Contributions of Dietary Protein and Zinc Deficiencies to Protein Energy Malnutrition

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SUMMARY

Some degree of zinc deficiency seems present in all cases of Protein-Energy malnutrition. Protein Energy Malnutrition (PEM) was induced in male Wistar rats fed either adequate (30ppm) or moderately deficient levels of zinc (6ppm) in diets containing either 0.4 or 20% spray-dried egg white. The protein-deficient rats developed PEM with oedema in 4 - 5 weeks regardless of their dietary zinc level. Except for disorders of the brain, protein deficiency was the major cause of most PEM signs - loss of appetite, growth failure, oedema, water accumulation in the liver, hypoalbuminaemia and mortality. Dietary zinc deficiency aggravated some of these to a small extent. Dietary zinc alone accounted for elevations of brain iron and sodium in both PEM and non-PEM rats. This suggests that zinc deficiency may significantly contribute to some of the symptoms of PEM.

INTRODUCTION

Although dietary zinc deficiency and Protein-Energy Malnutrition (PEM) differ in many of their symptoms, they share in common the symptoms - growth failure, apathy, skin disorders, loss of appetite, enlarged liver, hair abnormalities, learning disabilities and vitamin A accumulation in the liver[1]. It has been shown by many researchers[2,3] that kwashiorkor, apart from being initiated by protein deficiency, is also accompanied by zinc deficiency. PEM patients often show blood zinc levels of less than the normal 90 $\pm$ 10ug/dl1. The question has therefore been raised as to whether some of the symptoms of PEM, usually attributed to protein deficiency, may in fact not be due to the zinc deficiency which accompanies it.

This animal study was therefore undertaken to see if some light could be thrown on this question.

METHOD

Newly-weaned male wistar rats were randomly assigned to one of four diets. There were 9 to 12 rats/treatment. (Table 1)

Each diet was a mix of egg-white, corn starch, corn oil, vitamins and minerals that provided 4317kcal/kg diet.

TABLE 1: Design of Dietary Treatments

Treatment	Zinc mg/kg	Protein %
Low protein, low zinc (LpLz)	6	0.4
Low protein, High zinc (LpHz)	30	0.4
High protein, Low zinc (HpLz)	6	20
High protein, High zinc (control)	30	20

In the first of two studies, the animals were fed for 12 weeks. Rats were weighed daily for the first six weeks, their food consumption recorded and physical conditions noted. Any animal that died after developing PEM was weighed, its liver removed, blotted dry, weighed and stored frozen. On the final day of the study, all animals were weighed, killed and their livers stored as before. Livers were analysed later for moisture, total protein (by Kjeldahl procedure), zinc and iron by Atomic Absorption Spectrophotometry.

To confirm findings, the experiment was repeated with 12 rats/treatment. With rats taking 4 to 5 weeks to develop PEM in the first study, this study was terminated at the end of 5 weeks when all protein-deficient rats had developed PEM. In addition to the liver, mid-brain samples were also collected in this study. Apart from moisture, total protein, zinc and iron, liver and brain sodium were also analysed because of a publication [4] that came out while this study was underway.

Analysis of variance, t-tests and correlation procedures with the general linear model of the statistical analysis system (SAS) [5] were used to analyse the data.

RESULTS

Food Intake:

Regardless of the level of dietary zinc, food consumption of the rats on protein-deficient diets (LpLz & LpHz) began to fall by the end of the first week. This continued to the end of the 6-week food data collection. Rats on adequate protein but deficient zinc (HpL_z) consumed less food than the controls (HpHz).

Body Weights:

Rats on deficient protein began losing weight from the beginning of the study regardless of their levels of zinc intake. Rats on high protein gained weights with those on low zinc gaining a little less than the controls. Both groups of rats on low protein weighed less than 60% of the control weights by the 4th to 5th week of the study and also had oedema.

Oedema and Other Physical Symptoms

Irrespective of the level of dietary zinc intake, the protein-deficient rats developed oedema within 4 weeks of being on their diets. Their faces were bloated, much fluid accumulated on their chests and dorsal (upper) surfaces of their paws. Skin peeled off from their paws and tails along with generalised hair loss.

Liver Disorders:

The protein-malnourished rats had high moisture concentrations in their liver regardless of levels of dietary zinc intake. Their liver protein concentrations were very low. Fatty-liver was observed in no group. The PEM rats (LpLz & LPHz) showed significantly-elevated liver concentrations of zinc, iron and sodium regardless of levels of dietary zinc intake (Table 2).

