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To Dispel Darkness of Diabetes

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HYDROXYCHLOROQUINE: OLD WINE IN A NEW BOTTLE & SAROGLITAZAR: NEW KID ON THE BLOCK

*** Shaival Chandalia**

Hydroxychloroquine (HYQ) is a medication which has been used for decades by rheumatologists in the treatment of rheumatoid and other arthritis. It was found that in these patients, the risk of developing diabetes reduced dramatically. Hence there has been a vast amount of scientific literature regarding the efficacy and safety of the drug when used over a period of years in a patient. Let us examine this in a little bit of detail.

Efficacy:

What is the purported mechanism by which this drug works? This drug works by inhibiting insulin degrading enzymes resulting in a rise in insulin levels and/or the insulin remaining in circulation for a longer time. There are other important effects as well. Type 2 diabetes is an inflammatory condition. Various cytokines like interleukins and tumour necrosis factor-alpha (TNF-α) are elevated in the blood of diabetic patients. It is thus postulated that due to intrinsic anti-inflammatory effects of hydroxychloroquine, this results in amelioration of the metabolic changes and blood glucose levels in type 2 diabetic patients.

The third and fourth mechanisms involve an improvement in insulin sensitivity and in animal models preservation of beta cell function and mass. Through these mechanisms, it appears that hydroxychloroquine is uniquely suited to treat the burden of type 2 diabetes patients in our country, especially if they are reluctant to start insulin.

Who are the types of patients who will be benefitted?

The type of patients who are benefitted are those who are taking one or two oral drug therapies. For example, it has been shown that if a patient is on a sulfonylurea or a combination of sulfonylurea and metformin and is not controlled, hydroxychloroquine added as a second or third drug can achieve a reduction in HbA1c. Thus the unique mechanism by which hydroxychloroquine works results in an additive effect with other oral agents. This is because it addresses a different set of pathophysiologies of type 2 diabetes. In addition to oral agents, this drug can also be added to insulin. It results in a 30% reduction in insulin requirements and/or achieves good glycemic control in a patient who is uncontrolled on insulin. Thus, to summarize, hydroxychloroquine can be used at any stage of type 2 diabetes, like adding it as a second or third oral agent or finally, adding in patients who are on insulin. Thus, it indicates that it is a very robust drug in terms of its efficacy at even later stages of type 2 diabetes, where our commonly used medications start to lose steam.

What long term positive effects are seen?

Hydrochloroquine has been shown to reduce cardiovascular outcomes in one study. This may be partly due to its anti-thrombotic and anti-inflammatory effect. Of course, this needs to be tested in a prospective randomized controlled clinical trial in order to categorically confirm the results. But the current evidence is reassuring in this regard.

What are the side effects of this drug?

A lot has been said about the main side effect of this drug i.e. retinopathy. Suffice to say that it is very rare, only one out of a thousand odd patients in a rheumatological series. Also it increases with large cumulative doses of the

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drug. At the doses recommended for type 2 diabetes, it will not be seen at all in the first five years. Hence, the drug can be used safely for 5-7 years without checking the fundus (retina) of the patient except at baseline. After 5 years, a yearly retina evaluation is mandatory and if there is any sign of retinopathy, the drug should be stopped. Also, in some one with pre-existing retinopathy, the drug should not be initiated.

To summarize, hydroxychloroquine is an inexpensive, safe drug for type 2 diabetes, which can be used as add on to oral agents or insulin at all stages of type 2 diabetes. Monitoring of retinopathy is required after the first five years of use.

SAROGLITAZAR

The new kid on the block is saroglitazar or Lipaglyn. An innovation of an Indian company, Zydus Cadila, it is a "saro" or (good in Gujarati) glitazar. Thus the molecule owes its name to the place from where it derives its origin.

What are the glitazars?

Glitazars are molecules which bind to PPAR alpha and gamma. PPAR (peroxisome proliferator-activated receptor) are nuclear transcription factors which regulate a wide variety of genes. In simple parlance, they switch on and off a number of genes, resulting in widespread metabolic effects. Saroglitazar is the only glitazar which is currently marketed anywhere in the world, as previous glitazars like muraglitazar fell afoul of the regulatory authorities due to unacceptable side effects. Saroglitazar, is a PPAR-alpha agonist with milder PPAR-gamma agonist action. PPAR-alpha is involved with regulation of lipid metabolism, while PPAR-gamma is involved with regulation of glucose metabolism. Hence the interest in modulating two PPAR elements.

Close cousins of Saroglitazar are pio and roziglitazone or the thiazolidinediones. They are principally PPAR-gamma agonists. Both have been approved for treatment of type 2 diabetes. They have excellent insulin sensitizing actions and are potent anti-hyperglycemic agents. Their use has dampened a little bit due to some of the side effects seen with the glitazones like weight gain and increased risk of heart failure and bone fractures. However, they remain part of the armamentarium of treatment of type 2 diabetes, especially helpful in reducing insulin resistance. On the other hand, sole PPAR-alpha agonists are molecules like fenofibrate that regulate triglycerides.

What are the main actions of Saroglitazar?

