidemiological observational studies and clinical trials of Ayurvedic drugs. Developments in human genomics like the concept of 'Prakriti' or Ayurgenomics which undertakes individualized drug therapy or personalized medicine is quite promising. This effort will maximize drug efficacy and minimize drug toxicity leading to the concept of pharmacogenomics in Ayurveda, which on "translation" into clinical practice may open up novel possibilities.

Translational research is the process of applying knowledge from basic science and clinical trials to techniques and tools that address critical medical needs. Unlike applied sciences, translational research is specifically designed to improve health outcomes and the research findings are moved from the researcher's bench to the patient's bedside and community. Principles of Ayurveda have been developed over time using evidence-based clinical observation and philosophical assumptions. Hence, there is a dire need of interdisciplinary integrative research to validate and translate that knowledge to a vibrant science. Diagnosis and treatment must correlate with systems biology concept. The recent "omics"-level knowledge should be incorporated in therapeutic regimen. Combinatorial therapy according to 'Prakriti' type is elucidated by Ayurgenomics. It should be carried on for further research. "Bedside to bench" approach in research may give us critical information.

It appears that the Ayurveda knowledge system is itself structured as a translational model - with *Tattva* (principles) translating to *Śāstra* (theoretical constructs) and *Śāstra* translating to *Vyavahāra* (practical applications). Thus the whole system is designed to translate knowledge into action that is of benefit to society- *lokānugrahapravṛttaḥ śāstravādaḥ*.^[29] In other words, the purpose of the Śāstra, especially in the context of medicine, is to improve quality of human life, and not to be confined within the limits of academic explorations. The three tier structure of the knowledge system of Ayurveda is aimed to ensure that academic insights get translated into practical application. Translational research involves the application of knowledge gained through basic research to studies that could support the development of new products. In

today's market based economy, the outcomes of translational research become tangible in the form of products.

Integrative approach by Predictive, Preventive and Personalized Medicine (PPPM) pave the way for the new strategies to advance pre/diabetes care.^[30] Predictive, Preventive and Personalized Medicine (PPPM) is the concept of an integrative medical approach based on a paradigm shift from reactive to preventive medicine. The rationale for PPPM relates to the recognition that (a) prediction of populations at risk for a disease (e.g., diabetes mellitus) should lead to prevention of its development and progression and (b) treatment/intervention strategies should be on the basis of individualized patient information profile. This integrated approach should provide the opportunity for a better approach to health promotion thereby reducing morbidity and mortality and associated costs.

Commonly Used Medicinal Plants for the treatment of Diabetes



Gymnema sylvestre R. Br.



Syzygium cumini (L.) Skeels.



Trigonella foenum-graecum L.



Momordica charantia L.



Allium sativum L.



Ginkgo biloba L.

CONCLUSION

Diabetes care requires a multidisciplinary approach via a coordinated effort to bring together the various support services in a timely and effective manner. Principles of Ayurveda have been developed overtime using evidence-based clinical observation and philosophical assumptions. Translational Ayurveda implements ideas of translational medicine, taking into account Ayurveda's unique health care principles and their application in patient care.

Hence, there is a need of interdisciplinary integrative research to validate and translate that knowledge to a vibrant science. Diagnosis and treatment must correlate with systems biology concept. The final goal of translational medicine is to help patients with a more rapid development of new diagnostics, medicinal products, and new medical knowledge for treating diseases, giving access to care for people at reasonable costs. The integrative medicine approach that combines conventional and alternative therapies with an emphasis

on natural, less invasive, evidence-based option is well suited for the management of diabetes.

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