Attachment 1.

Library (2)

Date 20.11.86

ETHICAL REVIEW COMMITTEE, ICDDR,B.

Principal Investigator DR. TARIQ HASSAN Trainee Investigator (if any) 25

Application No. 86-036 Supporting Agency (if Non-ICDDR,B) SEARLE FRA

Title of Study SACOLENE IN CHOLERA 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)

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

Hassan

Principal Investigator

NOV 20 1986

Trainee

SECTION I - RESEARCH PROTOCOL

1.	TITLE:	SACOLENE IN CHOLERA
2.	PRINCIPAL INVESTIGATOR:	Dr. Tariq Hassan
	CO-INVESTIGATORS:	Dr. R.N. Mazumder
		Dr. F.C. Patra
		Professor Roger Eeckels
	COLLABORATIVE INVESTIGATOR:	Professor J.F. Desjeux
3.	STARTING DATE:	January 1987
4.	COMPLETION DATE:	December 1987
5.	TOTAL DIRECT COST:	US $ 45,000.00
	SOURCE OF FUNDING:	SEARLE FRANCE
6.	SCIENTIFIC PROGRAMME:	This protocol has been approved by the Clinical Sciences Division.

Signature of Acting Associate Director, Clinical Sciences Division

Date: 19 11 1986

ABSTRACT SUMMARY

To evaluate the antisecretory effect of Sacolene a methylated casein preparation, in cholera, a double blind random controlled trial is proposed. Sacolene contains methylated casein and sucrose. It is empirically used and commercially distributed as an oral antidiarrhoeal medication. The active principle is methylated casein. In this trial, 50 adult male patients with cholera will be treated with Sacolene (16 g/day) and 50 comparable patients will receive a placebo. All patients will enter the study after initial rehydration with intravenous acetate electrolyte solution. The patients will receive the usual treatment for cholera (maintenance of hydration by ORS and feeding) given in this institution, but no antibiotics will be administered. Response to treatment will be evaluated by comparing between the study and placebo groups, stool volume/4 hours, total volume of liquid stools and duration of diarrhoea Any unpleasant effects of the treatment will be recorded. All ethical guidelines for clinical trials at ICDDR,B will be followed. This study is an effort to a potentially simple and effective antidiarrhoeal therapy specifically by examining the efficacy of methylated casein in cholera.

8. REVIEWS

a. Chairman, Ethical Review CommCommittee: ----------

b. Chairman, Research Review Commitee: ----------

c. Director, ICDDR,B: ----------

SECTION II: RESEARCH PLAN

BACKGROUND

Dehydration due to cholera can now be effectively treated with oral rehydration fluid containing glucose and electrolytes. ORS rehydrates but does not inhibits the secretion induced by cholera toxin. Appropriate antimicrobial agents will benefit patients with specific bacterial diarrhoeas including cholera (12,15) However, multiple drug resistant Vibrio cholerae have been reported (9,16).

Antisecretory drugs are another therapeutic approach. In various animals a large number of pharmacological agents have been shown to inhibit intestinal secretion in various animals induced by cholera toxin and E. coli enterotoxins (review by Rabbani, 1980). However only few of these drugs have clinical effects in man. They also have some drawbacks, e.g., chlorpromazine produces dose - dependent sedation in children, berberine is bitter and is more active in E. coli diarrhoea than in cholera. It is thus important to continue looking for safe and possibly efficacious antisecretory drugs.

Sacolene may be such a compound. It contains methylated casein, as its active principle, and sucrose. It is marketed in France and the francophone African countries and prescribed in acute and chronic diarrhoeas. (6,18,1-8,10,11,18,19). Methylated casein is prepared by precipitating casein from skimmed cows milk with lactic acid, and methylating it with formaldehyde (18). This results in a polymerization of the casein molecules, making

methylated casein still more poorly soluble in water than its parent compound.

Caseins are one of the major proteins found in milks. Caseins are amphoteric phosphoproteins containing 15% nitrogen, 0.7% phosphorous, and about 0.8% sulphur. The aminoacid sequence of bovine casein is known and consists of 209 residues. The approximate molecular weight is 23,6000. The aminoacid composition of methylated casein is very similar to that of casein itself, except for a decrease in lysine and tyrosine residues (21).