Saroglitazar is a PPAR alpha and weak PPAR-gamma agonist. Hence, it has an impact on lipid metabolism as well as glucose metabolism. Hence the indication for use of saroglitazar is dyslipidemia, especially hypertriglyceridemia in patients with type 2 diabetes not controlled on statin therapy. This is due to the PPAR-alpha action. A bonus effect is the PPAR-gamma effect which results in reduction in blood glucose levels. In fact when compared to pioglitazone as treatment for type 2 diabetes, it was non-inferior to pioglitazone in one study. However, it has not yet been approved for treatment of type 2 diabetes. One advantage of saroglitazar over pioglitazone is that weight gain, fluid retention and tendency for increased heart failure does not occur. Similarly, one advantage of saroglitazar over fenofibrate is that the risk of rhabdomylosis is not increased when combined with statin.

An unmet need in theraputics fraternity is the treatment of NASH. NASH or non-alcoholic steatohepatitis is now fuelling an epidemic of chronic liver disease or cirrhosis which is increasing in our country. There is some preliminary data that saroglitazar could be used as treatment of fatty liver and NASH to reduce inflammation and prevent progression to cirrhosis. This would be an exciting new development, much awaited in the field of hepatology if confirmed in an ongoing randomized controlled trial. Currently pioglitazone is used in treatment of NASH, although it's use is limited due to the weight gain seen with it.

Another fact which needs to be studied is the effect of saroglitazar on long term cardiovascular

outcomes. It remains to be proven whether saroglitazar added to a statin to treat diabetes and dyslipidemia, will offer any cardiac mortality or survival benefit. We need more data in this regard.

What are the side effects of saroglitazar?

Saroglitazar is surprisingly well tolerated. The weight gain that is seen with pioglitazone does not occur with saroglitazar. However, long term data is needed for better understanding of the utility and limitations of this drug.

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MANAGING RESISTANCE & NON-ADHERENCE OF PATIENTS IN TYPE 2 DIABETES: IMPORTANT ROLE OF EDUCATORS

* Meenakumari

Type 2 Diabetes Mellitus is a metabolic disorder which is non-communicable and it results in elevation of blood glucose, mostly associated with morbid conditions like high blood pressure, dyslipidaemia, obesity and synergistic interactions among the patient, family and health care team. It arises from less release of insulin hormone (insulin deficiency) which regulates blood glucose levels and also insulin which is available in the system is not efficiently used by the cells of the body (insulin resistance).

Unfortunately, often, its immediate complications are not well recognized and they go unnoticed leading to further complications in management of the patient's health. It is however most important and necessary to control the disease and prevent increase in complications. A broad based plan should be made in which the patient, his family and service provider are integral parts and play important roles for prevention and cure. This ensures better, continued, and uninterrupted use of prescribed drugs, and reduces non-compliance to treatment by the patient himself or herself. This approach prevents more complications. The medical personnel can be excellent educators for educating the patient with the best medical advice but due to shortage of time they are usually unable to study the requirements of each patient individually and then educate the patient on a one to one basis. A physician is usually engaged more in a regular examination of the patient and prescription of drugs, and the more time consuming process of education and building awareness of each individual patient may be required. Also real time observations of the conduct, behaviour and perceptions of each patient so as to provide tailor made solutions for each patient may not be possible due to paucity of time. Therefore, the role of an educator becomes necessary and he or she is required in such a way that he or she works in detail with the patient on one to one basis to educate the patient and make him aware and knowledgeable about the several parameters of disease management.

EDUCATOR PROGRAM FOR HEALTHCARE PROVIDER

This paper makes an effort to point out some of the most important and immediate and far reaching effects of the lack of an educator in the management of this disease, and highlighting the need of appropriate educator training of educator in addition to the medical personnel who are expected to prescribe the drugs for the patient. Expectedly, the educator would ensure that the patient does take the drugs prescription seriously and also follows the regimen prescribed by the physician, so that the prescribed drugs do produce successful results without any wastage of time, effort and money.

The administration of many drugs may need to be strictly enforced by educating the patient on various aspects of the prescribed medicines and regimen.There are also other issues which need to be addressed. They are monitoring of the changes in the health of the patient from time to time and response of the patient to the prescribed medicines. For example it is necessary to discuss, formulate and enforce a meal plan with active cooperation of the patient and caregiver. It is also pointed out that the educator has a duty and opportunity to observe the progress and plan and bring about any desired changes in the psycho-social behavior of the patient. It may not be possible to dwell on all the aspects of the educator program which may have an effect on

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the health and quality of life of the patient, but we will discuss some of them.

PSYCHOLOGICAL AND SOCIAL PRESSURES ON PATIENT

Also there are psychological and social pressures on the patient which affect compliance of the Diabetes education involves a combination of one or all of the following issues:

Modification of dietary practices, weight management, regular exercise, biochemical monitoring of the body fluids that is blood , urine etc., foot care, use of drugs, technical skills like blood sugar monitoring at home.

Diabetes mellitus is recognized as a lifestyle disorder and is known to be complex demanding strict discipline and regimen. Diabetes education can play a very important role in the management of this disease.

NON-ADHERENCE AND NON-COMPLIANCE BY PATIENT

It is very well known that noncompliance to the therapy is highly prevalent and has been linked to increase in morbidity, mortality, healthcare costs and also lower level of quality of life. Fortunately OPD management with readily available glucose lowering, BP lowering, cholesterol lowering medications can control the disease and also reduce the risk of complications. Along with medication, lifestyle modification, regular exercise, and diet control needs to be followed on a long term basis.

