COMPARATIVE TRIAL OF DACCA SOLUTION AND A W. H. O. SUGGESTED SOLUTION IN CHOLERA AND NON-CHOLERA DIARRHOEA

M. Mujibur Rahaman and M. A. Majid

Physiological replacement of lost fluid and electrolytes is the principal rationale behind the formulation and use of various intravenous electrolyte containing solutions in the treatment of cholera and other acute diarrhoeal deseases. Ringer's lactate, 2:1 Saline: Lactate regimen and Dacca intravenous solution are some examples of such fluids extensively used in the rehydration of cholera as well as non-cholera diarrhoea with dramatic results. Dacca intravenous solution, used in many thousands of cholera and non-cholera diarrhoeal patients at the hospitals of the Cholera Research Laboratory and in many parts of Bangladesh has a composition of Na^+ = 133, K^+ = 13, HCO_3^- = 48, and Cl^- = 98 mEq/l. It now contains acetate as the base precursor instead of bicarbonate, thereby simplifying the manufacturing process. Prior to infusion in small children however, glucose has to be added to prevent the development of hypoglycemia in small number of young children.

As the concentration of sodium in stool is considerably lower in small children with cholera compared to adults and as its concentration is also low in non-cholera diarrhoea compared to cholera, a new formulation for intravenous fluid has been proposed where the concentration of sodium was reduced to 118 mEq/l and chloride to 88 mEq/l. Glucose was added to make it 1% or 44 mM/l. This solution called the Diarrhoea Treatment Solution (DTS). According to some authorities is most suitable intravenous solution for use in all kinds of acute diarrhoea and cholera. On advice of the World Health Organization (WHO), Geneva, a clinical trial was carried out to compare the effectiveness of Dacca Solution (DS) and the D T S in the treatment of cholera.

MATERIALS AND METHODS

Selection of patients:

Small children, adolescent and young adults who arrived at the hospital of the Cholera Research Laboratory with a history of recent onset of diarrhoea and moderate to severe dehydration requiring admission for intravenous therapy were included in the study. No patient with complications like fever, convulsions, pneumonia or severe malnutrition was included in the study. They were kept in a separate ward during the study. Each patient was weighed, vital signs were recorded and 4 ml of femoral arterial or venous blood were drawn for the following analysis: pH, haematocrit, glucose serum specific gravity, serum electrolytes: sodium, potassium, bicarbonate and chloride.

All patients were treated with the same basic regimen. Intravenous fluids, Dacca Solution (DS) or Diarrhoea Treatment Solution (DTS) were infused to alternate patients. If the patient had been severely dehydrated, a volume of fluid which was approximately 10% of his body weight was rapidly infused. In moderate dehydration, the amount of fluid used was usually 7% of the body weight. Full hydration was achieved in almost all cases in less than 4 hours. Vital signs were recorded every hour during the first 4 hours and eight hourly thereafter. No food was allowed during the first 24 hours. Distilled water was kept at bedside for drinking ad libitum. Biochemical studies of blood were carried out at 4, 24, 48 and 72 hours.

All stool and urine passed were carefully collected which was facilitated by selecting male patients. Spot samples of stool were also collected whenever possible by rectal catheters for the estimation of sodium, potassium and bicarbonate at intervals mentioned above.

Vomiting was not a problem in any of these study patients although provision was made for collecting vomitus.

No antibiotic was given to these patients during the continuation of the study for 72 hours. If diarrhoea lasted beyond the 72 hours or if the patient was vibrio or shigella positive, tetracycline or ampicillin was prescribed for the next five days.

pH was determined immediately in some cases in anaerobically drawn heparinized arterial blood using Corning model 12B Blood Meter with thermostatically controlled temperature compensator. Sodium and potassium levels were measured in National Instrument Laboratories flame photometer with internal lithium standard. Bicarbonates were

estimated in Van Slyke manometric apparatus. Chlorides were measured on Marius chloro-counter. Serum specific gravity was estimated by an American Optical TS meter. Glucose was estimated by the method of Nelson and Somogyi.

Rectal swabbing was carried out on admission and at 24 hours by using sterile swabs. Immediate plating at the bedside was done on gelatine-taurocholate-tellurite media as well on MacConkey's agar and Salmonella-Shigella agar. Readings were taken at 24 hours after incubation at 37°C. Positive isolates were confirmed by biochemical techniques and agglutination by specific antisera.

RESULTS

All patients in the study recovered fully and none developed major complications.