It has been found that methylated casein is resistant to the acidic action of the gastric juice and to the action of trypsin and chymotrypsin. In quasi-physiologic conditions, no formaldehyde is released from methylated casein.

Methylated casein is not expected to cross the intestinal barrier for several reasons: (i) the intestinal mucosa is almost impermeable to intact proteins especially high-molecular weight ones (13); (ii) the molecular weight of methylated casein is not known, but it is certainly several times higher than that of casein, (iii) after contact with cholera toxin, intestinal mucosal permeability to proteins is not changed (14). It should also be stressed that casein is being used in the treatment of cow's milk protein intolerance. Therefore no systemic effects are anticipated.

Recently, Peyrot and others have investigated in vivo the effect of methylated casein on intestinal water and ion transport in isolated jejunal loops of rats treated with cholera toxin (21). The authors reported that 10 mg/ml methylated casein in

the rat jejunum significantly inhibits water and electrolyte secretion induced by cholera toxin. This action is evident within 20 minutes, is exerted directly on the luminal side of the epithelium and is dose dependent. Methylated casein stimulates neutral NaCl absorption (whereas glucose stimulates electrogenic Na+ absorption). In vitro, the antisecretory effect was found to be caused by a reversal of the net Na+ and Cl- fluxes from secretion to absorption. Methylated casein does not interfere with intestinal function in the absence of stimulation by cholera toxin. More particularly, it does not interfere with the stimulation of Na+ absorption by glucose.

Clinical use: Sacolene is commercially available in France since 1979. It is sold at a price of 90 Taka = (20 F.F.) per 6g g. It is reimbursed by the French social security and the production price is obviously much lower than the market price. No side effects of any importance have been reported. In 12 studies, a total number of 3258 patients with diarrhoea were given Sacolene. No accidents were reported except for some minor possible side effects (see table 1).

In summary methylated casein is an antisecretory agent that has several characteristics that makes it a suitable candidate for anti-cholera drug; (i) it inhibits the action of cholera toxin in animal studies; (ii) it is fast acting, the action begining within 20 minutes of administration and lasting for 3 hours; (iii) it acts in presence of cholera toxin, but not on the normal gut; (iv) it produces additive Na+ absorptive effect to that of glucose;(v) it is acting from the mucosal side; (vi)

it is being used as an antidiarrhoeal agent in human beings, without any important side-effects. This list of characteristics is very close to the list produced by W.H.O. requirements on drug development with reference to treatment of diarrhoea (24). To a large extend this project will be similar to testing a traditional drug of known safety but not yet proven efficay.

OBJECTIVES:

Primary objective

To see whether Sacolene reduces fluid loss in cholera.

Variables are:
1. stool output in ml/kg per 4 h and
2. total volume of liquid stools, in ml.

These variables will be interpreted taking into account ORS intake, plain water intake, vomitus, urine volume and gain in weight.

Secondary objectives

To detect side effects related to Sacolene, if any.

Variables are:
1. Nausea (number of patients)
2. Vomiting (in ml and number of patients)
3. Abdominal pain (number of patients)
4. Abdominal discomfort (number of patients)

Rationale

Well conducted experimental in vivo studies have shown, rather unexpectedly, that methylated casein, an inoccuous anti-diarrhoeal preparation, blocks the action of cholera toxin on the rabbit intestinal epithelium. If this action also occurs in patients, methylated casein could be a simple low cost orally active antisecretory agents of value in cholera patients.

B. SPECIFIC AIMS : To test the antisecretory properties of methylated casein in cholera patients having high purging rates.

METHODS AND PROCEDURES

Study population

The study will be carried out in adult cholera patients in the study ward of the Dhaka Hospital of International Centre for Diarrhoeal Disease Research, Bangladesh, Dhaka.

Inclusion criteria

1. Only men will be studied for convenience of collecting stool and urine
2. Age : above 15 years
3. History of onset of watery diarrhoea (3 or more watery stools) within last 24 hours.
4. No prior treatment with antibiotic or antidiarrhoeal drugs.
5. Stool should be positive for Vibrio cholerae by dark field microscopy
6. Baseline purging of 20 ml/kg or more over 4 hours before allocation to treatment.
7. Voluntary agreement after informed consent to participate in the study until cessation of diarrhoea.

