chment 1.

Date 21/1/1991

E SHEET) ETHICAL REVIEW COMMITTEE, ICDDR,B.

cipal Investigator Dr. F.C. Patra Trainee Investigator (if any) _____

ication No. 90-022 (Revised) Supporting Agency (if Non-ICDDR,B) _____

e of Study Evaluation of diets d on cooked rice powder ..... .clinical trial using factorial design

Project status:
(✓) New Study
( ) Continuation with change
( ) No change (do not fill out rest of form)

le 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 Committee:
✓ Umbrella proposal - Initially submit an overview (all other requirements will be submitted with individual studies).
✓ Protocol (Required)
✓ Abstract Summary (Required)
✓ Statement given or read to subjects on 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
✓ 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.
2. Examples of the type of specific questions to be asked in the sensitive areas.
3. An indication as to when the questionnaire will be presented to the Cttee. for review.

gree to obtain approval of the Ethical Review Committee for any changes lving the rights and welfare of subjects before making such change.

F.C. Patra

20/1/91

SECTION I - RESEARCH PROTOCOL

1.	Title	:	Evaluation of diets based on cooked rice powder luquified by amylase rich germinated wheat cereal flour and yoghurt in persistent diarrhoea: a controlled clinical trial using factorial design.
2.	Principal Investigator	:	Dr F.C. Patra
	Co-investigators	:	Senior Medical Officer - 1 Medical Officer - 1 Trainee Research Fellow-1 M.A. Wahed
	Project Co-ordinator	:	Dr D. Mahalanabis
3.	Starting date	:	December 1990
4.	Expected Completion date	:	June 1993
5.	Total Direct Cost	:	US$ 175559.00
	Source of Funding	:	SDC/UNICEF
6.	Scientific Division	:	This protocol has been approved by the Clinical Sciences Division

Signature of Associate Director, CSD ---------- D Mahalanabis

Date: ---------17/12/90---------

7. ABSTRACT SUMMARY

Management of persistent diarrhoea still poses a formidable challenge to the clinicians. The very limited success that has been achieved in this field perhaps can be entirely attributed to dietary manipulations of these category of patients. In the proposed study we plan to evaluate the role of yoghurt and partially hydrolysed starch by adding amylase rich-germinated-cereal flour (ARGC) in an effort to improve the diet for infants and young children with persistent diarrhoea.

A total of 180 patients will be studied. A randomised factorial design for a clinical trial will be used to test two factors i.e. use of yoghurt in place of milk and use of partially hydrolysed cooked rice powder in place of cooked rice powder alone. Patients will be randomised into four groups. One group will receive rice powder plus milk; the second group will receive partially hydrolysed cooked rice powder by adding ARGC flour plus milk; the third group will receive a diet based on cooked rice power plus yoghurt, and the fourth group will receive partially hydrolysed cooked rice powder by adding ARGC flour plus yoghurt.

Sealed envelops containing treatment allocation based on a randomisation chart prepared by using permuted block of random numbers of variable block length will be used. Intake of these specialised diet, breast milk intake, stool output and duration of diarrhoea will be the outcome measures.

8. Reviews:

i. Ethical Review Committee: ----------

ii. Research Review Committee: ----------

iii. Director, ICDDR,B: ----------

SECTION II - RESEARCH PLAN

A. Introduction:

1. Objective:

To evaluate the role of diets based on (a) Yoghurt as a milk substitute for a milk plus precooked rice powder based diet and, (b) partially hyudrolysed precooked rice powder (by adding amylase rich germinated cereal flour) as a rice substitute for a milk plus precooked rice powder based diet in infants and young children suffering from persistent diarrhoea.

