

REVIEW BOARD ON THE USE OF HUMAN SUBJECTS, ICDDR,B.

22

Principal Investigator Dr. AYESHAMOLLA Trainee Investigator (if any) _____

Application No. 79-010 Supporting Agency (if Non-ICDDR,B) ATOMIC ENERGY CENTRE, DA

Title of Study Absorption of vitamin A and zinc status in diarrhoea of different etiology. Project status:
 New Study
 Continuation with change
 No change (do not fill out rest of form)

Circle the appropriate answer to each of the following (If Not Applicable write NA).

Source of Population:

- (a) Ill subjects Yes No
- (b) Non-ill subjects Yes No
- (c) Minors or persons under guardianship Yes No

Does the study involve:

- (a) Physical risks to the subjects Yes No
- (b) Social Risks Yes No
- (c) Psychological risks to subjects Yes No
- (d) Discomfort to subjects Yes No
- (e) Invasion of privacy Yes No
- (f) Disclosure of information damaging to subject or others Yes No

Does the study involve:

- (a) Use of records, (hospital, medical, death, birth or other) Yes No
- (b) Use of fetal tissue or abortus Yes No
- (c) Use of organs or body fluids Yes No

Are subjects clearly informed about:

- (a) Nature and purposes of study Yes No
- (b) Procedures to be followed including alternatives used Yes No
- (c) Physical risks Yes No
- (d) Sensitive questions Yes No
- (e) Benefits to be derived Yes No
- (f) Right to refuse to participate or to withdraw from study Yes No
- (g) Confidential handling of data Yes No
- (h) Compensation &/or treatment where there are risks or privacy is involved in any particular procedure Yes No

5. Will signed consent form be required:

- (a) From subjects Yes No
- (b) From parent or guardian (if subjects are minors) Yes No

6. Will precautions be taken to protect anonymity of subjects Yes No

7. Check documents being submitted herewith to Board:

- Umbrella proposal - Initially submit overview (all other requirements will be submitted with individual studies)
- Protocol (Required)
- Abstract Summary (Required)
- Statement given or read to subjects of nature of study, risks, types of questions to be asked, and right to refuse to participate or withdraw (Required)
- Informed consent form for subjects
- Informed consent form for parent or guardian
- Procedure for maintaining confidentiality

NA Questionnaire or interview schedule

* If the final instrument is not completed prior to review, the following information should be included in the abstract summary

1. A description of the areas to be covered in the questionnaire or interview which could be considered either sensitive or which would constitute an invasion of privacy.
 NA
2. Examples of the type of specific questions to be asked in the sensitive areas.
 NA
3. An indication as to when the questionnaire will be presented to the Board for review.
 NA

I agree to obtain approval of the Review Board on the Use of Human Subjects for any change involving the rights and welfare of subjects before making such change.

Ayesha Molla
Principal Investigator

Trainee

79-010

Rec'd 12/19/79

SECTION - I - RESEARCH PROTOCOL

1. Title: Absorption of vitamin A and Zinc status in diarrhoea of different etiology.

2. Principal Investigators: Dr. Ayesha Molla
Dr. Abdul Majid Molla

Co-Investigators: Dr. M.M. Rahaman
Dr. P.K. Bardhan
Dr. A.H. Khan - Atomic Energy Centre, Dacca.

3. Starting Date: September 1979

4. Completion Date: July 1980

5. Total Direct Cost: \$ 5940 - Incremental cost \$ 1566

6. Availability of funds:
(a) Scientific Director's remarks:-

(b) Controller's remarks:-

7. Abstract Summary

Vitamin A absorption and relative importance of Zinc status for the metabolism of Vitamin A will be studied during and after recovery in 40 patients with cholera and E. coli selected at random. After an overnight fast D-xylose absorption test will be done on the patients. Next morning vitamin A absorption test will be done after giving 7500 IU vitamin per kg of body weight. On the same day they will be further given an intramuscular injection of 50,000 units of water miscible vitamin A to saturate the liver store of vitamin A. Oral Zn as $ZnSO_4$ will be given to ten patients from each aetiology and the other ten will receive placebo. At the time of discharge a second vitamin A absorption test will be performed which will enable us to estimate the effect of Zn on the vitamin A absorption and its mobilisation from the liver into the plasms. This study should lead us to an important understanding of vitamin A absorption during diarrhoea and also should explain the importance of the presence of adequate level of zinc for effective metabolism of vitamin A.