Exclusion criteria

1. Gross blood and mucous in stool
2. Inability to maintain oral medication due to vomiting.

Sample size calculation

We assume that the patient to patient variability in stool output and duration of diarrhoea from patient to patient will follow the same pattern observe by Molla et al. (17).

From published report the mean stool output during the first 24 hours is 156 ml/kg and the standard deviation is 109 ml/kg. The expected reduction in stool output is 50% i.e. 78 ml/kg. Calculations are as below:

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

$\alpha = \cdot 05$

$\beta = \cdot 10$

power = 90

Thus n =

$$= \frac{2 \times 10 \cdot 5 \times (109)^2}{(78)^2}$$

41 Patients will be required in each group and in two groups, 82. To test this, the total number of patients included in this study will have to be 100.

Enrollment of subject

a. Informed consent

Each patient, or his attendant, will be explained to the nature of the study and only those who give voluntary written consent will be included. The patients have the right to withdraw from the study at any stage, without affecting further care.

b. Assessement of eligibility

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

c. Baseline examination

A standard history and complete physical examination will be carried out accordingly to a proforma.

- Micro-haematocrit and plasma specific gravity.
- Serum electrolyte and total CO_2.
- Rectal swab for V. cholerae
- Dark-field for V. cholerae

d. Subject allocation

The trial will be conducted in a double blind design and patients will be randomly assigned to receive either Sacolene or placebo, using a permutted block design. This will ensure the distribution of equal numbers of cases in each groups.

It is proposed that Sacolene and the placebo will be supplied by the French manufacturer (SEARLE, FRANCE) free of cost.

Intervention

a. Composition of sacolene and placebo. Sacolene per sachet of 6 g contains 2 g of methylated casein with 3.8 g of sucrose. Placebo will contain per sachet 2 g of microcellulose and 3.8 g of sucrose.

b. Description of the schedule

All patients admitted to the trial will be cared for by doctors and nursing staff assigned to the study. The nurses have gained experience in earlier metabolic studies. Immediately after his weight having been recorded, the patient will be put on a cholera bed allowing for accurate and separate collection of stools and urine. The vomitus will be measured in ml every 4 hours.

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 two parts.

1. Initial rehydration phase
2. Maintenance phase

Initial rehydration phase

Admitted into the ward before randomisation, patients will be rehydrated by intravenous acetate solution (Dhaka fluid). Patients with severe degree of dehydration will receive 100 ml/kg over a period of 2 to 4 hours. If the patient has a purging rate greater than 24 ml/kg for 4 hours, he will be randomly assigned either to the treatment or placebo group.

Maintenance phase

This phase starts after signs of dehydration are corrected. The study will start at this stage of the treatment. The diarrhoeal stool loss will be replaced weight for weight by WHO ORS based on 4 hourly stool weights, until diarrhoea ceases. Careful measurement of fluid intake, including feeds, and of stool, vomitus and urine output during this period will be recorded. Body weight and clinical examination will be repeated 4 hourly.

In all patients laboratory tests will be done at the begining of the study (i.e., microhaematocrit, plasma specific gravity, plasma electrolytes and TCO2). These tests will be repeated after 24 hours and at discharge. Patients will be discharged from the study after cessation of diarrhoea. Stool culture for V. cholerae will be done on admission, and at

discharge.

DRUG ADMINISTRATION

The treatment group will receive a loading dose of 4 g of Sacolene and 2 g every 4 hours unitil the cessation of diarrhoea. The same administration schedule will be followed for the placebo group.

Feeding

The patients will be given standard hospital diet, consisting of rice, dal, fish and vegetables.

Antibiotics

No antibiotics will be given to the patient.

Free water

Water will be offered during the maintenance phase, and accurate record of this intake will be kept.

WORKING DEFINITIONS

Cessation of diarrhoea

The end point of diarrhoea is considered as the time at which the last liquid stool has been passed.

Soft stool

Soft stool may be defined as a stool which can be poured down and takes the shape of a container.

Formed stool

Formed stool may be defined as a stool which does not take the shape of a container.

Treatment failure

If clinical signs of dehydration reappear during the maintenance phase supported by rising haematocrit and plasma specific gravity values and if this requires resumption of intravenous therapy, the patient will be considered as treatment failure. These patients will receive intravenous acetate 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 till the cessation of diarrhoea.

Data analysis

1. Pre-treatment clinical data will be analysed to assess comparability between the two groups of patients. They will be presented in a table including the variables, the number of patients for each variable, the mean and standard deviation, median and range for each of the two groups.