2. Background:

Persistent diarrhoea is defined as the diarrhoea which starts acutely but continues beyond their usual course of illness; for the purpose of this protocol an acute diarrhoea persisting longer than 14 days is considered to be persistent diarrhoea. Following the discovery of oral rehydration therapy - a simple and highly effective treatment of dehydration - persistent diarrhoea has emerged as an important cause of mortality and adverse nutrititional consequence in children in developing countries. Diet management is an important component of case management strategy of persistent diarrhoea in infants and young children. Considerable amount of research has gone into designing diets which provide adequate energy and nutrients and at the same time do not aggravate the clinical course of persistent diarrhoea. In infants and young children with severe persistent diarrhoea a diet based on chicken meat, vegetable oil and

glucose (in low concentrations) has been shown to be beneficial (1,2). Recently a less expensive diet, improvised from locally available ingredients i.e. rice powder, egg white, glucose, vegetable oil and salts has been found to be highly absorption efficient and effective in infants and young children with persistent diarrhoea at ICDDR,B (3).

Yoghurt is a traditionally used food in this subcontinent. It is believed to be an easily digestible preparation of milk so is often consumed during diarrhoeal illnesses. It can be very easily prepared at home. Yoghurt is prepared by adding lactobacillus bulgaricus and streptococcus thermophilus to the milk. The lactose content of yoghurt is 20 to 30% less compared to that of yoghurt. Fermented milk (yoghurt) based diets have also been shown to be useful in mild persistent diarrhoea in an out-patient based sutdy in Algeria (4). Yoghurt has a lower concentration of lactose than milk and contains bacterial β-galactosidase which is inactive at the usual pH of yoghurt but becomes activated in the small intestinal pH and further assists in the hydrolysis of lactose (5, 6, 7). In human studies it has been shown that yoghurt allows lactose absorption by lactose deficient subjects (5, 6, 7).

Germinated wheat cereal flour prepared in our laboratory has a high concentration of amylase (8) and when a small amount is added to a rice porridge it liquifies (9). Semi-quantitative thin layer chromatography of this liquified porridge showed that the complex starch in rice is broken down into maltodextrins of variable chain length, maltotri-

ose, maltose and a small amount of glucose (8). Such a liquified porridge based diet may be considered as a poor man's semi elemental diet. However, such a diet has not been tested in infants and young children with persistent diarrhoea.

It has been postulated that a mixture of a cereal plus milk could be the basis of first line dietary treatment in infants and young children with persistent diarrhoea and has been in use at the Clinical Research Centre of ICDDR,B. A partially hydrolysed cereal may render added efficiency to such a diet; and finally replacement of milk by an equivalent amount of yoghurt (milk fermented by adding labtobacillus bulgaricus + streptococcus thermophilus) may render such a diet even more absorption efficient. In this study we propose to evaluate

a) the role of yoghurt and

b) the role of partially hydrolysed rice starch (by adding ARGC flour) in improving the diet for infants and young children with persistent diarrhoea.

3. Specific objectives:

Could the use of a diet based on (a) Youghurt plus pre-cooked rice powder as such or partially hydrolysed by adding amylase rich germinated cereal (ARGC) flour and (b) Milk plus pre-cooked rice powder as such or partially hydrolysed by adding amylase rich germinated cereal (ARGC) flour be beneficial to infants and young children suffering from persistent diarrhoea i.e. maintain or improve the nutrition

during this phase without increasing the stool frequency and volume.

B. RATIONALE/SIGNIFICANCE

This study will assist in the development of an inexpensive ready to prepare energy dense and easily assimilable diet for infants and younger children with persistent diarrhoea.

C. RESPONSE VARIABLES

1. Stool output (gms per kg) daily and cumulative for 5 days.
2. Post-intervention duration of diarrhoea.
3. Weight change over 5 days of treatment.

D. METHODS AND PROCEDURES:

Study design and Sample size:

Trial design considerations.

A factorial design for a clinical trial will be used to test two factors i.e. use of yoghurt in place of milk and use of partially hydrolysed cooked rice powder in place of cooked rice powder in a diet composed of a cereal /milk mixture. Patients will be randomised into four groups: 1) one group will receive a diet based on cooked rice powder plus milk, 2) group two will receive partially hydrolysed cooked rice powder (by adding ARGC flour) plus milk, 3) group three will receive a diet based on cooked rice powder plus yoghurt, and 4) group four will receive partially hydrolysed cooked rice powder (by adding ARGC flour) plus