(8) Reviews:

(a) Research Involving Human Subjects: _____

(b) Research Review Committee: _____

(c) Director: _____

(d) BMRC: _____

(e) Controller/Administrator: _____

SECTION II - RESEARCH PLAN

A. INTRODUCTION

1. Objectives:

The overall objective of this study is to assess the nutritional status especially vitamin A and Zn level of the patients with diarrhoea due to different etiology. Since the actions of vitamin A and Zn are known to be interdependant the other objective of this project is to study the influence of Zn on the absorption of vitamin A in malnutrition and diarrhoea.

2. Background:

Vitamin A deficiency is widely known to be the cause of xerophthalmia and nightblindness in both man and animals. Besides, in absence of adequate dietary intake of vitamin A or its precursor for a reasonable length of time, several abnormalities can occur. Increased keratinization of epithelial line, loss of weight, loss of appetite, reduced turnover of mucus secreting cells are noteworthy. Vitamin A deficiency usually accompanied by protein energy malnutrition is also closely related with increased frequency of infection and impaired nutritional status of the individual. There are two kinds of vitamin A malnutrition, namely hypervitaminosis and hypovitaminosis. Hypervitaminosis is rare but hypovitaminosis is quite common particularly in developing countries among the people in slum area and having poor economy. To have good assessment of true vitamin A deficiency there is some difficulties. The nutrients which are not stored in the body, an equilibrium exists between the tissue and plasma. In these cases plasma level reflects the level in the body as a whole.

This is not the same for vitamin A which is stored entirely in liver. Therefore, the plasma vitamin A level does not necessarily say the true status of vitamin A level of the body. In 1963 the United States Interdepartmental Committee on Nutrition for National Defense (1) recommended that the "deficiency" should be considered when the plasma level becomes equal to or less than 10 µg/dl.

Absorption of Vit.A during Diseased States

Low vitamin A ~~level~~ in plasma can be associated with different conditions like parasitic infestation, liver disease, low protein intake and diseases which interfere with digestion, absorption, transport, storage or metabolism. Children are the most susceptible group of population who can have all these diseased condition and ultimately become victim of the deficiency state. An absorption study was performed by a group of scientist in India (2) to assess labelled vitamin A absorption in children during infection. It was found that during respiratory infection and during acute diarrhoea, absorption of Vitamin A was grossly impaired. The same group (3) reported another study of diminished absorption of vitamin A in children with Ascariasis/having after anthelmintic treatment. Recently Dilip Mahalanabis *et.al.* (4) observed malabsorption of water miscible vitamin A in children with giardiasis and ascariasis. Prompt improvement in absorption was noted after eradication of the infestation. Thus repeated attacks of diarrhoea or other gastrointestinal infections may enhance the vitamin A requirements specially in children whose vitamin A storage in the liver is poor. However, the mechanism of vitamin A absorption during infection is not clearly understood. / marked improvement

It was stated (3) that this defective absorption was not due to mal-absorption of fat, since steatorrhoea were not present in any of these study subjects. Therefore, the mechanism of vitamin A absorption needs to be studied in these diseased states.

