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SECTION I - RESEARCH PROTOCOL

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- I. TITLE : Efficacy of different Cereals (Maize, Millet, Sorghum) based oral rehydration solution in the management of acute diarrhoea in children.
- II. PRINCIPAL INVESTIGATORS : 1. Dr. Patrick R. Kenya
2. Dr. H. W. Odongo
- III. CO-INVESTIGATORS : 1. Dr. L. W. Okombo
2. Mrs. B. N. Were
3. Medical officer (to be named later)
- COLLABORATING INVESTIGATORS : 1. Dr. A. M. Molla
2. Dr. S. K. Nath
3. Dr. Ayesha Molla
4. Dr. F. C. Patra
5. Dr. Asma Khanam
6. Dr. A. Bari
- CONSULTANT : Dr. W. B. Greenough III
- IV. STARTING DATE : 1st May 1985
- V. COMPLETION DATE : 30th April 1986
- VI. TOTAL DIRECT COST : KHS US \$
- VII. AVAILABILITY OF FUNDS : AGA KHAN FOUNDATION

The protocol has been approved by the Project Development Committee.

Walter Kahane
Chairman
Project Development Committee
I.C.D.D.R.B.
24/12/84

02 JUL 2002

ABSTRACT SUMMARY:

Studies in ICDDR, B and Calcutta have proved that rice based ORS is superior to standard WHO/UNICEF ORS in terms of reduction in stool output vomiting, acceptibility and calorie supplementation. Following this, ICDDR, B is continuing a longitudinal field study and also implementing rice ORS in its Dhaka Hospital with success. Though rice is universally available, it is not the staple cereal in all parts of the world. Thus, it is essential to study the other common cereals in Kenya to assess their efficacy when used as a replacement of Glucose or Sucrose in the ORS for the management of acute diarrhoea. Keeping that view in mind , a randomized control trial is planned to study three Cereals; Maize, Sorghum and Millet in the ORS preparation in appropriate quantity 60 grams to liberate approximately 40 g. of Glucose which is equivalent to 50 g. rice powder. A total of 200 children with acute diarrhoea, will be studied. After inclusion into the study during the first 24 hours, children from 4 months to 59 months will be offered only ORS. For the next 24 hours onwards, they will receive food as well as ORS. Accurate record of fluid plus food intake and all kinds of output will be maintained. The efficacy will be determined on the basis of ORS intake, stool output, urine output, serum specific gravity and gain in body weight. On the basis of the above criteria the suitable ceral will be recommended to the Ministry of Health, Kenya for wider application and utilization at both village and health facility levels.

REVIEWS:

- A. Research involving human subjects - both Kenya and ICDDR, B _____
- B. Research Review Committee - MRS Kenya; ICDDR, B _____
- C. Director KEMRI (Kenya Medical Research Institute)
- D. Director MRC (Medical Research Centre) - Kenya
- E. Administrator - KEMRI/MRC - KENYA

A. INTRODUCTION

Aim of the Study:

Studies in ICDDR, B effectively replaced glucose or sucrose in ORS packet by rice powder (1). Subsequent studies in Calcutta as well as in ICDDR, B have shown that rice powder (50g-80g/L) reduces the stool volume, vomiting and duration of diarrhoea and provides more calories (2,3,4). Though rice is univesally available, different geographical areas in the world use different cereals as staple food. The availability, acceptibility and cost effectiveness may vary according to a particular grain for the specific country. Hence, clinical trials should be carried out to see the efficacy of different cereals like Maize, Millet and Sorghum in acute diarrhoea as a substitute for glucose in the ORS packets. This protocol aims at conducting a clinical trial in acute diarrhoea in Kenyan children to study the efficacy of different cereal based ORS (Maize, Millet and Sorghum).

B. SPECIFIC OBJECTIVES

To study the efficacy of different cereal based ORS in terms of
(a) Stool Volume (b) Vomitus Volume (c) Serum Electrolytes
(d) Duration of Diarrhoea (e) Urine Volume and (f) Weight Gain

C. BACKGROUND

About one in every 10 children born in developing countries dies of diarrhoea before reaching the age of 5 years. Oral rehydration therapy (ORT) can substantially reduce this heavy toll. ORT means

drinking a solution of water, sugar and electrolytes to replace the water and salts lost by the body during diarrhoea. This corrects dehydration which is the direct cause of diarrhoeal deaths. Making this simple, inexpensive and effective treatment available throughout the world is a major public health challenge.