yoghurt. Acceptibility tests of these diets will be undertaken initially before embarking on the study. The composition of diets are shown in Table 1. The osmolality of these diets (2 hour after adding ARGCF) does not exceed 360 mosm/kg. Children receiving yoghurt based diet will be compared with those who will not receive yoghurt based diet irrespective of whether the diet contains hydrolysed or unhydrolysed rice and children receiving partially hydrolysed rice based diet will be compared with those who do not receive apartially hydrolysed rice based diet irrespective of whether the diet contains milk or yoghurt. First order intraction between the effect of yoghurt and partially hydrolysed rice (i.e. ARGC treated) will also be evaluated. This design will reduce the sample size requirement considerably.

Eligibility criteria:

1. Male children aged 5 months to 23 months with diarrhoea lasting over 14 days but less than 30 days duration;
2. Infants exclusively or largely on breastmilk will not be included in the study.
3. Absence of severe malnutrition i.e. gross marasmus, kwashiorkor or marasmic kwashiorkor;
4. Absence of associated systemic infections and/ or complications.
5. Frank blood and mucus in the stool (dysentery positive) will not be eligible for the study.
6. Parents are willing to give informed consent.

7. History of previous diarrhoeal episode(s) and prior use of any antibiotics for the present episode will not disqualify a patient for inclusion into the study.

Sample size:

We assume that an yoghurt based diet will reduce the daily stool volume by 30% compared to the diet based on milk. In a recently reported study from ICDDR,B (Roy SK et al. unpublished) the average stool output in a group of infants with persistent diarrhoea was 98 gms per kg on day one (estimated standard deviation of 65) and the average stool output on day 3 was 84g with an estimated standard deviation of 56g. The calculated sample size for the group receiving yoghurt based diet is then estimated to be about 80 in each group (at 5% level of significance and 80% power). Therefore the total sample size is 160; we add 20 for deviated course. The total sample size therefore is 180 i.e. 45 in each of the four groups. If we assume that use of hydrolysed rice further improves the yoghurt based diet so that stool output is reduced by 40% compared to rice + milk diet the sample size would be 44 per group. This comparison is between group 4 and group 1; therefore the sample size of 45 in each group as calculated earlier is adequate.

Enrollment of subject:

About 70,000 patients annually attend the Treatment Centre of ICDDR,B. About 300 of these patients present with persistent diarrhoea. Patients who report to the Out Patient Department of ICDDR,B during working hours (8:30 a.m. to

5:00 p.m.) and who fulfill the eligibility criteria will be enrolled into the study. Written informed consent will be taken before entering a patient into the study.

Baseline examination:

A baseline history, physical examination and other social and anthropological data will be recorded on a pre-tested data form (Annex-1). The baseline history, physical examination will include:

- Identification of the subject
- Duration of symptoms prior to admission.
- Details of any treatment given for the illness before admission.
- Feeding history before and during the present illness.
- Hydration status according to the WHO guidelines.
- Anthropometric measurements i.e. body weight, height (recumbent length), mid upper-arm circumference.
- Mother's education, housing condition, parents occupation.

Initial observation period

Before entering into the study each patient will be observed overnight till the following morning. During the period the patients will be offered the standard hospital diet for chronic diarrhoea and will be rehydrated by rice based ORS. During this period the patient's stool output will be measured and frequency of stool will be noted. If the patient fails to pass 3 diarrhoea stools during this period then he will not be eligible to enter into the study.

Allocation to treatment group (randomisation):

Randomisation will only take place after the patient has been defenitely entered into the study.

The study cannot be blinded because of the appearance of the diets. Randomisation tables will be prepared using random permuted blocks of variable lengths. Serially numbered sealed envelopes corresponding to the serial numbers of the patient to be recruited into the study will contain treatment allocation according to the randomisation code.

After the patient has been definitely assigned to the study and admitted to the ward the sealed envelope containing the serial number of the study patient will be opened to ascertain the treatment group the patient belongs to.

The randomisation list and sealed envelopes will be prepared by a responsible and appropriately trained person who is not otherwise associated with the study.