2. The outcome variables (stool output ml/kg per 4 h, total volume of watery stools and duration of diarrhoea) will be analysed taking into account the distribution. If the latter is normal, the t-test will be used, if not, the Mann-Whitney U test will applied. Computations will be done on a PC using the 'Statpack' software. The data will be presented in a table including the name of the variables,the number of patients, and the appropriate measures of central tendency (mean or median) and of dispersion (standard deviation or range).

FACILITIES REQUIRED

1. Office space - The existing office space will be utilized
2. Laboratory space - No additional laboratory space will be needed
3. Hospital beds - The present clinical research ward will be used
4. Rent, communication and utilities - Not required

COLLABORATIVE ARRANGEMENTS

This protocol will be carried out at ICDDR,B in collaboration with Dr. J.F. Desjeux, Director "Unite INSERM, 290 Hopital St Lazare, 107, rue du Faubourge St. Denis, 75010, Paris, France". Searle France, the manufacturer of SACOLENE, will supply free of charge the drug and the placebo, in identical packets. The code will be kept by Searle and second copy by Dr Desjeux. Drug and placebo packets will be marked with two different letters (A and B) the significance of which will be first of the code.

Searle France will give institutional support to ICDDR,B by a gift of US $45,000, half of it to be transferred at the beginning of the study, the second half at the successful completion of the mid point of the study (50 patients).

TABLE 1

SUMMARY OF PUBLISHED CLINICAL STUDIES ON SACOLENE IN 3258 PATIENTS WITH DIARRHOEA

Ref.		No. of patients	Age (years)	Dose (g/day)	Duration of treatment (days)	Side-effect
1	Sacolene	30	34-70	8-16	5-15	0
2	do	30	18-60	6	15	1 Constipation 1 Nausea
3	do	775	adults	4-8	15	9 constipation
4	do	40	20-90	4-12	8-30	0
5	do	31	17-87	6-12	3-23	2 vomiting
6	do	30	(3/12-29/12)	1	5-9	0
7	do	149	0-70	0.5-4	5	0
8	do	2033	15-90	4-12	55	1 constipation 1 nausea-vomiting
10	do	30	36	3	10-60	2 constipation
11	do	40	61-93	4-6	10	1 constipation
18	Sacolene Placebo	20 20	3/12-12/12	2-4	5-10	0; Biology undisturbed
19		50	<40-80	4	5	1 abdominal pain
TOTAL		3258	0-90	0.5-16	3-60	19 (0.6%) 14 constipation 4 nusea of vomiting 1 abdominal - pain.

COMMENTS

- Aetiology of the diarrhoeas is not well defined
- Patients had acute diarrhoea, chronic diarrhoea, irritable bowel disease or post surgical problems (in the elderly).
- No study on cholera was ever done.

ABSTRACT SUMMARY FOR ETHICAL REVIEW COMMITTEE

1. The fundamental objective of this study is to evaluate the therapeutic antisecretory effect of Sacolene, a methylated casein preparation. This study will be conducted in 100 adult patients with cholera. Methylated casein has been shown to possess antisecretory activity in experimental animals: it acts from the luminal side of the intestine, being not resorved. It is being used as an oral antidiarrhoeal medication. It reverses net Na^+ and Cl^- fluxes from secretion to absorption in presence of cholera toxin. It is accepted to be completely safe for human use in Europe, and no side- effects of methylated casein have so far been reported.

2. After a base-line observation of 4 hours, patients will be randomly assigned to a treatment and placebo group. Those assigned to the treatment group will be given 16 g per day of Sacolene untill diarrhoea stops. Stool volume will be measured in every 4-hours period. All patients will receive acetate-electrolyte solution intravenously for initial rehydration but no antibiotics. All the patients will receive the usual treatment in this institution: maintenance of hydration with ORT and feeding after initial rehydration.

3. Informed consent will be obtained from each patient before allocating to treatment.

4. Confidentiality of clinical records will be maintained. All data will be abbreviated and will be published without references to the patients name and identity.

5. No personal interview is required.

6. Three ml of venous blood will be drawn at admission, after 24 h and 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 management.

