Attachment 1.

Date 23.08.87

ETHICAL REVIEW COMMITTEE, ICDDR,B.

Principal Investigator Dr R. Haider

Trainee Investigator (if any) 29

Application No. 87-019

Supporting Agency (if Non-ICDDR,B)

Title of Study Management of acute diarrhoea in diabetic patients

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 a 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)

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

R Haider

Principal Investigator

OCT 28 1987

Trainee

87-019

23.08.87

SECTION I - RESEARCH PROTOCOL

1. Title: MANAGEMENT OF ACUTE DIARRHOEA IN DIABETIC PATIENTS

2. Principal Investigator: Dr. R. Haider

   Collaborative Principal Investigator: Prof. A.K. Azad Khan

   Co-Investigators: Dr. S.K. Roy

   Dr. N.H. Alam

   Consultants in ICDDR,B: Dr. A.N. Alam

   In BIRDEM: Dr. H. Mahtab

3. Starting date: January 1988

4. Completion date: June 1989

5. Total Direct Cost: US $28,533.00

   Source of funding: -

6. Scientific Division: This protocol has been approved in Clinical Sciences Division

Signature of Clinical Sciences Division Head

18.8.87

Date

7. Abstract Summary

Forty-five patients of both sexes with diabetes, aged 15 years and above, with dehydration from acute diarrhoea will be studied in a randomized trial with three different oral rehydration solutions. They will be studied (i) to evaluate the fluctuations in the blood sugar level produced by administration of rice-ORS and glycine-ORS, as compared with those produced by WHO ORS, as well as (ii) to assess the efficacy of different ORS in reducing the severity and duration of diarrhoea. All three oral rehydration solutions will be citrate based. Patients with mild and moderate dehydration will be rehydrated with one of the oral rehydration solutions, and will be studied until the cessation of diarrhoea. After initial rehydration, patients will be given a standard diabetes diet. Levels of blood glucose and ketone bodies will be monitored, and glucose loss in the urine will be measured. Careful records of intake and output will be kept. The patients will remain under strict medical supervision of the investigators and will be discharged after cessation of diarrhoea.

8. Reviews:

a. Ethical Review Committee: ----------

b. Research Review Committee: ----------

c. Director:----------

SECTION II - RESEARCH PLAN

A. INTRODUCTION:

1. Objective

To find an effective oral rehydration solution for diabetic patients with acute diarrhoea which will not adversely affect diabetic control.

2. Background

Definition and classification of diabetes mellitus

For the present study, we are following the definition and classification of diabetes mellitus as proposed by WHO Expert Committee on Diabetes Mellintus in 1985 (WHO Technical Report Series 727).

Diabetes mellitus afflicts large number of people of all social conditions throughout the world. In the USA, about 6% of adults have diabetes. The proportion is roughly comparable to that of European countries. Even in USA, 50% of the diabetics are undiagnosed. Although rates are thought to be lower in developing countries; it appears that the prevalence of this disease is increasing. Prevalence of diabetes tend to be moderate to high in urban areas in Asia, Africa, and Latin America. Studies on Pima Indians show that rates of diabetes are four times higher that of US population. The highest prevalence rates are reported in the people of Nauru, the Micronesian group having 34.4% and the Polynesian group 6.2% (WHO 1985). In a study in Norway on 5930 adults, it was found that the prevalence rate was 1.8% (Jorde R, 1962). Nilsson et al., (1964) in a random sample of the adult population of Kristianstad, Sweden, reported 8 of 300 (2.7%) had known diabetes. In Birmingham, England, the College of General Practitioners carried out a survey from 1960-61 with five years and 10 years follow-up. The rate of known diabetes was 0.6% and

after more comprehensive screening, the apparent frequency went upto 1.2%. In Australia, the Busselton survey (Welborn et al. 1968; Bowyer et al., 1974) revealed the rate of occult diabetes to be 1.7% in adults; whereas previously known diabetics were 2.35%. Reported prevalence rates from India (Ahuja MMS, 1979) are 2.1% in urban areas and 1.5% in rural areas and that from Singapore city is 1.99% (Cheah et al., 1979).