Standard case management and the experimental treatment:

Immediately after enrollment of the patient into the study, the degree of dehydration will be assessed by the WHO criteria (5). Severely dehydrated patients will be given intravenous Acetate (Dhaka solution Na-133, K-13, Cl 98, Acetate-48, in mmol/L) solution 100 ml/kg over a period of 2-4 hours till the signs of dehydration are fully corrected. Mild to moderately dehydrated patients. will be rehydrated by WHO recommended ORS. 50 to 100 ml/kg (body wt.) of ORS will be given by spoon in 3 to 4 hours till the signs of dehydration are fully corrected. No feed will be offered during the rehydration period.

After the patient is fully hydrated the study diet as per the randomisation will be offered to the patient. Diets will have approximately 70 kcal per 100 grams, similar to energy concentration of human milk.

140 ml/kg/day of the diets will be offered in 2 to 3 hourly feeds on day one and day two (98 kcal/kg/day) and then will be increased to 150 ml/kg/day (105 kcl/kg/day) on day 3 and 4 and on day 5 & 6 upto 170 ml/kg/day (119 kcl/kg/day) will be offered. 40% of the calories in the diet will be provided by yoghort or milk. The methods for preparation of the diets and their composition are given in Annexure B.

During the study period following the start of the feeding regimen the patient's hydration will be maintained by WHO ORS. If the patient becomes severely dehydrated then he will be rehydrated rapidly with intravenous Dacca solution (100 ml/kg) in about 2-4 hours following which ORS will be given in quantity to match the stool volume every 4 hourly.

Breastfed infants will continue to receive breast feeding. Intake of breast milk will be measured by weighing the infants before and after each breast-feed.

Each study diet for each patient (each feed) will be prepared separately in the metabolic kitchen adjacent to the metabolic ward. Sufficient quantity for each feed will be prepared. Feeds once prepared will not be stored. All feeds will be given by spoon. In case the child vomits during or immediately following the feeds the amount vomited will be measured and equal amount of feeds will be given to the child immediately or during

the next feeding schedule if vomiting occurs following the feeds. Quantity of diet consumed will be determined by weighing the container before and after each feed. Aliquots of feeds at random will be stored for future analysis.

Stool output will be measured every 4 hourly by diaper methods. Diapers made of cotton, gauze and polythene sheets will be prepared and weighed, and the weight written in each diaper and kept in a polythene bag by the side of the patient. After each stool, the soiled diaper will be replaced by a dry diaper and the soiled ones will be kept in another polythene bag till the time of weighing every 4 hourly. Weight of the stool volume will be determined by the difference of weight between the soiled diapers and dry diapers.

Urine will be separated from mixing with the stool by applying urine collection bags to the penis. After passage of each urine the bags will be changed and the volume of urine will be determined by measuring it in a volumetric cylinder.

ORS dispensed in bottle will be kept by the bed side of the patient. ORS will be fed by spoon. Amount of ORS consumed will be determined every 4 hourly.

Duration of diarrhoea will be recorded from admission into the study to the time of last diarrhoeal stool. If on day 5, the diarrhoea has not stopped the observation will be truncated for stool output, but observation will continue upto day 7 for dura tion (i.e. to note the time when diarrhoea ceased). If diarrhoea does not stop at the ending of day 7 then the observation will be truncated.

Laboratory procedures (routine):

1. Stool for microscopy on admission.
2. Stool for culture for *V. cholerae*, Shigellae sp[illegible]nd Salmonella on admission. E. coli colonies will be saved and tested for LT and St toxins.
3. Elisa for rotavirus on admission.
4. Blood for CBC, electrolytes, HCT, and specific gravity on admission, and on day 2 to assess hydration and if necessary on clinical grounds subsequently.
5. Urine routine and culture, x-ray and blood culture if necessary.
6. Patient will be weighed naked at the time of admission, and subsequently once every day in a balance with the sensitivity of 5 grams.
7. Stool reducing substances and stool pH will be monitored once daily in each patient. If indicated the number of stool specimen tested will be 2 or 3 in a day in selected patients.