Presentation of results:

Only a part of the results of a total of 69 patients suffering from cholera and 31 from non-cholera diarrhoea are presented here. Since the incidences of electrolyte imbalance and hypoglycemia were predominantly found in small children, their results are presented separately from those of the older children. The adults were grouped together with older children.

It may be noticed here that a comparatively small number of patients belonged to the non-cholera diarrhoea groups. These are in addition to those presented last year on non-cholera diarrhoea group. This result is presented here because they were carried out in one single series during an epidemic of non-cholera and cholera diarrhoea.

Particulars of patients:

Ages, weights on admission and discharge and the number of patients studies in the various age groups are shown in table 1. They were comparable although the numbers were rather small in the non-cholera diarrhoeal group.

Rate of correction of dehydration:

The amount of I.V. fluid used depended on the degree of dehydration in each case and were assesed on the clinical basis. Table 2 shows the admission values of plasma specific gravities

and those after hydration at four hours and at subsequent intervals. There were virtually no difference in the rate of correction of dehydration between the D S and D T Solution.

Serum sodium level:

Serum sodium levels (without correcting for serum water) are shown in table 3. It is clear that there are little differences in the levels of sodium between the two solutions. There were three cases of serum sodium level 125 mEq/l or below which were detected in the D T S group and two in the D S group with cholera. Since sodium level was not corrected at four hours in the D T S group, the patients were withdrawn from the study and given normal saline. The two hyponatraemia cases in the D S group corrected the level of serum sodium to a reasonable degree and infusion of sodium chloride solution was not required. No such hyponatraemia was detected in the non-cholera group.

Intake of water by mouth:

Distilled water in measured volumes were kept at the bedside of the patients. It was known to the patients that this water could be drunk ad libitum but no attempts were made to encourage them to drink. Table 4 shows the mean intake of water at 4 and 24 hours in all the groups. It is clear that there is some degree of fluctuation in the intake of water in individual cases but no differences could be detected between the D S and D T S groups. The varying load of sodium did not seem to affect the intake of water in any way.

Excretion of sodium in urine:

Urine could be collected in a relatively small number of cases during the first 24 hours. If an intake of sodium in excess of what the body needs is infused, the extra amount should be excreted by the kidney. Table 5 shows this very clearly. It is obvious that a higher amount of sodium was put out in the urine in patients receiving D S which had a higher level of sodium compared to those receiving D T S with a lower level. It is, therefore, clear that the excessive load of sodium is within the capacity of the kidney to handle. It is worth mentioning that those with hyponatraemia passed urine completely devoid sodium.

Blood sugar:

D T Solution is formulated with 44 mM/l of dextrose to combat hypoglycaemia in small children whereas dextrose has to be freshly added in D S Solution . Table 6 shows the values obtained in the study groups at intervals. The blood levels of glucose on admission were the highest in all groups. There was a significant fall in the level of blood glucose after initial hydration in almost all groups measured at the 4th hour. Two patients in the 5 years or less age groups were found to have chemical hypoglycemias of less than 40 mg/100 ml when infused with dextrose-free D S but no convulsions or other signs of hypoglycemia were seen. This was corrected in one of the patients even the patient continued to receive the same dextrose-free D S. No hypoglycemic was detected in the older age groups. Cholera patients aged 5 years or less had a slightly higher level of blood sugar at the fourth hour when infused with the D T S which contains dextrose. It was probably effective in keeping the level of glucose at a slightly higher level compared to D S.

Serum K^+:

There was no difference in the contents of potassium between the solutions. It was interesting to note that there was a gradual and sustained lowering of potassium level with the continuation of diarrhoea as shown in table 7. Potassium of 13 mEq/l was not enough to protect the patients from getting hypokalaemic inspite of the fact that potassium-rich foods like meat and vegetables were given.

Serum CO_2^-:

All patients were admitted with acidosis which was not fully corrected at four hours as shown in table 8. The CO_2^- level however, was normal by 24 hours.

Requirement of I V and output of stool:

The rate of infusion of fluid is usually highest on admission when the patients are dry and has to be rehydrated. As expressed in ml/kg/hour, (table 9) this rate was highest in the cholera. It was somewhat less in non-cholera diarrhoea. The output through stooling followed the same pattern as shown in table 10. The duration of diarrhoea is usually less in the non-cholera diarrhoea.