Diabetes in Bangladesh

West et al. (1966) reported the prevalence rate of diabetes mellitus in Bangladesh (then East Pakistan) to be 1.5% in the age groups 30 years and above which was lower as compared to Uruguay, Venezuela and Malaysia. In Bangladesh (Ibrahim et al., 1979) have shown that 30% of the diabetics are less than 40 years of age. Data on 19,000 patients revealed a family history of diabetes in 27.62%, parental in 18.2, and that of siblings in 12.33%. In 1983 Mahtab et al. carried out a survey in a rural and semiurban community near Dhaka city. The combined prevalence of diabetes mellitus and Impaired Glucose Tolerance in these two communities was 0.7% in the population above 15 years. The prevalence of known diabetics in this survey was 0.14% while that of newly discovered cases was 0.56%, a four fold difference which may be expected in communities with poor health awareness. Therefore, in the total population of 100 million in Bangladesh, 350,000 might be expected to suffer from diabetes mellitus.

Screening for diabetes mellitus in 2240 healthy male workers in two textile mills in Bangladesh (Ali et al., 1985), showed 51 subjects to have glycosuria, out of which 12 turned out to be diabetic, a prevalence rate of 0.53%. The number of registered diabetics in BIRDEM till May, 1987 is 59,209 in Dhaka city alone. However, when these patients have diarrhoea,

they are either treated by general practioners or referred to ICDDR,B. In the treatment centre of ICDDR,B, where average attendance of out-patients varies from 150-300 every day, the number of diabetics coming with diarrhoea is 6-8 per month, even though they have an institute catering especially to their needs, free of any medical charge, which is the Bangladesh Institute of Research on Diabetes, Endocrine and Metabolic Disorders (BIRDEM). Most of them receive oral hypoglycemic drugs or dietary control only. Few are insulin requiring diabetes. This is not surprising since low prevalence of IDDM (Insulin dependent diabetes mallitus) is a phenomenon noted in developing countries (Zimmet, 1983). If diabetic patients with diarrhoea are referred from BIRDEM, then the number attending ICDDR,B will increase.

Diarrhoea in diabetic cases

Diarrhoea in diabetes can be broadly classified into two categories. In the first category is diarrhoea as a complication of diabetes, usually called 'diabetic diarrhoea', the term being first used in 1936 (Bargen et al.), to describe unexplained diarrhoea associated with severe diabetes. The typical patient has insulin dependent diabetes mellitus that is poorly controlled, in addition to advanced neuropathic and other diabetic complications (Katz et al., 1976; Scarpella et al., 1978) and will not be included in the study. The second category includes the acute diarrhoeal diseases affecting the general population, and diabetics affected as part of that population. Although the exact incidence of such diarrhoea in diabetic population is unknown, it is likely to be the same as that in the general population. Diarrhoea presents as a serious problem for the diabetic patient. Acute gastroenteritis is one of the frequent and difficult situations in which diarrhoea may be accompanied by nausea and

vomiting. The situation is further complicated in the diabetic patients by the omission of insulin at that time in the belief that they are unable to keep food in the stomach, and avoid food entirely. This may lead to disaster in the insulin requiring diabetic and they have to be instructed accordingly and every effort should be made to prevent dehydration. When diarrhoea develops suddenly, it may lead to hypoglycemia in the patient who has already taken his usual full dose of insulin for that day (Jenson 1973) Dehydration should be prevented or corrected as soon as possible, preferably by the oral route, since it has been shown to be one of the foremost factors responsible for exacerbating infection in the diabetic patient, whereas elevation of blood glucose is listed as an unlikely factor (Younger et al., 1973). There is some evidence that dehydration resulting from hyperglycemia and polyuria may enhance the extent of infections. Pillsbury & Kulchar (1935) noted that a disturbance in the fluid balance of rabbits resulted in marked increase in the extent of an experimental staphylococcal skin infection. Mosenthal (1935) and other investigators have regarded the polyuria and dehydration accompanying prolonged and marked glycosuria, rather than hyperglycaemia to be responsible for the diminished resistance to infection seen in diabetics.

Metabolism in diabetes: (Ganong 1983)

The following Figures illustrate the complexities of the metabolic abnormalities in diabetes.