Special laboratory procedures:

Total energy content of the feed will be determined by ballistic bomb caloriemetry (Gallenkamp). Nitrogen content of the feeds will be determined by micro-kjeldahl method (10), fat by vande kamers method (11) and carbohydrates by substracting these from total energy. Viscosity of the diets will be measured settes, U.S.A.using a viscosimeter Brookfield Engineering labs. Massachussettes, U.S.A.

Deviated course of the study:

Patient will be withdrawn from the study in case of non-compliance. If the patient is removed from the hospital before the end of the study or because the patient required unscheduled treatment for serious intercurrent illness and the planned diet treatment can not be continued. All records of the patients illness will be kept and considered at the time of analysis. If the patients purging leads to occurrence or reoccurrence of severe dehydration in any patient which necessitates I.V. therapy (to correct dehydration) two times or more in 24 hours following the 1st 48 hours of the study period will be considered as treatment failures. These patients will be withdrawn from the study and will be offered the chicken based diet which is the most effective diet for chronic diarrhoea in the present set up in ICDDR,B.

At the time of discharge from the study the dietary advice followed in this centre for these patients will be given. There will be no home visits for follow up of these patients. If they come to the hospital for further advice they will report to the chronic diarrhoea team.

Trial organisation:

Facilities and patient population:

About 300 patients with chronic diarrhoea come to the treatment centre of ICDDR,B each year. If the patients are enrolled into this study during the working hours, it is expected that it will take 2 years to study the requisite number of patients. After enrollment patient will be kept in the study ward.

Data collection and Analysis:

The data forms will be entered into a micro computer using a data entry template. The pre-intervention data will be summerised and compared among the groups. Significance tests will be carried out using standard parametric tests for quantitative outcome variables. The distribution of data will be examined for validity of such tests and if necessary appropriate transformation will be carried out before conducting the tests. Otherwise non-parametric tests will be used.

Analysis of variance for factorial designs will be used to evaluate the role of yoghurt and the role of partially hydrolysed rice powder in the diet and their effect on the daily stool output, comulative stool output for five days and on the duration of diarrhoea. Their first order interaction will also be evaluated. SPSSS PC+ software will be used for all statistical analysis. We anticipate that, in a small number of children, information on the duration of diarrhoea will be truncated; therefore, the duration will also be compared using servival analysis techniques and the significance of the difference will be evaluated by Log Rank Test.

Definitions:

1. Duration of diarrhoea after admission into the study: The time in hours from initiation of the study diet until passage of the last liquid or semiliquid stool prior to three formed stools or prior to 24 hours during which no stool is passed.

2. Stool output: The stool weight in grams per kg of admission body weight expressed per time period e.g. per 24 hours and for the entire duration of observation (i.e. 5 days or till cessation of diarrhoea).

3. Food intake: The weight of the food consumed in grams per kg of admission body weight expressed by time period e.g. per 24 hours and for the entire duration of diarrhoea.

4. ORS intake: The volume of ORS taken in ml per kg of admission body weight expressed per time period. e.g. per 24 hours and for the 5 day study period or less.

5. Breast milk intake: Weight of breast milk expressed by time period e.g. per 24 hours and for the entire study period.

References:

1. MacLean WC et al. Nutritional management of chronic diarrhoea and malnutrition, primary reliance on oral feeding. J Pediatr 1980;97:316-323.

2. Larcher VF, Shepherd R, Francis DEM and Harries JT. Protracted diarrhoea in infancy. Arch Dis Child 1977;52:597-605.

3. Roy SK et al. Persistent diarrhoea: clinical efficacy and nutrient absorption with a rice based diet. Arch Dis Child 1990;65:294-297.

4. Boudraa G, Toughami M, et al. Effet compares du yaourt et du laitsur la diarrhee persistante du nourrisson et de l'infant: resultants preliminaries. In:Les laits fermentes. Actualite de la recherche, pp. 229-132. Paris, John Libbey Eurotext Ltd. 1989.

5. Dewit D, Boudraa G, et al. Breth hydrogen test and stools characteristics after ingstion of milk and yogurt in malnourished children with chronic diarrhoea and lactase defi ciency. Journal of Tropical Pediatrics 1987;33:177-180.

