|| ISSN(online): 2589-8698 || ISSN(print): 2589-868X ||
International Journal of Medical and Biomedical Studies
Available Online at www.ijmbs.info
Volume 2, Issue 6; November-December: 2018; Page No. 47-52

"PROTEIN METABOLISM DEFICIENCY"

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Article Info: Received 04 November 2018; Accepted 2 December. 2018
Cite this article as: Kukreti, S., & Saxena, S. (2018). "PROTEIN METABOLISM DEFICIENCY". *International Journal of Medical and Biomedical Studies*, *2*(6).
DOI: https://doi.org/10.32553/ijmbs.v2i6.64
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Conflict of interest: No conflict of interest.

ABSTRACT:
Metabolism is a complex process that involves a series of chemical reactions in the human body. Alterations in these metabolic processes constitute the disturbances of metabolism causing metabolic disorders. When studying the pathological mechanisms of protein deficiencies it is necessary not only to take into account the composition of the diet. This research discusses the oral aspects of metabolic diseases.
Key Words: Metabolism diseases, protein deficiency syndromes, IEMS, MSUD.

1. INTODUCTION:

The definitions proposed by the joint FAO/WHO Expert committee (1962) are unsatisfactory: protein and calorie deficiencies are considered under a single general heading and a distinction is made between kwashiorkor and marasmus solely on the basis of the presence or absence of oedema (see also Kerpel-Fronius, 1957). The aim of the present article is to discuss protein deficiency syndromes on a physio-pathological basis and to illustrate some of the conclusions with examples. When studying the pathological mechanisms of protein deficiencies it is necessary not only to take into account the composition of the diet but also to distinguish between the different circumstances under which the deficiency syndrome sets in. Has the deficiency existed since birth, or at least since the very early stages of life, thus preventing the organism from developing? Or has an otherwise healthy organism suddenly been submitted to a deficient diet, and when? Studies of protein malnutrition induced during the growth period (such as a child weaned on to a protein-deficient diet) or when growth has been completed [such as an adult abruptly put on to a generally deficient and thus also protein-deficient diet, as was achieved experimentally by Keys et al. (1950) or observed in Europe during the Second World War (Medical Research Council, 1951; Poliakov, 1964)] will be discussed and the main characteristics of protein malnutrition that make their appearance under different circumstances described.

2. MATERIAL AND METHOD:

The estimated burden of IEM is 3-4/1,000 live births1. About 20 percent of acute illnesses in

newborns in the developed countries are due to IEMS. Indian data on IEMS are scanty. According to an ICMR multicentric study ~ 5 percent of genetic causes of mental retardation are due to IEM2. Other studies have quoted a figure of 0.5-2.5 percent. In a study at AIIMS, over 2,000 cases were screened for IEMS and 1.9 percent was found to have amino acid disorders. Common disorders reported were homocystinuria, alkaptonuria, maple syrup urine disease (MSUD) and non-ketotic hyperglycenemia (NKH)4. The disorders in which specific dietary management is the primary management strategy are phenylketonuria (PKU), homocysti-nuria (HCU), pyridoxine non-responsive, maple syrup urine dis-ease and galactosemia. Many others like urea cycle disorders and organic acidurias may require low protein diets along with other treatment modalities. The clinical manifestations of IEMS are variable and non specific most of the times. Table I summa-rises the manifestations and management of some common IEMS.

2.1 Principles of Therapy For IEMS5

Dietary management requires an understanding of both normal nutritional requirements and the basic biochemical defect. The principle strategies of management are:

