Attachment 1. 30

ETHICAL REVIEW COMMITTEE, ICDDR,B.

Date 13/12/85
19-12-83

Principal Investigator DR. F.C. PATRA

Trainee Investigator (if any) _____

Application No 85-038

Supporting Agency (if Non-ICDDR,B) _____

Title of Study: Oral rehydration therapy with Alanine-glucose ORS a controlled clinical trial

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).

1. Source of Population:
   (a) Ill subjects (Yes) No
   (b) Non-ill subjects Yes (No)
   (c) Minors or persons under guardianship (Yes) No
2. 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)
3. 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
4. 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.

(PTO)

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

Jakir Hossain Patra

Principal Investigator

Trainee

Non-Collaborative

83-038
19-12-83

SECTION I - RESEARCH PROTOCOL

1. TITLE: ORAL REHYDRATION THERAPY WITH ALANINE-GLUCOSE ORS: A CONTROLLED CLINICAL TRIAL.

2. PRINCIPAL INVESTIGATOR: Dr F.C. Patra

CO-INVESTIGATORS: Dr S.K. Nath
Dr R.N. Mazumder
Dr A. Islam
Dr A.N. Alam

CONSULTANTS: Dr D.A. Sack
Prof. R. Eeckels

3. STARTING DATE: 1 January 1986

4. COMPLETION DATE: 31 December 1986

5. TOTAL DIRECT COST: US $ 32,778.00

6. SCIENTIFIC PROGRAMME: This protocol has been approved by the Pathogenesis & Therapy Working Group.

Signature of Acting Associate Director, PTWG: for: ----------

Date: 17/12/85

7. ABSTRACT SUMMARY:

In a double blind randomized study a total of 90 male patients aged 6 years and above and suffering from acute diarrhoeal dehydration will be studied in two groups to evaluate the efficacy of an alanine-glucose based oral rehydration solution and to compare it with the standard WHO recommended oral rehydration solution (ORS). The electrolyte composition of the study ORS will be similar to the WHO recommended citrate based ORS, but 90 mmole of alanine an aminoacid will be added to one litre of ORS containing 90 mmol of glucose per litre of solution. The control group will receive the standard WHO recommended citrate containing ORS. All the patients will be initially rehydrated by intravenous acetate solution followed by the administration of either of the ORS. All the patients will be studied till the cessation of diarrhoea. All the patients will receive oral tetracycline therapy for 48 hours and all of them will be fasted for 24 hours followed by the introduction of appropriate feeds. Careful record of intake and output will be kept. The patients will be kept under strict medical supervision by the investigators and will be discharged from the hospital after cessation of diarrhoea.

8. REVIEWS:

(a) Ethical Review Committee: ----------

(b) Research Review Committee: ----------

(c) Director: ----------

SECTION II - RESEARCH PLAN

A. Introduction:

1. Objective.

The objective of the present study is to assess the possibility of reducing the magnitude and duration of diarrhoea, in addition to replacing the diarrhoeal losses using an alanine-glucose oral rehydration solution in older children and adults with acute diarrhoea in a controlled clinical trial comparing with the currently WHO recommended glucose ORS.

2. Background.

Glucose-linked enhanced absorption of sodium and water from the small intestine is largely intact during acute diarrhoea of diverse aetiology and forms the basis of glucose-based oral rehydration fluids for acute diarrhoea (1). The present WHO recommended oral rehydration formula contains 2 g of glucose per 100 ml of ORS is a powerful therapeutic tool and is capable of replacing the need for intravenous therapy in 80-90% of clinically dehydrated patients, who would have been treated intravenously by conventional criteria. In other wards such an ORS can adequately correct the deficiency of moderate to severe dehydration due to acute diarrhoea and can replace the on-going losses provided the rate of diarrhoeal stool output does not exceed certain limit. However compared to intravenous treated controls oral rehydration therapy neither reduces nor increases the magnitude of diarrhoeal