The importance of diarrhoeal disease in Kenya is reflected by the Ministry of Health's morbidity data (5). The Ministry of Health established a health information system where the 29 most commonly treated diseases are reported from all the provinces, hospitals, health centres and dispensaries whether government or non-government. Currently, the information is published on a quarterly basis in the health information bulletin. According to the reports, malaria, acute respiratory diseases, skin diseases and intestinal helminths are the top 6 diseases commonly treated at the outpatient departments in Kenya. Diarrhoea ranked third as a cause of morbidity in Nyanza and Western Provinces, fourth in the Coast and Eastern and fifth in Central Province (5).

From existing mortality statistics for Kenya, we may conservatively assume that at least 22,000 children in the country below the age of five die annually from various causes assuming a death rate of 23 per 1,000 in the pre-school range and 30% of these being caused by diarrhoea disease.

Recently, ICDDR, B developed a rice based ORS in which 30 g. of rice powder was used in place of 20 g. of glucose or 40 g. sucrose (1) while the electrolytes remained same as was recommended by WHO. Using a higher concentration (50 g/L) of rice, another group in Calcutta showed that rice based ORS was superior to glucose based ORS in terms of reducing stool volume and duration of diarrhoea (2).

Being a cereal rice based ORS has several advantages, for example -

- * It is cheap and readily available.
- * Being food is easily acceptable.
- * Rice starch being digested by intraluminal enzymes, liberates glucose molecules slowly into the intestinal lumen and at the mucosal surface.
- * For the same reason it does not cause rise of osmolality and is free from the effects of excessive osmotic pressure.
- * Hence, a higher amount of carbohydrate can be used in the ORS which provides more calories.
- * Being available at every home it can eliminate the logistic problem of carrying and storing the most bulky ingredient of ORS packets. Similarly, the distribution problem is reduced if not avoided altogether and self sufficiency can be achieved.
- * Most importantly, it reduces the stool volume and duration of diarrhoea.

Because of the above mentioned advantages, ICDDR, B conducted a trial with the highest amount of rice powder (80 g.) which goes into solution in one liter of water without making the solution too thick to drink, in acute cholera both in children and adults. This study involving 400 patients was conducted in a busy treatment centre under minimum supervision during a cholera epidemic. The results of this study confirmed the findings that rice based ORS is superior in terms of reduction in stool output and intake of ORS (3). However, another metabolic balance study was carried out in adults as well as in children with 80 g. rice powder/L. In this study, 52 children and 144 adults were studied in depth and many Clinical Parameters were recorded and biochemical estimations were carried out.

These results clearly showed rice ORS reduced stool output and ORS intake by 50 percent, vomiting by 80 percent and compared to glucose ORS it has four (4) times more calories while rehydrating equally well as reflected by weight gain and serum specific gravity. Rice ORS is as effective in correcting acidosis or other biochemical abnormalities. The higher amount of starch as reflected by the amount of glucose present in the stool before and after hydrolysis did not lead to any clinical inefficacy in most cases. However, in some young children mild diarrhoea was continued and associated with spilling higher amount of sugar in the stool. For this reason, the amount of rice powder was brought down from 80 g/L to 50 g/L and a small trial showed that the reduction in stool output and vomiting was maintained nearly to the same level as in 80 g/L.

Hence, it was decided to use 50 g. rice powder per liter of ORS in the subsequent trials. The next logical step was to extend the rice based ORS into the field as well as in the treatment centre of ICDDR, B. This was preceded by a pilot study about the feasibility and acceptibility of rice ORS. Some of the results of this feasibility study are presented in Table 1. The large field study started from September 1983 to compare the efficacy and nutritional impact of rice ORS with that of glucose ORS in under five children in a two year longitudinal study in Chandpur. The study is going on and the preliminary results already indicate that rice ORS significantly reduces the prolonged diarrhoea in children. However, this longitudinal field studies will provide us with many important results.

Having completed all the above mentioned studies cereal based ORS clearly merits a more wider application. ICDDR, B has already started its clinical application in the treatment centre from 1st December 1983 and within two months there had been a switch from the sucrose-based ORS to rice-based ORS. All the three cereals (maize, millet and sorghum) are used in various parts of Africa, Kenya included, as staple food in different forms. Particularly in the Western part of Kenya, maize is widely grown and used in various forms such as ugali (bread) and uji (a thin porridge). Sorghum and millet were in the past widely used in the same region in the same forms. Recently, these two cereals have become less popular due to westernization of the population. However, the Kenyan government is trying to rehabilitate them in view of their high nutrient values and ability to resist adverse climatic conditions.