- Dietary reduction of substrates, frequently protein or amino acids, associated with the formation of the toxic metaboli-ties, for example, phenylalanine in PKU, protein restriction in urea cycle defects, galactose/lactose in galactossemia.
- Replacement of essential nutrients that are deficient as a result of the metabolic block, for example, cystein in HCU.
- Co-factor therapy: Pharmacological doses (up to 100 times the nutrient requirement) of specific vitamins to induce non-functional enzyme activity.
- Enhancement of excretion or product utilisation to form non-toxic metabolites like sodium benzoate in urea cycle disorders.
- The choice of therapy depends on the enzyme defect and its consequences but must be constructed to allow the child to grow and develop normally.
- Dietary therapy should be started as early as possible as during the initial years the developing brain is most sus-ceptible to the toxic effects of the substrate and its by products.
- In most situations, dietary therapy has to be continued throughout life.
- The requirement of protein and essential amino acids must normally be provided in the diet. The total nitrogen require-ment may be lower than normal for infants with organic acidaemias and urea cycle defects. Non-essential amino acids should be provided, ideally in the same proportion as in human milk. Table II gives the normal amino acid requirement.
- Frequent measurements of plasma amino acids and other meta-bolites is essential for monitoring deficiencies and control of the disorder.

2.2 Low protein diets:

IEMS of the catabolism of amino acids which lead to the accumula-tion of toxic metabolites such as ammonia not of specific amino acid require restriction in dietary protein along with high energy intake. These patients will usually tolerate the amount of protein which is just adequate for growth. In these situations, an arbitrary protein intake is prescribed and fine control is usual-ly difficult. Alterative means of removing toxic metabolites is to be considered (Benzoate in urea cycle disorders). Protein should normally provide 6 per cent of the total dietary energy except during relapses. In severe forms, adequate protein supplementation may be difficult.

2.3 PRACTICAL ASPECTS Ongoing management

Protein: In low protein diets, protein should be of high biolog-ical value but dietary variety should be kept in mind. In infancy, human milk or whey-based infant formulae are ideal protein sources. Later other foods such as cereals, pulses, milk, etc are introduced. Protein

substitutes are available for specific IEMS but essential fatty acids, energy and conventional food are to be supplemented.

Fruits and vegetables: Fruits and vegetables are mostly permitted without measurement except in few disorders like classical MSUD.

Energy: Proteins cannot be utilised for growth unless adequate dietary energy is available. Protein restricted diets are frequently low in energy.

Table 1:

Total protein and amino acids (g)		Theoretical initial intake of phenylalanine from natural protein (mg)	
0 to 1	100 to 130kcal	3 to miximum 4	50 to 60
1 to 2	90 to 100 kcal	2.4 to 3.5	30 to 40
2 to 4	80 to 100 kcal	2 to 3	25 to 40
4 to 6	80 to 100 kcal	2 to 3	25
6 to 8	70 to 90 kcal	2 to 2.5	15 to 25
8 to 14	55 to 75 kcal	1 to 1.5	As tolerance
over 14	45 kcal	1	As tolerance
Pre-conception and pregnancy	-	Minimum 1 (>50g/day)	As tolerance, increasing with the demands of the foetus in the second half of pregnancy

Maple syrup urine disease: In MSUD the intake of leucine, isoleucine and valine has to be restricted. The levels for leucine are maintained between 100-700 umol/lit and between 100-400 umol/lit for valine and isoleucine. This is a very difficult disorder to manage, and more so without availability of commercial diets. A modified Indian diet can be prescribed but there are no long-term experiences available. The intakes should vary at different age groups and the diet needs modi-fication accordingly.

3. MATERIAL AND METHOD:

A low methionine and high cysteine diet helps in maintaining intellectual development. The introduction of dietary therapy is worthwhile at any age, but is very expensive for the Indian patient, as commercially produced low methionine and high cysteine formulae are not available and need to be imported. Therefore, most of the times, one has to plan a special diet for patients, using locally available foods. These diets aim to provide 25-45 mg/kg/day of methionine in infants and 8-10 mg/kg/day of methio-nine in teenagers. Plasma levels of methionine are to be main-tained between 0.03-0.1 mmol/1 and cystine levels between 0.037-0.085 mmol/1. Although, ideally, quantitative measurements of plasma methionine are required, the same information can be obtained by paper chromatography after careful standardisation. Table VI gives a list of restricted and unrestricted food items in homocystinuria. Since wheat and pulses are to be restricted, the caloric density of the diet can be increased by mixing sago or arrowroot powder in wheat flour. A prototype diet for a 10 kg child is shown in Table VII. It is difficult to increase the cystine content of this diet without inadvertently increasing its methionine content. Therefore, these diets are not as effective as commercial diets. Trial of treatment with Pyridoxine and folic acid (1-5 mg/d) is worthwhile in all the cases. Treatment with betaine (trimethylglycine; 6-9 g/d) which serves as a methyl group donor, produces clinical improvement in patients unresponsive to pyridoxine.