Non adherence to the therapy is common among patients suffering from chronic diseases. An individual's failure to use prescribed medication contributes to adverse clinical outcome and can increase hospital admissions, causing increase in cost of the treatment multiple times. This is in fact a huge burden to individuals/to society/ to the nation. Psychological issues are crucial in determining adherence to treatment.

NON-ADHERENCE DEFINITION AND SYMPTOMS

WHO has defined adherence as "the extent to which a person's behaviour – taking medication, following a diet and /or executing lifestyle changes, corresponds with agreed recommendations from a health care provider". Noncompliance/non-adherence has to be identified and addressed appropriately in entirety without prior assumptions.

Pattern of Non-adherence

Primary non-adherence: After consulting the Physician patient fails to buy the medication and does not start the treatment.

Non Persistence: Patient starts taking treatment but discontinues after the very first dispensation. This may be because he/she becomes symptom free, after starting medication. Noncompliance in this situation may be due to lack of awareness/ education.

MAJOR FACTORS LEADING TO NON-ADHERENCE

Patient's refusal to accept the disorder, fear about future, associated anxiety can lead to discontinuing the medication or switching to alternate medication.

Psycho-socio-economic factors: Anger is a common reaction to major changes in day to day routine. Majority consider this as a social stigma which prevent them from following dietary modifications in social gatherings. In today's era it is a disease of upper, middle and lower socio-economic strata hence affordability for the patient rests on their financial status and is also a cause of long term mental stress to individual as well as family. On many occasions lack of money compels the person to stop treatment.

Patient physician relationship: Physician treating a person with chronic disease should be empathetic to the patient. This will in turn ensure regular follow up, adherence to the treatment and consistency in the life style modification from time to time.

Therapy related factors (complex regimen) should be explained in detail and the prescription should be designed as easily understandable.

INTERVENTION TO ENSURE COMPLIANCE:

Systematic education/counselling by a professional diabetic educator:

Message based method can be adopted for literate and reliable patients. Regular follow up can be ensured by empathetic approach and building confidence among the beneficiaries by the health care team. Health education through regular awareness programs in small groups help to build confidence among patients and their family to manage the disease.

Shifting of doctors and shifting to alternate medicine can be prevented by better patient and health care team interactions. Majority believe in so-called natural treatments like drinking bitter gourd juice, Neem juice (bitter), Jamun juice, etc. These beliefs should be modified at individual level. Counselling regarding effects and adverse effects of treatment, unhealthy diet needs to be done during follow up visits. Unrealistic attitude towards the disease compels the patient to find multiple excuses to avoid medication/diet control/exercise. Such patients need systematic education, which is one of the most important components of Diabetes management. Any chronic disease necessitates empowerment of the diseased which is only possible through education.

EDUCATOR PROGRAM DESIGNED FOR COMPLIANCE:

Education programme has to be implemented at all clinics which manage chronic diseases.

Objective of education: A successful education program should break the initial barriers of denial and non-adherence and kindle interest in the mind of the target group. It should lend hope and dispel despair. The target should be able to understand the disease. The information so imparted should empower the patient and the care giver to undertake day-to-day self-management.

A successful behaviour change can improve control of disease management, long-term outcomes and quality of life. Any person in the healthcare system can become an educator by undergoing systematic training programs. Group interaction among patients can also improve compliance. One-to-one sessions are important as survival skills are better taught. Group sessions can be used for greater motivation, interaction and constructing conceptual frameworks.

CONTENT OF EDUCATION PROGRAM

One-to-one program of a newly detected diabetic should cover all aspects of disease management comprehensively. It consists of:

- Explaining the disease
- Diet and exercise; its importance as well as why to do it continuously
- Meal planning (tailor made).
- Explain the medication dose, pre/post meal and important side effects.
- Hypoglycaemia – cause, symptoms, detection and management
- Sick day routine: Nutrition and medication on sick day; when to meet health providers. Blood sugar monitoring at home by glucometer is an integral part of diabetes management to be taught by the educator.
- Day-to day care of foot; selection of footwear to be explained
- Insulin (when prescribed): selection of site of injections, rotation of sites, storage instructions, injection techniques, side effects including hypoglycaemia to be explained during each visit to improve compliance which in turn will improve “quality of life”.

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HYPO ADIPONECTIN LINKED TO OBESITY AND T2DM

*** Harsheen Chaudhary**

Adipose tissues located beneath the skin consists of adipocytes. Adipocyte filled with a droplet of triglyceride appear in a small group joined by a connective tissue which serves as a storage site for the body's energy reserves and is considered as an endocrine organ. Adipocytes secrete adipokines such as tumour necrosis factor -α, interleukins, plasminogen inhibitor type 1, leptin, resistin and adiponectin, they particularly function to control appetite, increase insulin sensitivity and in some cases promotes inflammation and atherogenesis.

Adipose tissue consists of white and brown adipose tissue. Brown adipose tissue primarily functions to transfer the energy from food into heat. While white adipose tissues (WAT) is the major energy storage site which stores energy in the form of triglycerides during nutritional abundance and releases FFA's during deprivation. WAT also secretes adipokines which affect the activity of insulin through changes in insulin sensitivity and modulating the action of insulin. Adiponectin produced in white and brown adipose tissue is a key modulator for insulin sensitivity and glucose tolerance. It functions to maintain a balance between energy and fat storage and accounts for 0.01% of the plasma protein. Its action is primarily to increase its concentration in the injured vessels and inhibit the activity of TNF-A and decrease its expression in macrophages.

