Library ①

ETHICAL REVIEW COMMITTEE, ICDDR,B.

Principal Investigator Dr. G.H. Rabbani

Application No. 84-041

Title of Study RANDOMIZED, CONTROLLED TRIAL OF BERBERINE TO INHIBIT FLUID LOSS IN NON-CHOLERA DIARRHOEA.

Trainee Investigator (if any) ②

Supporting Agency (if Non-ICDDR,B)

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.

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

G-H-Rabbani

Principal Investigator

Trainee

SECTION 1 - RESEARCH PROTOCOL

1. TITLE: RANDOMIZED, CONTROLLED TRIAL OF BERBERINE TO INHIBIT FLUID LOSS IN NON-CHOLERA DIARRHOEA.

2. PRINCIPAL INVESTIGATORS: Dr. G.H. Rabbani, and Dr. T. Butler

3. STARTING DATE: 1 October 1984

4. COMPLETION DATE: 30 September 1985

5. TOTAL INCREMENTAL COST: US $ 9,300.00

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

Signature of Programme Head: _____

Date: _____

7. ABSTRACT SUMMARY:

After our initial success with Berberine in cholera, now we will attempt to study the effect of Berberine in reducing secretory diarrhoea in patients with severe non-cholera diarrhoea. The study and control groups will each consist of 20 adult patients with darkfield negative stools for V. cholera. After a period of 4 hours of observation to ascertain the basal purging rate, patients in the study group will be given a dose of Berberine Sulfate equal to 10 mg/kg. Purging rate will then be quantified over the next 24 hours and rates in the treatment and control groups compared. Side effects of treatment if any will be noted.

8. REVIEWS:

(a) Research involving human subjects: _____

(b) Research Review Committee: _____ _____

(c) Director: _____

SECTION II - RESEARCH PLAN

A. INTRODUCTION:

1. Objectives

To investigate the clinical efficacy of Berberine sulphate as an antisecretory agent in patients with non-cholera diarrhoea.

2. Background

Our recent success of Berberine in the treatment of cholera prompted us to further examine its effects in other types of non-cholera diarrhoea, such as E. coli diarrhoea. In our previous randomized, controlled trial at ICDDR,B, Berberine sulphate (400 mg) significantly reduced stool volume (35-40%) in a group of 120 adult subjects with severe cholera (Butler T, Rabbani GH, 1984). In toxigenic E. coli infection, intestinal fluid loss occurs by a biochemical mechanism similar to that of cholera, i.e. production of a toxin (ST or LT) and subsequent activation of adenylate cyclase and the specific necleotide (cAMP or cGMP). In experimental animals, E. coli ST induced diarrhoea can be effectively inhibited by berberine (Sack RB, et al 1982). Therefore, we anticipate that the drug might have antisecretory activity in man and may be useful in the treatment of diarrhoea produced by toxigenic strains of E. coli. The drug is safe and we did not find any instances of untoward effects after a 1200 mg dose in adult subjects in the previous study.

Toxigenic E. coli is the major cause of dehydrating diarrhoea in the rural community of Matlab (Black et al 1982) and also among the hospitalized patients at the Dhaka Station (Stoll et al 1983). Although mild to moderate degree of clinical severity is common, the fluid-loss may be considerable and sometime life threatening, death may occur in untreated cases, especially in young children. E. coli is prevalent through out the world and is the major pathogen associated with the travellers diarrhoea. Although cholera is a more severe disease, is it limited to the endemic regions of Asia and is responsible for only 5-10% of total diarrhoeal cases in no-epidemic season.

Therefore if an agent can be found such as berberine, which reduces fluid-loss in E. coli diarrhoea, it might have widespread usefulness. This will also produce evidence that the durg which acts against cholera also is useful in non-cholera diarrhoea such as E. coli diarrhoea.

Berberine is an alkaloid (berberine sulfate mol.wt. 384.4) derived from the plant Berberis aristata, the Indian Barberry,or Tree turmeric. It has been known to indigenous Indian and Chinese medicine for several thousand years. The yellow alkaloid berberine is a bitter extract of the root, bark, and wood. It has been traditionally used as a tonic, astringent, diaphoretic, antipyretic, and purgative, in cases of splenomegaly and jaundice, in remittent and intermittent fevers, in neuralgia, in bilious complaints, and in diarrhoea.