Metabolism of Vitamin A

To understand the mechanism of vitamin A absorption a simple account for vitamin A metabolism is to be given here. It is already established (5) that retinol (vitamin A alcohol) circulates in blood attached to retinol binding protein (RBP) a specific protein which inturn is bound to prealbumin (PA). Under normal condition these three proteins interact in a molar ratio of 1:1:1. The presence of RBP and PA is essential for proper utilisation of vitamin A. In protein calorie malnutrition RBP and PA are significantly decreased (6) and simultaneously the transport of vitamin A from liver becomes affected. A third substance Zinc is essentially involved in vitamin A metabolism. Zinc was reported to be necessary for normal mobilization of vitamin A from the liver (7). J.R.Duncan et.al (8) reported possible interaction between vitamin A and Zn in pregnant rats. Combined vitamin A and Zn deficiency had teratogenic effect on the foetus. This study also proposed that Zn may interact with vitamin A metabolism at the line of vitamin A transport from the liver to preipheral tissue.

Diseases due to Zn deficiency

Numerous studies (9-12) were performed to establish the clinical symptoms associated with Zn deficiency. The well known symptoms are dwarfism and hypogonadism, growth retardation, testicular atrophy and loss of appetite. Acrodermatitis enteropathica is a well known condition of Zn deficiency.

- 4 -

Besides, Zn deficiency is also known to be associated with Kwashiorkor (13), coeliac disease (14) and disaccharidase deficiency (15). Symptomatic zinc deficiency has also been detected in patients with regional enteritis (16). Malabsorption due to pancreatic insufficiency, steatorrhoea, gastrectomy, intestinal mucosal disease and parasitic infection all these are known to cause Zn deficiency (17). Mechanism of Zn absorption from the gut is not clearly understood. Some recent studies from experimental animals indicate that a zinc binding ligand is secreted into the intestinal lumen by the pancreas and it appears to facilitate the uptake of zinc by the intestinal epithelial cells. Whether the same mechanism exists for man is not established. One may speculate that a lack of the zinc binding ligand may cause malabsorption of Zn. Zinc therapy has been described in cases with malabsorption with marked improvement (15). In specific two cases, one being a female aged 71 yrs and the other a male aged 7 months had a marked clinical progress with zinc therapy (300 mg $ZnSO_4 \cdot 7H_2O$ /day) and (30mg $ZnSO_4 \cdot 7H_2O$ /day) respectively. The patients plasma value for Zn showed a raised level coinciding with clinical improvements in their condition (15).

Vitamin A and Zinc level in Bangladesh

In Bangladesh a large percentage of population is suffering from malnutrition which predisposes to various types of infection and diarrhoea leading to malabsorption. Moreover eighty percent of total energy intake here is consumed as rice, which is a poor source of both vitamin A and Zn. The mean adult intake of vitamin A and its precursor is about half of the recommended value of 3500 IU per day (18). There is of course a seasonal variation of vitamin A intake, increasing in May and June due to availability of seasonal fruit.

From a study done by Ken Brown et.al (19) in children nutrition unit, Dacca, Bangladesh it was reported that the mean serum vitamin A and carotene level were $5 \mu\text{g}/\text{dl} \pm 5$ and $39 \mu\text{g}/\text{dl} \pm 26$ respectively among the outpatients, as compared to village means of $14 \pm 8 \mu\text{g}/\text{dl}$ and $87 \pm 6 \mu\text{g}/\text{dl}$. No study on Zn level in Bangladeshi population has been done yet. According to the report of a joint WHO/USAID meeting (1) vitamin A of $10\mu\text{g}/\text{dl}$ plasma is regarded as high risk level. On the otherhand safeguards are also needed to control continuous overdose of vitamins. During acute hypervitaminosis the following symptoms may be observed, e.g. nausea, vomiting, headache and diarrhoea. However, these symptoms often occur following a single administration of high dose capsules (110-165mg or 200,000-300,00 IU) and they are transient, do not cause any permanent damage to tissues. In the present study the absorption of vitamin A and its relation with the Zn status during and after diarrhoeal illness will be evaluated. The information derived from this study would be very helpful in proper management of the recovery phase of the patients.

3. Rationale:

In Bangladesh all degrees of vitamin A deficiency is prevalent. This is particularly true in subjects with malnutrition. Diarrhoea precipitates malnutrition and thus can cause vitamin A deficiency. Studies have shown that infestation of giardia and other worms can cause malabsorption of vitamin A. So far no study has been done to show the absorption of vitamin A during the acute infections diarrhoea. Besides, Zn deficiency has been shown to interfere with mobilization of vitamin A.