SOME LOGISTICS IN PREPARATION OF THE CEREAL BASED ORS

Various logistics involved in the preparation of ORS are discussed to evaluate if these will deter the use, and implementation of cereal based ORS. The logistics are as follows:

- 1.) Boiling of the cereal based ORS - It is obligatory to boil the cereal based ORS in order to make a homogenous solution. This is both an advantage and a hindrance in the preparation of the ORS. Different expert committees expressed concern about the contamination of ORS by coliform bacteria and advise the use of pure, clean or drinkable water. Thus, boiling the cereal based ORS and using it within 6-12 hours almost eliminates the chance of contamination and avoids the confusion about which water to use. Time and fuel are required which may be considered a constraint. But the constraints should be weighed against the extra benefit from cereal based ORS.

Is boiling necessary ?

Boiling of the cereal based ORS is not only obligatory but also scientifically advantageous. Most cereals contain about 80% starch and 80% of the starch is converted into monosaccharide if the hydrolysis of the polysaccharide depends on hydration of the starch (6). The hydration of the polysaccharide occurs during heating of the starch. Amylase has specificity for internal α -1.4 Fructose bonds, α -1.6 bonds are not attacked. The products of the digestion by amylase are mainly the disaccharide maltose, the trisaccharide dextrin, and limit dextrans.

Being acted upon the disaccharides at the intestinal surface the final product glucose produced is released at the mucosal surface. Di, oligo and polysaccharides not hydrolysed by amylase and/or small intestinal surface enzymes, reach the colon where bacterial actions release monosaccharides and also many other degradation products which can cause fluid secretion, increase motility, cramps, irritation and distension. Hence, full hydration of starch will ensure full hydrolysis and minimum degradation product(6).

2.) Fuel cost and time for preparation

Boiling for preparation for rice ORS needs fuel and time. Is it cost effective compared to the standard ORS which does not need boiling? In almost all over Bangladesh and many other regional countries, mothers use rice powder (freshly prepared or stocked at home) boiled in milk or water as the supplementary feed for young children. This practice is becoming more and more regular in wider areas of Bangladesh with the deteriorating economic condition. In Kenya uji or thin porridge is in traditional use normally as the weaning food of the children and also during diarrhoea. Though the logistics may seem very complicated in mass scale preparation in the hospital set up, it will not be much of extra work to a mother who will use home based ingredients which is normally required for the supplementary feed for her child. The cost for preparation of one or half a liter for the child will not involve much extra cost. Moreover, the cost and logistics of the cereal based ORS must be weighed against the benefits like reduction in stool output, duration of diarrhoea,

increased calorie content and lower risk of contamination.

Criteria for Selecting Possible Cereals for Clinical Trials:

Depending on the satisfactory fulfillment of the following criteria a cereal would be selected for a trial. An ideal cereal would be :

- * Available and cheap.
- * Easily digestible.
- * Preparations must be easy for using the ORS.
- * Must be acceptable to the target population.
- * Should be used by a large number of people as staple.
- * Biochemical composition must be satisfactory e.g. must have adequate carbohydrate in order to liberate sufficient glucose molecules.
- * Must be free from any side effects or stigma in the community.

Considering all the above points the following cereals qualify for a clinical trial:

- * Wheat
- * Maize
- * Millet
- * Sorghum

Non cereals like cassava, potato and coconut water can also be tested.

Composition of the Different Cereals to be Used for Trial:

Table 2 present the composition of the different cereals proposed to be used in this trial (7,8,9). It is clear that corrected for the moisture content different cereals have adequate carbohydrate, although potatoes have lower carbohydrate because of the high water content. The amino acid content of the cereals are also comparable and if used in the right proportions and in the right form these cereals should work as Glucose substitute in the ORS. Invitro hydrolysis in ICDDR, B showed that the Glucose content of Maize, Millet, Sorghum, Wheat and Potato are approximately 70%, 67%, 66%, 70% and 20% respectively. Studies by Lebenthal et al (10) showed that 85% of the children recovering from acute diarrhoea can tolerate and absorb the Glucose polymers from the corn syrup. These information suggested that the proposed cereals will qualify and have the theoretical potentials to work if used in ORS. Based on the Glucose content of different cereals the compositions of the proposed ORS per litre are shown in Table 3.