Mixed with honey it is applied externally to aphthous sores, abrasions, and ulcerations of the skin[2].

The pioneer study of berberine in experimental cholera was Datta and Panse's 1962 work[3]. They used infant rabbits and found that berberine alone among several indigenous plants tested prevented diarrhoea and death when given both before and 8 hours after infection. The authors did not, however, find berberine to be vibriocidal.

Subbaiah and Amin in 1967 found berberine sulphate useful in the prevention of experimental Entamoeba histolytica infection in 3-4 week-old golden hamsters, and tolerated by the animals up to a dose of 100 mg/kg[4]. Amin, Subbaiah, and Abbasi assessed the antimicrobail activity of berberine sulfate in 1969, and found that it was more potent than chloramphenicol and tetracycline against V. cholerae and was also bactericidal against this organism. Datta, however, found that berberine was less active than tetracycline and chloramphenicol[6], and Nair, Modak, and Venkatraman found it to be vibriostatic rather than vibriocidal[7].

In clinical trials in 1967 berberine was shown to be more effective than chloramphenicol in the treatment of cholera and nonspecific diarrhoea[8]. Further clinical studies in India in the late 1960's and early 1970's confirmed the drug's clinical efficacy in diarrhoeal disorders - these include studies by Kamath (1967)[9], Deshpande (1969)[10], Sharda (1970)[11], Sharma et al (1970)[12], and Desai et al (1971)[13]. In 1975 Gupte showed that berberine was effective and well tolerated at a dose of 10 mg/kg/day in the treatment of giardiasis, with efficacy somewhat less than that of standard therapies[14].

Raswat, a traditional crude dried preparation of Berberis aristata, was also effective against cholera toxin-induced diarrhoea at a dose of 1-2 mg/kg[18].

Earlier, Dutta and co-workers had shown that oral administration of berberine to infant rabbits 18-24 hours before the intra-intestinal administration of cholera toxin prevented the development of diarrhoea or significantly prolonged survival time, whereas berberine given later was ineffective[6]. They related this result to the finding by Bhide et al that the concentration of berberine in the blood of infant rabbits reaches a maximum 8 hours after G.I. tract administration with some drug still detecteble after 72 hours[19]. Mekawi showed that 0.3 mg of berberine injected I.M. protected mice from death from cholera infection, and also showed that the drug protected them against cholera toxin[20].

Further studies by Akhter and coworkers showed that berberine given orally significantly prolonged the latent period and reduced the frequency and severity of diarrhoea in dogs provoked by Inpomoea turpethum root, a potent traditional prugative preparation. Berberine did not prevent diarrhoea caused by magnesium sulfate or castor oil. At a dose of 10 mg/kg it reduced intestinal motility in mice, and was more effective when given intra-peritoneally than when given orally[21].

Recent experimental work has continued to confirm berberine's efficacy as an anti-secretory agent. Swabb and co-workers tested the effects of luminal berberine in the cannulated, perfused rat ileum using ^{14}C polyethylene glycol as a nonabsorbable marker.

They found that berberine reduced cholera toxin-induced secretion of water, Na, Cl, and HCO_3 in a concentration - dependent manner but did not alter normal ileal water and electrolyte transport. The effect of berberine on toxin-induced secretion became evident 60-80 minutes after exposure and was reversed 60-80 minutes after removal of berberine from the perfusate. Berberine also prevented the development of cholera toxin - induced villous tip edema[22]. Sack and Frochlich found that berberine sulfate inhibited by approximately 20% secretory responses to the heat-labile enterotoxins of V. cholerae and E. coli in rabbit ligated intestinal loop.

The drug was effective when given both before and four hours after toxin administration, and by both intraluminal and parenteral administration. It did not inhibit the stimulation of adenylate cyclase by cholera enterotoxin and caused no histological damage to intestinal mucosa. Berberine also inhibited secretion due to the E. coli heat-stable enterotoxin in the infant mouse[23,24].

The study of berberine pharmokinetics in humans is now possible thanks to the development of sensitive and specific assay methods for detecting the drug in fluids (e.g., urine)[25,26].