6. Kolars JC, Levitt MD, et al. Yogurt - an autodigesting source of lactose. The New Enmgland Journal of Medicine. 1984;310:1-3.

7. Savaiano DA, ElAnouar AA, et al. Lactose malabsorption from yogurt, pasteurized yogurt, sweet acidophilus milk, and cultured milk in lactase-deficient individuals. Savaiano DA, Elanouar AA, et al. The American Journal of Clinical Nutrition. 1984;1219-1223.

8. Wahed M.A. Personal communication.

9. Mosa AC, Svanberg U. Preparation of weaning foods with high nutrient density using flour of germinated cereals. UNU Food and Nutrition Bulletin. 1983;5(2):10-14

10. Henry RJ. Clincial Chemistry: Principles and Technics. 1964. Herper & Row, New York.

11. Vande Kamer JII, Ten Bokkel Huiniuk II, Weyers IIA. Rapid method of determination of fat in feces. J Biol Chem 1949;177:347-55.

Abstract Summary for Ethical Review Committee

1. The study aims at evaluating the role of a mixture of rice cereal and milk as the basis for first line of dietary treatment in infants and young children with persistent diarrhoea as is routinely done at ICDDR,B. Cereals will be offered in two forms (1) Pre-cooked rice powder and (2) Pre-cooked rice powder liquified by Amylase rich germinated wheat flour. Similarly milk will be offered in two forms (1) Milk as such and (2) Yoghurt prepared from this same milk. The age range of the patients is 5 months to 23 months.
2. There is no potential risk involved.
3. The children will be under constant observations by the physicians, study ward nurses, health assistant and volunteers. Apart from the above variation in diet, the case management will not deviate from the one followed at ICDDR,B.
4. During data analysis only the I.D. number of the patient will be used and complete confidentiality will be maintained.
5. Written informed consent will be obtained from the authorised legal guardians or parents before the patients are included in the study.
6. Stool samples will be taken on admission for microscopy and culture.
7. Venous blood samples (2 ml) will be taken on admission and repeated on day 2. Blood will be analysed for hct, Sp. gravity, electrolytes and TC, DC, and Hb%. This is a routine procedure.

8. Patient will be given the usual care offered to all the patients in the ICDDR,B and under no circumstances appropriate treatment will be withheld from the patient.

TABLE 1

Composition of the diets

1. Cooked rice powder plus milk:	
Milk powder	6.0 gram
Khai (cooked rice) powder	13 gram
Water up to	100 gram
Energy content	75 kcal/100 g
2. Partially hydrolyzed cooked rice powder plus milk:	
Milk powder	6.0 gram
Khai (cooked rice) powder	13.0 gram
Amylase rich germinated cereal flour (ARGCF)	2.0 gram
Water up to	100 gram
Energy content	75 kcal/100 g
3. Cooked rice powder plus yoghurt:	
Yoghurt prepared from 6 gram of milk powder	
Khai powder	13 gram
Water up to	100 gram
Energy content	75 kcal/100 g
4. Partially hydrolyzed cooked rice powder plus yoghurt:	
Yoghurt prepared from 6 gram of milk powder	
Khai powder	13 gram
ARGCF	2 gram
Water up to	100 gram
Energy content	75 kcal/100 g

Pop-rice powder - Annexure-B

Pop-rice is used as a traditional snack in the Indian sub continent and is readily available in the local market. Pop-rice will be procured from the local market in bulk. It will be warmed upto 40^{o}C in an oven before grinding in an electric grind. The pop-rice powder will be stored in polythene bags.

Amylase rich germinated cereal flour (ARGCF)

This is prepared from wheat in the biochemistry lab and is available in powder form. It is rich in amylase.

Milk - Whole milk powder fed routinely to the patient in the Clinical Research Centre will be used.

Yoghurt - Youghurt will be prepared in the traditional manner (as it is done in the household) using the whole milk powder used in the Clinical Research Centre. Quality of yoghurt will be checked from time to time by measuring its lactose content which should be 20-30% less than the milk.