Adiponectin structure:

Belonging to the complement factor C1q family it is a 244 amino acid. The cysteine residue situated at the amino-acid terminal is involved in disulphide bond formation. Adiponectin is determined by the APM1 gene in the 3q27 chromosome is indicated as the primary region for the occurrence of type 2 diabetes mellitus and metabolic syndrome.

FUNCTIONS OF ADIPONECTIN

The primary function of adiponectin is to signal that the body has the capacity to store fat. With the increase in energy expenditure, adiponectin enhances the expression of genes involved ß-oxidation of fatty acids. Furthermore, adiponectin is known to enhance the expression of insulin-stimulated tyrosine phosphorylation, insulin receptor, acetyl co-a carboxylase, glucose uptake, reduction in molecules of gluconeogenesis and insulin substrate, thereby, reducing the molecules involved in gluconeogenesis. A recent study conducted by Kadowaki T concluded that, with the administration of ACRP3 there is increased fatty acid oxidation in muscles with a reduction in hepatic glucose output resulting in decrease insulin resistance and further improvement in glucose metabolism in diabetic patients. Adiponectin is also found to decrease the action of adhesion molecule-1, endothelial cell adhesion molecule-1, E-selectin in endothelial cells and decreases the attachment of monocytes in TNF-α cells and increases the activity of anti-inflammatory cytokines.

* Dietician and CDE at Ayush Clinic

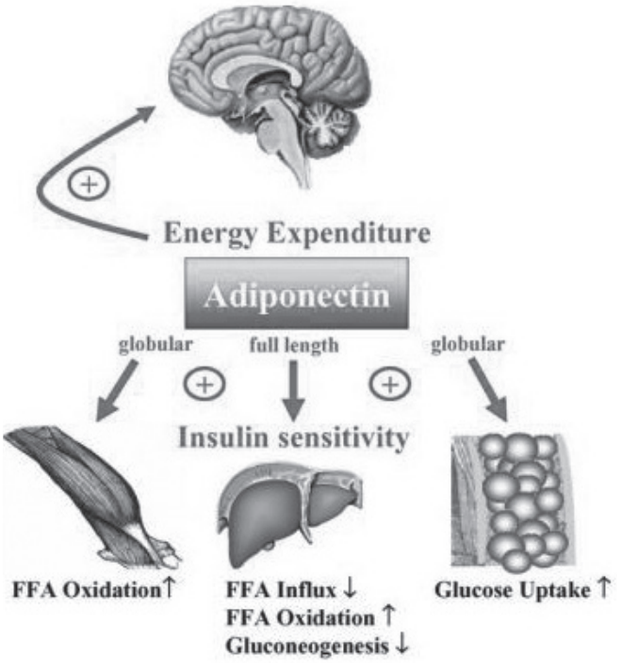

Figure 1: Functions of adiponectin in adipose tissue, liver and skeletal muscle.
(Fasshauer et al. 2004)

FACTORS INFLUENCING PLASMA ADIPONECTIN LEVELS:

Accretion of abdominal fat is an independent risk factor for the occurrence of insulin sensitivity and type 2 diabetes mellitus, it may also lead to a reduction in the adiponectin levels with increased oxidative stress in adipose tissue. Soy Protein, fish oils and linoleic acid have been found to increase plasma adiponectin levels. However, a carbohydrate-rich diet is also known to decrease plasma adiponectin levels.

Oxidative stress is also considered as one of the factors to decrease the action of adiponectin.

Females particularly, tend to have higher adiponectin levels as compared to the male counterpart.

Thus, the plasma adiponectin level is affected by multiple factors, including gender, ageing, and lifestyle.

ADIPONECTIN AND ENERGY METABOLISM

Adiponectin's major action is in skeletal muscle and liver. In muscle, through the AMPK pathway and PPAR-γ, the sensitivity to insulin is increased. In the liver, the activity of glucose transporters is increased with a further reduction in the expression of gluconeogenesis. The activity of fatty acid oxidation is also increased with a decrease in inflammation via PPAR- γ. It is often noted that the activity of AMPK pathway is directed by adiponectin, hence with a decrease in adiponectin, there would be an increased activity of gluconeogenesis and a decrease in glucose transporters.

In the liver, insulin sensitivity is enhanced by promoting phosphorylation of insulin receptor and IRS-1. In the pancreas, adiponectin increases the activity of cell proliferation by stimulating insulin secretion. In adipose tissues, the basal glucose uptake is increased with enhancement in insulin-stimulated glucose uptake through AMPK.

ADIPONECTIN AND OBESITY

Obesity is caused because of increased energy intake and decreased energy expenditure resulting in excessive fat accumulation. One of the major causes of the increase in the incidence of obesity is because of a change in the environment and social behaviour. Filippi E scrutinizes the association of plasma adiponectin levels and insulin sensitivity and found plasma adiponectin levels associated change in insulin sensitivity especially in obese patients and not lean patients.

Hypoadiponectinemia is an independent risk factor for the development of metabolic

syndrome. Mets characterized by increased CRP, inflammatory cytokines and abdominal adiposity. Low HMW (high-molecular weight adiponectin) can be one of the possibilities of developing the risk of MetS.