stool output in infants and children aged under 5 with rotavirus diarrhoea (2) and cholera (3). In adults with secretory diarrhoea caused by cholera the diarrhoeal stool output even may increase by 15 to 20%, when the patients are treated with ORS (4,5). Presently used ORS containing 2 g % glucose stimulate optimum sodium absorption except in 2 to 4% of clinically dehydrated hospitalised infants with acute diarrhoea, who may develop temporary malabsorption of glucose and for whom ORS may worsen the diarrhoea (1). Our present state of knowledge suggests that almost all water soluble organic molecules which are absorbed from the small intestine enhance the absorption of sodium and water. Examples are D-hexoses, amino acids, dipeptides and some water soluble vitamins (6). In vivo perfusion studies in human volunteers (7) and in animals (8) suggest that the faster the absorption of an organic molecule the greater is the linked absorption of sodium and water. If the sodium concentration in the oral rehydration solution is kept constant at a desired level as detected by the need of therapy (9) the concentration of water-soluble organic compounds can not be increased beyond certain limits as it would raise the osmolality for above that of plasma and would impose as osmotic penalty (8), (i.e. osmotic back flow of water from the plasma to gut lumen due to unabsorbed organic molecules) and would negate the beneficial effects of increased absorption. If however the organic molecules are absorbed rapidly the adverse osmotic effect may be largely eliminated. From human perfusion studies it has been shown that alanine is readily absorbed from the small intestine and its absorption rate increases with its increasing concentration (10).

In the presence of alanine there is significant enhancement of both sodium and water absorption and this stimulated absorption of sodium increases with increasing concentration of alanine (10). Alanine is a white odourless crystalline powder with a sweetish taste and soluble in water (11). It is present in many food stuffs and has been used as a dietary supplement (11). Alanine 50 g daily by mouth in divided doses reversed hypoglycaemia and ketosis and reduced muscle catabolism in obese subjects starved for 2 weeks (12). Alanine also is a potent stimulant of glucagon secretion (13). Alanine is also the primary endogenous glucogenic substrate released by muscle and extracted by the liver during startation (14). The glucose-alanine cycle in muscle has been fully documented (15), Alanine is formed by transamination from pyruvate and becomes a carrier of nitrogen to the liver where its carbon skeleton enters the glucogenic pathway and the amino group is transformed to urea (15). Naline et al have shown a marked improvement in sodium and water absorption in patients with cholera by using a mixture of glycine (110 mmol/1) and glucose (110 mmol/1) (16). Controlled clinical trials conducted recently in Calcutta using either 5% puffed rice powder substituted for glucose or adding 111 mmol of glycine to a litre of ORS in the treatment of dehydrated infants with acute diarrhoea have shown a significant reduction in stool output (50%) duration of diarrhoea (25%) and volume of fluid required for rehydration and fluid balance (40%) (17,18).

We postulate that a modification in the actual substrate composition of WHO recommended ORS i.e. addition of 90 mmol of alanine and decreasing the glucose content to 90 mmol in a litre

of ORS to reduce the osmolality, could eventually act like an absorption promoting drug by decreasing the stool volume, duration of diarrhoea and intake of oral rehydration solution.

The present study has been designed to test this hypothesis in a controlled double blind clinical trial comparing the new formula with the currently WHO recommended one. The glucose content (90 mmol/l) of this alternative formulation is still in between the range of glucose concentration (56 to 140 mmol/l) which was found to exert maximum effect on water and sodium absorption (19). Its total osmolality is 400 mosm/l which is slightly higher than the currently WHO recommended ORS (331 mosm/l).

It has been decided to use a more stable base precursor sodium citrate in place of sodium bicarbonate taking into account the result of the recent study (20) which has shown that citrate works as well as bicarbonate in correcting acidosis.

If this study successfully demonstrates these additional benefits of oral rehydration, it would be an important contribution to expand its use through-out the world.

B. Rationale:

Although the proper replacement of water and salt losses is the main therapeutic goal in the treatment of acute diarrhoea, the possibility of reducing at the same time the magnitude and duration of diarrhoea has a great psychological and practical importance both to patients (or parents) and physicians.

METHODS AND PROCEDURE:

Study population.