Composition of the diet:

Diets will have similar calorie content as human milk. 40% of the calorie will be supplied by the milk and the rest 60% by the rice powder.

To prepare 100 g of the feed the required quantity of the ingredients are as follows.

Milk powder - 6.0 gr

Khai (pop-rice) powder - 15 gr

Water upto 100 gr

The calculated energy density of this diet is 75 Kcal per 100 gr.

For diets containing AFGCF 2 gr of ARGCF will be used and 13 gr of pop-rice powder will be used for 100 gr of feed. The calculated calorie density of this feed is 75 Kcal/per 100 gr.

Water used to prepare the ARGCF treated feeds will be heated up approximately upto 40^{o}C to facilitate the enzyme hydrolysis of the starch.

The measured osmolality of the ARGCF containing feeds from fifteen minutes to two hours after adding ARGCF is 315-350 mosm per kg.

Clinical Trial of ARF based weaning food in persistent diarrhoea in infants and children (Feeding trial)

	1st year	2nd year
Personnel	US$	US$
Medical Officer - NOC (25%)	2871	2871
Medical Officer - NOA (25%)	1872	1872
Paediatrician (25%)	6000	6000
Research Trainee (Doctor)		
Fellow (1) (100%)	3000	3000
Data management & Statistics trainee fellow (100%)	1500	1500
Dietician GS5 (100%)	4224	4224
Clerk (20%)	900	900
Secretary (10%)	621	621
Ayah (4) (100%)	4800	4800
Data Manager - GS5 (25%)	660	600
Trainee Health Asstt.- 3 (100%)	4000	4000
Trainee Laboratory Research Fellow - 1 (100%)	1500	1500
	31948	31948
Equipment		
Data managemet (software & hardware)	5000	
High precision balance for test weighing (one unit)	4000	
Precision balance for measuring stool (one unit)	500	
Blender (one unit)	1050	
	10550	
Laboratory Costs		
Stool M/E (200 tests)	400	
Stool culture (V. cholerae & ETEC, Shigella - (200 tests)	2000	
Stool for Rotavirus (200 tests)	2000	
Stool sugar (1000 tests)	2000	
LT & ST (50 tests)	500	
Stool osmolality (300 tests)	900	
Stool electrolytes (300 tests)	1500	
Urine routine (200 tests)	600	
Blood:		
TC, DC (200 tests)	600	
Hct, sp. gravity (500 tests)	1500	
Electrolytes (300 tests)	2000	
XRAY - chest & abdomen (100)	500	

For metabolic collection:

Metabolic analysis:

Total calorie estimation -	
200 stool samples	2000
200 food samples	2000
Total nitrogen	
200 stool samples	2400
Viscoscity - 200 food samples	1000
Patient Hospitalisation	
30x5x180	27000
Supplies & materials (stock,non-stock)	5000
Urine collection bags (1000)	2000
Polythene sheets (1000)	500
Others	
Printing, publication,	1000
xerox	500
Medical illustration	500
Staff clinic	500
Transport	1000
Post & Communications	700

Summary

	1st year US$	2nd year US$
Personnel	31948	31948
Equipment	10550	
Laboratory	21900	
Supplies & material	7500	
Patient hospitalisation	27000	
Others	4200	
Total	103098	31948
Overhead 30%	30929	9584
GRAND TOTAL	134027	41532

Total for 2 years = US$ 175559.00

Consent Form

Dietary manipulation is the mainstay of treatment of persistent diarrhoea. These category of patient progressively become malnourished as the illness is prolonged in nature. They have loss of appetite and the absorption capacity of the intestine is less compared to that of healthy children.

Liquified porridge contains partially digested food which will be easily digested in the intestine of these patients. We plan to offer one out of these four types of diets. (1) Pre-cooked rice powder and milk, (2) Liquified pre-cooked rice powder and milk, (3) Yoghurt and pre-cooked rice powder, (4) Yoghurt and liquified pre-cooked rice powder.

Liquification of the rice powder is done by adding very small quantity of germinated wheat cereal powder to it.

By random selection your baby will get one of these four types of feeds every 4 hourly. If your child is breast fed he will be allowed to have breast feeding as usual.