Both vitamin A and Zn deficiency is likely to be common in Bangladesh. This study will provide informations on the absorption of vitamin A during diarrhoea of different etiology. Furthermore, it will establish the role of Zn on the absorption and mobilization of vitamin A. These informations will be extremely valuable in the nation wide distribution of vitamin A and prevention of blindness program.

B. SPECIFIC AIMS

- (1) To assess vitamin A and Zn status in patients with acute diarrhoea of different aetiology.
- (2) To study the absorption of vitamin A during diarrhoea after recovery.
- (3) To study the relative influence of Zn on the vitamin A absorption and metabolism.

C. METHODS OF PROCEDURE

1. Subject

Patients with acute diarrhoea and suggestive history of cholera and E. coli will be taken into the study. Subjects with moderate to severe dehydration and mild to moderate degree of malnutrition will be selected at random basis. Patients with any complications like respiratory disease, high fever and severe malnutrition will be excluded from the study. In each group of aetiology, 80 patients will be selected. Only weaned children between 3-10 years of age will be taken into the study. In each aetiology of diarrhoea, patients will be divided into two major categories as cholera with parasites present or absent and E.coli with parasites present or absent. Each group will again be subdivided into malnutrition present and malnutrition absent for the sake of simplicity different varieties of parasites and different degrees of malnutrition will not be further classified at this stage. As much as possible 80 age matched control subjects with no history of enteric disease will be studied. Patient distribution is explained in diagram 1.

2. Clinical procedure

On admission detailed history about diet and symptoms relating to the vitamin A deficiency will be taken. In addition to routine clinical examination biochemical and anthropometric measurements will be carried out. Biochemical parameters will include Hct, TC, DC, total protein albumin ratio, stool and urine analysis. Anthropometric measurements will include weight, height, weight for age, height for age and mid-arm circumference. Signs of vitamin A deficiency like Keratomalacia, Xerophthalmia, bitots spot will be noted when present. Rectal swab will be cultured for cholera and toxigenic E. coli. Neutral fat globules will be examined under microscope to assess the steatorrhoea.

3. Study design

On admission 2 cc venus blood will be drawn for TC, DC, Hct. sp. gravity and also electrolytes if clinically indicated. The patient will be rehydrated with intravenous fluid only. After 24 hr. of admission patients will be fasted overnight and d-xylose test will be carried out. The level of xylose will be analysed in 2 cc. blood collected 1 hr. after feeding 5 gms d-xylose. Next morning in empty stomach vitamin A absorption test will be carried out by feeding 7,500 IU of vitamin A palmitate per kg of body weight. 2.5 cc of blood will be drawn before giving vitamin A and 2.5 cc four hours after for estimation of vitamin A and Zn. Immediately after this 50,000 units of water miscible vitamin A will be injected intramuscularly to restore the liver vitamin A store. Patients will be

discharged after clinical recovery. 14 mg of Zn as $ZnSO_4$ will be supplied to 10 patients in each sub group and the other 10 will receive placebo.

Antibiotics will not be given to the study patients because the effect of antibiotics on vitamin A and zinc absorption and interaction are unknown. Patients will be followed up after two weeks. Repeat vitamin A absorption test will be done to all patients as described earlier. The second vitamin A absorption test enable us to compare the effect of Zn on the vitamin A absorption and its mobilization into the plasma. Whether zinc is directly responsible for better absorption or hepatic mobilization will not be made clear by this study. At the discharge biochemical and anthropometric measurements will be repeated.

