

THE JOHNS HOPKINS MEDICAL JOURNAL

VOLUME 132

ORAL FLUID THERAPY OF CHOLERA AMONG BANGLADESH REFUGEES¹

D. Mahalanabis, A. B. Choudhuri, N. G. Bagchi,
A. K. Bhattacharya and T. W. Simpson

*The Johns Hopkins University
Center for Medical Research and Training
Calcutta, India*

Received for publication January 12, 1973

INTRODUCTION

A crucial field trial of oral electrolyte solutions in the treatment of cholera was carried out in India during the summer of 1971 when the disease appeared in a population of war refugees. Observations made during the epidemic substantiated the usefulness of oral therapy in circumstances of this kind. Realistic estimates of what one might expect from this mode of therapy led to a formulation of practical guidelines to its use and limitations.

The development of a simple and effective method for oral replacement of fluid and electrolytes in cholera makes an interesting story. In the normal human bowel, glucose is rapidly and actively absorbed, mainly from the duodenum and jejunum (1). It had been demonstrated, both in laboratory animals and man, that glucose absorption from all or part of the small bowel is accompanied by increased absorption of sodium and water (2-4). Furthermore, glucose absorption remains intact in cholera patients and, in spite of the effects of the enterotoxin, still enhances the absorption of water and electrolytes (5-7). Controlled clinical studies of hospitalized patients had demonstrated the effectiveness of oral glucose-electrolyte solutions as adequate maintenance therapy in cholera and other severely dehydrating diarrheal diseases (5-9). Furthermore, field trials had subsequently confirmed the efficacy of primary oral therapy when adequate supplies were available and trained personnel were on hand (10).

Could this method be used in a critical situation in which there were inadequate treatment facilities, an extreme shortage of parenteral fluids and only a few persons trained in cholera therapy? These were exactly the limitations that faced responsible agencies of the Government of India, the West Bengal government and voluntary relief organizations when cholera erupted in the Bangladesh refugee population during the summer of 1971. The needs were clear and full-scale use of oral fluid therapy appeared to be the only practical option. The Johns Hopkins Center for Medical Research and Training in Calcutta (JH-CMRT) offered its help during this critical period and our professional and paramedical personnel went to work immediately in cooperation with governmental and voluntary agencies.

¹ This work was supported by National Institutes of Health Grant No. 2R07A110048-11 ICC (Washington) and by a special grant from the Christian Agency for Social Action, World Council of Churches (Geneva).

Reprint requests to Dr. Simpson, Department of Pathobiology, The Johns Hopkins University School of Hygiene and Public Health, 615 North Wolfe Street, Baltimore, Md., 21205

THE PROBLEM AND THE EARLY APPROACH

By the end of May 1971 over six million people from East Pakistan, now Bangladesh, had fled the civil war and sought refuge in India. The outbreak of cholera in the monsoon months of June and July created enormous problems. The disease attacked people already devitalized by exhaustion, starvation and exposure. A heavy death toll occurred in the refugee camps, where there was an estimated case fatality ratio of 30% from cholera and cholera-like diarrheal diseases (Figs 1 and 2).

Available resources for the treatment of cholera were mobilized but basic handicaps still existed. The huge amounts of intravenous fluids that would be required, plus the problems of transport and lack of trained personnel for their administration, represented an almost insurmountable logistical problem in treating cholera effectively under such circumstances by the standard methods currently in use. We suggested the use of oral fluids as the only recourse in this situation. On the basis of previous experience cited above we were reasonably sure that orally administered electrolyte solutions with glucose would be satisfactory for maintenance of fluid and electrolytes *after* shock and severe acidosis had been corrected by intravenous fluids. Partial initial replacement of fluid loss might be provided orally. An important clue lay in the fact that, when given early in the disease *before* the onset of hypovolemic shock, oral fluid replacement therapy alone apparently could prevent fatal dehydration (11).

We organized two teams for cholera therapy including oral rehydration. Both teams worked along the border between India and East Pakistan where the need was greatest. Apart from the simple humanitarian service, we sought to evaluate the feasibility of oral therapy with locally available materials, to be administered under extremely difficult conditions. Practical recommendations for cholera therapy in similar situations have been worked out subsequently with the help of able consultants in Calcutta and elsewhere (12). We report here the observational basis of these recommendations as it grew from our experience among the Bangladesh refugees.

