

3. Clinical studies

3.1 Evaluation of comparative efficacy of Cefuroxime axetil and Tetracycline in the treatment of cholera in adults.

Investigator: M.K. Bhattacharya

Acute watery diarrhoea caused by *Vibrio cholerae* is an important cause of hospitalization at the I.D. Hospital, Calcutta. The number of children dying each year from diarrhoea has decreased over the past decade from 5 million mainly because of the success of oral rehydration solution (ORS) therapy. Several drugs, namely tetracycline, furazolidone and trimethoprim-sulfamethoxazole (TMP-SMX), have been found to be effective in reducing stool volume, duration of diarrhoea and faecal excretion of vibrio in patients with cholera. Recently, we observed from our hospital based surveillance system for diarrhoeal diseases that *Vibrio cholerae* strains (01 and 0139) are uniformly resistant to furazolidone, nalidixic acid and partially resistant to ciprofloxacin and norfloxacin due to indiscriminate use. Moreover, the isolated strains of *Vibrio Cholerae* non01 non0139 strains are resistant to TMP-SMX (53%) and tetracycline (56%) which constitutes 30% of the total isolation of vibrio cholerae strains.

Cefuroxime is a second generation cephalosporin. It is highly active against gram-negative and gram-positive bacteria in (*in vitro*). Isolated strains of *Vibrio cholerae* are uniformly susceptible to cefuroxime. A study was undertaken to evaluate the safety and efficacy of cefuroxime in the treatment of cholera in adults with moderate to severe dehydration. A total of 128 cases of acute watery diarrhoea were studied. Out of 128 cases 68 cases received cefuroxime and 60 cases received tetracycline. Of these 128 cases, 46 cases were positive for *V Cholerae*. Out of 46 cases, 27 cases received Cefuroxime and 19 cases received Tetracycline. Both the drugs were equally effective in the treatment of cholera in adults in respect to duration of diarrhea, volume of stool and consumption of ORS. Hence, Cefuroxime can be kept as an alternative to Tetracycline for treating Cholera in adults caused by multi-drug resistant strains of *V Cholerae*.

3.2 Impact of Lactobacillus (Lactic acid bacteria) in children with acute watery diarrhoea

Investigator: P. Dutta

This is a hospital based, randomized, double blind clinical trial to evaluate the role of Lactobacillus (Lactic acid bacteria) therapy on the outcome variables (stool output, duration of diarrhoea, consumption of fluid therapy) of acute watery diarrhoea in children.

The study is in progress at the Dr. B.C. Roy Memorial Hospital for Children, Kolkata in double blind fashion. One hundred forty male children of all nutritional groups (except severe malnutrition) aged between 6-24 months suffering from acute watery diarrhoea (Passage of more than 3 liquid stools within last 24 hours period) of < 3 days duration with some dehydration were included in this study.

Children who were exclusively breastfed, aged less than 6 months and more than 24 month, associated with other systemic infection or any complication or chronic underlying disease or severe malnutrition for which they need extensive care were excluded from this

study. Children who received antibiotic before admission and whose parents refused to give consent were also excluded from the study.

Informed written consent was obtained from the parents of the children after explaining the details of the study procedure before inclusion in the study.

After selection, complete history was taken from parents and thorough physical examination was done and findings were recorded in a pre-designed proforma. Stool samples were collected in sterile MacCartney's bottle on admission for detection of various established enteropathogens. Children were weighed unclothed on admission using weighing scale with a sensitivity of 1 gm, length and mid arm circumference of the children were also recorded.

After selection of the patient, two dispersible Lactobacillus tablets (each Lactobacillus tablet contains 60 million spores of Lactobacillus (Lactobacillus sporigen). or placebo tablets were administered two times a day according to a random number in a double blind design for a period of 5 days even after cessation of diarrhoea. Lactobacillus and placebo tablets were identical in colour, shape, size and test and were prepared in blister strips and these strips were numbered for specific patient.

After enrollment in the study, the degree of dehydration was assessed by the WHO criteria. All the patients received standard (WHO recommended) oral rehydration therapy at the rate of 75-100 ml/kg body weight for 4 hours for correction of initial dehydration. Oral rehydration solution at the rate of 50-100 ml per loose stool was also given to maintain the hydration status till cessation of diarrhoea. The patient, who developed severe dehydration during the study period, received I.V. fluid (Ringer's lactate solution) as per WHO guideline (treated as recipient of unscheduled IV fluid). The patient who developed complication was withdrawal from the study and treated according to the hospital treatment protocol.

All the children received the normal hospital diet including breast-feeding. Patients were weighed after rehydration and then every morning between 10.00 - 10.30 AM and also followed up till recovery or up to 5 days even if they did not fulfill the criteria of recovery within that period. Daily records were noted on the pre-designed proforma. Intake and output charts were maintained every 8 hourly till recovery or up to 5 days. Urine was separated from stool and volume was measured. Amount of fluid intake (ORS, plain water, I.V. fluid and other liquid food) was also measured. Stool was measured after collection in pre-weighed diaper and the measurement weight was sensitive up to 1 gm. Patients were discharged from the hospital when they fulfilled the recovery criteria (recovery was defined as passage of soft stool or normal stool or no stool for last 18 hours) even before 5 days. Prescribed tablets were supplied to the parents to continue upto 5 days if discharged before 5 days. If the patients condition deteriorated in spite of 3 days therapy, then they were considered as treatment failure and were treated according to the standard treatment of the hospital. Patients who developed complication during the study period and deviate from the study were also termed as treatment failure. Parents received nutritional advice for their children (at least one extra meal or liquid food/day) during the recovery period. Parents were also advised to attend hospital if the patient develops any complication within 15 days of discharge.

Though 140 patients were included in this study, data could not be analysed as the study is in progress in double blind design.