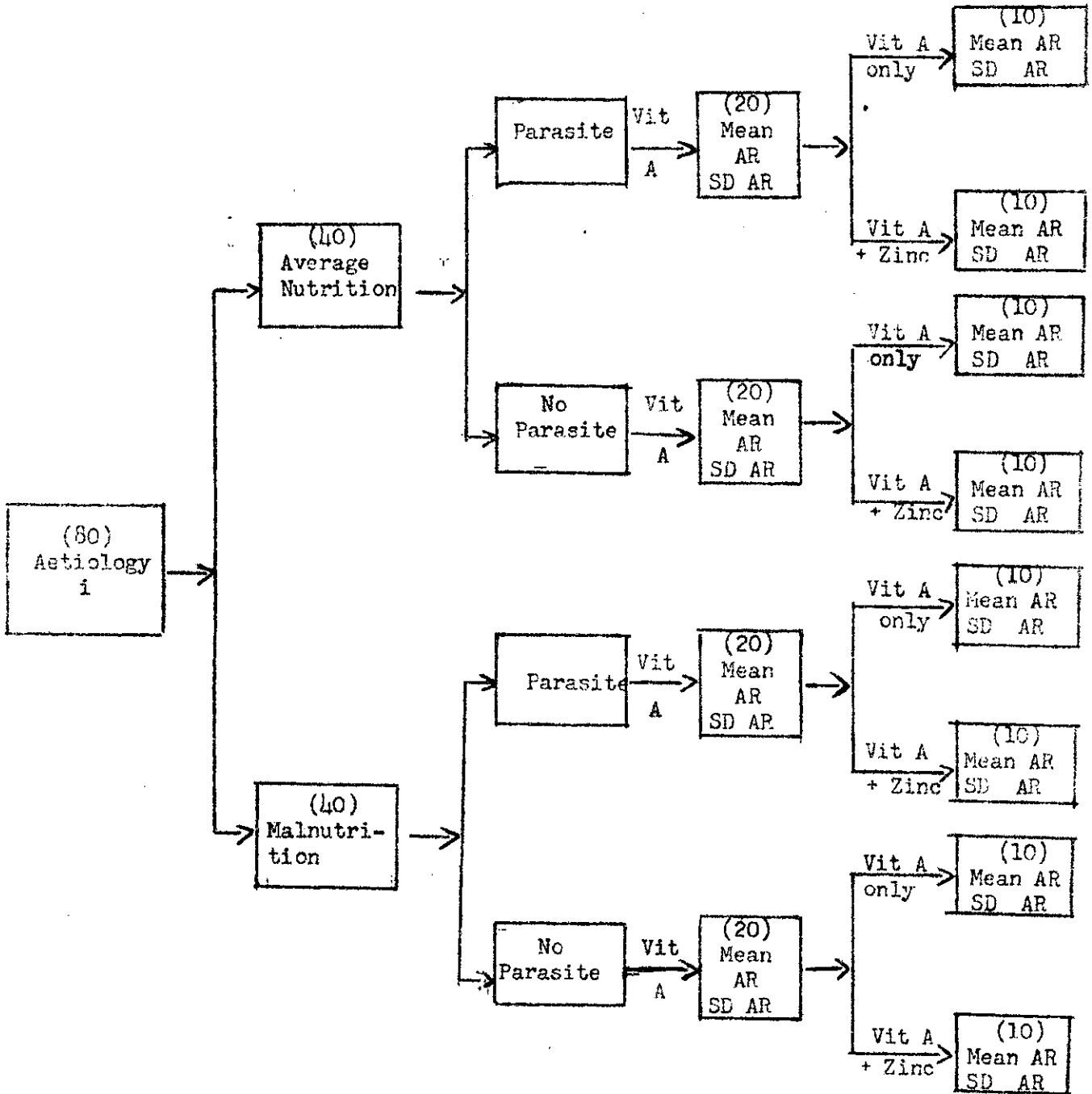
Vitamin A will be analysed flurometrically as described by Hunsen et. al. (20). Zinc in plasma will be estimated by Dr. A.H. Khan, Head, Chemistry Division, Atomic Energy Centre using a very sensitive modern analytical method known as protein induced X-ray Emission (PIXE) analysis in his own laboratory, Dacca.