Composition of stool:

Spot stool could not be obtained by rectal catheters in many cases at the prescribed intervals. The mean level of sodium in cholera was around 100 mEq on admission and increased somewhat at 48 hours (table 11). However, there was a great flactuation in its lessor amount of sodium. Bicarbonate measured on spot samples of stool from cholera patients were also appreciably less than 50 mEq/l and were even lesser in non-cholera diarrhoea.

The K^+ levels in patients where spot samples could be obtained were approximately 30 mEq/l, (table 13) much higher than the 13 mEq/l added in D S or D T S. In many cases it was extremely high which accounted for the development of hypokalaemic.

Discussion and conclusion:

The study confirmed what was observed last year in a study on a limited number of patients suffering from non-cholera diarrhoea.

The higher concentration of sodium in the D S was not harmful to any patients. It actually may have helped those patients who were admitted with hyponatraemia during the last season. If there was sodium in excess of the requirement, it did not cause hyponatraemia or other complications. The excess load was handled by the kidneys as was evident in the higher rate of loss of sodium. On the otherhand, stool composition showed that loss of sodium is not as high as have been reported, possibly on the basis of studies carried out in a selected group of heavy purgers. It was, of course, much lower in non-cholera diarrhoea, but their number in this study were low. D T S solution therefore would be closer to being "Universal" if the sodium levels in stool are used as a guide. However, we had to take out a number of hyponatraemic patients from the D T S group once the serum levels were known. Since malnutrition associated with hyponatraemia is going to remain as a problem in developing countires, it is useful to have some solutions available which will correct this state. Infusion of D T S may actually lower the level of serum sodium

Glucose levels in blood seems to fall rapidly with hydration, probably by shutting off the secretion of epinephrine produced during shock. None on D T S developed chemical hypoglycemia whereas two children did show levels of glucose less than mg/100 ml while on D S. However it was interesting to note that 44 mM/l of glucose in the D T S was not adequate in preventing the rapid initial fall in the levels of glucose.

Patients belonging all group develop hypokalaemia whether they receive D S or D T S. This had been found to be true also in earlier studies.

It seems there is no "Univarsal" solution which could be used in all cases of diarrhoea.

TABLE 1

COMPARATIVE TRIAL OF DACCA SOLUTION AND DIARRHOEA TREATMENT SOLUTION - PARTICULARS OF PATIENTS.

	Cholera				Non-cholera Diarrhoea			
	≤ 5 yrs.		6 yrs.+		≤ 5 yrs.		6 yrs.+	
	DS	DTS	DS	DTS	DS	DTS	DS	DTS
Number	20	13	17	19	4	7	9	11
Age (Yrs)	4.2	4.4	9.6	8.4	2.04	3.5	10.1	10.8
	(1.2)	(0.7)	(1.9)	(1.7)	(1.7)	(1.4)	(2.5)	(1.6)
Weight in Kg. Admission	10.4	10.4	18.3	15.6	8.4	9.9	18.4	21.2
	(2.6)	(2.2)	(5.1)	(3.6)	(1.7)	(1.6)	(4.6)	(4.6)
Weight in Kg. Discharge	11.3	11.4	19.4	16.5	9.0	10.5	19.5	22.1
	(2.9)	(1.9)	(5.1)	(3.6)	(2.0)	(1.8)	(4.9)	(4.4)

Figures ( ) ± Sd

TABLE 2

SERUM SP. GR.

	Cholera				Non-cholera Diarrhoea			
	≤ 5 yrs.		6 yrs.+		≤ 5 yrs.		6 yrs.+	
	DS	DTS	DS	DTS	DS	DTS	DS	DTS
Time in hour No.	12	13	17	19	4	6	9	10
Admission	1.035	1.034	1.036	1.036	1.031	1.031	1.032	1.034
4	1.027	1.028	1.026	1.028	1.024	1.024	1.025	1.025
24	1.024	1.025	1.025	1.027	1.024	1.023	1.024	1.025
48	1.025	1.025	1.025	1.026	1.023	1.025	1.026	1.026

TABLE 3

SERUM Na^+ (mEq/L)