MECHANISM OF LOW ADIPONECTIN LEVELS AND INCREASED RISK OF DIABETES MELLITUS

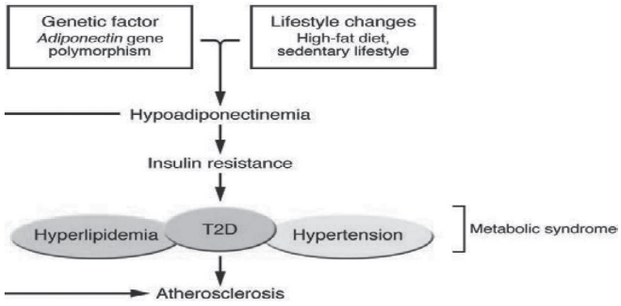

Figure 1: Hypothesis suggesting reduced adiponectin levels and increase the risk of type 2 diabetes, metabolic syndrome and atherosclerosis, (Kadowaki et al. 2006)

Genetic factors such as SNP 276 in the adiponectin gene and with external environmental conditions such as changes in lifestyle with a diet that is high in fat and reduced physical activity results in a decrease in the plasma adiponectin levels. Furthermore, reduced adiponectin levels may play a role in the development of atherosclerosis.

Asian Indians are particularly known to be susceptible to type 2 diabetes since they have, obesity phenotype characterized by lean BMI, central adiposity and high body fat percentage and increased insulin resistance.

ADIPONECTIN AND ADIPONECTIN RECEPTORS AS THERAPEUTIC TARGETS

It is noted that thiazolidinediones, increased adiponectin levels with a tremendous decrease in insulin resistance.

TZD MEDIATED INCREASED ACTIVITY OF ADIPONECTIN

One of the widely used drug for the treatment of diabetes. Its primary role is to increase insulin sensitivity by enhancing glucose disposal in the skeletal muscle and suppress the activity of gluconeogenesis in the liver. TZD particularly enhance adiponectin action, however, it also decreases insulin resistance through adiponectin independent pathways. It is observed that plasma adiponectin levels tend to rise with the administration of TZD. The mechanism for this is, TZD generates small adipocytes that express adiponectin, which enhance the activity of PPAR-γ and further increase the number of adipocytes, resulting in increased insulin sensitivity. Independently, TZD has known to decrease the size of adipocyte, serum FFA, expression of TNF-α and resistin, thus contributing to the amelioration of insulin resistance in skeletal muscle. Interestingly, even treatment of insulin-sensitive subjects with the TZD rosiglitazone for 2 weeks results in a 130% increase in adiponectin plasma levels.

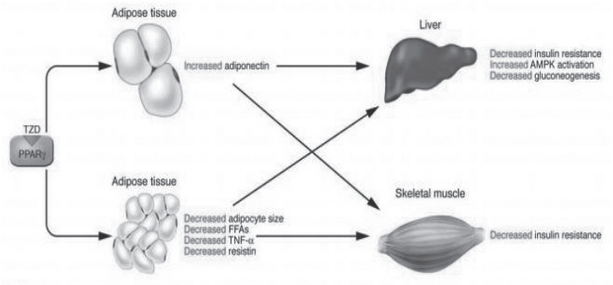

Figure 3: Action of therapeutic medicine in skeletal muscle and liver, (Kadowaki et al. 2006)

CONCLUSION

Adiponectin concentrations tend to decrease with an increase in visceral fat along with a

decrease in energy expenditure. However, it is suggested that exercise may help to augment the plasma adiponectin levels and reduce the risk hypo adiponectin associated obesity and type 2 diabetes mellitus.

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QUESTION AND ANSWERS

Q. What is the role of probiotics in diabetes?

We all know colon harbors the largest number of bacteria. These bacteria play multiple roles such as improving immune system, production of certain vitamins in the gut, preventing growth of pathogenic bacteria and maintaining acidic pH of the vagina. Research has shown that microbiome plays a vital role in vast array of diseases such as diarrhea, Crohn's disease and Ulcerative colitis. Most importantly, certain bacterial flora is associated with diabetes mellitus and metabolic syndrome.

Type 2 diabetes is known to be associated with inflammation and oxidative stress and increased incidence of dysbiosis. Alteration in intestinal microbiota is also attributed as one of the cause of diabetes as it can lead to increased intestinal permeability and mucosal immune response. Increase in intestinal permeability is the result of reduced expression of certain proteins which causes translocation of bacterial lipopolysaccharides (LPS) from the membrane of gram negative bacteria. The result is endotoxemia, inflammation, impaired glucose metabolism, insulin resistance, obesity and diabetes.

There are many reasons for dysbiosis in diabetics and obese patients. One such cause is highly processed diet like high SFA, reduction in oligosaccharides and phytochemicals. Diet plays a pivotal role in regulation of intestinal flora. Therefore, processed diet

Probiotics are now an important part of treatment of diabetes. According to WHO/FAO, probiotics are live microorganisms which when consumed in adequate amounts, will confer health benefits to the host. Lactic acid bacteria from genera Lactobacillus, Streptococcus, Enterococcus, genus Bifidobacterium, some yeast and E.coli are most common types of organisms which are proved to be probiotics. Majority of probiotics strains belong to lactic acid bacteria which convert sugar to lactic acid. Lactic acid produced creates an acidic environment, thereby inhibiting growth of pathogens.