Foods Prepared from Sorghum, Maize and Millet:

Since the cereals like Maize, Millet and Sorghum are common staple in Kenya, a summary of different kinds of food prepared from these cereals is provided in this protocol. Maize, millet and sorghum are used for food preparation in several ways. Millet and Sorghum flour is also produced by grinding the grain on a traditional stone. The list of common food items are provided below:

Ugali (bread): is prepared from any of the three types of cereal flour. Water of a given wuanntity is boiled, the flour is added and mixed with it until it hardens to an acceptable solid consistency. All this is done while on fire. The prepared ugali is eaten with stew or vegetables.

Uji (thin porridge): Water of given quantity is let to boil, at the same time a proportionate amount of cereal flour is mixed with old water in a different container and stirred into a fine mixture. This mixture is then added to the boiling water and stirred continuously until it boils. It is then left to boil until a desired consistency is achieved.

In different parts of the world these cereals are prepared in different ways:

Injera, a sorghum preparation which is a traditional bread made from sorghum and eaten in Ethiopia (11). The best quality sorghum injera is made from the dehulled grain. Injera is usually eaten with a kind of stew called wot which is made of vegetable, pulses and meat. Adults and children even 2 years of age normally take injera as staple.

Sorghum roti, is one of the most popular sorghum food consumed in India. Roti is consumed with several side dishes like vegetables, dhal, meat, milk or curd. Procedure for sorghum roti preparation is the same as wheat roti preparation. However, sometimes sorghum flour dough is occasionally mixed with other grains like green gram, chickpea and wheat in different preparations.(12).

Tortilla, made from both sorghum and maize are mostly eaten in Central America. Making tortillas is one of the most important task of women in the society. The grain is first winnowed by pouring it from one pan to another and sometimes it is washed before steeping with alkali. Steeping time ranges from 20 to 25 minutes. After steeping, the grain is washed and ground into mass. The mass is shaped into a circle and baked in hot plate. Usually tortilla is made fresh everyday otherwise both maize and sorghum tortilla can turn soury the next day (13,14).

Ogi, a smooth, creamy, free-flowing thin porridge and tuwo, a soft binding thick porridge are two major staple foods prepared from sorghum in Nigeria. Ogi is eaten mostly at breakfast and lunch and tuwo is eaten mainly at lunch and dinner (15).

Couscous is a major sorghum food in the Sahelian zone of West Africa. It is steamed granulated product made from cereal flour. Couscous can be precooked directly into a steamed product which is eaten with sauce. Couscous can be sun dried and stored indefinitely and reconstituted in milk for eating sauce (16). Millet is used for preparation of almost all of the foods mentioned, however, sorghum and maize are preferred by the people.

3.) Rationale:

- (a) The advantages of Cereal based ORS over standard WHO/UNICEF ORS have been well proven in case of rice in Dhaka as well as in other Centres. But rice is not the main staple throughout the world. Different parts of the world have different staples which will determine the availability and choice by the people of that particular country. Hence, it is essential that different cereals be given trial and out of which several specific cereals can be selected for trial and subsequent use in the country.
- (b) Because of their similar composition it is presumed that other cereals like Millet, Maize, Sorghum, Wheat and Cassava will be effective replacement of Glucose in the ORS.
- (c) Before recommending the ORS based on the above cereals it is essential to test the efficacy in a well controlled set up in countries where the cereals constitute staple.

- (d) Hence, it is proposed in this protocol that the cereals like Maize, Sorghum and Millet will be studied in Kakamega District, Kenya and based on the result of this study recommendations will be made to the Kenyan Government for wider applications and utilization of the above mentioned cereal based ORS.

C. Methods and Procedures

1. Preparation and composition of the oral rehydration solution to used in the study:

Although the techniques for preparation of food from the various cereals is different, the preparation of ORS will be same for all cereals. The dry cereal grains will be milled into flour first, a definite amount of specific cereal flour will be boiled in a little over a liter (1100 mls.) of water for 5-7 minutes and cooled. After adding the electrolytes, the ORS will be stirred and served to the patients. The composition of different cereal based ORS is given in Table 3. Once prepared the different ORS will be deisgnated as follows during the study:

- 1.) Maize ORS
- 2.) Sorghum ORS
- 3.) Millet ORS
- 4.) WHO/UNICEF ORS

2. Selection of Patients

The study aims at testing the efficacy of different cereal based ORS in children with acute diarrhoea. Patients will be selected according to the clinical criteria as mentioned below. Diarrhoea will be defined as three or more loose stool in 24 hours.