The study will be carried out in dehydrated older children and adults with acute watery diarrhoea in the study ward of the International Centre for Diarrhoeal Disease Research, Bangladesh, Dhaka.

Inclusion criteria.

Age - from 6 years and above.

Sex - males only, for convenience of separately collecting stool and urine.

- Three or more loose or watery stools per day for no more than 24 hours.
- Clinical signs of severe dehydration.

Exclusion criteria.

- Clinical signs of shock
- Clinical evidence of concomitant systemic illness (i.e. pneumonia, sepsis etc.).
- Clinical signs of complete ileus
- Clinical evidence of severe malnutrition
- Oral antibiotic treatment within 48 hours prior to admission.
- Previous attack of diarrhoea within the two weeks before the present illness.
- Gross blood and mucus in stool on admission.

Sample size calculation:

We assumed that the variability (σ^2) in stool output and duration of diarrhoea from patient to patient will follow the same pattern as observed by Molla et al (21) and Islam et al (22) respectively.

Stool output:

1. HO : Stool output will be reduced by 25%

$$n = 2 (Z\alpha/2 + Z\beta)^2 \frac{\sigma^2}{d^2}$$

α = 0.05, power 90% , β = 0.10

$(Z\alpha/2 + Z\beta)^2$ = 10.5 from normal tables

From published report (21), we have total stool volume = 316 ml/kg.

We expect to reduce this volume by 25%.

The reduced volume = 237

$\therefore d$ = 79 mg/kg (i,e, 316-237)

From the combined sample we have σ=101.6

$$n = 2 \times 10.5 \times \left(\frac{101.6}{79}\right)^2 \simeq 35 \text{ per group}$$

Total sample size will be 35 X 2 = 70

Duration of diarrhoea:

2. Duration of diarrhoea will be reduced by 40%

From the unpublished result (22) (please see enclosed table) the mean duration of diarrhoea $\simeq$ 36.8 hr

40% duration d = 14.7

Estimate of standard deviation from the referred table comes out to be 22.4 = σ

α = 0.05, power 90%, = β 0.10

$$= 2 \times 10.5 \times \left(\frac{22.4}{14.7}\right)^2 \simeq 48 \text{ per group}$$

So for stool volume we have n = 35 per group and for duration of diarrhoea we have n = 48 per group.

We can take the average 42 patients per group

So that the total sample size will be 84 for the whole study.

We plan to increase this total sample size by about 8-10% to get the statistical protection i.e. α = 0.05 and power 90%.

Here the effective total sample size is taken to be 90 which will be equally divided between the study and the control group.

This sample size we consider to be sufficiently large for this study. In my previous submission we found the sample size based on published results (18) to be equal to 70. Now this has been increased to 90 which seems to be a quite large sample.

Enrolment of subjects.

a. Informed consent.

Each child's mother or the father and the older patients or the attendant will be given an explanation as to the nature of the study and only those who give voluntary written consent (informed consent form is enclosed) will be included in the study. Parents and the patients reserve the right to withdraw from the study at any stage without affecting further care of the patient.

b. Assessment of eligibility.

Patients will be assessed and included into the study according to inclusion and exclusion criteria anf informed consent.

c. Baseline examination.

A standard history and complete physical examination will be carried out accordingly to a proforma. The following laboratory tests will be performed on admission.

- micro hematocrit and plasma specific gravity
- serum electrolyte and total CO_2
- fresh stool/rectal swab for enterotoxigenic E. coli and V. cholerae.
- fresh stool for microscopy.

The above blood test will require 3.0 ml blood.

d. Subject allocation.

The trial will be conducted in a double blind design and patients will be randomly assigned to receive either the improved ORS formulation (i.e. glucose alanine based ORS formulation) or WHO recommended ORS. The randomization will be stratified into two age groups i.e. 6 years to 12 years and more than 12 years and above.

It is proposed that the improved ORS packets and standard ORS packets will be supplied by WHO incorporating appropriate randomisation in the serial number of packets.