	Cholera				Non-cholera Diarrhoea			
	≤ 5 yrs.		6 yrs.+		≤ 5 yrs.		6 yrs.+	
	DS	DTS	DS	DTS	DS	DTS	DS	DTS
Time in hour No.	20	13	17	20	4	5	9	11
Admission	133.5	132.0	134.0	134.4	141	137	136.4	137.1
	(3.3)	(4.4)	(3.2)	(5.0)	(2.1)	(2.4)	(2.3)	(3.3)
4	133.6	133.5	135.6	135.0	138	135	138.0	136.4
	(2.6)	(3.5)	(3.5)	(2.2)	(2.7)	(3.7)	(2.1)	(3.0)
24	134.7	135.3	136.8	135.2	137	136	138.3	137.5
	(2.7)	(3.5)	(2.5)	(2.9)	(2.1)	(2.9)	(2.2)	(3.1)
48	135.5	135.0	136.5	134.8	137	136	137.2	137.0
	(3.1)	(3.9)	(2.0)	(2.8)	(2.6)	(2.5)	(2.1)	(2.9)

TABLE 4

ORAL INTAKE (ML/KG/HR)

		Cholera				Non-cholera Diarrhoea			
		≤ 5 yrs.		6 yrs.+		≤ 5 yrs.		6 yrs.+	
		DS	DTS	DS	DTS	DS	DTS	DS	DTS
Time in hour	No.	20	11	17	19	4	6	9	11
4		1,39	0,99	1,33	0,56	1,4	1,5	1,78	0,88
		(1,53)	(1,36)	(3,09)	(1,34)	(1,2)	(1,7)	(2,28)	(1,09)
24		3,57	3,54	3,47	3,09	2,9	2,5	2,15	2,01
		(1,35)	(1,51)	(1,49)	(1,42)	(1,0)	(1,1)	(1,12)	(1,28)

TABLE 5

EXCRETION OF SODIUM IN URINE
DURING THE FIRST 24 HOURS (mEq)

	Cholera				Non-cholera Diarrhoea			
	≤ 5 yrs.		6 yrs.+		≤ 5 yrs.		6 yrs.+	
	DS	DTS	DS	DTS	DS	DTS	DS	DTS
No.	11	10	17	20	4	5	8	10
	12,5	4,3	55,5	17,8	15,4	13,2	67,6	33,9
	(10.3)	(3,8)	(49.3)	(25,9)	(14,2)	(8.2)	(37,6)	(24.7)
	p<0.05		p<0.01		N.S.		N.S.	

TABLE 5

BLOOD SUGAR (MG/100 ML)

	Cholera				Non-cholera Diarrhoea			
	≤ 5 yrs.		6 yrs.+		≤ 5 yrs.		6 yrs.+	
	DS	DTS	DS	DTS	DS	DTS	DS	DTS
Time in hour / No.	20	13	17	19	4	6	9	10
Admission	120.7	125,1	115,7	124,2	77.0	101,0	96.3	109,1
	(67.5)	(67,4)	(29,9)	(69,3)	(18,6)	(24,3)	(37,7)	(31,1)
4	49.2	60.5	64.4	64.9	63,5	68,5	61.2	59.4
	(12.8)	(17,9)	(12,6)	(14,1)	(8,4)	(12,0)	(11,5)	(13,7)
24	68.8	77,8	68,4	70,7	65.0	70,7	60.8	95,3
	(11.6)	(40,7)	(13,8)	(16,5)	(8,7)	(15,6)	(21,6)	(13,0)
48	71,8	65,1	72,6	71,6	56,5	69,3	63,0	63,5
	(25,4)	(24,6)	(21,4)	(23,3)	(8,6)	(3,6)	(12,0)	(7,9)
*	p<0,001	p<0,01	p<0,001	p<0,001	N,S.	p<0,05	p<0,02	p<0,001

* Fall of glucose level in 4 hrs.

TABLE 7

SERUM K^+ (MEQ/L)

	Cholera				Non-cholera Diarrhoea			
	≤ 5 yrs.		6 yrs.+		≤ 5 yrs.		6 yrs.+	
	DS	DTS	DS	DTS	DS	DTS	DS	DTS
Time in hour No.	17	12	17	20	4	6	9	11
Admission	4.5	4.4	4.3	4.6	4.1	4.0	4.2	4.0
	(0.9)	(0.9)	(0.5)	(0.9)	(0.6)	(0.4)	(0.7)	(0.4)
4	4.0	4.1	4.3	4.3	3.5	3.6	3.8	3.9
	(0.7)	(1.1)	(0.4)	(0.7)	(0.6)	(0.4)	(0.4)	(0.5)
24	3.5	3.6	3.6	3.6	3.4	3.8	3.6	3.7
	(0.4)	(0.7)	(0.5)	(0.5)	(0.6)	(0.4)	(0.3)	(0.4)
48	3.6	3.3	3.7	3.6	3.8	4.1	3.6	3.3
	(0.7)	(0.5)	(0.4)	(0.5)	(0.3)	(0.6)	(0.3)	(0.3)