2.1 Criteria for Selection of Patients

The criteria for selection are presented in Table 5.

Male children (4 months - 59 months) with 3 days or less history of diarrhoea having moderate to severe degree of dehydration without history of prior medication will be selected for the study. Because of difficulty in urine collection which is critical in this study, only male patients will be selected. Any patient with history of blood dysentery, severe malnutrition and signs of any other systemic infection will be excluded from the study. Stool and rectal swabs from all patients will be sent for V. Cholerae, salmonella, shigella and E. Coli culture. E. Coli isolates will be tested for LT and ST toxins. Patients or guardians of the patients will be informed about the study procedures and only after the informed consent is obtained, patients will be admitted into the study ward. Suspected shigella patients showing pus cells greater than 20/HPF or having clinical signs of toxemia will also be excluded from the study. During the study period, antibiotics will not be prescribed and those needing antibiotics on clinical grounds will be taken out of the study and appropriate therapy will be started.

3. Sample Size

Three groups of cereal based ORS (maize-ORS, millet-ORS and sorghum-ORS) will be compared to WHO-ORS group. A sample size of 50 children aged 4-59 months will be recruited per treatment group and control group. Distribution of patients is shown in Table 4.

4. Randommization Procedure

This will be a randommized study in a clinical set up and cannot be blinded because of the distinctive colour of the solutions made of different cereals. A random Table will be prepared with same numbers of patients for each of the cereals and control. Then a small ticket for each patient will be prepared and put inside a box. On admission of a patient, nurse on duty will pick one of the tickets from the box and assign the patient to the study group accordingly. This will ensure elimination of any bias.

5. Laboratory Investigations on Admission and During the Study:

On admission some routine laboratory investigations are necessary for normal clinical care. These will include: blood for TC, DC, Hb, HCT, serum electrolytes, urine for urinalysis, rectal swab for culture for salmonella, shigella, V. Cholerae and E. Coli. Rectal swabs/stool for testing rotavirus will be preserved in deep freeze -10 degrees Centigrade and later will be transferred to Nairobi for ELISA tests. E. Coli isolates will be tested for ST and LT toxins in Nairobi.

6. Initial Clinical Procedure

Admission weight and height of the patients will be taken and the study physician or one of the investigators will examine the patient thoroughly to assess the degree of dehydration and exclude any complication or systemic infection. Patients with severe dehydration will receive initial rehydration by intravenous $\frac{1}{2}$ st. Darrow's solution and the amount will be determined as follows:

- * Severe dehydration: Fluid equal to 10% of the admission body weight to be administered over 4 hours (17).

After initial hydration is accomplished each patient will be re-assessed clinically for suitability to start oral therapy. Patients with moderate dehydration will be started directly on ORT. ORS will be used only to maintain the on going losses in the stool, urine and vomitus. Stool, urine and vomitus all will be collected separately and will be measured at eight hours interval.

The following measurements will be carried out during the study period

- a. Weight and height on admission, and weight at 8 hour intervals
- b. Vital signs (P. T. R) on admission and at 4 hourly intervals
- c. Hydration status and clinical assessment at 8 hourly intervals
- d. Blood for Hb, Spgr and serum electrolytes on admission ,
24 hours
- e. Measurements of intake and output every 8 hours.

ORS will be measured accurately and be fed by the mothers or attendant under the close supervision of the study nurses. Measured quantities of plain drinking water will be allowed to each child. Clinical evaluation will include examination of the skin elasticity, mucous membrane and signs of over hydration. Patients will be under constant observation of the study nurse, clinical officers trained in pediatrics and specially assigned to the project under the supervision of the investigators. Special attention will be paid to the acceptability of the ORS and feeling of well being by the patient or as judged by the parents. Acceptability will be measured by criteria like taste, nausea or vomiting, amount of ORS consumed and by asking how he liked to drink it. In children for the first 24 hours only ORS will be allowed and after than ORS, food and measured quantity of plain water. If food is offered for the first 24 hours glucose from food participate in the hydration and will interfere in assessing the efficacy of the ORS alone. Study will be continued until first soft stool appears.