7. Any untoward reaction associated with therapy will be noted and treated accordingly.

8. Benefits to the patients involved in the study will be a proper treatment of diarrhoeal illness under close supervision. General benefits to society include the possible identification of an useful antidiarrhoeal drug for cholera.

9. No retrospective hospital record will be used.

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24. WHO/CDD/DDM/82.3.

SECTION III - BUDGET

1. Personnel services:

Name	Position	% effort	US Dollar
Dr. T. Hassan	Principal Investigator	100%	3600.00
Dr. R.N.Mazumder	Co-P.I.	100%	3600.00
Dr. F.C. Patra	"	30%	-
Prof. R. Eeckels	"	20%	-
Study Nurses - 2		100%	5000.00

Sub Total= 12,200.00

2.	Supplies and materials	1650.00
3.	Laboratory tests	3650.00
4.	Equipments	2500.00
5.	Patients hospitalization	17,500.00
6.	Transportation of materials	500.00
7.	Printing and reproduction	1000.00
8.	Computer and data entry	2000.00
9.	Travel	2000.00

Sub Total=30,800.00

GRAND TOTAL = US $ 43,000.00

Total project cost is US $45,000.00. The excess amount of US $2,000.00 will go to the Centre as an institutional help.

International Centre for Diarrhoeal Disease Research, Bangladesh

CONSENT FORM

SACOLENE IN CHOLERA

International Centre for diarrhoeal Disease Research, Bangladesh would like to carry out research on Sacolene for the treatment of diarrhoea in cholera. Sacolene is a widely used safe oral antidiarrhoeal medication used in France and in some African countries. It is thought to have the capability of reducing the diarrhoeal stool volume and duration of diarrhoea. The study will last till the cessation of diarrhoea and during this period the patient will be treated with Sacolene. The patient will receive intravenous acetate solution (Dhaka solution) for initial rehydration after which the drug will be administered by mouth and WHO ORS will be continued.

Stool, urine and vomitus of the patient will be measured every 4 hourly until the cessation of diarrhoea. Three millilitres (3 ml) of blood will be drawn from the patient on admission, after 24 hours and at discharge, to assess the degree of dehydration and assessment of therapeutic response. Stool culture will be performed at the time of admission into the study ward and at discharge.

All records of the patients in the hospital will be kept confidential with the Principal Investigator. Taking part in the study totally depends upon your decision. The patient will be provided with all the available treatment facilities in this hospital even if he does not allow himself to participate in this study voluntarily. If you agree to participate in this study, then please sign here and give your consent.

---------- ----------

Signature of the Investigator

Signature or Finger Print

of the patient/guardian.

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

আন্তর্জাতিক উদরাময় গবেষণা কেন্দ্র, বাংলাদেশ।

"কলেরায় অ্যাকোলিনের ব্যবহার"।

আন্তর্জাতিক উদরাময় গবেষণা কেন্দ্র কলেরায় অ্যাকোলিনের কার্যকারিতা পরীক্ষা করতে ইচ্ছুক। অ্যাকোলিন ফ্রান্স এবং আফ্রিকার দেশসমূহে ডায়রিয়াজনিত রোগে ব্যবহৃত হয়ে আসছে। ইহা নিরাপদ মুখে যাবার ঔষধ। ইহা পাতলা পায়খানার পরিমাণ ও সময় কমাতে আশ্চর্য্য করতে পারে। এই ঔষধ খাওয়ানো ডায়রিয়া বন্ধ না হওয়া পর্যন্ত চলবে। প্রাথমিকভাবে রোগীকে কলেরা অ্যালাইন দিয়ে পানি শূন্যতা দূর করা হবে এবং তারপর ORS খাবার অ্যালাইন দেয়া হবে যতক্ষন পর্যন্ত ডায়রিয়া থাকে।

এই গবেষনা কোষ হওয়ার আগ পর্যন্ত রোগীর মল, মূত্র ও বমি ৪ঘন্টা অন্তর অন্তর মাপ হবে। ভর্তির সময়, ২৪ ঘন্টা পর ও ছুটির সময় ৩মিঃ রক্ত নেয়া হবে যার মাধ্যমে দেহের ডায়রিয়াজনিত পানি শূন্যতা যাচাই করা হবে ও এই ঔষধের কার্যকারি নির্ণয় করা হবে। রোগীর পায়খানা ভর্তির সময় এবং ভাল হবার পর পরীক্ষা করা হবে। এ সকল পরীক্ষার ফলাফল রোগীর শুচিকিৎসায় ব্যবহৃত হবে।