4. Data analysis

Absorption rate (absorbed IU/supplied IU x 100) will be the unit of measurement and the dependent variable. Diagram 1 shows how each aetiology of diarrhoea (chol, E.coli and control) will be divided and subdivided according to nutritional status and parasite load. It also shows how treatment of vitamin A and zinc will be given.

Each aetiological group will have eight treatment subgroups. Absorption rate for each subject will be found out. Mean and standard deviation for each treatment subgroups, each subgroups of nutrition and parasite will be calculated. T test will be performed to see the difference of between the absorption rates of any two groups or subgroups or treatment subgroups. Analysis of variance technique will be applied to test the absorption rates differences of subgroups and groups as a whole.

DIAGRAM 1



D. SIGNIFICANCE

Diarrhoea of different etiology causes malabsorption or loss of many nutrients. As diarrhoea in Bangladesh is extremely common, the status measurement of vit A and its absorption during diarrhoea will be of immense value. Besides, diarrhoea can precipitate malnutrition and vit A deficiency is more common among malnourished persons. Studies have shown that in a zinc deficient subjects vit A supplementation may not be adequate. Thus establishment of the influence and role of zinc on the vit A absorption and metabolism is very important. This study is likely to have highly significant contributions on these fields.

E. FACILITIES REQUIRED

1. Hospital facilities, nursing and physician attendance will be required. The same nurse and physician may also be attending other study patients.
2. One research assistant will be needed for measuring vitamin A level from the plasma samples.

F. COLLABORATIVE ARRANGEMENTS

This study will be done in collaboration with Dr. A.H. Khan, Head, Chemistry Division from ATOMIC ENERGY CENTRE, DACCA.

SECTION - III - BUDGET

A - DETAILED BUDGET

1. PERSONNEL SERVICES

<u>Name</u>	<u>Position</u>	<u>% of Effort</u>	<u>Annual Salary</u>	<u>Project Requirement</u>	
				<u>Taka</u>	<u>Dollars</u>
Dr. Ayesha Molla	Principal Investigator	30 %	Tk. 86,388/-	25,916/-	1726
Dr. A. Majid Molla	Principal Investigator	15 %	Tk.120,000/-	18,000/-	1200
Dr. M.M. Rahman	Consultant	5 %	Tk.126,480/-	6,324/-	421
Dr. A.H. Khan	Co-Investigator	5 %	No cost to ICDDR,B	-	-
A Research Assistant (to be named)		50 %	Tk. 18,432/-	9,216/-	614
				<u>Tk.65,606/-</u>	<u>\$ 4374</u>

2. SUPPLIES & MATERIALS

	<u>Amount Required</u>	
	<u>Tk.</u>	<u>Dollar</u>
Laboratory Reagent -		
Vitamin A acetate crystals 0.1 gm (100 vials) (IGN Pharmaceuticals)	-	250
Chloroform (25 litre)	-	200
Ethanol 95% for flurometry (40 litre)	-	4480
Petroleum ether (40 litre)	-	250
Vitamin A capsule		supplied by UNICEF
Water miscible vitamin A (200 vials) 100,000 units / ml	500	400
Oral glucose packet - 2000	3000	200
	<u>Tk.3500/-</u>	<u>\$ 5780</u>

3. <u>EQUIPMENT</u>	None	<u>Amount required</u>	
		<u>Tk.</u>	<u>Dollar</u>
Other laboratory facilities	Includes existing glassware etc.	-	-
4. <u>PATIENT HOSPITALIZATION</u>			
(i) No of patient days - 1200	Tk.150.00/day	7,80,000/-	12,000
(ii) Clinical pathology			
Dark field - 160 test	Tk.1.00/test	160/-	11
Sereny test - 160 test	Tk.3.00/test	480/-	32
5. <u>OUTPATIENT CARE</u>			
	None	-	-
6. <u>ICDDR,B TRANSPORT</u>			
	None	-	-
7. <u>TRAVEL AND TRANSPORTATION OF PERSONS</u>			
	None	-	-
8. <u>PRINTING AND PUBLICATION</u>			
		5,000/-	334
		<hr/>	<hr/>
		1,85,640/-	12,377
		<hr/>	<hr/>