Intervention.

a. Composition and preparation of the oral rehydration formulations

Sufficient number of packets per patient will be prepared by WHO and then coded according to randomisation list. The external apprarance of the packets will be same except for the serial number of patients.

Composition of the improved ORS formulation.

Sodium chloride	-	3.5 g
Potassium chloride	-	1.5 g
Trisodium citrate dihydrate	-	2.9 g
L-Alanine	-	8.1 g
Glucose	-	16.2 g

When diluted in 1 litre of water this ORS will have Na 90, Cl 80, K 20, HCO_3 equivalant 30, L-alanine 90, and glucose 90 all in mmol per litre.

Composition of ORS in control will be the same as in the WHO recommended tri-sodium citrate dihydrate based ORS formula.

b. Description of the schedule.

All patients admitted to the trial will be cared for by doctors and nursing staff assigned to the study. Nurses already experienced in metabolic collections in earlier studies will be assigned to the study. Immediately after recording weight and assigning the appropriate serial number the patient will be put on a cholera bed designed to make accurate measurement of stool and urine separately. The container with the assigned ORS and the cups will be kept by the bedside of the patient to facilitate measured intake. The vomitus will be mopped with the pre-weighed gauze and measured by the difference in weight. Intake and output will be recorded in a specially disigned record sheet every 4 hours untill discharge from the study.

All fluid therapy will be divided into two parts.

i. Initial rehydration phase

ii. Maintenance phase.

Initial rehydration phase:

Once admitted into the study and randomised patients will be rehydrated by intravenous acetate solution (Dacca solution). Patient with severe degree of dehydration will receive 100 ml/kg over a period of 2 to 4 hours.

Maintenance period.

This phase starts after signs of dehydration are corrected. The diarrhoeal stool loss will be replaced by ORS as per the randomization, weight for the weight based on every 4 hourly stool weights untill diarrhoea ceases. Careful measurement of fluid intake including feeds and stool output and urine during this period will be recorded. Body weight and clinical examination will be repeated at 8 hours after admission and every 24 hours thereafter. In all patients laboratory tests will be repeated at 8 hours after starting the study (i.e. microhematocrit, plasma specific gravity, plasma electrolytes and TCO_2). These tests will also be repeated at 24 hours and at discharge. Patients will be discharged from the study after cessation of diarrhoea.

Feeding.

All the patients will be fasted for initial 24 hours period. After 24 hours all the patients will be given standard hospital diet consisting of rice, dal, fish and vegetables etc.

Antibiotics.

All the patient will be given oral tetracycline therapy 50 mg/kg/24 hrs to older children divided into 4 equal doses and 500 mgs 6 hourly to adults for the initial 48 hours. A antibiotic therapy will commence after initial 24 hours of the study.

Free water

Water will be offered during maintenance phase and accurate record of its intake will be kept.

Treatment failure:

If signs of dehydration re-appear during the maintenance phase supported by hematocrit and plasma specific gravity, which necessitates intravenous therapy the patient will be considered as treatment failure. These patient will receive intravenous acetate solution (Dacca solution) till signs of dehydration are fully corrected and then maintained on ORS. Input and output measurements and other procedures outlined for other patients will still be carried out and recorded.

Ascertainment of response variables.

a. Response variables.

- Duration of diarrhoea in hospital
- Diarrhoea stool volume 0-8 hr, 0-24 hrs, 24-48 hrs, 0 - till cessation of diarrhoea.
- Weight gain
- Amount of ORS consumed till cessation of diarrhoea

- Hematocrit, plasma specific gravity
- Urine volume.

b. Working definitions.

- Cessation of diarrhoea: The end point of diarrhoea is considered as the time at which the last liquid stool is passed provided the next stool is semisolid or solid.

- Volume of diarrhoea: The stool weight from admission till cessation of diarrhoea measured to the nearest one gram.

- Severe vomiting: Vomitus in an amount equal to or exceeding fluid intake.

- Glucose intolerance: Glucose malabsorption (stool sugar more than 0.5 g%) plus treatment failure due to high stool output.

c. Data analysis.