রোগীর চিকিৎসার যাবতীয় তথ্যাদি গোপন রাখা হবে। এই গবেষণায় অংশগ্রহন করা কিংবা না করা সম্পূর্ন আপনার ইচ্ছাধীন। অংশগ্রহন না করলেও আপনি এ হাসপাতালের প্রচলিত নিয়মানুসারে শুচিকিৎসা পাবেন।

যদি আপনি এ প্রস্তাবে রাজী থাকেন তবে নিম্নে স্বাক্ষর করুন অথবা বামহাতের বুড়া আংগুলের টিপসই দিন।

গবেষকের স্বাক্ষর

রোগীর স্বাক্ষর / টিপসহি

CLINICAL TRIAL OF SACOLENE IN CHOLERA

Study No. / / / /

Name of the subject: _____

Hospital admission number / / / / / / /

Date of admission to study / / / / / / / / / /
Day Month Year

Age in years / / /

HISTORY AND PHYSICAL

Admission body weight (kg) / / / / / /
Kg g

Temperature (°C) / / /

Radial pulse/min / / /

Respiration/min / / /

Duration of diarrhoea before adm (h) / / /

Clinical status of dehydration (Mod=1, Sev=2) / /

Dark field examination for V. cholerae (Positive=1, Negative=2) / /

Rectal swab culture for V. cholerae on adm day (Positive=1, Negative=2) / /

DISCHARGE NOTE

Duration of diarrhoea / / /

Weight (kg) / / /

Dx. _____

Outcome: _____

DATA COLLECTION SHEET

PRETREATMENT PERIOD

Study No. /___/___/___/

Date /___/ Day /___/ Month /___/ Year

Time /___/ hr /___/ min /___/ hr /___/ min

Weight (kg) /___/ kg /___/ g

OUTPUT

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

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

Urine (ml) /___/___/___/

Vomit (ml) /___/___/___/

INTAKE

I.V. cholera fluid (ml) /___/___/___/

Feeding (Absent=1, Present=2) /___/

Nausea (Absent=1, Present=2) /___/

Abdominal pain (Absent=1, Present=2) /___/

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

Other symptoms (if yes, specify)

INCLUSION CRITERIA

Male /___/ 15 years /___/ Diarrhoea 24 h /___/

No drug /___/ Vibrio cholerae /___/

Purging rate 20 ml/kg /___/ · Informed consent /___/

Day /__/ Study No. /__/__/__/

Date /__/__/ /__/__/ /__/__/
Day Month Year

/__/__/ /__/__/ HOURS POST TREATMENT PERIOD

Time of collection from /__/__/ hr /__/__/ min /__/__/ hr /__/__/ min

OUTPUT

Stool volume (ml) /__/__/__/__/

Stool consistency (Watery=1, Soft=2, Formed=3) /__/

Urine (ml) /__/__/__/__/

Vomit (ml) /__/__/__/__/

INTAKE

Drug given (No=1, Yes=2) /__/

WHO ORS fluid ingested (ml) /__/__/__/__/

Plain water ingested (ml) /__/__/__/__/

Feeding (No=1, Yes=2) /__/

Nausea (Absent=1, Present=2) /__/

Abdominal pain (Absent=1, Present=2) /__/

Abdominal discomfort /__/

Other symptoms or signs (if yes, please specify)

Blood collected (No=1, Yes=2) /__/

Contd...

/ / / / / / HOURS POST TREATMENT PERIOD

Time of collection	/ / / hr	/ / / min	/ / / hr	/ / / min

OUTPUT

Stool volume (ml)	/ / / /
Stool consistency (Watery=1, Soft=2, Formed=3)	/ /
Urine (ml)	/ / / /
Vomit (ml)	/ / / /

INTAKE

Drug given (No=1, Yes=2)	/ /
WHO ORS fluid ingested (ml)	/ / / /
Plain water ingested (ml)	/ / / /
Feeding (No=2, Yes=2)	/ /

Nausea (Absent=1, Present=2)	/ /
Abdominal pain (Absent=1, Present=2)	/ /
Abdominal discomfort	/ /
Other symptoms or signs (if yes, please specify)	
Blood collected (No=1, Yes=2)	/ /