In type 2 diabetics, probiotics have shown to reduce inflammation, oxidative stress markers and improve glycemic control. Specific probiotics strains alter gut flora, affect intestinal integrity and also reduces LPS transmission from gut lumen into the circulation. This leads to reduction in release of pro-inflammatory cytokines which is the main cause of inflammation.

In few RCTs , use of probiotics in patients with diabetes have shown to reduce fasting blood sugar, insulin levels, improve HbA1c and insulin resistance.

Probiotics are also known to improve antioxidants status such as of glutathione peroxidase and superoxide dismutase in diabetics.

Probiotics also increase HDL cholesterol. It is because cholesterol is lowered due to prevention of bile salt recycling. Since probiotics deconjugate bile salts, which are then not able to be reabsorbed and hence excreted from the body.

Bifidobacteria and Lactobacillus are most commonly used strains in supplements and functional foods. Different species of Lactobacillus can be found in our homemade curd, such as L.casei, L. acidophilus and L.lactis. Consumption of curd has been shown to reduce glycemic curve and HbA1c. Additionally, Yakult, a commonly consumed probiotics, contains 6.5 billion Lactobacillus. casei.Shriota (LcS). But, a serving a size of 80ml bottle contains 11gm of sugar. Hence, natural source of probiotics is most advisable for a diabetic.

Samina Burhanpurwala

Q. Should we advice weight loss pills in diabetes?

Weight loss is often the metabolic Holy Grail for endocrinologists. It is often difficult to achieve, and often there are no good modern medicines to alleviate the problem of obesity.

Modern medicines for weight loss have had a chequered past, often being withdrawn after being marketed due to unacceptable side effects. Example rimonabant and sibutramine. The reason we are unable to find a drug which would reliably reduce weight is that obesity is a field which is mired in insufficient knowledge. Our knowledge of the brain and its appetite centre as well as peripheral and central inputs of obesity is a rudimentary one. As our knowledge of the neurological sciences grows, so will the tools with which we can deal with the pandemic of obesity.

In the Indian scenario, there are a couple of oral medications which can be used in obesity. There is also an injectable medicine, called a GLP-1 analog which is approved for weight loss, however since we are discussing pills, we will leave this out of the discussion.

The two pills that are available are orlistat and topiramate. Orlistat is a fat blocker which prevents the fat in the food from being absorbed through the GI tract. It is not very effective and often associated with perturbing side effects like diarrhea, fecal incontinence and flatulence.

The second pill is topiramate, which is actually an epileptic drug which is used off-label for weight loss. It is approved in the United States, as a combination of topiramate with phenteramine, a sympathetic nervous system-stimulating medication for weight loss. It is quite effective as a weight loss tool with a good amount of weight loss. However, it is to be used carefully in patients with a history of kidney stones and since it is an anti-epileptic medicine, it is to be withdrawn gradually.

As the nature of weight loss is not as easy one, it follows that there is a proliferation of alternative medicine supplements- Ayurvedic, homeopathic and herbal supplements to help bridge the gap. None of these have been tested rigorously, and some of them are prepared by quacks who can mix thyroid hormones, diuretics, sleeping pills and transquilizers in the pills to produce weight loss. One must be careful when using Ayurvedic and herbal supplements as to the content of these pills. If it is only herbs and leaves and does not contain heavy metals, then it is probably safe. However, there are a number of sad stories of patients being treated with alternative medicine

supplements and developing kidney damage due to unknowingly ingesting heavy metals like lead, gold, silver or arsenic in these pills. In the United States, there are a few other agents for weight loss and these like Lorcaserin will be coming to India soon.

To summarize, weight loss pills especially safe ones are few and for between. Diet and exercise, is probably the safest way if applied effectively and if an additional boost is required, orlistat and/or topiramate should be used judiciously by the treating endocrinologist.

Shaival Chandalia

Q. Are multivitamins a blanket prescription in diabetes?

Multivitamins are probably among the most prescribed medicines in the world. This article seeks to address the issue as to whether there are pros and cons to the use of multivitamins.

First let us talk of the advantages. Vitamin D deficiency and Vitamin B12 deficiency are very common problems in our country. Vitamin D is a vitamin or might even be considered a pro-hormone and is involved in calcium metabolism. Normally, vitamin D is synthesized in our skin when ultraviolet light reaches the skin. Inspite of living in a tropical country with abundant sunlight, vitamin D deficiency is very common because pollution prevents the ultraviolet part of sunlight from reaching the skin. Also, our food products like milk are not fortified with vitamin D. Hence, vitamin D deficiency is very common. Thus a multivitamin with vitamin D will help in that regard.

Secondly, vitamin B12 deficiency is also a very common disorder in our population. Vitamin B12 is obtained from animal products hence its deficiency is largely seen in our vegetarian (sometimes vegan) population. Also metformin, the most commonly used anti-diabetic drug is associated with vitamin B12 deficiency. Hence, B12 supplementation would be an essential part of the treatment regimen of patients who are vegan (or predominantly vegetarian) and/ or on metformin. Instead of giving vitamin D and Vitamin B12 supplement separately, a multivitamin containing both (and other vitamins) would serve the same purpose with added economy.

What are the disadvantages?

