80-044

308

International Centre for Diarrhoeal Disease Research, Bangladesh

Office Memorandum

TO : Dr. K.M.S. Aziz

FROM : Director

DATE: November 13, 1980

SUBJECT : REFEREED PROTOCOL FROM BMRC FOR ETHICAL REVIEW.

Professor Kamaluddin Ahmed has indicated his willingness to have his protocol reviewed by our Committee. I see no objection to going ahead and satisfying the BMRC request to this.

WBG:abn

MEDRESCON

বাংলাদেশ মেডিক্যাল গবেষণা পরিষদ
BANGLADESH MEDICAL RESEARCH COUNCIL

Public Health Institute
(2nd Floor)
Mohakhali, Dacca-12

বাংলাদেশ মেডিক্যাল গবেষণা পরিষদ
(জনস্বাস্থ্য ইনস্টিটিউট)
মহাখালী, ঢাকা-১২

Ref. No. BMRC/Ec/79-80/1,113 Date... 6-11-...1980

Dr. K.M.S.Aziz,
Scientific Director,
International Centre for Diarrhoeal
Disease Research, Bangladesh,
Mohakhali, Dacca-12.

Dear Sir,

Please find enclosed protocol from Dr. Golam Nabi, Member-Secretary of the Trial Committee and Officer-in-Charge, National T.B. Control, Shymoli, Dacca to try a drug of herbal origin on human subject.

As our Ethical Committee is not working at present, you are requested to kindly place it to the Ethical Committee of ICDDR,B for opinion.

Thanking you in anticipation.

Yours sincerely,

A.K.Khan
6.11.80

(Prof. A. K. Khan)
Director.

THE INSTITUTE OF NUTRITION AND FOOD SCIENCE
UNIVERSITY OF DACCA
DACCA-2, BANGLADESH

Phone : 256238
Cable : NUTRITION DACCA

No. 441/INFS/80-81 Immediate. Dated 4.11.80

Dr. Golam Nabi
Syamoli T.B.Clinic
Dacca.

Dear Dr. Nabi,

The toxilogical tests on Hirtacin have been done by us on albino male rats weighing about 200 gms. Test were carried out on 25 animals. Another sets of 10 rats served as control. They were all given laboratory stock diet. The experimental group had equivalent of hirtacin 200 mg per animal daily, mixed with the diet i.e. 2 gm/kg for 3 months with no adverse effect comparing well with the control group. They did not suffer from any loss of weight. They were sacrificed at the end of 3 months for gross examination(antopsy). Nothing abnormal was observed. In addition following Biochemical determinations were also made :

(a) Hemoglobin	(13.92 ± 0.36)
(b) Liver xarthine oxidase	(247.17 ± 8.61)
(c) Serum choline esterase	(67.5 ± 5.21)
(d) S.G.O.T.	(29.83 ± 3.54)
(e) S.G.P.T.	(22.33 ± 2.25)

The proposed human dose will not exceed 500 mg for 35-40 Kg body weight.

Yours sincerely,

Sd/-Illegible.
(K. Ahmad)
Director.

Govt. of the People's Republic of Bangladesh,
National T.B.Control Project,
Sher-E-Bangla Nagar, Shyamoli, Dacca.

Dr. Gulam Nabi,
Officer-in-Charge.

Misc.No.1-C1/80(Drug Trial)-TBCP- 525 Dt. 15.10.1980

To

The Director,
Medical Research Council,
Govt. of Bangladesh,
Public Health Laboratory Building,
Mohakhali,
Dacca.

Subject:- Permission for doing a trial on herbal drugs against Tuberculosis on humanbeings.

Dear Sir,

I am to inform you that the recent Anti-TB. drugs though give almost 100% cure but they have also some disadvantages. Everywhere in the world Scientists are working hard for a new anti-TB. drug which is safe and potent.

Institute of Nutrition and Food Science, University of Dacca claim to have invented a drug which is effective against Tuberculosis. For this, they wrote a letter to Director General of Health Services for doing trial of this drug on human being. Accordingly the D.G., Health Services formed a Committee with a Chairmanship of Dr. A.F. Hussain, Director, I.E.D.C.R., Dacca and Member Secretary to myself.

The Committee make a proposal for this trial and protocol is attached herewith.

I, therefore, hope that you would be kind enough to give permission for doing this trial on human being as it is a new drug.

Yours faithfully,

(Dr. Gulam Nabi)
Member-Secretary of the
Trial Committee &
Officer-in-Charge,
National T.B.Control Project,
Shyamoli, Dacca.

Attachment 1. Date

ETHICAL REVIEW COMMITTEE, ICDDR,B.

Principal Investigator Trainee Investigator (if any)

Application No. 80-044 Supporting Agency (if Non-ICDDR,B)

Title of Study 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.