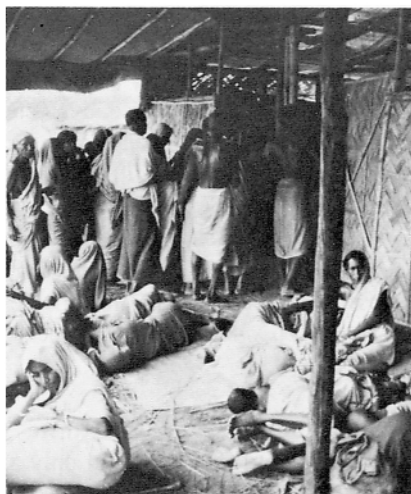


Fig 1. Refugees from East Pakistan, now Bangladesh, seeking food and medical attention at a temporary camp in India, near Bongaon, West Bengal.



Fig 2. Young cholera victim from the refugee camp, brought by family to emergency treatment center early in his illness, when oral therapy is most likely to be effective.

LOCATION, LOGISTICS AND SUPPLIES

Both of our treatment teams converged during the peak of the epidemic at a place called Bongaon, quite near the border where refugees were still crossing in great numbers. The treatment center was located at the subdivisional hospital in Bongaon. Two cottages with 16 beds, originally built to accommodate patients with infectious diseases, were used as cholera wards. When we arrived on June 24, 1971, an estimated 350,000 refugees were living in the vicinity of the town, with an additional daily influx of about 6000 more. The meager resources of the town were strained to the limit.

We arranged a continuous shuttle of vehicles on the 50-mile run from Calcutta to Bongaon, carrying personnel, medication, food and supplies to the center. Our own reserves of intravenous saline-lactate solution stocked originally for cholera research soon were depleted. Parenteral fluids of various sorts were then supplied by other agencies. These included limited quantities of isotonic saline solution, isotonic saline solution with 5% glucose, Ringer's solution with lactate and Krebs-Ringer's solution (without lactate). Such multiplicity of fluid formulas could not be avoided under the circumstances, but was hardly ideal. Daily supplies of parenteral fluids were unpredictable and never adequate in amount.

The oral solution that we elected to use consisted of 22 gm glucose (as commercial monohydrate), 3.5 gm sodium chloride (as table salt) and 2.5 gm sodium bicarbonate (as baking soda) per liter of water. When dissolved, the mixture gives an approximate electrolyte composition of sodium 90 mEq, chloride 60 mEq and bicarbonate 30 mEq per liter, and 121 mM glucose. This is the simplest formula, containing the minimum number of ingredients, previously found to be effective in severely ill patients with cholera (8). Potassium citrate or other potassium salt could have been added to advantage but was not readily available locally in sufficient quantity.

Glucose-salt packets were prepared in Calcutta; of necessity at first in the JH-CMRT library room. Each of the three components of the mixture was carefully weighed by separate technicians and poured into a small polyethylene bag in assembly-line fashion. Another technician inserted a descriptive label with instructions for dissolving in water; then he sealed one end of the bag with a hot iron. Two sizes of glucose-salt packets were made: one for a final volume of four liters and the other for sixteen liters of fluid. In the field, the dry powder was added to clean drinking water and dispensed from drums directly into the patients' cups.

The cost was calculated to be 11 Indian "paise," or about 1½ cents in United States currency, per liter of fluid. All materials and equipment for packaging and dispensing were obtained locally. Packets for preparation of about 50,000 liters of oral solution were supplied by our "salt factory" for use by us and other voluntary agencies working among Bangladesh refugees.