Fig.1: Disordered blood glucose homeostasis in insulin deficiency

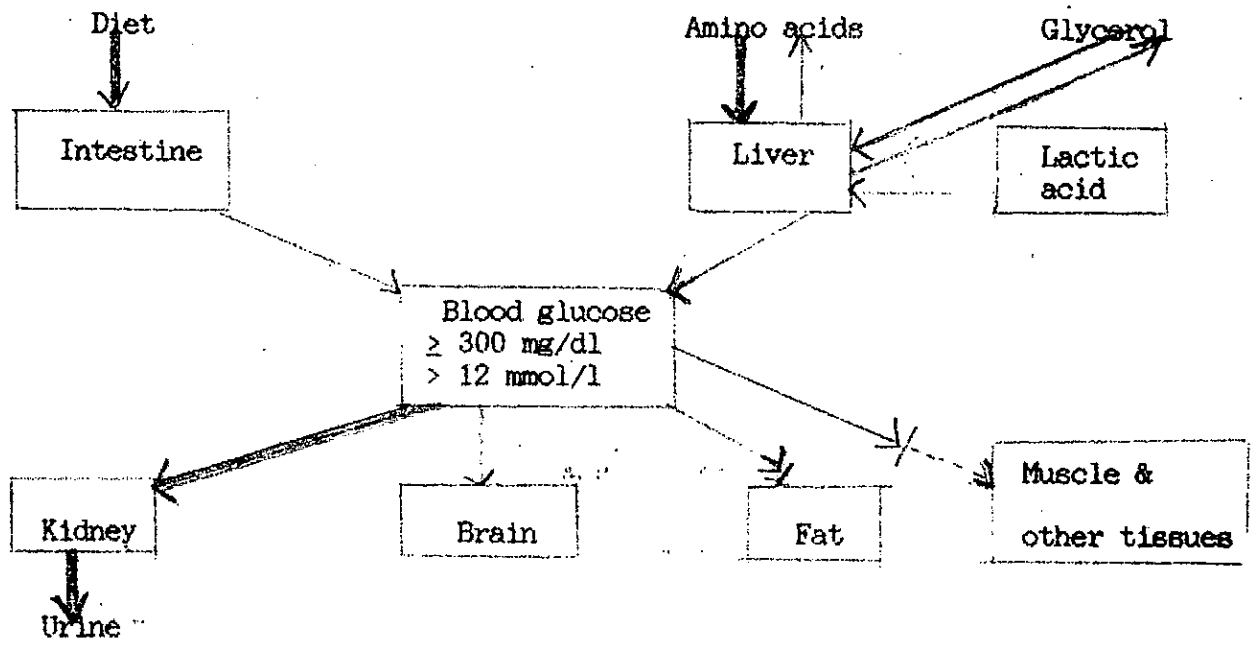
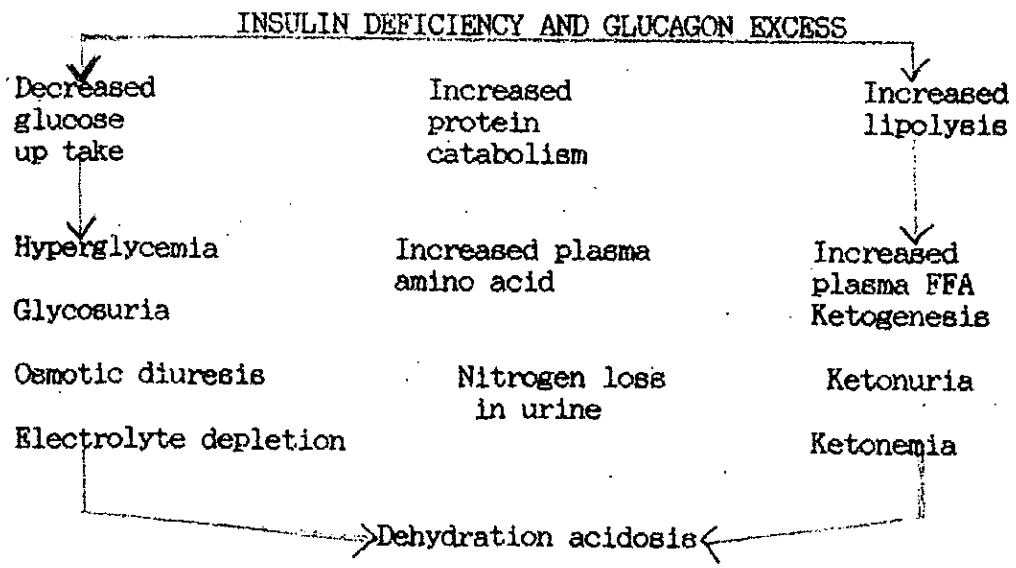


