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NUTRITIONAL FACTORS AND DIABETES

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ABSTRACT

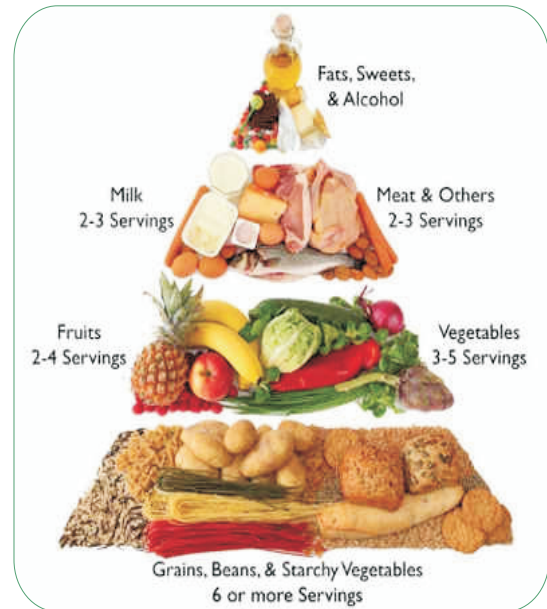
There are various stages in the progress of diabetes. Initially there is impaired fasting glucose then impaired glucose tolerance then NIDDM and finally IDDM. Beta cells of the pancreas are highly susceptible to oxidative stress. Oxidative stress results when there is an imbalance between pro-oxidants and anti-oxidants, in favour of pro-oxidants. If oxidative insults are mild there is repair and recovery. If the oxidative insults are severe, instead of repair and recovery, there is complete damage. Oxidative stress is associated with generation of Reactive Oxygen Species (ROS). These activate immune cell (i.e. Macrophages and 2 types of T cells). There is production of 2 types of cytokines. One type is proinflammatory (e.g. interleukin 1, tumor necrosis factor, interferon gamma) and the other type is protective (IL-2, IL-4 and IL-10). Some nutrients have protective effects and some harmful effects.

KEYWORDS: Nutritional Factors, progress of diabetes, pro-oxidants and anti-oxidants.

INTRODUCTION

Harmful effects are seen with high intake of simple sugars, high intake of total fats as well as n-6 fats, high intake of iron, copper fluoride, cyanogens, alcohol, tobacco, preservatives and pesticides. All these generate free radicals or ROS. These substances are termed pro-oxidants. An adequate intake of n-3 fatty acids, sulphur containing/branched amino acids and micronutrients (manganese, zinc, selenium, chromium, magnesium, vit k, vit A, vit B.C.E. Beta-carotene and flavanoids) all have a protective effect.

As regards fats, different types of fats have different



effects on glucose homeostasis and insulin sensitivity. Various studies done in this respect are :

- i. Seven Countries Study 1995
- ii. Nurses Health Study 2000
- iii. Nurses Health Study 2001

The Seven Countries Study (Netherlands/Finland) showed a positive association with saturated and total fat, inverse association with fish intake and no association with total carbohydrates. The Nurses Health Study done in 1879 subjects followed up for 10 years using a diet assessment food frequency questionnaire showed an inverse association with whole grain, total and cereal fiber and no association with glycolic index or glycolic load.

The Nurses Health done in 2507 subjects in U.S.A. given a food frequency questionnaire to look for outcome of diabetes showed an inverse association with vegetable fats and PUFA, positive

association with trans fats and no association with total fats. Fatty acids are made of basic elements. Carbon, Oxygen and Hydrogen. Carbon atoms are linked together in a chain. A fatty acid chain can consist of 4 to 28 carbon atoms depending upon which it is classified as short, medium or long chain fatty acids.

Fatty Acids :

A fatty acid chain can consist of 4 to 28 carbon atoms depending upon which it is classified as short, medium or long chain fatty acids, They can be saturated, monounsaturated or polyunsaturated.

Mono unsaturated Fats :

Here 2 hydrogen atoms have dropped off from adjacent carbon atoms in the middle of the chain. This double bond is a weak spot causing the chain to link. As linked chains cannot bunch snugly together, these fats are less solid and more apt to be fluid at room temperature.

Polyunsaturated Fatty Acids (PUFA) :

Carbon chain carries hydrogen atoms, in saturated fats the carbon chain has as many hydrogen atoms as possible attached to it. In unsaturated fats the chain had fewer hydrogen atoms attached. They have more number of hydrogen atoms dropped of the chain form 4 to 12. The fewer the hydrogen atoms, the more links it has and the more links chain has the more fluid the fat is.