PLAN OF THERAPY

To make the most effective use of our limited resources for the benefit of the largest possible number of patients, we employed a very simplified treatment regimen. In severe cases, intravenous solutions were given initially to attain at least partial correction of the fluid deficit and to combat shock and acidosis. Severely ill adults may require less than three liters intravenously during the initial six to eight hours if oral supplementation can be provided (7, 9-11). Daily supplies of parenteral fluids were usually sufficient to meet these minimal needs, but sometimes we had none at all for periods of 24 hours or longer. Oral glucose-electrolyte solution then was given for further correction of dehydration and acidosis, and to replenish continued loss of water and electrolytes in the stools. Patients with mild to moderate dehydration, *without* signs of hypovolemic shock, were given oral glucose-electrolyte solution alone from the beginning. The solution was started as soon as patients would take it, usually between

one and four hours after admission; it was continued until cessation of watery diarrhea. Because salt packets were widely distributed and solutions freely shared, tabulation of amounts consumed by individual patients was not possible. Very rough estimates suggest a range of 10 to 20 liters each for adults from admission until cessation of diarrhea, consistent with previous, better-controlled observations (7, 9, 10).

Potassium in the form of dihydrogen phosphate salt was administered orally to children on an individual basis. Green coconut water, with a potassium content of approximately 70 mEq/L, was given when available. Adults and large children were given oral tetracycline (when available) in a dosage of 250 mg every six hours for 48 hours; small children received half this amount on the same schedule. A normal diet was resumed as soon as possible even though the diarrhea had not completely stopped.

OUTCOME OF THE FIELD EXPERIENCE

The height of the cholera epidemic occurred near the end of June 1971. Daily admissions of cholera patients at the Bongaon center reached a peak of about 200 and more than 3000 patients were treated in the first three weeks. The cottage facilities soon were overloaded and patients had to be placed on the floor. Finally a point was reached when literally no more floor space was available. One hundred canvas cots were sent from Calcutta and set up in a large tent beside the cottages, but the bed situation remained critical. Two adults, or as many as four children, were often huddled on the same cot. The pressure of new admissions forced us on many occasions to discharge patients after 24 hours, with only oral fluids and a small quantity of tetracycline for use on return to the camp – fortunately only a few of them needed readmission for continued diarrhea. The admission rate dropped below 60 per day after mid-July and tapered off to a trickle by the end of August.

Over 3700 patients with a clinical diagnosis of cholera were treated under our supervision during eight weeks between June 24 and August 30, 1971 (Table I). The case fatality ratio was 3.6%. Treatment in the separate tent was exclusively under control of the JH-CMRT staff and served eventually as our demonstration ward. About 1200 patients were treated here with only 12 deaths, representing a case fatality ratio of only 1% among these particular patients.

Paramedical workers and relatives of patients were instructed to give oral solution freely to all patients as soon as they were able to take fluid by mouth. Patients took the oral solution avidly when they were dehydrated; when hydration

TABLE I
Summary of Mortality from Cholera
and Cholera-Like Diarrheas at
Bongaon Treatment Center,
June 24 through August 30, 1971

Patient population	Admissions	Number of deaths*	Case fatality ratio
Entire center	3703	135	3.6%
JH-CMRT demonstration unit only	1190	12	1.0%

*Approximately half of the patients died before any rehydration therapy could be started.

was achieved they preferred to have plain water instead of salt solution. Although vomiting was common, most patients retained enough oral salt solution to maintain hydration. Paramedical workers (and even physicians) had to be convinced that a massive volume of fluid needed to be given, particularly in the initial stages. Failure of oral hydration could usually be traced to the fact that, in the absence of supervision, not enough fluid had been given by attendants.

Patients and their families usually accepted the oral solution as a form of treatment. However, some of them thought that intravenous fluid was a more impressive form of therapy and tried to cajole us into using some of our scarce supply, even though the patients were doing well on the oral solution alone. In areas such as Bengal where people are familiar with cholera, "saline" is widely known to be the cure. We called the oral solution "drinking saline," thus enhancing its acceptance as medication of real worth. Vomiting, however, was a major psychological barrier to the acceptance of oral therapy by the patients, their relatives and paramedical workers; constant persuasion was needed to maintain adequate oral intake in the face of this distressing symptom.

Workers not previously familiar with cholera therapy usually were able to start intravenous drips after only two days of training, although they were not experienced enough at that point to judge the requirements for parenteral fluid restitution and maintenance. The use of oral fluid therapy partly circumvented this difficulty since parenteral fluids were not used in the mild and moderately severe cases without shock.