In summary, berberine has been shown to be an effective anti-secretory agent in cholera and other diarrhoeal dyndromes by a great deal of experimental work in various animal models. Some evaluation in humans was also carried out with encouraging results, but there has been no published study of a human trial in more than ten years.

Berberine is marketed in India and Japan, and presumably widely used in those countries as an anti-diarrhoeal medication as well as in other disease states. The published reports suggests that it is safe in humans but no definitive knowledge of possible side-effects exists. These may include some or all of the effects observed in animal studies, including hypotension[27] and sedation[28]. It would seem reasonable to study the efficacy and spectrum of clinical effects of berberine in a controlled trial for if it is really a potent, safe anti-secretagogue it may make a significant contribution to our management of cholera and other severe secretory diarrhoeal diseases.

Rationale:

Toxigenic E. coli is the most frequent pathogen associated with watery diarrhoea in children and adults, it is also the most common bacterial cause of diarrhoea in travellers. In terms of clinical severity it stands next to that produced by Vibrio cholera. Since berberine works against cholera, it may also work against toxigenic E. coli because both the toxins produce pathogenic effects by similar mechanism. A controlled randomized study of berberine's efficacy in non-cholera diarrhoea may substantiate this knowledge and provide sound justification for using this inexpensive and safe drug in the treatment of non-cholera diarrhoea.

B. SPECIFIC AIMS: See objectives

C. METHODS AND PROCEDURES:

Study population. This will be a randomised, parallel, and controlled clinical study. The study will be carried out in 100 adult patients with severe non-cholera diarrhoea. Patients will be selected from the Treatment Centre and will satisfy the following admission criteria.

Inclusion criteria:

1. Onset of watery diarrhoea within previous 24 hours.
2. Darkfield negative stools to exclude patients with cholera.
3. No history of current use of Tetracycline
4. Voluntary agreement to participate in the study
5. Baseline purging rate of at least 100 ml per hour as observed in the Treatment Centre over a period of 4 hours.

Randomization. After admission to the study ward patients will be randomly assigned to either - (a) treatment group or (b) control group. Patients will be stratified by purging rates and will be randomized using a random number table.

Low purging group	=	100-200 ml stool/h as baseline rate
Moderate purging group	=	200-300 ml stool/h as baseline rate
Severe purging group	=	More than 300 ml/h as baseline rate.

Drug administration: After purging has been observed for 4 hours, patients assigned to group (a) will receive berberine sulfate at a dose of 10 mg/kg. In a 40 kg adult, the total dose will be 400 mg and will be given as 400 mg in a single dose for 24 hours.

Berberine sulphate - 10 mg/kg (total 400 mg), single dose for 1 day = 50 pts

Control subjects - No treatment = = 50 pts

Exclusion criteria:

Patients having any of the following conditions will be excluded from the study. Patients who:

(a) are known or suspected to be pregnant or are breast-feeding;

(b) have a known allergy or hypersensitivity to the study medications;

(c) are not able to comply with the study procedures as outlined in the protocol;

(d) are not expected to maintain oral medication due to vomiting;

(e) have any other concurrent medical condition that might interfere with the evaluation of the study medication.

(f) have clinical evidence of severe malnutrition.

Exclusion criteria during the course of the study:

Subjects who acquire any of the following conditions during the course of the study will be excluded from further participation in the study. Subjects who:

(a) exhibit any adverse reaction warranting discontinuation of the study medication;

(b) have V. cholera isolated from the stool specimens as confirmed by bacteriologic culturing (drop out);

(c) acquire any intercurrent illness or condition that might interfere with the evaluation procedures in this study (drop out).

In these intances, further treatment will be given by the investigators.

Dropout accounting:

Subjects who do not complete the study will be replaced according to the guidelines in this protocol. This will be done in order to preserve the study population as close as possible 100 completed subjects.

Monitoring and Treatment:

All patients will receive I.V. hydration to match their stool losses. The latter will be quantitated by 8 hours periods for 24 hours (3 eight-hour periods) as long as each patient has significant diarrhoea. Stool cultures will be done. Colonies that are typical of E. coli will be picked and kept preserved, until they are tested for toxin production using standard procedures. Oral feedings will be minimal (e.g., bread, milk) for the first 24 hours, after which regular meals will be provided. Each patient's B.P. and level of consciousness will be recorded for every 8 hour period, and any significant changes in physical condition will be noted.