After admission and again on the 2nd day a small quantity of blood will be taken from your child for laboratory tests. These tests will help your child as well as the physician who will be able to decide the quantity of fluids or other medicines that might be necessary for treatment, depending on the results of these tests.

Stool and urine, samples of your child will also be examined. Your child will be weighed daily and each time before and after breast feeding. Your child will be provided with other treatments and medicines which will be judged appropriate.

The results from this study might in future help other children suffering from prolonged diarrhoea.

If you agree upon the above mentioned conditions and allow your child to participate in this research please sign (or give your thumb impression) below. If you don't allow your child to be studied he will get all necessary available treatment in this hospital. By allowing your child to participate in the study you also have the right to withdraw your child from the study at any time you may wish without assigning any reason to us.

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Principal Investigator	Guardian
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Witness	Date

সম্মতি পত্র

দীর্ঘস্থায়ী ডায়রিয়া চিকিৎসায় খাবারের ভূমিকা গুরুত্বপূর্ণ। রোগ দীর্ঘস্থায়ী হবার কারণে এই সমস্ত রোগী ধীরে ধীরে অপুষ্টির শিকার হয়। সুস্থ্য বাচ্চাদের তুলনায় এই শিশুদের খাবারের রুচি এবং পরিপাক ক্ষমতা কমে যায়।

তরলীকৃত শিশু খাদ্যে আংশিক পরিপাক অবস্থায় খাবার থাকে, যা এই শিশুরা সহজে হজম করতে পারে। এরকম চার প্রকার খাবারের যে কোন একটি শিশুকে দেয়া হবে : (ক) সেদ্ধ করা চালের গুঁড়ো ও দুধ, (খ) তরলীকৃত সেদ্ধ করা চালের গুঁড়ো ও দুধ, (গ) সেদ্ধ করা চালের গুঁড়ো ও দহু, (ঘ) তরলীকৃত সেদ্ধ করা চালের গুঁড়ো ও দহু।

চালের গুঁড়োর সাথে সামান্য পরিমান অংকুরিত গমের গুঁড়ো মিশিয়ে তরল খাবার তৈরী করা হয়।

নির্ধারিত ক্রম অনুসারে আপনার শিশু উক্ত চার প্রকার খাবারের যে কোন একটি প্রতি ৪ ঘন্টা পর পর খাবে। বুকের দুধ খেলে তা আগের মতোই চলবে।

ভর্তির সময় এবং পুনরায় দ্বিতীয় দিনে আপনার শিশুর সামান্য পরিমান রক্ত নিয়ে ল্যাবরেটরী পরীক্ষা করা হবে। এই পরীক্ষার দ্বারা শিশুর কতটা স্যালাইন বা অন্য ঔষধ লাগবে তা জানা যাবে।

এছাড়া আপনার শিশুর মল ও মুত্র পরীক্ষা করা হবে। প্রতিদিন একবার এবং বুকের দুধ খাবার আগে ও পরে শিশুর ওজন মাপা হবে। শিশুর জন্য প্রয়োজনীয় অন্যান্য প্রয়োজনীয় চিকিৎসা ও ঔষধ দেয়া হবে।

এই পরীক্ষার ফলাফল ভবিষ্যতে অন্য শিশুদের দীর্ঘস্থায়ী ডায়রিয়া চিকিৎসায় সাহায্য করতে পারে।

আপনি যদি উল্লিখিত শর্তে রাজী থাকেন এবং আপনার শিশুকে এই গবেষণায় অংশগ্রহণ করাতে চান, তাহলে নীচে সই (বা টিপ সই) দিন। আপনি গবেষণায় অংশ না নিলেও আপনার শিশু এই হাসপাতালের সকল প্রয়োজনীয় চিকিৎসা পাবে। গবেষণায় অংশ সেবার পরও যে কোন সময় ইচ্ছা করলে কোন কারণ না দেখিয়ে আপনি আপনার শিশুকে গবেষণা থেকে সরিয়ে নিতে পারবেন।

প্রধান গবেষক

অভিভাবক