TABLE 2 Composition of Rat Liver and Mid-brain after 5 Weeks on Diet

	Liver		Mid-brain	
	Sodium (mg/g dry wt)	Iron (ug/g dry wt)	Sodium (mg/g dry wt)	Iron (ug/g dry wt)
LPLz	5.17 ± 0.45[a]	1.09 ± 0.10	7.08 ± 0.13	121.0 ± 10.8
LPHz	4.59 ± 0.31	1.06 ± 0.05	6.72 ± 0.20	101.4 ± 9.0
HPLz	2,16 ± 0.07	0.23 ± 0.03	7.09 ± 0.13	124.5 ± 5.8
HPHz	1.93 ± 0.05	0.16 ± 0.01	6.64 ± 0.09	87.1 ± 8.3

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Brain Disorders:

The brain had a different picture from that of the liver (Table 2). The level of dietary protein showed no effect on the concentrations of the brain minerals measured. The rats on the low zinc diets showed elevations of both sodium and iron in the brain regardless of levels of protein intake.

DISCUSSION

Using the Welcome classification for PEM[6], the PEM rats from this study (under 60% weight of controls plus oedema) were marasmic-kwashiorkor models. The kwashiorkor signs of oedema and skin peeling were present. Their elevated liver moisture probably explains the liver enlargement seen in PEM. The elevation of minerals such as sodium in the liver must have contributed to the water accumulation there. The absence of fatty-liver in these PEM rats agreed with the findings of Patrick and Mackay[7] who showed in baby baboons that PEM developed without fatty liver if sucrose (the fructose content specifically) was missing from the diet. Cornstarch was the source of carbohydrate used in this study.

The finding of sodium and iron elevation in the mid-brain as a result of low-dietary zinc also agreed with the findings of Wallwork[8], showing alterations of various mineral concentrations in the rat brain as a result of dietary zinc deficiency. Zinc deficiency appears to cause malfunctioning of sodium transport in some cells of the body[4] and also hampers proper nerve impulse generation in some neurons of the brain9. Thus the zinc-deficiency of PEM may be an important contributor to the brain pathologyof PEM [10,11].

In man, these findings suggest an important role for dietary zinc in the prevention and treatment of PEM. They also help explain why recovery from PEM is slowed down[12,13] when dietary zinc intake is inadequate during PEM treatment.

The importance of adequate zinc in current weaning food formulations in the third world, for example, must not be overlooked. Oberleas and Prasad[14] have long suggested zinc-supplementation of high-protein vegetable mixtures formulated to treat kwashiorkor. Until supplementation with zinc is affordable, whole-grain cereals rich in available-zinc and other nutrients must be the first choice in high-protein vegetable food formulation. Commercial high-protein and weaning food manufacturers must definitely be encouraged to consider this.

It is concluded that the dietary zinc deficiency of PEM does contribute to its symptoms. It may be principal contributor to the brain malfunction of PEM while the protein deficiency takes major responsibility for the other symptoms of PEM.

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Co-Chairman: Thank you very much Dr. Asibey-Berko. This paper is now open for discussion and comments. I will again start. Dr. Asibey-Berko, did you differentiate protein deficiency from Protein Energy Malnutrition. Are they almost the same?

Speaker: When you have 60 to 80% of the standard weight for age with the presence of Oedema then you have kwashiokor. But when you have 60 % to 80% of the standards weight for age, without Oedema, then you simply have malnourishment. And then too, when the weight is less than 60% of the standard weight for age, with the presence of Oedema, then you have marasmic kwashiorkor. But when the weight is less than 60% of the standard weight for age without Oedema, then you have marasmus. This is why I am saying that the models we got, actually represent marasmic kwashiorkor models.

Co-chairman: I think, if we say Protein Energy Malnutrition exists, we should have abnormal metabolism in protein or carbohydrates or may be lipid metabolism. Just low body weight does not mean there is malnutrition. Maybe there is undernutrition. But when you say mal, it means abnormalities in metabolism.

Speaker: I agree with you.