Adverse Reactions:

All adverse reactions, regardless of severity will be recorded on the appropriate record(s) provided in the case report forms.

Overdose Management:

In case of an overdose of berberine, symptomatic and supportive therapy may be required, as well as the following:
If the amount ingested is considered dangerous or excessive, vomting will be induced, unless the patient is convulsing or comatose or has

lost gag reflex in which case gastric lavage will be performed using a large-bore tube. If indicated patient will be followed with charcoal. There are no specific antidotes.

Concomitant Medications:

Medications which is considered necessary for the patients welfare and which will not interfere with the study drug or its evaluation may be given at the discretion of the investigator. Administration of all such concomitant medications will be recorded on the appropriate page of the case report.

D. SIGNIFICANCE:

The aim of the study will be to test the efficacy of berberine as an antisecretory agent in non-cholera diarrhoea in a controlled randomized manner, as well as to identify any negative side effects of the drug.

Data analysis: Patients in the treatment and control groups will be compared with regard to baseline purging rate, purging rate after treatment, and duration of diarrhoea. Each patient's baseline purging rate will be compared with his rate after treatment. Appropriate tests of statistical significance will be employed, e.g., student's 't' test for comparison of measn and S.D.'s of stool volumes.

E. FACILITIES REQUIRED:

1.	Office space:	Present office space will be used
2.	Laboratory space:	The present Laboratory will be utilized.
3.	Hospital resources:	100 adult patients will be studied.
4.	Animal resources:	Suckling mice will be utilized for toxin assay
5.	Logistic support:	None
6.	Major equipment:	None
7.	Others:	None
8.	Transport:	None

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ABSTRACT SUMMARY:

Controlled trial of Berberine as an antisecretory agent in non-cholera diarrhoea.

1. This study will be conducted with 100 adult patients with non-cholera diarrhoea and severe purging. It will test Berberine sulfate, which as been shown to be an effective anti-secretory agent in cholera and E. coli toxin induced diarrhoeas in a number of animal experiments and some human trials. Berberine is synthesized and marketed in India and Japan and is beleived to be safe for human use; it has been found to be essentially free of side effects at a dose of 10 mg/kg/day.

2. The patients will be randomly assigned to treatment and control groups. They will be observed for 4 hours so that their baseline purging rate may be ascertained. Those assigned to the treatment group will then be given a dose of Berberine equal to 10 mg/kg body weight. Stool volumes will thereafter be measured during 8 hours periods for 24 hours. Patients will be rehydrated by the I.V. route. The study should not subject either treatment or control group patients to any significant risks. It is not expected that serious side effects of berberine administration will be found.

3. Not applicable

4. Patient confidentiality will be maintained. All data will be abbreviated and will be published without reference to the subjects' name and identity.

5. Informed consent will be obtained from each patient enrolled in the study.

6. No personal interview is required.

7. Benefits to the patients involved in the study will be the cost-free treatment of diarrhoeal illness. General benefits to society include the possible identification of a valuable anti-secretory drug in non-cholera diarrhoea.

8. No retrospective hospital records will be used. No biological specimens except stool will be taken from the subjects.

SECTION III - BUDGET

1. Personnel:

Investigators	Position	% time used	Annual salary	Project requirement Taka	Project requirement Dollar
Dr. G.H. Rabbani	Principal Investigator	50%	Tk.90,000	Tk. 45000	-
Dr. T. Butler	Co-Investigator	10%	-		$ 5000

2. Patients hospitalization:

   100 pts X Tk. 150 X 3 days = Tk. 45,000

3. Laboratory tests:

   Stool culture for cholera (100X2tests) = $ 200

   Infant mouse for E. coli toxin assay (100)= $ 300

   Biochemistry = None

   Hematology = None

4. Out patient care = None

5. Travel of person = None

6. Transportation = None

7. Printing and Reproduction = $ 100

8. Contractual services = None

9. Computer time = $ 100

BUDGET SUMMARY

		Taka	Dollar
1.	Personnel services	-	6,800
2.	Supplies and equipment	-	500
3.	Patients hospitalization	-	1,800
4.	Out patient care - Nil		
5.	Transportation - Nil		
6.	Travel of person - Nil		
7.	Transport of things - Nil		
8.	Tent., etc. - Nil		
9.	Printing & Reproduction		100
10.	Computer		100
			$ 9,300