SAMPLE SURVEYS DURING THE EPIDEMIC

A survey was made of a sample population of the patients to determine the age distribution (Table II). Children below six years of age constituted 38% of the patient population, in contrast to only 14% in the general refugee population. Our patient population thus was heavily weighted with infants and young children, who pose much greater therapeutic problems than adults.

Rectal swabs were taken from 108 patients for culture at the Cholera Research Centre of the Indian Council of Medical Research, Calcutta. About 79% of swabs yielded *Vibrio cholerae* with 92% of isolates being classical biotype (during recent years in the Calcutta area, biotype El Tor has been predominant).

TABLE II
Estimated Age Distribution in
Study Patients in Comparison with
General Refugee Population Samples

Age group	General population* Bangladesh refugees		Patient population Bongaon treatment center	
	No.	Percentage	No.	Percentage
0-5	62	14%	620	38%
6-15	164	36%	457	28%
>15	226	50%	555	34%
Total	452	100%	1632	100%

*J. Rohde and P. Gardner, International Rescue Committee, personal communication.

DISCUSSION

A simple method of treatment may save lives in the cholera-affected areas of the world. Therapy of cholera by simplified oral glucose-electrolyte solutions thus assumes importance. While our studies of necessity were observational rather than quantitative, several strong impressions emerged. The following specific points can be made:

Our experience during the cholera epidemic among Bangladesh refugees confirmed the feasibility of prepackaging the glucose-salt mixture and taking it to the field in dry form. This procedure eliminates error in measuring the ingredients on the spot and greatly reduces the cost of transport. Large soluble tablets which could be dissolved in one liter of water have been suggested as a convenient way of distributing and stockpiling the materials for oral therapy in areas where they are likely to be needed, but manufacturing and packaging costs would undoubtedly be relatively high. Furthermore, it has been found that an average teaspoon when carefully levelled gives reproducible results (8); this we verified by preparing successive liter lots of solution and analyzing for electrolytes and glucose². Accurate measurement by volume would expedite packaging the glucose-salt mixture by eliminating the tedious weighing procedure.

The prepackaged glucose-salt mixture with enclosed instructions in unmistakably simple terms makes therapy much easier for people with no previous training or experience. Intelligent people in camps and villages can be taught to recognize cholera-like diarrhea and start oral replacement early. This was attempted by newspaper accounts and radio announcements during the Bangladesh crisis and apparently reached many people in the area.

To be most effective, oral fluid therapy must be given *early* in the course of the illness. As with intravenous fluids, one must convince physicians and paramedical workers of the *massive* fluid requirements during the initial phase of rehydration. When circumstances preclude weighing patients or measuring stool output in the usual ideal manner, attendants need to be urged simply to give *as much fluid as the patient can take by mouth*. Overhydration from oral fluids was not observed at Bongaon, where this was the procedure.

Vomiting during the initial phase of rehydration is perhaps the greatest barrier to effective oral therapy. Vomiting is probably associated with hypovolemia or with continuing acidosis; it must be met by *rapid* administration of appropriate fluids by *any available route*, including oral administration or nasogastric gavage. This point cannot be overemphasized and is an important key to successful therapy.

Results of treatment in the Bongaon center, with a case fatality ratio of less than 4%, compare favorably with results of standard therapy in well-organized modern treatment centers. We believe that many more persons were provided effective treatment and more lives saved than if we had depended entirely on the use of available parenteral fluids administered only by trained personnel.

²Four liters of the JH-CMRT oral solution required the following amounts of dry ingredients, measured by volume: sodium chloride, as table salt, 4 level teaspoonfuls; sodium bicarbonate, as baking soda, 3 level teaspoonfuls; commercial glucose (as used in soft drinks), 20 level teaspoonfuls.

SUMMARY

Confirmation of the effectiveness of orally administered electrolyte solutions with glucose in the treatment of cholera without hypovolemic shock was obtained by a crucial field trial during the cholera outbreak that erupted in the summer of 1971 among Bangladesh refugees at Bongaon, West Bengal, India. Extremely adverse logistic and administrative conditions prevailed. A total of 3703 patients, including severe cases treated initially by limited supplies of parenteral fluids and mild to moderately severe cases treated by oral therapy alone, were admitted to the Bongaon treatment center; the overall case fatality ratio was 3.6%. A special demonstration unit provided treatment for 1190 of these patients with case fatality ratio of 1%.