While one would intuitively feel that by adding harmless multivitamins to a patient's medication list, you cannot do wrong, there is a downside. A very instructive study showed that in an elderly patient population, the use of multivitamin or shall we say multiple vitamins was associated with an increased risk of death. The study found that when the pill burden increased for the elderly patients, they were often taking these multiple vitamins regularly, at the expense of their important regular medication like blood pressure, diabetes and other essential medications. Hence the risk of death increased. Hence the lesson to be learnt is that one good multivitamin to cover most deficiencies, would be in order to be prescribed to all diabetic patients. But one must not overdo this, as patients may start taking multiple vitamin pills at the expense of more important daily medications

Shaival Chandalia

RECIPES

CHICKEN QUINOA BIRYANI

Ingredients:

- Quinoa — 20 grams (raw)
- Chicken — 100 grams
- Onion — 1
- Tomato — 1
- Low fat curd — 150grams
- Oil — 20 grams (approx 1 tbsp)

Method:

- Blanch the quinoa and keep aside.
- Wash chicken thoroughly and remove thin layer of fat from it to make it lean protein source.
- Marinate chicken with curd, garam masala, red chilli powder, turmeric powder, ginger-garlic paste, coriander powder, lemon juice and salt to taste.
- In a pressure cooker, heat the oil. Add tempering ingredients like cloves, bay leaf and cardamom. To this add finely chopped onion, green chilli and mint leaves.
- Add ginger-garlic paste till the raw smell goes away.
- Add tomato and saute till it turns soft.
- Add marinated chicken and saute 2-3 mins. Cover it and cook well for for 6-7 mins more.
- Add 1/2 cup curd, 1-2 cups water and allow it to boil.
- Once it starts boiling, reduce the flame and cook for more 3 mins.
- Layer it with quinoa and toss it.

Nutrition profile per serving (Serves 1)

Energy (Kcals)	Protein (gms)	Carbohydrates (gms)	Fats (gms)	GI
626	29.5	34	22.4	Low

Note:

- It is a high protein, gluten free and healthy recipe for a diabetic.
- A good recipe for lunch/dinner for a person with gluten sensitive enteropathy (Celiac disease).
- Can have with salad or soup to incorporate fiber.

AMARANTH TIKKI

Ingredients

- Amaranth seeds 50 grams
- Capsicum 1
- Bread crumbs 15 grams
- Onion 1
- Oil 25 grams (approx 2 tbsp)

Method:

- Boil 1 cup of water and add the amaranth seeds. Stir well.
- Cover the bowl and lower the heat. Let it simmer for 15-20 mins.
- When completely cooked, can season with pepper powder and keep it aside.
- In a pan, add oil and saute finely chopped garlic and onion. To this, add finely chopped capsicum and stir fry for 2-3 mins.
- Add lemon juice, garam masala powder, coriander powder, red chilli and stir well. Can add amchoor and black pepper. Remove from the heat and keep aside.
- Add this prepared mixture to boiled amaranth. Mix well and let it cool until easily handled.
- Make pattice. Coat the tikkis with bread crumbs or amaranth flour.

Nutrition profile per serving (3 Pattice)

Energy (Kcals)	Protein (gms)	Carbohydrates (gms)	Fats (gms)	GI
360	5.1	27.5	26.8	Low

Note:

- It is a high protein, high calcium snack.
- Can have as a healthy snack at tea-time. But portion size will have to be reduced for a diabetic.

MYTHS AND FACTS

Myth: Same diet should be followed by all diabetics

Fact: There is no one-size-fits-all diet for all diabetics. All the diets are customized according to the patient's biochemical parameters, lifestyle, medications and nutritional requirements. All the diet regimens work differently which help in managing blood sugar, from a diet of normal calorie, carbohydrate, protein, fat proportion to a very low calorie diet (VLCD) for weight reduction. The calories also vary, from an isocaloric diet to a diet with 500 kcal less than current intake(for obese subjects) to a 500 kcal added diet (for lean subjects).

Myth: All diabetics will eventually develop heart disease

Fact: Risk factors for diabetes and heart disease are hypertension, obesity, high cholesterol, insulin resistance and physical inactivity. Though risk factors for all 3 remain the same, a good glycemic control will retard the development of heart disease.

Myth: Drinking water can flush out sugar from body and thereby cure diabetes

Fact: In general, it is recommended to have adequate water intake (~3-4 Lit) to keep up electrolyte balance, help digestion of food and promote nutrient absorption. Water intake can be higher amid the day when activity level is high. However, it is not possible to wash out your sugars just by drinking water. You can definitely control diabetes with a healthy diet, being physically active, taking prescribed medications and having a regular check up with your medical team. Remember that extra water intake may be harmful in a patient of kidney, heart and liver disease.

Myth: Diabetics can have a high fat diet, since it doesn't affect blood sugar

Fact: Since protein and fats take longer time to digest, they do not cause as sharp a spike in blood sugar levels as seen with indigestion of simple carbohydrate foods. When talking of dietary fat, it is important to see the type of fats consumed- MUFA/ PUFA/ SFA. At present, most diets are rich in SFA (meat, poultry, dairy products, coconut oil, and peanut butter) which is one of the main cause of insulin resistance in diabetes. High fat diets also increase blood cholesterol, which is again one of the risk factors for heart disease and stroke.