7. Clinical Failure and Indications for Discontinuation of the Study

Following are the indications for declaring a patient as clinical failure:

- * Excessive vomiting making the patient unable to drink.
- * Negative gut balance as indicated by weight loss more than the admission.
- * Reappearance of signs of severe dehydration.
- * Any sign of electrolyte imbalance e.g. extreme restlessness, lethargy, excessive vomiting, etc.

When all or more than two of the above mentioned signs are present, one of the investigators will examine the patient, take body weight, blood for serum electrolytes and spgr. The patient will be declared as therapeutic failure and transferred to routine clinical care.

Analysis of Data

Flow sheets for the study will be prepared and for each study patient, a flow sheet will be filled in. Information in the flow sheet will be analyzed and paired t-test will be done to compare between the results among the patients receiving the two types (control versus cereal) of oral rehydration solutions. Tables will be prepared (model - enclosed Tables 6 & 7) to compare the results of the therapy of the types of solution used.

From the results, calculations will be made to assess the following aspects for all types of ORS.

- a. Effect of therapy on weight gain, stool output, change in the serum specific gravity, urine output etc.
- b. Biochemical parameters like serum electrolytes and serum glucose.
- c. Net stool output at 8 hour periods.

8. Significance

The results of this will provide information about the efficacy of different cereals to be used in the ORS. Thus, this study will provide information necessary to formulate ORS based on cereals other than rice. If successfully implemented, different parts of the world would have low cost, more efficient and home made ORS which will have significant contribution in the treatment of diarrhoea and possibly help reduce the nutritional effect of diarrhoea. This will help to bring the diarrhoea treatment to the mother at home as the technology required is very simple and can easily be transferred.

9. Facilities Required

1. No new office space is required.
2. Laboratory facilities for routine microbiology, biochemistry and clinical pathology are adequate.
3. Hospital resources - the study will utilize the patients selected from the out patient. Initially, a maximum of four patients will be studied at a time. With growing experience number of the patients can be increased.
4. Animal resources - will be necessary for E. Coli toxin assay in Nairobi/CMR.
5. Statistical Data Analysis - Help of Statistical Unit/MRS will be utilized. However, the present computer capacity at MRC is not adequate for the purpose of this analysis.
6. A new deep freezer 8 cft. is required for preservation of samples.
7. New weighing scales are to be provided.

Statistical Analysis:

The following variables will be considered during analysis:

- amount of intake of ORS
- amount of output of (a) stool, (b) vomitus and (c) urine at different interval of time after the administration of ORS
- duration of diarrhoea after administration of ORS
- gain in body weight

This means all of these variables for each type of ORS will be compared with those of standard WHO ORS using t-statistic. While comparing the proposed ORSs taking at a time, F-statistic can be used.

Abstract Summary for Ethical Review Committee

1. Taken from P. 1 - Abstract Summary
2. There is no significant risk. The cereals to be used in this study are being used as staple food in different parts of Kenya and mainly in the study population both for adults and children. The carbohydrate and protein content of all the cereals are adequate and less likely to produce hypoglycaemia.
3. The study will be carried out in Kakamega Provincial Hospital. Patients will be screened before admission for any possible disease or any other complication. Moreover, patients will remain under constant supervision of a nurse, an experienced clinical officer and a medical officer. Appropriate measures will be taken whenever any complication arises.
4. Only hospital in patient number of the patient will be used during analysis of the data.
5. Informed consent will be obtained from the guardian of the patient after full explanation of the procedure in the local language.
6. No detail interview except relevant history of illness.
7. All patients benefit from the study. ORS with glucose is used as a standard diarrhoea therapy all over the world. It is anticipated that the group of patients treated with different cereal based ORS will provide effective rehydration and also supply adequate calories which might help in early rehabilitation.
8. Hospital records and body fluids like stool, urine, vomitus and 3 mls. of blood will be required.