Fig. 2: Effects of insulin deficiency



The efficacy of oral rehydration therapy in replacing the loss of fluid and electrolytes in watery diarrhoea is now well established (Chatterjee 1953, Harrison 1954, Meneghello 1960). The discovery of glucose facilitated transport of sodium and water in the small intestine (Shultz et al., 1964), and the fact that this process remains intact during acute diarrhoea of diverse etiology, forms the basis of glucose-based oral rehydration fluids for acute diarrhoea (Hirschorn, 1980). Glucose being expensive, and not easily available in some countries, it was replaced by sugar (Sack et al., 1978), and since even sugar is not easily available in the rural areas of developing countries, it was further replaced by gur or molasses (Islam et al., 1980). Recent studies using cereal (rice powder) have shown good results in Bangladesh (Molla et al. 1982) and in India (Patra et al., 1982). Rice based ORS has been shown to reduce stool output and ORS intake by 40-50%, and vomiting by 60% compared to glucose ORS. It rehydrates more efficiently as shown by gain in body weight and change in serum specific gravity. Rice based ORS effectively corrects the biochemical abnormalities and maintains them within normal limits.

Studies have shown that almost all water soluble organic molecules which are absorbed from the small intestine enhance the absorption of sodium and water; examples are hexoses, aminoacids, dipeptides, tripeptides and some water soluble vitamins (Shultz et al. 1977). When an amino acid such as glycine is added to glucose containing ORS, the adverse osmotic effect or osmotic penalty (Patra et al., 1984) i.e., osmotic back flow of water from plasma to gut lumen due to unabsorbed organic molecules is largely eliminated due to rapid absorption of the organic solutes (i.e., glycine and glucose), which in turn stimulates absorption of a larger quantity of sodium and water. It has been shown that patients treated

with glucose or glycine solution achieved a positive water and electrolyte balance within the first eight to twelve hours of oral therapy (Nalin et al., 1970).

A randomized non-blind trial of glucose tolerance test, in two groups, four in each, was conducted with glucose and rice in diabetic patients 18 years and above in BIRDEM, Dhaka. Patients who were given an oral glucose load, were seen to have a higher level of blood glucose which they continued to maintain for the next one hour. However, the patients given rice showed a gradual drop in the blood glucose level, the 2 hour post prandial blood glucose being even lower than the initial fasting level. Thus it was seen that the patients given rice, remained well within the safety range (unpublished observation).

Magnitude of the problems

According to Ahuja's study in India (1971), prevalence of diabetes is age related, being the highest in the age group 40 years and above. With prospective increase in longevity of life, with economic advancement and changes in dietary practice, the potential risk of diabetes may increase further as has been experienced in developed countries in the West. Migration of population to urban areas also seems to augment prevalence of diabetes.

Hypothesis: ORS containing Rice and Glycine as base is safer and more effective than WHO-ORS for treatment of diabetic patients with acute dehydrating diarrhoea.

3. RATIONALE

Although the proper replacement of water and salt losses is the main therapeutic goal in the treatment of acute diarrhoea, the possibility of preventing too much fluctuation in the blood sugar level as well as reducing the magnitude and duration of diarrhoea, will have a great practical and psychological importance to both the diabetic patients and their physicians. Most of the diabetics who attended Diarrhoea Treatment Centre during the past year did not take WHO ORS at home since it contains sugar and some were even reluctant to take the rice ORS. The present study will show which one of the above oral rehydration solutions is best for diabetic patients, and shall be recommended for them.

B. SPECIFIC AIMS

1. To assess the fluctuation of blood glucose level after administration of rice-ORS, glycine-ORS, and WHO ORS to diabetic patients with acute watery diarrhoea.
2. To identify the most appropriate oral rehydration solution for diabetics with acute diarrhoea.
3. To evaluate the effect of different oral rehydration solutions on the clinical course of diarrhoea in diabetic patients.

C. METHODS OF PROCEDURE

Sample size

Since there are no reference data considering fluctuations in blood sugar level with the different ORS regimes, we refer to our own experiment carried out with glucose and cooked rice in diabetic patients, without diarrhoea.