The oral solution provided sodium 90 mEq, bicarbonate 30 mEq and chloride 60 mEq per liter, along with glucose 22 gm per liter (121 mM), prepackaged for mixing with water in the field. Potassium supplementation was given orally on an individual basis. Advantages of the oral solution included local availability of ingredients, minimal cost of preparation and transport, ease of administration, safety in the hands of inexperienced personnel after only brief instructions, early accessibility of treatment and reasonable effectiveness especially when used very early in the course of the disease prior to extreme dehydration, shock and acidosis. In severe cases, considerable sparing of intravenous fluids resulted from the adjunct use of the oral solution.

ACKNOWLEDGMENTS

We wish to thank Dr. H. L. Saha, former Director of Health Services of West Bengal, Dr. A. Mondal, Director of the WHO-ICMR Cholera Research Centre, and Dr. K. N. Neogy, Professor of Microbiology of the Calcutta School of Tropical Medicine, for their counsel and encouragement.

Dr. S. P. Dey, WHO-ICMR Cholera Research Centre, did the bacterial cultures on specimens submitted from the Bongaon treatment center.

REFERENCES

1. Wiseman, G.: Absorption from the Intestine. Academic Press, London, 1964.
2. Curran, P. F.: Na, Cl, and water transport by rat ileum in vitro. *J. Gen. Physiol.*, 43:1137, 1960.
3. Fordtran, J. S. and Dietschy, J. M.: Water and electrolyte movement in the intestine. *Gastroenterology*, 50:263, 1966.
4. Malawar, S. J., Ewton, N., Fordtran, J. S. and Ingelfinger, F. J.: Interrelation between jejunal absorption of sodium, glucose and water in man. *J. Clin. Invest.*, 44:1072, 1965.
5. Pierce, N. F., Banwell, J. G., Mitra, R. C., Caranasos, G. J., Keimowitz, R. I., Mondal, A. and Manji, P. M.: Effect of intragastric glucose electrolyte infusion upon water and electrolyte balance in Asiatic cholera. *Gastroenterology*, 55:333, 1968.
6. Hirschhorn, N., Kinzie, J. L., Sachar, D. B., Northrup, R. S., Taylor, J. O., Ahamad, S. Z. and Phillips, R. A.: Decrease in net stool output in cholera during intestinal perfusion with glucose containing solutions. *New Eng. J. Med.*, 279:176, 1968.
7. Nalin, D. R., Cash, R. A., Islam, R., Molla, M. and Phillips, R. A.: Oral maintenance therapy for cholera in adults. *Lancet*, 2:370, 1968.
8. Sack, R. B., Cassels, J., Mitra, R., Merrit, C., Butler, T., Thomas, J., Jacobs, B., Choudhuri, A. and Mondal, A.: The use of oral replacement solutions in treatment of cholera and other severe diarrhoeal disorders. *Bull. WHO.*, 43:351, 1970.
9. Pierce, N. F., Sack, R. B., Mitra, R. C., Banwell, J. G., Brigham, K. L., Fedson, D. S. and Mondal, A.: Replacement of water electrolyte losses in cholera by an oral glucose electrolyte solution. *Ann. Intern. Med.*, 70:1173, 1969.
10. Cash, R. A., Nalin, D. R., Rechat, R., Reller, B., Haque, E. and Rahaman, A.: Results of a clinical trial of oral therapy in a rural cholera treatment center. *Amer. J. Trop. Med.*, 19:653, 1970.
11. Nalin, D. R., Cash, R. A. and Rahaman, M.: Oral (or nasogastric) maintenance therapy for cholera patients in all age groups. *Bull. WHO.*, 43:361, 1970.
12. Rohde, J. E., Mahalanabis, D. and Gardner, P.: Guideline to the Management of Common Medical Problems among Bangladesh Refugees. The Little Flower Press, Calcutta, 1971.