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

Principal Investigator

Trainee

Abstract Summary

80-044
Rec'd 1/12/80

The herbal preparation under investigation is made up of a local plant extract. It has been found in invitro experiments as well as in animal studies that it has very potent antibiotic action against a number of pathogenic micro-organisms, and it promised to be useful in many infections specially pulmonary tuberculosis. It has been found to be completely non-toxic even to the extent 2 gm./kg of body weight (oral administration). The dose to be used in the treatment of tuberculosis will not exceed 500 mg. for a human patient weighing 35-40 kg.

In this trial for the evaluation of the drug young adults having pulmonary tuberculosis as indicated by examination of sputum (A.F.B. positive) and X-Ray radiography will only be used. They would have taken no previous medication. There would be no difficulty in seeking their consent to be a subject of the study. There is absolutely no physical, psychological, social, risk. In case of any unexpected side effect of the drug the investigator would be free to withdraw the medicine and use appropriate measures. The patients will be given identification numbers and there is no fear of divulging confidentiality or anonimity. There is no need for withholding information from the subject on the course of the treatment and results being obtained. This study does not involve an interview except what is needed to take the medical history. This study would need some body fluids namely sputum, urine and blood for routine examination. The study will last three months when they will be indoor patients in the Institute of Chest Disease. After that there will be follow-up by home visits.

The potential benefit to the individual and to the society is enormous-as the drug will be cheap and made of only locally available indegenous ingredients. All other known drugs of tuberculosis are expensive and have deleterious side offects.

TRIAL OF A DRUG (HIVACIN) OF HERBAL ORIGIN ON CASES OF PULMONARY TUBERCULOSIS.

Description of the drug :

It is a preparation from a local herb, The plant has been used as a food (vegetable) in Bangladesh and also used in folklore medicine in the treatment of various infections such as diarrhoea, dysentery etc. It is known to produce no adverse effect on health or any other untowered symptoms. However, the potential of the herb as a drug has missed recognition.

There is no prejudice or opinion against the plant from the point of view of religion or culture. In the laboratory of this Institute (INFS,DU) the plant has been investigated for its potential therapeutic property . It has been found to be effective against the growth of various pathogenic microorganism Streptococci, E.coli, Salmonella, Pseudomonas etc. but most importantly against Mycobacterium tuberculosis. Every experiment on the toxicity of the drug have been done. It has been found that daily 1 gm/kg of body weight is of no harm whatsoever.

It is now proposed that study be undertaken to determine the efficacy of the drug in the treatment of pulmonary tuberculosis in human subjects.

Protocol :

Background :

The present anti-tubercular drugs, though gives almost hundred percent cure have the following disadvantages : -

i) They cannot be used singly, but needs to be administered in combination.

ii) The combination of drugs needs to be taken continuously for not less than one year.

iii) All are not equally potent and some are costly, some are toxic.

So costs of drugs, long duration of treatment and occasional toxic effects have all contributed in the rise of large number of unwanted failure cases and this has been major deterrant in the control of tuberculosis in many countries.

In view of the above facts, search for a new, safe and potent anti-tubercular drug has been continuing all over the world. The dapratment of Biochemistry of the University of Dacca claims to have invented a drug which is effective against pulmonary tuberculosis.

Objectives :

This trial aims at evaluating the efficacy of the new drug, its toxic effect, if any on the patients suffering from pulmonary tuberculosis .

Base line of the area from where the patient will be selected.

1. Dacca city area and around the Dacca city where after 3 months the patients can be easily followed up upto 12 months.

2. Patients can be selected from any socio-economic condition if patients agree to put on trial drug.

3. Health situation as regards tuberculosis : -

As we know that prevlenece of pulmonary tuberculosis is equally distributed in cities, urban towns and villages. Prevalence rate of Smear positive is 4% and sputum positive is 5%.

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4. Facilities available in the area :

Only two specialised Institutes for diagnosis and treatment of tuberculosis are present in Dacca , one is National T.B.Control Project and other is T.B.Control and Training Institute. There is also 500 bedded Tuberculosis & chest disease hospital in Mohakhaly, Dacca.

Methods and Materials :

Section of patients for trial :

(i) Number : The total number will be 100 (one hundred). They will be divided into two groups . Group A & B. Each group will get 50. Every alternate patient will be put on alternate group.

Group A will be trial group treated by new drug only. and Group B will be treated by known anti-TB. drugs.- Inj.Streptomycin 1 Gm. daily + INH 300 mg. + TB1 150 mg for 3 months then Stop streptomycin Inj. and continue INH 300 mg + TB1 150 mg. daily for 9 months more.

(ii) The patients will be selected at National T.B.Control Project Shyamoli, which maintain an well attended out patient department. The criteria of section shall be as follows :-

a) Age - 15 years to 45 years.

b) Sex - Both sexes (Pregnant Woman and women with amenorrhoea will not be eligible for inclusion in the trial)

c) Sputum should be positive for A.F.B. from Army Pathological Laboratory by direct microscope.

d) X-Ray of chest P.A. view should reveal shadow suggestive of Pulmonary tuberculosis.

e) Patients should have no history of taking any anti-T.B. drugs in the past.

f) Patient should not have any association with illness.