With 95% confidence limit (Type I error) and 80% power (Type II error) the sample size in each group is calculated with the help of the formula -

$$\frac{2 \times SD^2}{\text{Difference}^2} \times \text{Power} \qquad \text{(Cochran et al)}$$

Our experiment showed.

X1 (or the blood glucose level 2 hours after glucose) = 15.2 mmol/l

and X2 (blood glucose level 2 hours after rice) = 11.5 mmol/l

and SD = 3.0 mmol/l

$$\frac{2 \times 3^2 \times 7.9}{(15.2 - 11.4)^2} = \frac{18 \times 8}{(3.8)^2}$$

$$= \frac{18 \times 8}{14} = 11 \text{ per group}$$

For cancellation, four more patients may be taken in each groups

i.e. 12 + 3 = 15

So in all (15 X 3) = 45 patients will be taken into the study, to be distributed randomly in three treatment groups with the help of a random table.

Randomization procedure

The study will be randomized but not blinded because of the whitish colour of the rice ORS. A random table will be used to allocate the number of patients for each of the ORS group.

Comparibility of the study patients

Study patients will be selected according to the criteria described in subsequent section. Since this protocol will only accept patients with mild to moderate dehydration as may exist in the community they will be directly assigned to the different rehydration therapy group.

ENROLMENT OF SUBJECT

a. Assessment of eligibility:

Patients included into the study will be those who have been diagnosed by BIRDEM to be diabetic, according to the WHO criteria which are:

A single blood glucose estimation in excess of 10.0 mmol/l (180 mg) in venous whole blood or 11.1 mmol/l (200 mg) in venous plasma in a patients with symptoms of diabetes.

For epidemiological or population screening purposes the two hour value after 75 g oral glucose load may be used alone. The patient is said to be diabetic if this value is >10 mmol/l in venous whole blood, or > 11.1 mmol/l in venous plasma.

The inclusion criteria for the study are: Adults of either sex, age more than 15 years, insulin requiring/on oral hypoglycemic or on diet control only, with a history of onset of watery diarrhoea during the last 48 hours.

Exclusion criteria

Female patients suspected to be pregnant, patients with other illnesses or patients suspected to have complications such as ketoacidosis will not be included in the study.

b. Informed consent: Each patient will be explained about the study, and only those who give voluntary written consent will be included in the study.

c. Baseline examination: Complete history will be taken and thorough physical examination will be carried out according to a proforma. The following laboratory investigations will be performed

on admission:

Blood: Blood glucose, free fatty acids, Hct, TC, DC, electrolytes, (Na, K, Cl, TCO2) creatinine, plasma protein and specific gravity. 4 ml blood will be required.

Urine: Reducing substance, ketones.

Stool: M.E., D/F, C/S for V.cholerae and enterotoxigenic E.coli

Subject allocation

The patients will be randomly assigned to receive either the rice-based ORS, glycine ORS or WHO ORS as described previously.

Composition of oral rehydration solution

ORS Citrate		Electrolytes	
Composition			
Sodium chloride	3.9 g	Na^+ mmol/l	90
Trisodium citrate dihydrate	2.9 g	Cl^- "	80
Potassium chloride	1.5 g	K^+ "	20
Glucose, anhydrose	20 g	HCO_3^- "	10
Water	1000 ml		

Rice ORS: 50 gm rice powder will be used in place of glucose.

Glycine ORS group will receive ORS with 111 mmol/l of glycine added, in place of glucose.

Description of the schedule

All patients admitted to the trial will be cared for by doctors and nursing staff assigned to the study. Immediately after recording weight and assigning the proper serial number, the patient will be put on a cholera cot, 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. A preweighed bowl will be kept by the bedside for collection of vomitus. Intake and output will be recorded in a specially designed record sheet every 4 hours until discharge from the study. All fluid therapy will be divided into 2 parts:

i) Initial rehydration phase; ii) Maintenance phase

i) Initial rehydration phase

After admission into the study and randomization, the initial investigations will be performed and the patient with moderate dehydration will be rehydrated by any one of the oral rehydration fluids. Intravenous acetate solution (Dhaka solution) will be used only in case of persistent vomiting and difficulty in compliance for initial rehydration, along with any of the ORS fluids. Patients with mild dehydration will receive 50 ml/kg of the oral rehydration fluid assigned to them over 2 h according to the WHO guidelines. Any stool output during this time will be replaced by the ongoing rehydration fluid.