CLINICAL TRIAL OF BERBERINE IN NON CHOLERA DIARRHOEA

Data collection sheet

Name of the subject: _____ _____

Hospital admission number: /___/___/___/___/___/___/

Date of admission to study: Day /___/___/ Mon /___/___/ Year /___/___/

Age in years: /___/___/

Sex: /___/ (Male = 1, Female = 2)

HISTORY AND PHYSICAL:

Admission body weight (kg): /___/___/ /___/___/

Oral temperature (^{O}F): /___/___/___/ /___/___/

Blood pressure (mmHg): Systolic /___/___/___/ Diastolic /___/___/___/

Radial pulse/min: /___/___/___/

Respiration per/min: /___/___/

Duration of diarrhoea before admission (hours): /___/___/

Clinical assessment of dehydration: /___/ (Mild=1, Mod=2, Sev=3)

Previous medication: /___/ (None = 1, Yes =2)

Dark-field exam for V. cholera: /___/ (Positive = 1, Neg = 2)

Rectal swab culture for V. cholera: Admission day /___/ (Pos=1, Neg=2)

Second day /___/ (Pos=1, Neg=2)

Known allergy to Berberine: /___/ (Yes =1, No = 2)

BASE-LINE STOOL ASSESSMENT (FIRST 4 H OBSERVATION AFTER HYDRATION)

Time stated: _____

Time end: _____

Stool volume (ml): /___/___/___/___/

Stool consistency: /___/ (Watery = 1, Soft=2, Semisoft=3, Formed=4)

Urine volume (ml): /___/___/___/___/

Vomit (ml): /___/___/___/

Intravenous fluid given (ml): /___/___/___/___/

Plain water ingested (ml): /___/___/___/

Milk ingested (ml): /___/___/___/

Body weight (kg): /___/___/ /___/___/

Stratification by purging rates: /___/ Mild=100-200 ml/h (code=1)
Mod =200-300 ml/h (code=2)
Sev = 300 ml/h (code=3)

Randomization: /___/ (Treatment group=1, Control group=2)

Treatment: Berberine (400 mg) Given /___/ Note time: _____

If the subject vomited after the drug admisinstration, please note the time of vomiting occured:

Hours /___/___/ Min /___/___/

Nausea: /___/

Adbominal pain: /___/

Abdominal discomfort: /___/ (Absent = 1, Present = 2)

Hospital No.: _____

FIRST 8 HOUR POST TREATMENT PERIOD:

Time of collection: _____ _____

OUTPUT:

Stool volume ml: /___/___/___/___/

Stool consistency: /___/ Watery=1
Semi-soft=2
Soft=3
Formed=4

Urine volume (ml): /___/___/___/___/

Vomit (ml): /___/___/___/

Nausea: /___/

Abdominal pain: /___/ Absent = 1, Present = 2

Abdominal discomfort: /___/

INTAKE:

I.V. fluid given (ml): /___/___/___/___/

Plain water ingested (ml): /___/___/___/

Milk ingested (ml): /___/___/___/

SECOND 8 HOUR POST TREATMENT PERIOD

Time of collection: ___ _____ _____ ___

OUTPUT:

Stool volume (ml) /___/___/___/

Stool consistency: /___/ Watery=1
Semi-soft=2
Soft=3
Formed=4

Urine volume (ml): /___/___/___/___/

Vomit (ml): /___/___/___/

Nausea: /___/

Abdominal pain: /___/ Absent = 1, Present = 2

Abdominal discomfort: /___/

INTAKE:

I.V. fluid given (ml): /___/___/___/___/

Plain water ingested (ml): /___/___/___/

Milk ingested (ml): /___/___/___/

THIRD 8 HOUR POST TREATMENT PERIOD

Time of collection: ___ __ _____ __ __

OUTPUT

Stool volume (ml): /___/___/___/___/

Stool consistency: /___/ Watery=1
Semi-soft=2
Soft=3
Formed=4

Urine volume (ml): /___/___/___/

Vomit (ml): /___/___/___/ Nausea: /___/ Abdominal pain: /___/

Abdominal discomfort: /___/

INTAKE

I.V. fluid given (ml): /___/___/___/___/

Plain water ingested (ml): /___/___/___/

Milk ingested (ml): /___/___/___/

SUBJECT STUDY NO. _____

No Adverse Effects Noted [ ]