HOW KNOWLEDGEABLE ARE YOU?

1. Gastroparesis symptoms may improve with dietary changes along with prokinetics such as
   a. Vitamin C
   b. Pregabalin
   c. Valproate
   d. Metoclopromide

2. Deficiency of insulin is linked to
   a. Reduced gluconeogenesis
   b. Reduced glyogenolysis
   c. Reduced lipolysis
   d. Reduced protelolysis

3. Which is the most important source of blood glucose during last hours of a 48 hour fast
   a. Muscle glycogen
   b. Acetoacetate
   c. Liver glycogen
   d. Amino acids

4. Typical dyslipidemia in metabolic syndrome is
   a. Raised HDL, decreased TG, normal LDL
   b. Raised TG, decreased HDL, normal LDL
   c. Raised LDL, decreased HDL, normal TG
   d. Raised TG, raised LDL, normal HDL

5. Tuning fork used to test vibration sense is:
   a. 128 Hz
   b. 512 Hz
   c. 256 Hz
   d. 126 Hz

6. Which nutrient doesn't have an inverse relationship with blood pressure?
   a. Sodium
   b. Potassium
   c. Calcium
   d. Magnesium

7. Target blood pressure in patient with diabetes having proteinuria is:
   a. 130/85 mmHg
   b. 140/90 mmHg
   c. 130/75 mmHg
   d. 125/75 mmHg

8. Hyperkalemia is not a side effect of which drug?
   a. Enalapril
   b. Irbesartan
   c. Valsartan
   d. Furosemide

9. The commonest form of laser therapy used for retinopathy is
   a. Argon
   b. Xenon
   c. Neon
   d. Helium

10. Which of the following is not nephrotoxic?
    a. Cadmium
    b. Gentamicin
    c. Metformin
    d. Lithium

ANSWERS:

1) d 2) c 3) d
4) b 5) a 6) a
7) d 8) d 9) a
10) c

DIABETES TODAY

Dr. Chandalia's DENMARC in collaboration with Help Defeat Diabetes Trust and Association for Diabetes Care and Prevention (ADCP) presents to you Diabetes Today Magazine

Help Defeat Diabetes is a non-profit public trust whose main objective is promoting education and awareness in people suffering from diabetes as well as people in those at increased risk.

It is a lifestyle magazine that demonstrates how to live fully each and every day while managing diabetes.

Who can subscribe?

Professionals working in the field of diabetes education, patients, relatives of patients and anyone else who is interested in diabetes.

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BOOK REVIEW

RSSDI text book of Diabetes Mellitus; Editor-in-Chief: H B Chandalia, Executive Editor: G R Sridhar, Editors: A K Das, S V Madhu, V Mohan, P V Rao

Jaypee Brothers Medical Publishers; New Delhi; 2014; pages 1457; Price Rs 2995

The third edition of RSSDI Text Book of Diabetes Mellitus (D M) has been published six years after the second edition. It is authored and edited by those clinicians and professors who have been teaching and practising diabetes over many years within the country. A few chapters are contributed by Non-resident Indians. As pointed out by the editor-in-chief, this edition has undergone considerable revision. The material published both within the country and outside till the end of 2013 has been critically analysed and included. A few topics which are paid scant attention in other books, like-the complexity of insulin resistance, the criteria applicable to metabolic syndrome in Asians,challenges in the management of children and elderly with diabetes,musculoskeletal manifestation of diabetes, malnutrition modulated diabetes, Latent Autoimmune Diabetes in Adults (LADA), neonatal diabetes and the role of Yoga and relaxation techniques are unique to this book.

The flow chart on the management of diabetic ketoacidosis available in this book should be in possession of all ICUs. The colour pictures of retinopathy, foot lesions, skin diseases and musculoskeletal manifestation are well presented. The role of alternate therapy is extensively discussed. The guidelines for the beginner to organise a diabetic clinic and optimal health care for diabetes amidst diversity of social, economic and regional food habits is noteworthy. The limitation of stem cell therapy as of now is a good reminder. Some controversial issues are discussed in individual chapters. Much alike the chapter on A Glimpse in the Future, I wish a full chapter was devoted to controversies in diabetes. New chapters added in this edition are valuable and discuss important current issues. These include Sleep and Type 2 diabetes-mellitus, Early-onset Type 2 DM, Nutrient blockers and Bromocriptine, Insulin Pump Therapy, Glycemic Management in Hospitalized Patients, Continuous Glucose Monitoring System, Vitamin D and DM, HIV in Diabetes, Diabetes and Cancer.

The appendix is retained from the previous edition and gives a wealth of information applicable to Indian subjects like BMI and waist circumference and laboratory values in S I and conventional units.The index has attained perfection.The novel feature of this edition is mentioning the chapter number on the right edge of each page.

The book will prove to be valuable to students, physicians, diabetologists, endocrinologists and providers of diabetes care. It should be on the shelf of every medical library. The availability of this book has made the Western text books redundant. The single volume covering so many topics is bulky and heavy. I wish it was brought out in two volumes.

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CERTIFIED DIABETES EDUCATOR COURSE

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Help Defeat Diabetes Trust (HDDT) is a registered, non-profit public trust, having amongst its many objectives, the main objective of promoting education and awareness about diabetes among people from different fields.

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Please include biographical information, including affiliation of all authors and email of corresponding author.

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