ROLE OF PROTEINS IN RELATION TO DIABETES MELLITUS

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Though the mechanism of metabolism of carbohydrate and protein is different, they take place simultaneously in the human system and are closely integrated to each other. It is seen that protein malnutrition in young adulthood leads to a malnutrition related diabetic syndrome in many developing countries.[1] The possibility that malnutrition in early infancy and childhood can result in partial failure of the $-cell function and clinical onset of diabetes later in life deserves further study.[2]

With experimental models of protein malnutrition it has been possible to reproduce the impaired glucose tolerance and decreased insulin secretory response to glucose in human Kwasbiorkor.[3-7] *In vitro* experiments on rats show that insufficient protein diet for a limited period results in diminished insulin secretory response to glucose after the rats are returned to an adequate diet.

That protein malnutrition affects the insulin secretion and glucose tolerance has been shown by Ingemar Swenne and Workers[8] on experimental animals of same age and sex divided into two groups: one fed with low protein diet and the other fed the normal diet for a limited period of time. Subsequently, when both the groups were treated with a diet of high nutritional efficiency, it was seen that there was no change in weight gain and growth in protein malnourished rats compared to normal rats. However, in malnourished rats impairment of glucose tolerance and an increased hypoglycemic response to exogenous insulin was seen. These observations indicate that the impairment of glucose tolerance in protein malnutrition is caused by deficient insulin secretion rather than by changes in peripheral insulin action. On a diet of higher nutritional efficiency, the serum insulin levels of malnourished rats remain lower than the normal rats indicating a functional impairment of pancreatic islets due to protein malnutrition which is also irreversible.

When different tissue samples of normal and protein malnourished rats were analysed[9], it was observed that malnutrition resulted in decrease in pancreatic size, diameter and volume of pancreatic islets. It was also observed[9] that stimulation of pancreas with glucose load as well as with synthetic stimulators like A 23187 (Calcium ionophore which elicits first phase of insulin secretion)

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and TPA (4-B-phorbol-12 myristate-13 acetate which stimulates the second phase of insulin secretion) resulted in insulin secretion in both the groups. When insulin secretion was expressed as MU insulin/ml/mg. dry pancreatic weight, it was observed[5,8,7] that, there was no significant difference in insulin secretory capacity of pancreas in low protein and normal-fed rats. Since the pancreatic size was decreased in protein malnutrition it resulted in proportionately lesser insulin secretion.

Different tissue samples of both the groups were analysed for DNA[10,11] and protein[12] content and Protein/DNA ratio was used as an index of cell size. It was observed that in normal rats Protein/DNA ratio was increased with age, whereas, in protein malnourished rats the ratio was lower compared to normal rats of the same age. Even on treatment with a diet of higher nutritional efficiency in later life, the ratio remained lower in protein malnourished rats compared to normal rats. Persistent reduction of Protein/DNA ratio in malnourished animals and humans[13] indicates that despite the treatment with an adequate diet, the increase in cellular proteins and growth in size are impaired as insulin stimulates protein biosynthesis and cytoplasmic growth rather than cell replication [1]V[5].

It is observed that in human Kwashiorkor[16] and experimental protein malnutrition[17,18,19] there is atrophy and disruption of normal pancreatic morphology and reduction in islet number, total islet mass[20] and size of individual)3-cells.[18] Possibly, in such animals normal pancreatic cell size and cell number required to maintain an adequate insulin secretion is not attained and as a result they are unable to respond to diabetogenic stimuli and nutritional challenges and are vulnerable to diabetes in later life.

While planning a diet of diabetic patient, the natural starch-protein interaction also may be taken into consideration. A study conducted by Rao and co-workers[21] showed that various factors influence the rate of digestion of starch such as the nature of starch[22], the natural starch-protein interaction,[23] the presence of fibres and anti-nutrients such as lectins, phytates and enzyme inhibitors[24,25]. Nearly 10 to 20% of the starch in wheat flour is malabsorbed and it was interesting to find that[23] removing gluten from the wheat flour eliminated the malabsorption and subsequently adding back gluten to the gluten-free wheat flour did not reverse the effect. These observations raised the question whether the natural starch-protein interaction is responsible for the reduced digestibility of starch and if so what are it's implication in terms of gastro-intestinal physiology in malabsorption states like celiac disease[26] which is usually associated with diabetes.

In vitro experiments by Rao[21] showed that the natural starch-protein interaction decreased the starch-digestion products in dialysate. In their experiments, white bread, gluten-free bread and gluten-free bread+gluten (externally added) were used. They observed that concentration of starch digestion products was significantly low for white bread compared to gluten-free bread and subsequent addition of gluten to gluten-free flour did not decrease the concentration of starch digestion products. These observations indicate that removal of gluten from wheat flour results into increased amylolytic digestion *in vitro.*

Such studies may be used to identify the foods of potential use for inclusion in diets of diabetic patients[27]. High protein starchy foods such as legumes are especially useful in diabetic diet[28] as they show reduced digestibility[29] and lower glycemic response compared to other cereals whose protein content is nearly half that of legumes.

Possibly the wheat flour contains granules with starch molecule in central core surrounded by protein net-work and this protein net-work may inhibit the action of enzyme on starch in the gastro-intestinal tract. Possibly the same type of natural starch-protein interaction may account for decreased glycemic response of legumes. Although, the presence of such protein coated starch in legumes is not yet confirmed protein isolates of legumes are found to be in close association with carbohydrates[30].

Obese adolescents kept on hypocaloric diet show inter-relationship between glucose and nitrogen balance. It is observed that in such cases with added glucose nitrogen balance becomes significantly more positive. Added dietary carbohydrate stimulates pancreas for insulin secretion which in turn stimulates protein biosynthesis[31] and inhibits net protein catabolism from skeletal muscle.[32]

The protein requirement of an individual varies according to age, sex, and physiological conditions. Normally the protein content in the diet is 1 g /Kg body weight. In India, the recommended dietary allowance is 55 g./day for male and 45 g./day in females. In young children there is an increased need for proteins and this must be kept in view while preparing a dietary plan for juvenile diabetes. In a diet plan of juvenile diabetes, protein requirement is 72 g./day. For an obese diabetic, the daily protein requirement is 40 g. A complete diet plan for the juvenile diabetics and for maturity on-set type of diabetes is as follow:

Diet Plan

Constituents (in g./day)	Juvenile diabetes	Maturity on-set diabetes
Proteins	72	40
Fat	57	33
Carbohydrates	310	135

Summary

Dietary protein deficiency causes altered carbohydrate metabolism in children, adult humans and animals. The decreased insulin release in such malnourished condition results in a condition similar to diabetes mellitus. Lowered protein/DNA ratio in many tissues may be related to lowered capacity for insulin secretion. The effect of natural starch-protein interaction of high protein starchy foods such as legumes are especially useful in diabetic diet as they show reduced digestibility and lowered glycemic response. Inter-relationship of glucose and protein in obese adolescents during hypocalorie diet therapy shows that nitrogen balance is significantly more positive with added glucose. The protein requirement under different states of diabetes mellitus shows that the juvenile diabetes has an increased requirement for proteins, whereas, the maturity onset type has a decreased requirement for proteins

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