SUSPECT DRUG INFORMATION

Drug _____

Total Daily Dose/Units+ _____ Route PO

Treatment Start/End _ _/ /_ _ _/ /

Reason _____ STUDY DRUG

SUSPECTED ADVERSE REACTIONS

AR	Adverse Reactions	Dates Onset	Dates End	Duration	Sev *	Out-come **
1						
2						
3						
4						

* Severity:
1=mild
2=moderate
3=severe

** Outcome:
A=alive with sequelae
R=recovered
S=still under treatment
D=died

Questions	AR-1 ***	AR-2 ***	AR-3 ***	AR-4 ***
Outpatient treatment required?	[NA]	[NA]	[NA]	[NA]
Hospital treatment required?	[ ]	[ ]	[ ]	[ ]
Was dose reduced?	[NA]	[NA]	[NA]	[NA]
Was drug discontinued?	[NA]	[NA]	[NA]	[NA]
Did reaction abate?	[ ]	[ ]	[ ]	[ ]
Was drug reintroduced?	[NA]	[NA]	[NA]	[NA]
Was dose increased?	[NA]	[NA]	[NA]	[NA]
Did reaction reappear?	[NA]	[NA]	[NA]	[NA]

***Y=YES, N=NO, NA=NOT APPLICABLE TO THIS STUDY. OTHER QUESTIONS REQUIRE A YES OR NO RESPONSE.

COMMENTS (Describe other relevant medical history, etc.)

_____

_____

_____

Trial of
Berberine

The International Centre for Diarrhoeal Disease Research, Bangladesh.

(Consent form)

I understand that I have diarrhoea from non-cholera infection and that I may need to be treated with intravenous fluids. I also understand that I am to be admitted to the hospital research ward where I will remain until the diarrhoea is over. I will be treated either with Berberine, which is a drug, which in India is used to treat diarrhoea, or with intravenous fluids alone. The purpose of treating me with Berberine is to find out if it really is effective in helping to stop diarrhoea caused by non-cholera pathogens.

I understand that I do not have to participate in this study and if I do not want to, I will not be refused proper treatment in this hospital. I also may withdraw from this study at any time without any penalty.

The records of my treatment will be kept confidential.

Signature of the Investigator/
Co-Investigator

Signature of the patient

Date: _____

বারবারিন ঔষধ গবেষণা

সম্মতি পত্র

আমি জানিতে পারিয়াছি যে আমার কলেরা নয় এরূপ জীবাণু সংক্রমিত ডাইরিয়া হইয়াছে আমাকে শিরায় স্যালাইন দ্বারা চিকিৎসা করা হইবে। আমাকে হাসপাতালে ভর্ত্তি করা হইবে এবং ডায়েরিয়া না ভাল হওয়া পর্যন্ত রাখা হইবে। আমাকে বারবারিন ঔষধের দ্বারা অথবা শুধু স্যালাইন দ্বারা চিকিৎসা করা হইবে। এই ঔষধ ভারতে ডাইরিয়ার জন্য ব্যবহার করা হয়। আমাকে বারবারিন চিকিৎসা দেবার উদ্দেশ্য হইল ইহার ডাইরিয়া রোগের উপর কার্যকারিতা পরীক্ষা করিয়া দেখা।

আমি আরও জানিতে পারিয়াছি যে আমি ইচ্ছা করিলে গবেষণায় নাও অংশ নিতে পারি, ইহাতে আমার স্বাভাবিক চিকিৎসার কোন প্রকার তারতম্য হইবে না। আমার ইচ্ছামত আমি এই গবেষণা হইতে নাম প্রত্যাহার করিয়া লইতে পারিব। আমার ডাক্তারী পরীক্ষার সকল কাগজপত্র গোপন রাখা হইবে।

গবেষকের স্বাক্ষর

তারিখ----------

রোগীর স্বাক্ষর/টিপসহি
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