B U D G E T - S U M M A R Y

	<u>US \$</u>
A. PERSONNEL	37,700
B. SUPPLIES AND MATERIALS	12,200
C. EQUIPMENT	1,850
D. PATIENTS HOSPITALIZATION	2,000
E. LABORATORY	6,500
F. CONSULTANTS' VISITS	<u>24,100</u>
	TOTAL US \$ <u><u>84,350</u></u>

B U D G E TA. PERSONNEL

	% Effort	Salary/ Annum (US \$)	Allowances and/or Transport (US \$)	Project Requirement (US \$)
Principal Investigator I	50%	-	4000	4000
Principal Investigator II	75%	-	3000	3500
Co-Investigators:				
Coordinator	25%	-	2000	2000
Medical Officer	100%	-	4000	4000
Public Health Nurse	100%	-	3500	3500
Microbiologist	10%	-	1600	1600
Virologist	10%	-	1000	1000
Clinical Officer (Paediatrics)	100%	-	2700	2700
Lab Technician	100%	1400	-	1400
Kenya Registered Nurse	100%	-	2000	2000
Community Nurses (5)	100%	1440 X 5	7000	7000
Study Clerk	100%	1000	-	1000
Cleaners (4)	100%	750 X 4	-	3000
Cook/Utensil Bottle Cleaner	100%	1000	-	1000
			T O T A L =	<u>US\$37,700</u>

B. SUPPLIES AND MATERIALS

	<u>US \$</u>
Stationery Goods	2500
Urine bags (3000)	3000
Buckets (20)	1000
Beds (20)	1000
Makintosh, Blanket & others	2500
Cereals	200
Utensils	400
Charcoal	750
Economical Charcoal Burner	100
Electrolytes	750
TOTAL =	<u>US\$ 12,200</u>

C. EQUIPMENT

	<u>US \$</u>
Measuring Scale (one)	250
Weighing Scale (big)	250
Measuring Jars	100
Disposable gloves	500
Pocket Computer	750
TOTAL =	<u>US\$ 1,850</u>

D. PATIENTS HOSPITALIZATION

Total Number of Patients	=	200
Average Hospitalization Days	=	5 days
Total Number of Hospital Days	=	1000 days
Cost Per Day	=	US \$ 2
Total Hospitalization Cost	=	<u>US \$ 2000</u>
T O T A L	=	<u>US \$ 2,000</u>

E. LABORATORY

	<u>US \$</u>
Deep Freezer	2000
Incubator	3000
Laboratory Supplies	<u>1500</u>
TOTAL US \$	<u>6,500</u>

F. CONSULTANTS VISIT DURING TWO YEARS TIME

Visit of consultants will consist of one investigator and a nurse or field supervisor for the field as well as for the clinical protocol.

Investigators are as follows:

Dr. A. M. Molla

Dr. S. K. Nath

Dr. M. A. Bari

Dr. W. B. Greenough III

Dr. Asma Khanan

There will be 4-5 nurses and two (2) field supervisors who will accompany the investigators. Depending on the availability of the time, each investigator will spend 15 days to one month in Kakamega. Each of the nurses and field supervisors will spend 2-4 weeks in Kakamega depending on the need of the protocols.

Budget for the Consultant's Visit

1. Air Ticket : Dhaka-Kakamega-Dhaka = US \$ 1800.00

Total Ticket Cost :

\$ 1800.00 X 8 = \$14,400.00 Say US \$ 15,000.00

2. Per diem for 130 days at the rate of US \$ 70.00/day

130 X 70 = US \$ 9,100.00

Total Cost = US \$ 15,000 + US \$ 9,100

= US \$ 24,100.00

Consent Form

Medical Research Centre is carrying out research to find out simple, effective and inexpensive treatment for diarrhoeal diseases. A cereal based oral rehydration solution in which the grain powder instead of glucose has been used with superior results to the standard oral rehydration solution (ORS). MRS would like to carry out further research on oral rehydration solution made of 60 g. flour of different cereals like maize, sorghum and millet along with the WHO recommended electrolytes in one litre of water. We would like to request you to allow your child to participate in this study. The study will last for 24 hours and during this period your child will be treated with either glucose electrolyte solution or cereal based oral rehydration solution. In addition to measurement of stool, urine and vomitus, 3 mls. of blood will be drawn on admission and at the end of 24 hours of treatment. The results of blood test will be mainly used to evaluate the effect of treatment. Your child will be allowed to go home after diarrhoea has stopped and other necessary treatments are completed. You may choose not to participate in this study and in any case appropriate treatment of diarrhoea as available in this hospital will be provided to your child.