Appropriate statistical methods will be applied to examine the following variables.

i. Pre-treatment clinical data to assess comparability

ii. Post-treatment clinical and laboratory data such as weight gain at 8, 24 hours and at discharge, duration of diarrhoea, stool output, intake of ORS, hematocrit, plasma specific gravity, serum electrolytes, rate of treatment failure and amount of unscheduled intravenous fluid used.

SECTION III - BUDGET

1. Personnel services.

Name	Position	% effort	US Dollar
Dr. F.C. Patra	Principal Investigator	50%	18,325.00
Dr. S.K. Nath	Co-Investigator	25%	1,181.00
Dr. R.N. Mazumder	Co-Investigator	20%	511.00
Dr. A. Islam	Co-Investigator	5%	288.00
Dr. A.N. Alam	Co-Investigator	5%	500.00
Dr. D.A. Sack	Consultant		
Prof. R. Eeckels	Consultant		
1 Clerk (study ward)		20%	360.00
			Sub Total=21,165.00

2. Supplies and Materials:

Supplies - Cotton and Gauze	100.00
Non stock item	100.00
Sub Total=	200.00

3. Laboratory tests:

Stool microscopy	129.00
Stool culture	1009.00
Blood electrolytes	1108.00
Serum specific gravity	184.00
Hematocrit	412.00

4. Equipments - nil

5. Data analysis 100.00

Sub total = 2942.00

6. Hospitalization of patients 10,710.00

7. Outpatient care - nil

8. Transportation 225.00

9. Transportation materisla - nil

10. Rent, communication, utility - nil

Sub total = 10,935.00

11. Printing and Reproduction:

Stationary goods	300.00
Xerox and mimiograph	150.00
Medical illustration	200.00

12. Contractual service - nil

13. Construction - nil

Sub total = 650.00

GRAND TOTAL = US $ 35,892.00

REFERENCES:

1. Hirschhorn N. The treatment of acute diarrhea in children: an historical and physiological perspective. Am J Clin Nutr 1980; 33:637-63.

2. Sack DA, Chowdhury AMAK, Eusof A, et al. Oral hydration in rotavirus diarrhoea: a double blind comparison of sucrose with glucose electrolyte solution. Lancet 1978;2:280-83.

3. Mahalanabis D, Sack RB, Jacobs B, et al. Use of an oral glucose-electrolyte solution in the treatment of paediatric cholera ... a controlled study. J Trop Pediatr 1974;20:82-87.

4. Pierce NF, Sack RB, Mitra RC et al. Replacement of water and electrolyte losses in cholera by an oral glucose-electrolyte solution. Ann Intern Med 1969;70:1173-81.

5. Hirschhorn N, Kinzie JL, Sachar DB et al. Decrease in net stool output in cholera during intestinal perfusion with glucose-containing solutions. N Engl J Med 1968;279:176-81.

6. Schultz SG. Sodium-coupled solute transport by small intestine: a status report. Am J Physiol 1977;233:E249-54.

7. Fordtran JS. Stimulation of active and passive sodium absorption by sugars in the human jejunum. J Clin Invest 1975;55:728-37.

8. Patra FC, Mahalanabis D, Jalan KN. Stimulation of sodium and water absorption by sucrose in the rat small intestine. Acta Paediatr Scand 1982;71:103-07.

9. Mahalanabis D. Rehydration therapy in diarrhea. In: Acute enteric infections in children: new prospects for treatment and prevention. Holme T, Holmgren J, Merson MH, Mollby R, eds. Amsterdam: Elsevier 1981:303-18.

10. Hellier MD, Thirumalai C and Holdsworth CD. The effect of amino-acids and dipeptides on sodium and water absorption in man. Gut 1973;14: 41-45.

11. Martindale. The extra pharmacopoeia edited by James EF Reynolds 28th edition, London. The Pharmaceutical Press 1982, P 48.

12. Genuth SM. Effects of oral alanine administration in fasting obese subjects. Metabolism 1973;22:927-937.

13. Donowitz M, Hendler R, Spiro HM, Binder HJ and Felig P. Glucagon secretion in acute and chronic pancreatitis. Ann Int Med 1975;83: 778-781.