Table 2:

Dietary exchanges in Phenylketonuria (Ref 7) (Common Indian foods) Vegetables (cooked)	**15 mg exchanges Amount (in tablespoonful)**
Green beans	5
Cabbage	8
Carrots	5
Cauliflower	3
Brinjal	1.5
Spinach	1
Gourd	3
Onions	4
Sweet potato	4
Fruits	Number
Apple	4 (small)
Guava	1/2 (medium)
Mango	1 (small)
Orange	1 (medium)
Papaya	1/2 (cup)
Watermelon	1/2 (cup)
30 mg exchanges	
Cereal	Amount (in tablespoonfuls)
Rice (cooked)	5
Wheat	2
Barley	3
Lentils	3
To avoid Meat, fish Chicken, eggs Urad dal	
To take ad lib (any amount) Sweets, jam Butter and ghee Sugar and honey Aerated water	

Dietary exclusion of galactose and lactose (from which galactose is derived) is necessary almost throughout childhood and major sources should probably be omitted throughout life. A nutritionally adequate galactose/lactose free milk substitute should be used during infancy and later as a supplement to diet. In later childhood occasional lactose free milk and calcium and vitamin supplements may suffice. Monitoring should ideally be done by measurement of galactose 1-phosphate levels in RBCS. Fortunately lactose free formulae are available in our country and this disorder can be managed with relative ease. Some people also recommend restriction of plant foods (pulses, beans, peas, spinach) during infancy and early childhood due to the presence of galactosides and nucleoproteins which are potential sources of galactose but opinions differ10,11.

4. RESULT AND DISCUSSION:

These disorders principally affect the liver and have nine different types depending on the enzymes involved. As carbohydrate metabolism

in the liver is responsible for glucose homeostasis, this group of disorders presents typically with hypoglycaemia and hepatomegaly (not in all types) Treatment is designed mainly to maintain normoglycemia and is achieved by continuous nasogastric infusion of glucose or oral uncooked starch. Uncooked starch acts as a slow release form of glucose.12 this is specially useful in Type I, III and VI but is most demanding in Type I.

Table 3:

Low methionine diet for a 10 kg child (Methionine allowance 25-45 mg/kg, Cal: 100-120/kg, Protein 2g/kg) (Ref 8) Cal	**Protein**		**Methionine (mg)**
Breakfast			
Buffalo milk	115	4.0	100
100ml + 1tsf sugar	20	-	-
Sago khichari (10g sago, 25g Potato, 1tsf oil)	110	1.0	6.0
Lunch			
Rice 50g cooked & drained + 1tsf ghee	220	3.5	25
Vegetable 1 Katori + 1tsf ghee	50	-	10
Curd 50 ml	60	2.0	50
+ Fruit 1	50	-	-
Tea			
50 ml milk	60	2.0	50
+ 1tsf sugar	20	-	-
2 arrowroot biscuits	50	-	-
Dinner			
Rice 50 g cooked & drained + 1tsf ghee	220	3.5	25
1 katori vegetable	50	1.0	10
1 katori dal masur cooked (25g raw)	70	1.25	10
Sweet semolina kheer (20g semolina+ 25 ml milk + 1tsf sugar)	120	3.50	55
TOTAL	**1215**	**21.75**	**341**

4. CONCLUSION:

Protein substitutes are available for specific IEMS but essential fatty acids, energy and conventional food are to be supplemented. These diets aim to provide 25-45 mg/kg/day of methionine in infants and 8-10 mg/kg/day of methio-nine in teenagers. Plasma levels of methionine are to be main-tained between 0.03-0.1 mmol/1 and cystine levels between 0.037-0.085 mmol/1. Treatment is designed mainly to maintain normoglycemia and is achieved by continuous nasogastric infusion of glucose or oral uncooked starch. Uncooked starch acts as a slow release form of glucose.12 This is specially useful in Type I, III and VI but is most demanding in Type I.

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