ii) Maintenance phase

This phase starts after signs of dehydration have disappeared. The diarrhoeal stool loss will be replaced by ORS as per the randomization, based on 4 hourly stool weights, until diarrhoea ceases. Careful measurement of fluid intake including milk, water, stool and urine output during this period will be recorded. Body weight and clinical examinations will be repeated at 8 hours after admission and every 24 hours thereafter. In all patients, the following laboratory tests will be carried out before starting the study. Complete blood count, blood glucose, FFA plasma

specific gravity, serum electrolytes, urine glucose and ketone. Blood for electrolytes and FFA will be repeated at 24 hours intervals and before discharge. Finger prick blood for glucose will be tested before breakfast and two hours after lunch every day with the help of a glucometer. Urine will be collected 8 hourly and the sugar estimated which will give the 24 hour urinary glucose loss. Patients will be discharged from the study after cessation of diarrhoea when stool is soft.

Diet

All the patients will be given standard diabetic diet according to WHO guidelines - dietary fat 25% of total daily energy intake, protein 20% and carbohydrate with natural fibre constituting the remaining food energy.

Oral hypoglycemic agents and insulin

Patients will be continued on the same anti diabetic treatment they were on previously (diet only, oral hypoglycemic or insulin) provided they can take the standardised diet described above. They will be given in addition Inj. Soluble Insulin 4 units 1/M hourly on appearance of Ketone bodies in the urine and this will be continued till the Ketone bodies disappear.

Treatment failure

If signs of dehydration reappear during the maintenance phase and the patient has to be given intravenous therapy, he/she will be considered as treatment failure and will be dropped from the study. If electrolyte imbalance develops, he/she will be treated along the same guidelines followed in our hospital for general patients.

ASCERTAINMENT OF RESPONSE VARIABLES

Response variables:

- Duration of diarrhoea in hospital
- Diarrhoea stool volume: 0-8 h, 0-24 h, 24-48 h, 24-48 h, 0 - till ceasation of diarrhoea
- Blood glucose levels on admission, before breakfast and two hours after lunch.
- Blood for free fatty acids on the next day of admission, after 24 hours and before discharge.
- Corresponding urine sugar - from 8 hourly urine collection to calculate 24 hr glucose loss
- Weight gain
- Amount of ORS consumed till ceasation of diarrhoea
- Hct, Sp. gravity, electrolytes and creatinine on admission and repeat electrolytes after 24 hours and before discharge.

Working definitions

Cessation of diarrhoea: The cessation 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 nearest one gram.

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

Analysis of data

i) Pretreatment clinical data to assess comparability among the groups.

ii) Post-treatment clinical and laboratory data such as weight gain at 4-24 h and at discharge, duration of diarrhoea, stool output, intake of ORS, blood glucose, Hct, plasma specific gravity, serum electrolytes and creatinine, free fatty acids urine glucose, rate of treatment failure and amount of unscheduled intravenous fluid used.

Appropriate statistical test will be selected and will be performed on micro computer.

D. SIGNIFICANCE

Since diarrhoea remains a significant problem for the developing countries, a large number of the diabetic population is likely to be affected, and it remains to be known which rehydration solution will be more appropriate for them.

E. FACILITIES REQUIRED

1. The present office space will be utilised.
2. Laboratory office - ICDDR,B and BIRDEM office will be utilised.
3. Hospital resources - Study ward and outpatient space will be required.
4. Logistic support - ICDDR,B computer facilities will be used.
5. Transport - ICDDR,B transport will be used.

F. Collaborative arrangements will be made between ICDDR,B and Prof. A. K. Azad Khan and Dr H. Mahtab from BIRDEM who will help in the referral and management of patients.