N-3 Fats

The 1st double bond is at carbon number 3. The parent molecule in the omega-3 family of fatty acids is alpha linolenic acid (LNA) which has 18 carbon atoms containing 3 double bonds which is also described as 18:3n3. When LNA is consumed in diet the body converts it into Eicosapentaenoic acid (EPA) and Docosahexaenoic acid (DHA) EPA-22:5n3. DHA-22:6N3. It takes 10 LNA's to convert into EPA. Main sources of linolenic acid are plant foods such as flaxseeds, walnuts, fenugreek. Almonds, rajmah. EPA and DHA are main sources of marine oils and seaweed. Vegetable seeds oils are a rich source of PUFA-6 fats. Our diet must have optimum proportions of fatty acids. Any fat which has high N6 content or high N6/N3 ratio becomes a harmful source for ROS.

Metabolic derangement that result from elevated N6/N3 ratio are Insulin resistance, IGT, Type-2 DM., central obesity, dyslipidemia. Deranged macrophage function, attenuated fibrinolysis increased platelet activity, microalbuminuria, hypertension and CHD.

N-6 has abundant source & supply, N-3 has limited source & supply. Walnuts have high N-3 but also has four times N-6, Soya also has high N-3 but also has ten times N-6. Coconut oil and ghee have a unique fatty acid composition. They have high saturated fatty acid content most of which is short and medium chain. They have low concentration of PUFA, low N6 as well as n3 and N6/N3 ratio is 3. Being highly saturated they can be easily stored without getting rancid or oxidized. They do not deplete antioxidants. Large content of Palmitic acid (C16) and Myristic acid (C14) present in these fats may have some antidiabetogenic action. Unlike long chain fatty acids, lower chain fatty acids present in these do not require beta oxidation and are readily utilized for energy requirements unlike N6 fats. They appear to be preferred energy substrates for endothelial cells of the colon and intestines. Deficiency of these is linked to inflammatory bowel disorders. Negligible content of N6 family is a major asset of these fats. No other fat has this quality. Our objective is to keep the use of N6 fats as low as possible and use an oil which has the lowest N6/N3 ratio. Ideal N6/N3 ratio should not be more than 5.

N6/N3 Profile

Saturated Fats	N-6	N-3	N6/N3 Ratio
Butter	2.5	1.5	1.5
Ghee	1.6	0.5	3.0
Coconut	1.5	0.5	3.0
Palm Oil	9.0	0.3	3.0
Unsaturated fats			
Mustard	13	8.6	1.5
Olive	8	0.7	11.3
Groundnut	28	0.8	35.0
Soya	51	7.0	7.3
Sesame	40	0.5	80.0
Corn	57	0.8	71.0
Sunflower	49	0.3	163.0
Sunflower	73	0.5	146.0

Vanaspati & Margarine

Vanaspati is an unnatural fat prepared by hydrogenation of unsaturated fats using metal ions catalyst so that it has the ill effects of both lipid toxicity and toxicity of metal ions. Margarine contains trans fatty acid which are associated with rise in lipoprotein (a), plasma TG and fall in HDL. All bakery and confectionary products as well as commercial ice-creams are made from these.

Cholesterol Phobia :

Ansel Keys in 1970 propagated cholesterol hypothesis based on the results of some studies which showed close association of CHD mortality to high levels of cholesterol. On the basis of these studies cholesterol became a 'risk factor' for CHD and saturated fats were labeled atherogenic, Unsaturated fats both mono and polyunsaturated become heart friendly.

1. Studies were done around 1970.
2. Biotechnology was not developed.
3. It was not known that Atherosclerosis and Heart disease are caused by oxidative stress.
4. Unsaturated fats are a major source of these free radicals.
5. While converting cholesterol, it converts LDL into small dense particles which are highly atherogenic.
6. At that time both N6/N3 were grouped together.
7. Saturated fats confined to land animals is a strong fat which is harmful and that is also due to its N6 content which is very high.
8. There are no adverse effects of other saturated fats seen in milk and coconut.
9. Cholesterol itself is innocent.
10. Only when LDL content gets oxidized it becomes harmful.

Vit. D and Diabetes :

Vit. D is immunosuppressive or immunomodulating, thus having a protective supplementation in infancy may protect Beta cell damage brought about by immunological insults. Vit. D deficiency progressively reduces insulin secretion and the glucose intolerance becomes irreversible. A variation in Vit. D requirements could arise from genetic differences in Vit. D processing depending on Apo 1 genotype. Apo 1 genotype individuals who have Vit. D receptor near beta cell can have Vit D deficiency and benefit immensely after supplements of Vit. D3. Patients who are mainly indoors, elderly or covered (Burkha) are seen more in our country.