14. Metcoff J. Maternal nutrition and foetal growth In Text book of Paediatric Nutrition Edited by Donald S Maclaren and David Burman 2nd edition, churchil livingstone Edinburgh, London, Melbourne and New York 1982 P 31.

15. Leleike NS, Murray C and Munro HN. Enteral support of the hospitalised child. In Textbook of Paediatric Nutrition Edited by Robert M Suskind. Raven Press. New York 1981; P 359.

16. Nalin DR, Cash RA, Rahman M et al. Effect of glycine and glucose on sodium and water absorption in patients with cholera. Gut 1970; 11:768-772.

17. Patra FC, Mahalanabis D, Jalan KN et al. Is oral rice electrolyte solution superior to glucose electrolyte solution in infantile diarrhoea. Arch Dis Child 1982;57:910-912.

18. Patra FC, Mahalanabis D, Jalan KN et al. In search of super solution: controlled trial of glycine-glucose oral rehydration solution in infantile diarrhoea. Acta Paediatr Scand, 1984;73:18-21.

19. Sladen GE and Dawson AM. Interrelationships between the absorption of glucose, sodium and water by the normal human jejunum. Clin Sci 1969;36:119-132.

20. Islam MR, Samadi AR, Ahmed SM et al. Oral rehydration therapy: efficacy of sodium citrate equals to sodium bicarbonate for correction of acidosis in diarrhoea. Gut 1984;25:900-904.

21. Molla AM, Ahmed SM and Greenough III WB. Rice based ORS decreases stool volume in acute diarrhoea. Bulletin WHO (in press).

22. Islam MR, et al. Treatment of cholera with a single dose of tetracycline. Submitted for publication.

ABSTRACT SUMMARY FOR ETHICAL REVIEW COMMITTEE

1. A total of 90 patients suffering from acute watery diarrhoea of less than 24 hours duration and with signs of severe dehydration will be studied in two groups. Patients with history of taking antibiotics 48 hours perior to admission and with clinical evidence of concomitant systemic illness (i.e. pneumonia and sepsis etc.) will not be included in the study. Also patients suffering from severe malnutrition will be excluded from the study.

2. The study group will receive an alanine-glucose based oral rehydration solution with similar electrolyte composition as that of the WHO recommended ORS, and the control group will receive the standard WHO recommended ORS.

3. Three ml of venous blood will be drawn at admission, at 8 hours after admission and 24 hours and again at discharge. This will be necessary to assess the state of hydration of the patient and to serve as a guideline for the subsequent fluid therapy and clinical cure.

4. All the patients will be initially treated with intravenous acetate solution followed by the oral therapy.

5. All the patient will be fasted for initial 24 hours.

6. Patients stool will be examined microscopically and also will be cultured to ascertain the cause of diarrhoea.

7. All the patients will receive oral tetracycline for 48 hours.

8. Any untoward reaction associated with therapy will be noted.

9. There is no potential risk involved in the study and every precaution will be taken to safeguard the interest of the patient.

10. All records will be kept confidential and will remain with the investigators.

11. Informed consent (signed or thumb impression) will be obtained from either of the parents or the relative or from the patients before enrollment into the study.

12. Interview of the patients or relatives will be taken only related to the history of present illness which will be of help for the clinical management of the disease.

13. The patients will be benefitted from the treatment of diarrhoeal illness. General benefit to the society will include possible widescale use of the alanine-glucose based ORS for the treatment of acute diarrhoeal dehydration.

14. No retrospective hospital record will be used.

CONSENT FORM

International Centre for Diarrhoeal Disease Research, Bangladesh (ICDDR,B) would like to carry out research on Alanine-Glucose oral rehydration solution (ORS) for the treatment of diarrhoea in children. This new alanine glucose ORS is palatable and is thought to have the capability of reducing the diarrhoeal stool volume and duration of diarrhoea in addition to replacing the diarrhoeal losses. Alanine-glucose ORS will be compared with the currently WHO recommended ORS for the treatment of acute diarrhoea. The study will last till the cessation of diarrhoea and during this period the patient will be treated with either alanine glucose ORS or WHO recommended ORS. The patient will receive intravenous acetate solution (Dacca solution) for initial rehydration after which the administration of either of the ORS will commence.