GRAND TOTAL : Tk.2,54,746/- Dollar 22,867

Incremental cost Tk.1,89,140 \$ 18,157

B - BUDGET SUMMARY

<u>CATEGORY</u>	<u>T A K A</u>	<u>DOLLAR</u>
1. Personnel	65,606/-	4374
2. Supplies	3,500/-	5780
3. Equipment	-	-
4. Hospitalization	1,80,640/-	12043
5. Outpatients	-	-
6. ICDDR,B Transport	-	-
7. Travel persons	-	-
8. Printing and Publication	5,000/-	334
	<hr/>	<hr/>
GRAND TOTAL:	2,54,746/-	22,531
	*****	*****

Incremental cost Tk.1,89,140/- \$ 18,157

REFERENCES

- (1) Vitamin A deficiency and Xerophthalmia. Report of a joint WHO/USAID Meeting in Jakarta. Nov. 1974, Page 29.
- (2) B. Sivakumar and Vinodini Reddy. Absorption of labelled vitamin A in children during infection. 1972. Br. J. Nutr. 27, 299.
- (3) B. Sivakumar and Vinodini Reddy. Absorption of vitamin A in children with Ascariasis 1975. J. Trop. Med. Hyg. 78, 114.
- (4) Dilip Mahalanabis, T.W. Simpson, Chameli Ganguli, A.K. Bhattacharjee and K.L. Mukherjee. Malabsorption of water miscible vitamin A in children with giardiasis and ascariasis. 1979. Am. J. Clin. Nutr. 32, 313-318.
- (5) Yves Ingenbleek, Henny George Van Den Schrieck, Philippe Denayen and Michel De Visscher. The role of Retinol binding protein in protein calorie malnutrition. Metabolism. 1975, 24, 633.
- (6) Frank Rees Smith, Robert Suskind, Ousa Thanangkul, Claus Leitzmann, Dewitt S. Gordan and Robert E. Olson. Plasma vit A, Retinol binding protein and prealbumin concentrations in protein calorie malnutrition. III. Response to varying dietary treatments. 1975, Am. J. Clin. Nutr. 28, 732-738.
- (7) J. Cecil Smith, Jr. E.G. McDanel, F.F. Fan and James A. Halsted. Zinc: A Trace element essential in vitamin A metabolism 1973, Science 181, 954.
- (8) John R. Duncan and Lucille S. Hurley. An interaction between zinc and vitamin A in pregnant and Fetal rats. J. Nutr. 1978, 108: 1431-1438.

- (9) Ronaghy, H.A. Reinhold, J.G., Mahloudji, M.Ghavami., P. Fox, M.R.S. and Halsted. J.A. Controlled zinc supplementation of malnourished schoolboys in Iran: increased growth and other effects. *Am.J.Clin. Nutr.* 1974, 27, 112.
- (10) Halsted, J.A. Ronaghy, H.A., Abadi, P. Haghshenass, M. Amirhakimi, G.H., Baraket, R.M. and Reinhold, J.G. Zinc deficiency in man. The shiraj experiment. *Am.J.Med.* 1977, 53, 277.
- (11) Halsted, J.A., Smith, J.C., Jr., and Irwin, M.I., A conspectus of research on zinc requirements of man, *J.Mutr.* 1974. 104, 345.
- (12) Eminians, J., Reinhold, J.G., Kfourey, G.A., Amirhakimi, G.H., Sharif, H., and Ziai, M., zinc nutrition of children in Fars province of Iran, *Am.J.Clin. Nutr.*, 1965, 17, 15.
- (13) Sandstead, H.H., Shukry, A.S., Prasad, A.S., Gabr, M.K., Hifney, A.E., Mokhtar, N., and Darby, W.J., Karwshiorkor in Egypt. I clinical and biochemical studies, with special reference to plasma zinc and serum lactic dehydrogenase, *Am.J.Clin. Nutr.* 1965, 17, 15.
- (14) Hellwege, H.H., Der Serumzinkspiegel and seine veränderungen bei einigen krankheiten en kindesalter, *Monatsschr. Kinderheilkd.* 1977, 119, 37.
- (15) MacMohan, R.A., Parker, M.L., and Mckinnon, M.C., zinc treatment in malabsorption, *Med. J. Aust.*, 1968, 2, 210.