Milk and Curds :

Contain conjugated linoleic acid (CLA) improves glucose tolerance. It also improves PPAR gamma response. Milk provides calcium, phosphorus, Vitamin D and sulfur containing aminoacids.

Antioxidants and Diabetes :

There are 3 categories of antioxidants i.e. primary, secondary and those offering functional dependence. Primary antioxidant defences in the body are superoxide dismutase, glutathione peroxidase catalase, uric acid, Secondary antioxidants are Vit. C, Vit E. A and carnitine. Functional dependence is provided by Zinc, Magnesium, Selenium and iron. Antioxidant deficiency predisposes to CAD as shown by population study of WHO (MONICA STUDY) and 595 elderly subjects from Moradabad Vit. E levels showed inverse correlation to CAD.

Common sense advice is to have 600 gms, fruits a secondary prevention and 400 gms. of fruits and as primary prevention. The Cambridge Heart Antioxidant Study (CHAOS) showed that alpha tocopherol (Vit.E) treatment substantially reduces the rate of nonfatal MI with beneficial effects apparent after 1 year of treatment.

Vit. C and Diabetes :

Diabetics have significantly decreases serum levels of ascorbic acid as compared to non-diabetics. Insulin facilitates the uptake and storage of Vit. C while hyperglycemia impairs it. Vit. C supplementation leads to a significant decrease in the levels of diene conjugates, lipid peroxidase and significant increase in the levels of reduced glutathione. When Vitamin E in active V form (tocopherol-0) Ascorbic acid reverts it back to the active form. Vitamin C reduces concentration of sorbitol in erythrocytes. There is a close link between Vit. C and Polyol pathway. Hyperglycemia produces depletion of NADPH which in turn depletes reduced glutathione. Vit. C reverses this. Ascorbic acid prevents glycosylation and formation of AGE products.

Vitamin A – Beta Carotene is a precursor of Vitamin A. Both have a role in immunity. Most diabetics are not likely to be Vitamin A deficient and mega doses of this has serious side effects and teratogenicity. No toxicity is associated with Beta carotene.

'B' Group Vitamins – Thiamine (B1), Riboflavin (B2) Nicotinic acid (B3), Pyridoxine (B6) and B12 all have an important role in glucose metabolism. B Vitamins are water soluble hence poor diabetes control will cause more excretion which could alter patient's requirements.

Although the occasional patient with diabetic neuropathy may respond to thiamine in pharmacological doses, there is no justification for routine thiamine supplementation. Nicotinamide functions as a component in coenzymes involved in glycolysis, fat synthesis and tissue repair. The precise mechanisms of the b cell protection is not known. Possibly there are beneficial effects in early onset IDDM. Pyridoxine deficiency has been commonly reported to occur in diabetics. In one study patients on insulin showed more deficiency than those on OHA's. Poor glycolic control is associated with more deficiency.

B6 has a regulatory effect on tryptophan metabolism. Certain catabolic metabolism of tryptophan such as quinolinic acid hydroxyanthranilic acid can impair carbohydrate of xanthurenic acid and hydroxyl kynurenine, former is known to reduce biological activity of insulin. Megadoses of Pyridoxine can actually worsen neuropathy.

Role of Trace Minerals 1) Chromium :

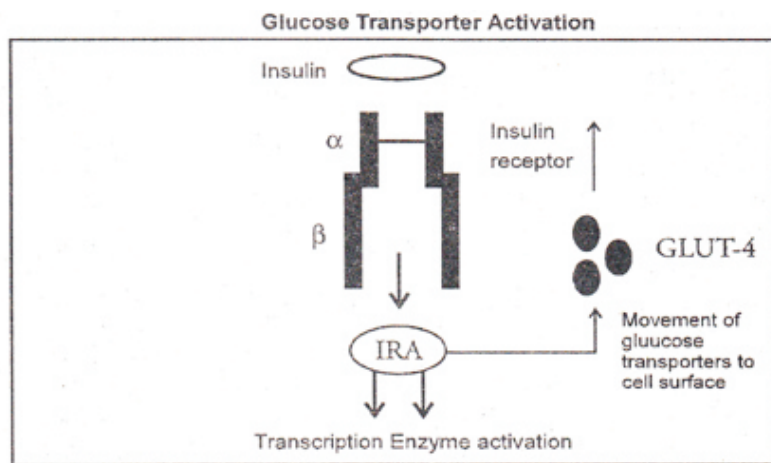
Glucose tolerance factor (GTF) is related to glucose homeostasis Natural sources are brewer's yeast, liver and kidneys. GTF enhances binding of insulin to receptor. Most diabetics are not chromium deficient although severe deficiency can lead to glucose intolerance.