Chairman's closing remarks: Ladies and gentlemen, we have had a most interesting morning, and we've had very informative papers. Practically as a layman in the field, it will be presumptuous of me to attempt a full summary of what has been delivered. However, I just want to highlight a few points which the lecturers brought to our attention. We started with the keynote address by Dr. Commey on Nutrition and Development. And he reminded us that, of the World's nearly 5 billion people, 38% are children and that only 25% of these children are in the developed countries. So all the provisions that have been made by pronouncements that have been made by the United Nations and other International Organisations, are benefiting perhaps only 25% of the possible target group. He emphasized the problem of malnutrition in early childhood. He lamented that, intervention projects to mitigate this have not yielded the right results because the food supplements have tended to go anywhere but the target groups. The intellectual development of the child he thought very much depended on his nutrition and he also posed the problem as to the role of the environment in subsequent development. Here is the child that is prone to poor intellectual development because of nutrition, because of parts of physiological changes in the brain and yet we also have the poor environmental situation which will make this worse.

He emphasized the place of breastfeeding particularly, in the developing countries, and made the point that promotion of breastfeeding is a responsibility for all health workers, doctors, nurses etc. He also emphasized the problems posed by inappropriate weaning practices preempting some of the papers that we subsequently heard. He also went on to the question of growth monitoring, the rejection of the traditional techniques that we had known, leaving a vacuum that we haven't filled, and told us a lot about what was happening in Thailand, using the VNAP project.

Then we moved on to Mrs. Lartey who told us about nutritional intake and milk yield in lactating mothers, a study of the milk yield, the Vitamin, a content, the protein nutritional content and the nutritional status of the infants born to such mothers. We had comparisons between what our mothers are producing and the production levels in the advanced countries. She showed that with the milk yield the average is 546 ml in 24 hours compared with 700 to 800 ml/day in the developed countries. But the protein content seems to be closer and of course the Vitamin A content is quite divergent. She discussed the effect this has on the growth of the infant. Some very interesting observations were made. That in the 2 to 40 month old period, in some of these values, the children in terms of length for age, weight for age and weight for length seem to do quite well. It generated some interest that in spite of these deficiencies the children in the 2 to 4 month age group do well. Problems of adaptations were discussed.

We had Dr. Shizuka telling us about her work in the Upper East Region in the Binaba district in which she concentrated on the 3 to 12 year old group which constituted 43% of the population in this area and made observations about the body weight, the mean height and the upper arm circumference, and found significant differences between a similar population in the Greater Accra area of the country. She made the recommendation that appropriate agricultural practices have to be introduced in this part of the country in order to ameliorate these differences.

Finally, we had Dr. Asibey-Berko who gave us the animal study of protein-calorie malnutrition in rats and made the observation that it is the food intake which determines the animals protein intake, and also their body weight. Zinc level seems to have little to do with the oedemas and enlargement of the liver which seems to be largely due to water and sodium. But the zinc deficiency shows its defect in the brain. He speculates that it might well be the cause of the kwashiorkor syndrome that it really has to do with the appetite and brain disturbance as a primary factor. Thank you very much.

Co-chairman's closing remarks: Malnutrition is prevalent mostly in developing countries and it has a significant health implication. As we discussed yesterday, infections are very common in this country. Unfortunately, malnutrition and infections often go hand in hand influencing each other. Infections or other diseases, aggravate nutritional status of the patient and lead to malnutrition. Conversely, malnutrition by lowering body resistance to diseases greatly predisposes infections and enhances their severity. The causes of malnutrition are complex and multifactorial as indicated by Prof. Commey's lecture. Everyone agrees that immediate causes of malnutrition is inadequate food intake in quantity or in quality. However, the causes of malnutrition are not so simple. There are many underlying causes. The problems may lie in food production, agricultural practices, eating habits, poor sanitation, low educational level and so on. Furthermore, socio-economic, cultural, ecological and political factors make the matter even more complex. Therefore, it is not an easy task to combat malnutrition and it cannot be solved solely by nutritionists. A broad multisectorial approach is needed to eradicate malnutrition.

This morning, we have discussed many aspects of nutrition issues in this country and important suggestions were made for improvement of the nutritional status of the people. However, we are still far away from the eradication of the nutrition problem in this country. So further efforts are clearly needed in all sectors such as agriculture, health, education and social welfare. Let us therefore continue every effort to improve the health of the people of this country. And I sincerely hope Noguchi Institute will continue to play a major role in solving the health problems not only of this country but also of the whole world.

Thank you very much.