After the patient has satisfied all the criteria ~~of section~~ he/she will be recommended admission in the Institute of Diseases of the Chest and Hospital, Mohakhali, Dacca where he/she will be admitted in a trial bed. The patient will stay in the hospital for 3 months. After their discharge, they will attend in National T.B.Control Project, Shyamoli every month for check up.

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After admission , before put on trial the patient will undergo the following pre-triall examination : -

a) Blood for T.C. & D.C., Hb. / ESR

b) Liver function tests namely : S.G.O.T., S.G.P.T., Alkaline Phosphatase and Serum Bilirubin.

c) Urine for Routine examination .

(d) Sputum for AFB by direct Microscopy.

According to the result of sputum examination - patient will be graded as Mild - +

Moderate - ++

Severe - +++

After the pretrial examinations are done and the administration of the drug will be started according to group :

While on the drug in hospital the patient will be assured periodically every fortnight. The periodical assessment will include the following : -

1) Clinical examination
2) Bacteriological Examination by direct Microscopy for A.F.B. and culture from the Army Pathological Laboratory.
3) Radiological :- X-Ray of the chest P.A. view for I.D.C.M.
4) Blood for TC., DC., Hb from Army Pathological Laboratory.
5) Evidence of advarse effect of the drug, if any.
6) Liver function tests will be added in every second fortnightly assessment. Patients found to have deteriorated in any periodic assessment will be taken out of the trial.

Those trial patients, who at the end of the three months of hospital stay, have shown definite improvement without any adverse effect, will be followed up for another nine months as out patients.

They will attend National T.B.Control Project every month.

During the nine months period the follow up the records of the patients will be assessed periodically every month for Ist. three months, every two months for remaining six months. Such assessment will be based on (a) Sputum Examination from Army Pathological Laboratory (b) Chest X-Ray from National T.B.Control Project Ist. three months and remaining 6 months every 2 months.

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Financial implication of the trial :

(1)	Senior Investigator - 5 - @Tk.1000/- P.M.	Tk.	15000/-
(2)	Junior Investigator - 5 - @Tk. 500/- P.M.	Tk.	7500/-
(3)	Sputum Examination (3x20x7x50)	Tk.	21000/-
(4)	X-Ray Examination of chest (1x20x7x50)	Tk.	7000/-
(5)	Liver function tests(100x2x50)	Tk.	10000/-
(6)	Other contingent expenses	Tk.	10000/-
	Total	Tk.	70,500/-

N.B: All money will be given by INFS of Dacca University. No expenditure will be incurred from Bangladesh Medical Research Council.

CONSENT FORM

Name of Patient -

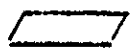
Age -

Sex -

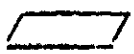
Address :-

The voluntary consent of the patient.

Agree to put on trial



Disagree



Signature/Thum Impression of the pati·

PATIENTS' CONSENT FORM

The Institute of Nutrition, Dacca University is conducting a study to see the effect of the indigenous herbal preparation (Oral) on patients suffering from tuberculosis. This has been found to be effective and well tolerated. This herbal medicine will be given to you orally as a part of your treatment against tuberculosis. Dr. Khurshid Jahan and other Physicians will examine you very closely. 1 ml of blood will be required to look for blood picture. You have the right to withdraw from the treatment programme at any stage if you like. If you agree to participate and cooperate with the study please sign your name or give left thumb impression below:

Name .....
or
LTI

Address .....

.....

.....

Hospital .....
No.

Hospital .....

Date .....

রোগীর সম্মতি পত্র

যক্ষ্মা রোগের উপর দেশীয় লতাগুল্ম ও ছোট গাছ-গাছড়া হইতে প্রস্তুত ঔষধের ফলাফল দেখার জন্য ঢাকা বিশ্ববিদ্যালয় পুষ্টি প্রতিষ্ঠান একটি গবেষণা কাজ হাতে নিয়াছে। এই ঔষধ যক্ষ্মার জন্য ফলপ্রদ ও সহনীয়। আপনার যক্ষ্মা রোগের জন্য গাছ-গাছড়া হইতে প্রস্তুত এই ঔষধ আপনাকে খাওয়ানো হইবে। ডঃ খুরশীদ জাহান এবং অন্য আর একজন ডাক্তার আপনাকে ভালভাবে পরীক্ষা করিবেন। পরীক্ষার জন্য আপনার শরীর হইতে ১ সি. সি. রক্তের দরকার হইবে। আপনি ইচ্ছা করিলে যে কোন সময়ে এই চিকিৎসা হইতে নিজেকে বাদ দিতে পারিবেন।

যদি আপনি এই চিকিৎসা করাইতে চান এবং আমাদের সাথে সহযোগীতা করিতে চান তবে নীচে আপনার নাম সই করুন অথবা টিপ সই দিন।

নাম----------

অথবা টিপ সইঃ

ঠিকানা----------

হাসপাতাল নম্বর---------

হাসপাতাল----------

তারিখ----------