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DETAILED BUDGET

1. Personnel services

Name	Position	% effort	No. of of months	No. of man month	Project reqmt.
Dr. Rukhsana Haider	Principal Investigator	20%	18	3.6	$ 2160
Prof. A.K. Azad Khan	Co-Investigator	-	-	-	-
Dr. S.K. Roy	" "	10%	18	1.8	1350
Dr. N.H. Alam	" "	10%	18	1.8	1260
Clerk (study ward)		20%	18	3.6	612
Dietician		10%	18	1.8	720
Research Officer		10%	18	1.8	630
Uerban Volunteer (CHW) - 2		100%	18	18	1800
				Sub-total:	8532

2. Supplies and materials

Drugs	1500
Hospital supplies & stationaries	1500
Non-stock supplies	1000
Sub Total	= 4000

3. Inter-Departmental Service

a.	Transportation of patients at end of study		500
b.	Patient hospitalization (45 x 7 d/p x $25/p) =		7875
c.	Laboratoy tests		
	Blood glucose, stup.	864	
	Blood Hct, TC, DC	240	
	Stool M.E.	84	
	Stool or rectal swab C/S	548	
	Urine stup for glucose	288	
	Urine test for Ketone	352	
			2376
d.	Xerox		300
e.	Medical illustration		200
e.	Computer charges for data analysis		1000
	Sub Total	=	$ 12251

4.	Travel international	2000
5.	Capital expenditure	
a.	Glucochek machine - 2	1200
6.	Other costs	
a.	Rent, communication and utilities	50
b.	Printing and reproduction	400
c.	Service charges	100
	Sub Total =	550

BUDGET SUMMARY

1.	Local salaries	US $	8532.00
2.	Supplies and Materials	US $	4000.00
3.	Other costs	US $	550.00
4.	Inter-departmental services	US $	12251.00
5.	Travel international	US $	2000.00
	Total direct operating cost	US $	27333.00
	Capital expenditure	US $	1200.00
	TOTAL DIRECT COST	US $	28533.00

ABSTRACT SUMMARY FOR ETHICAL REVIEW COMMITTEE

1. Forty five known diabetic patients, both male and female patients on insulin or oral hypoglycemia agent or only diet control as advised by BIRDEM, aged 15 years and above, suffering from acute diarrhoeal dehydration, will be selected for the study. Females suspected to be pregnant, patients with major systemic illness, or complications such as ketoacidosis will be excluded from the study.

2. Any untoward reaction associated with any of the three oral rehydration solutions will be noted and managed appropriately.

3. There is no potential risk involved in the study. Every precaution will be taken to safeguard the safety of the patients.

4. All records will be kept strictly confidential and will remain with the investigators. Code numbers will be used.

5. Informed consent (signed or thumb impression, will be obtained from the patients or the guardians of the patients enrolled in the study.

6. Interview will be taken only related to the history of the illness, and is needed for clinical management of the disease.

7. The patient will benefit from the treatment of diarrhoeal disease. General benefit will be both for the diabetic patients, and the physicians. The present study will show which one of the oral rehydration solutions (WHO, rice, or glucose ORS) is best for diabetic patients, and will be recommended for them. If however all these are found to be equally safe, then any of them can be confidently recommended.

8. No retrospective hospital records will be used.

9. The study will require fresh stool for microscopy and rectal swab for bacteriological culture on admission. 4 ml of venous blood will be drawn on admission, 3 ml after 24 hours and before discharge. The above tests will be necessary to assess the state of hydration of the patient electrolyte status and the glucose level in the subject which will serve as a guideline for subsequent fluid therapy and clincial management. One drop of finger prick blood will be tested for blood glucose, by a new, convenient technique daily before breakfast, and 2 hours after lunch.

CONSENT FORM

MANAGEMENT OF ACUTE DIARRHOEA IN DIABETIC PATIENTS

International Centre for Diarrhoeal Disease Research, Bangladesh is carrying out research to find an effective oral rehydration solution for diabetic patients with acute diarrhoea which will not upset their blood glucose level. In this study three types of oral rehydration solution will be used. They are standard WHO ORS, rice-based ORS, and glycine-based ORS. All of three have been proved effective in acute diarrhoea but we would like to find out which one is the best for diabetic patients.

If you agree to participate in the study the following procedure will be applicable for you.

1. You will receive any one of the above mentioned oral rehydration solutions according to a random table.

2. Your stool, urine and vomitus will be measured. 4 ml of blood will be drawn on admission for routine care and 3.5 ml after 24 hours and before discharge . In addition, finger prick blood will be tested daily by a new convenient technique for blood glucose level before breakfast and 2 hours after lunch. All the urine will be collected and tested for glucose and ketone bodies.