Stool, urine and vomitus of the patient will be measured every 4 hourly untill discharge from the study. Three millilitre of blood will be drawn from the patient on admission, at 8 hours, at 24 hours and at discharge to assess the degree of dehydration and assessment of therapeutic response. Stool for microscopic examination, and culture will be performed to determine the cause of diarrhoea. The result of the investigations will be used to evaluate the effect of treatment. The patient will be discharged from the hospital after cessation of diarrhoea and completion of the necessary treatment.

All records of the patients's treatment in the hospital will be kept confidential. Taking part in the study totally depends upon your cedision. The patient will be provided with all the available treatment facilities in this hospital even if you do not allow yourself/ the patient to participate in this study. If you agree to the proposal that yourself/the patient should participate in this study then please sign here.

_____
Signature of the investigator

_____
Finger print/Signature of the guardian/or the patient.

Relation to the patient: -----

Date: ----------

সম্মতি পত্র

আন্তর্জাতিক উদরাময় গবেষণা কেন্দ্র শিশুদের ডায়রিয়া চিকিৎসার জন্য এলানিন গ্লুকোজ মুখে খাওয়ার স্যালাইনের উপর গবেষণা করতে ইচ্ছুক। এই নতুন এলানিন গ্লুকোজ মুখে খাওয়ার স্যালাইনের স্বাদে সুস্বাদু। ইহা পাতলা পায়খানার পরিমান ও সময় কমাতে সাহায্য করে। উপরন্তু শরীরের ডায়রিয়াজনিত ঘাটতি পূরণে সহায়তা করে। ডায়রিয়ার এই নতুন স্যালাইনের সংগে প্রচলিত WHO স্যালাইনের কার্যকারিতার তুলনামূলক পরীক্ষা করা হবে। এই স্যালাইন খাওয়ানো ডায়রিয়া বন্ধ না হওয়া পর্যন্ত চলবে এবং এই সময়ে রোগী হয় এলানিন গ্লুকোজ অথবা শুধু গ্লুকোজ স্যালাইন খাবে। প্রাথমিক ভাবে রোগীকে আই, ভি স্যালাইন দিয়ে পানিশূন্যতা দূর করতে হবে তারপর উপরোক্ত দু'টি মুখে খাওয়ার স্যালাইনের যে কোন একটি দেওয়া হবে।

এই গবেষণা শেষ হওয়ার আগ পর্যন্ত রোগীর মল, মূত্র ও বমি ৪ ঘন্টা অন্তর অন্তর মাপা হবে। ভর্তির সময় ৮ ঘন্টা পর, ২৪ ঘন্টা পর ও ছুটির সময় ৩ মিঃ লিঃ করে রক্ত নেওয়া হবে যার মাধ্যমে দেহের ডায়রিয়াজনিত পানি শূন্যতা করা হবে ও এই স্যালাইনের কার্যকারিতা নির্ণয় করা হবে। এ সকল পরীক্ষার ফলাফল রোগীর সুচিকিৎসায় ব্যবহৃত হবে। ডায়রিয়া সম্পূর্ণ ভাল হওয়ার পর প্রয়োজনীয় চিকিৎসা দিয়ে তাকে বাড়ী পাঠানো হবে।

রোগীর চিকিৎসার যাবতীয় তথ্যাদি গোপন রাখা হবে। এই গবেষণায় অংশগ্রহণ করা কিংবা না করা সম্পূর্ণ আপনার ইচ্ছাধীন। অংশগ্রহণ না করলেও আপনার সন্তান এ হাসপাতালে প্রচলিত নিয়মানুসারে সুচিকিৎসা পাবে।

যদি আপনি এ প্রস্তাবে রাজী থাকেন তবে নিম্নে স্বাক্ষর করুন।

গবেষকের স্বাক্ষর

তারিখ----------

রোগীর স্বাক্ষর / টিপ সহি