- (16) Solomons, N.W., Khactor, K.V., Sandstead, H.H., and Rosenberg, I.H., Zinc nutrition in regional enteritis (RE), Am.J.Clin. Nutr., 1974, 27, 438.
- (17) Ananda S.Prasad. Zinc in human nutrition CRC critical review in clinical laboratory sciences. 1977.
- (18) Nutrition survey of East Pakistan, March 1962 January 1964. U.S. Department H.E.W., 1966.
- (19) Kenneth H. Brown, M.D., Abdül Gaffar, M.B.B.S., Sharif M. Alangir, M.B.B.S. Vitamin A deficiency, protein calorie malnutrition and infection in children. 1978. Submitted for publication.
- (20) Leland G. Hansen, M.P.H., and Warren J. Warwick, M.D. An improved assay method for serum vitamin A and E using fluorometry. Am.J.Clin pathol 1978, 70, 922-923.
- (21) Dawson, J.B. and Walker, B.E., Direct determination of zinc in whole blood, plasma and urine by atomic absorption spectroscopy, Clin, Chim. Acta., 1969, 26, 465.

Abstract Summary

In a study of 40 patients with cholera and E. coli, the absorption of vitamin A and the effect of zinc supplementation for its effective utilisation will be studied on admission and at recovery phase. Weaned children between 3-10 years of age will be admitted to ICDDR,B hospital and after thorough physical and clinical examination 2 cc of blood sample will be taken for determination of different biochemical parameters and also electrolytes if clinically indicated. The patients will be given intravenous fluid therapy only. After 24 hr. of admission patients will be fasted overnight and D-xylose test will be carried out. Next morning vitamin A absorption test will be done by feeding 7500 IU of vitamin A per kg. 2.5 cc of blood will be collected before and 2.5 cc 4 hr. after for estimation of vitamin A and zinc. Immediately after this an intramuscular injection of vitamin A (50,000 IU) will be given to the patients for saturating the liver store. At the same time 14 mg of zinc as Znso₄ will be fed daily to 10 patients with each etiology and the others will receive placebo.

Patients will be kept under careful observation and antibiotics will only be given if clinically indicated. On 12th day of admission vitamin A absorption test will again be done and all estimations stated earlier will be repeated.

1. Children are preferred because they are the most susceptible group of our population who are affected by diarrhoea and malnutrition. Informed consent will be obtained from the guardian.
2. There is no potential risk involved with the study.
3. Does not apply.
4. Patients will be anonymous.
5. Consent form is attached.
6. Does not apply.
7. The patients will be potentially benefitted by this study. We anticipate that vitamin A malabsorption occurs during diarrhoea and supplementation of the diet with vitamin A and zinc is a direct benefit of the subjects.
8. Blood samples will be needed for the study.

CONSENT FORM

ICDDR,B has undertaken a clinical study to estimate vitamin A absorption in diarrhoea and to see the effect of zinc supplementation on the absorption of vitamin A at admission and at the time of discharge. This will include initial blood examination for assessment of nutritional parameters (both biochemical and anthropometric). Your stool and urine will also be examined microscopically. Then you will be fed an oral dose of vitamin A. Before and after administration of this medicine each time 2.5 cc sample of blood will be taken for assessing your vitamin A and zinc concentration. After this you will be given an intramuscular injection of vitamin A for saturation of your liver concentration. From the same day you will receive 14 mg of Znso4 powder to eat everyday. On 12th day of admission vitamin A test will be again performed for estimation of vitamin A and zinc in your blood samples.

If you do not want to participate in the study you will still be taken care of. You can withdraw from the study at any time you want to and you will still be given full treatment.

Your signature

Date _____

Investigator's signature