3. The results of the investigations will be used to evaluate the effect of treatment which may benefit a vast majority of diabetic patients in future.

4. You will be required to stay until diarrhoea is stopped.

5. Taking part in the study totally depends upon your own decision. You will be teated to the best of our ability with all the available treatment facilities in this hospital even if you do not participate in the study.

6. You will have full rights to withdraw from the study at any time yet you will receive standard treatment of the hospital.

If you are willing voluntarily to join this study, please sign your name or put your left thumb impression on this consent form.

Signature of Investigator

Signature or LTI of patient/ guardian

Witness: ----------

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

সম্মতি - পত্র

আমি মিস, মিঃ, মিঃ, আর মিঃ
ডায়েবেটিস্ রোগীর ডায়রিয়ার চিকিৎসা :

আন্তর্জাতিক উপাময় গবেষনা কেন্দ্র ডায়েবেটিস্ রুগীর ডায়রিয়ার চিকিৎসায় একটা আশ্চর্যকরী খাওয়ার স্যালাইন উদ্ভাবনের জন্য গবেষনা চালিয়ে যাচ্ছে যাহা রক্তের গ্লুকোজের মাত্রার কোন তারতম্য ঘটাবে না। এই গবেষনায় মোট ৩ প্রকারের খাবার স্যালাইন ব্যবহার করা হবে। এগুলি হচ্ছে :- সাধারন ডব্লিউ, এইচ, ও, সলোনিত খাওয়ার গ্লুকোজ স্যালাইন, চাউলের গুড়া দ্বারা তৈরী খাওয়ার স্যালাইন এবং গ্লাইসিন দ্বারা তৈরী খাবার স্যালাইন। এর সবগুলিই ডায়রিয়া রুগীর চিকিৎসায় আশ্চর্যকরী প্রমর্মনিত হয়েছে। কিন্তু আমরা দেখতে চাই এর কোনটি ডায়েবেটিস্ রুগীর ডায়রিয়াতে সবচেয়ে ভালো।

যদি আপনি এই গবেষনায় অংশ গ্রহন করেন তাহলে আমরা নিম্নলিখিত পরীক্ষাগুলি করবো।

(১) আপনি উপরিলিখিত খাবার স্যালাইনগুলির যে কোন প্রকার খাবেন সেটা আপনার ভাগ্যে পড়বে।

(২) আপনার শারিরীক, পেশাব এবং রক্ত মাপা হবে। ভর্তির সময় ৪ মিঃলিঃ, ভর্তির ২৪ ঘন্টা পর এবং ছুটির সময় আরো ৩.৫ মিঃলিঃ রক্ত পরীক্ষার জন্য নেয়া হবে। তাছাড়া দিনে ২ বার সকালে খাওয়ার আগে এবং দুপুরে খাওয়ার ২ ঘন্টা পরে আপনার আঙ্গুল থেকে রক্ত নিয়ে রক্তের গ্লুকোজ মাপা পরীক্ষা করা হবে। আপনার পেশাব রাখা হবে এবং ৮ ঘন্টা অন্তর অন্তর গ্লুকোজ এবং কিটোনবডিজের জন্য পরীক্ষা করা হবে।

(৩) এই গবেষনার ফলাফল ফলপ্রসূ হলে ভবিষ্যতে অল্পে ডায়েরিয়া ~~ডায়েবেটিস্~~ রুগী উপকৃত হবে।

(৪) আপনার ডায়রিয়া ভালো না হওয়া পর্যন্ত আপনাকে হাসপাতালে থাকতে হবে।

(৫) এই গবেষনায় অংশ গ্রহন সম্পূর্ন আপনার ইচ্ছার উপর নির্ভরশীল। আপনি গবেষনায় অংশ গ্রহন না করলেও আপনার চিকিৎসা করা হবে।

(৬) আপনি যে কোন সময় গবেষনায় অংশ গ্রহন থেকে নিজেকে বিরত রাখতে পারবেন তবু ও আপনার চিকিৎসা দেওয়া হবে।

যদি আপনি এই গবেষনায় অংশ গ্রহনে সম্মত হন তাহলে অনুগ্রহ-পূর্বক আপনার নাম সহি/টিপসহি করুন।

প্রধান গবেষকের স্বাক্ষর

রুগীর সই/ টিপ সই

তারিখ

স্বাক্ষীর সই—