Finger print/Signature of the
Patient/Guardian:

Signature of the Investigator:

Date: _____

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Table 1

Results of home made Rice ORS sample analysis

Solutes	No. of sample (%)	m. mol/l Mean \pm SD	Range
Sodium	150 (100)	97 \pm 39	02 - 250
	23 (15.33)	45 \pm 14	02 - 70
	85 (56.6)	89 \pm 27	71 - 110
	42 (28)	144 \pm 21	111 - 250
Potassium	150 (100)	3.05 \pm 49	09 - 10.5
Glucose	17 (11.3)	304 \pm 49	157 - 371

Table 2

Mean Composition of Different Cereals Per 100 grams

	SORGHUM	MAIZE	WHEAT	MILLET	RICE
Energy	349	342	323	331	349
Moisture	11.9	15	11.3	11.2	12.6
Protein (g)	10.4	11.1	10.3	12.3	8.5
Fat (g)	1.9	3.6	2.4	4.3	0.6
Carbohydrate (g)	72.6	66.2	65	61	77.4
Fibre (g)	1.6	2.7	8.6	8.0	-
Phosphorus (mg)	222	348	355	290	280
Iron (mg)	5.8	2.0	15.5	12.9	2.8
Calcium (mg)	25	10	64	31	10

Ref: Nutritive value of Indian foods
 Gopalan C et al. National University of Nutrition
 Indian Council of Medical Research. Hyderabad 1982.

Table 3

Composition of the proposed ORS (one litre)

Cereal flour (50 g. rice equivalent)*		NaCl	Electrolyte (g/l)	
			NaHCO ₃	KCl
Maize	60 g.	3.5	2.5	1.5
Sorghum	60 g.	3.5	2.5	1.5
Millet	60 g.	3.5	2.5	1.5
Wheat	60 g.	3.5	2.5	1.5
Water	One litre			

* Amount fixed on the basis of glucose content after in-vitro hydrolysis

Table 4

Distribution of patients to different cereals

Cereal	No. of Patients
Maize	50
Millet	50
Sorghum	50
Control	50
T O T A L Four (4) Groups	200

Table 5

Criteria for Selection of Study Patient

Particulars	Selected	Excluded
Age (yrs)	4m - 59m	Less than 4 m and Greater than 59 m
H/O Diarrhoea	up to 3 days	Greater than 3 days
Sex	Male	Female
H/O antibiotics	No antibiotics	antibiotics
Blood count	Normal WBC	High count (greater than 15.000)
	Normal DiffCount	Shift to the left
Dehydration	Moderate to severe	Mild
<u>Stool Exam</u>		
Pus Cells	Up to 20/HPF	Greater than 20

Table 6

COMPARISON CHARACTERISTICS OF THE STUDY PATIENTS (Mean \pm SEM)

Criteria	Cereal - ORS	WHO - ORS	P
Age (yrs)			
Adm. Weight (kg)			
Adm. Hct			
Adm. Hb			
Adm. Ser. Spgr.			
Prev. illness (prior to adm.)			
Dehydration Status			
Mild			
Moderate			
Severe			
Serum Electrolytes	<u>On Admission</u>	<u>24 hours</u>	
Na ⁺ mmol/l			
K ⁺ mmol/l			
Cl ⁻ mmol/l			
TCO ₂ meq/l			
Serum glucose			

Table 7

TABLE TO COMPARE THE EFFICACY OF THE CEREAL BASED ORS WITH STANDARD WHO/UNICEF
ORS (Mean + SEM)

Parameters	Cereal ORS	WHO-ORS	P
<u>Stool output</u>			
a. Total volume (litres)			
1st 24 hrs.			
2nd 24 hrs.			
b. ml/kg/day			
1st 24 hrs.			
2nd 24 hrs.			
<u>Vomitus (ml/kg/day)</u>			
1st 24 hrs.			
2nd 24 hrs.			
<u>Intake of ORS (ml/kg/day)</u>			
1st 24 hrs.			
2nd 24 hrs.			
<u>Dv intake (ml/kg/day)</u>			
1st 24 hrs.			
2nd 24 hrs.			
<u>Intake of plain water (ml/kg/day)</u>			
1st 24 hrs.			
2nd 24 hrs.			

TABLE 7 (CONTINUATION)

Parameters	Cereal ORS	WHO-ORS	P
<u>Combined intake (ORS, IV, water) ml/kg/day</u>			
1st 24 hrs.			
2nd 24 hrs.			
<u>Urine output (ml/kg/day)</u>			
1st 24 hrs.			
2nd 24 hrs.			
Gain in body weight (% of adm. wt.)			
Failure, no. and %			