Glucose tolerance factor was discovered in 1957. In 1959, Cr. Was identified as the key mineral

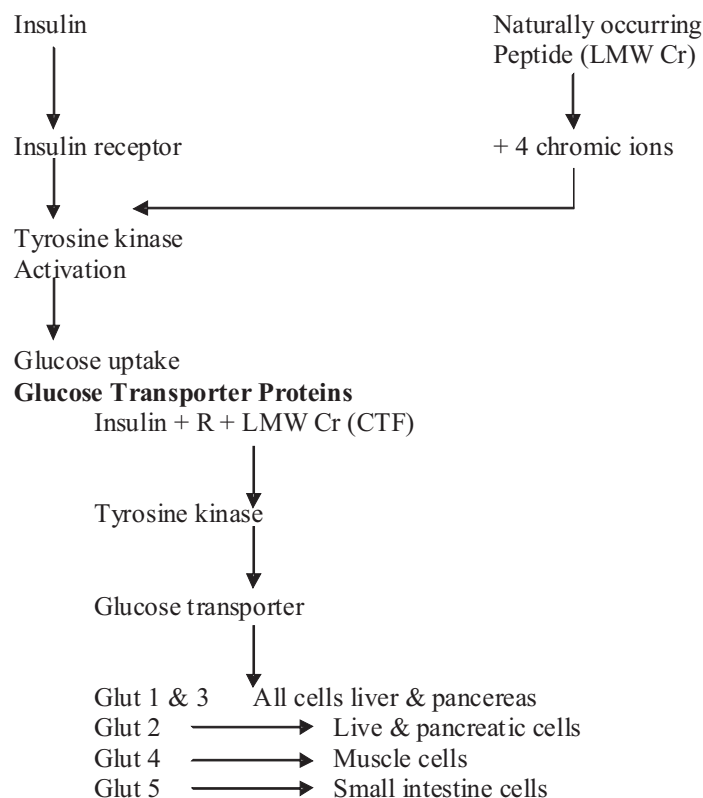
in GTF. GTF is necessary for insulin reduction, and insulin utilization, insulin resistance may be developed when there is inadequate Cr available to form adequate levels of GTF. Chromium is a multipurpose micronutrient required for regulation of glucose metabolism, fat metabolism and amino acid metabolism. It prevents loss of lean muscle mass, promotes weight loss and lowers cholesterol and lower triglycerides.

GTF Formation

- Nicotinic Acid
- + amino Acids
- + 4 Cr atoms
- Low Molecular wt. Cr. (CTP)



Cr. Molecular Aspect



Zink :

It is an essential component of enzymes in many metabolic pathways. Deficiency in some studies has been shown to be associated with reduced insulin secretion and increased insulin resistance. The effect of Zinc on insulin secretion is biphasic. Very high or very low plasma levels impair insulin secretion. Pharmacological doses of supplemental Zinc had no effect on glycated haemoglobin in diabetic patients. It improved T-cell response to phytohaemagglutinin stimulation without enhancing natural killer cell activity. Zinc status is important for the functional integrity of the immune system. Pregnancy related diabetic complications are seen more in zinc deficient women.

It may have beneficial effects on healing of venous ulcers in elderly subjects. A pharmacological dose (>250 mg. elemental zinc daily) has resulted in increased LDL and decreased HDL. Diabetics with poor control are at a high risk of Zinc deficiency, there are not clear cut guidelines for treatments.

Magnesium :

It is essential component of many enzymes and is second only to potassium in cellular concentration. It is important in maintaining the electrical potential in nerve and muscle membranes and also used in glucose homeostasis. It modulates glucose transport across cell membranes and is a cofactor in various enzymatic pathways involved in glucose oxidation. Diabetics with glycosuria and ketoacidosis may have excessive urinary loss resulting into deficiency. Hypomagnesemia can cause insulin resistance.

Selenium :

It is an important antioxidant and parallels many of the functions of Vit. E. Its deficiency is associated with poor reduced glutathione peroxidation and is also associated with certain form of cardiomyopathy.

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