TABLE 8

SERUM CO_2 (MEQ/L)

	Cholera				Non-cholera Diarrhoea			
	≤ 5 yrs.		6 yrs.+		≤ 5 yrs.		6 yrs.+	
	DS	DTS	DS	DTS	DS	DTS	DS	DTS
Time in hour No.	20	13	16	19	4	6	9	11
Admission	11.3	13,6	13,2	12,9	16,3	14,6	13,7	12,1
	(3.4)	(2,7)	(3,8)	(3,2)	(5,5)	(3,6)	(2,4)	(5,0)
4	18.3	20.7	20,3	21,9	17,2	19.9	21,4	20,5
	(3.5)	(2.8)	(4,3)	(3,2)	(4,8)	(3,0)	(3.0)	(2,6)
24	22.6	25,6	23,0	24,6	20,9	24,6	23,5	23,6
	(4.6)	(5,1)	(4.3)	(3,9)	(3,2)	(2,0)	(3.4)	(2,7)
48	21.9	27,1	23,3	25,3	18,5	22,8	25,1	22,4
	(2.7)	(5,5)	(3.7)	(5,3)	(1.4)	(4,3)	(3,6)	(2,7)

TABLE 9

STOOL OUTPUT (ML/KG/HR.)

		Cholera				Non-cholera Diarrhoea			
		≤ 5 yrs.		6 yrs.+		≤ 5 yrs.		6 yrs.+	
		DS	DTS	DS	DTS	DS	DTS	DS	DTS
Time in hour	No.	20	11	17	19	4	5	9	11
4		7.1	4.4	4.2	5.2	3.6	1.2	1.7	2.4
		(10.8)	(5.4)	(5.4)	(5.4)	(3.6)	(1.3)	(2.7)	(2.6)
24		10.9	9.1	6.1	7.0	4.8	2.0	1.4	1.2
		(9.6)	(5.9)	(4.5)	(4.5)	(2.3)	(2.3)	(1.11)	(0.8)
48		11.1	10.9	5.6	6.8	4.0	2.5	1.5	0.9
		(8.8)	(5.3)	(4.3)	(5.1)	(1.7)	(2.8)	(0.7)	(0.3)

TABLE 10

I.V. REQUIRED (ML/KG/HR.)

		Cholera				Non-cholera Diarrhoea			
		≤ 5 yrs.		6 yrs.+		≤ 5 yrs.		6 yrs.+	
		DS	DTS	DS	DTS	DS	DTS	DS	DTS
Time in hour	No.	20	11	17	19	4	6	9	11
4		27.7	27.2	22.1	24.6	20.6	21.0	23.1	19.5
		(10.8)	(4.9)	(6.4)	(5.1)	(3.7)	(3.8)	(4.3)	(3.4)
24		14.3	14.3	9.3	10.8	5.7	6.5	5.4	4.6
		(8.8)	(7.1)	(4.6)	(5.6)	(1.9)	(2.2)	(1.5)	(1.3)
48		12.3	14.1	7.2	8.8	3.9	4.7		
		(8.6)	(6.7)	(4.2)	(5.1)	(1.2)	(2.8)		

TABLE 11

STOOL COMPOSITION

Na^+ (mEq/L)

		Cholera				Non-cholera Diarrhoea			
		≤ 5 yrs.		6 yrs.+		≤ 5 yrs.		6 yrs.+	
		DS	DTS	DS	DTS	DS	DTS	DS	DTS
Time in hour	No.	17	10	17	17	4	3	7	9
0		101.9	106,3	107,2	113,6	48,8	90,0	87,8	99,4
		(23.4)	(22.9)	(19,4)	(15,7)	(37,6)	(8,6)	(28,4)	(18,8)
4		100,4	103,5	92,6	95,4	57,5	57,8	85,5	77,8
		(19,7)	(18,0)	(24,2)	(31,2)	(20,9)	(13,9)	(24,4)	(13,3)
24		105,6	108,2	108,8	103,4	42,7	95,3	94,0	81,0
		(23,8)	(14,6)	(14,9)	(17,5)	(9,0)	(30,6)	(12,9)	(30,5)
48		117,4	115,1	120,1	108,2				
		(13,1)	(8,8)	(6,5)	(22,1)				

TABLE 12

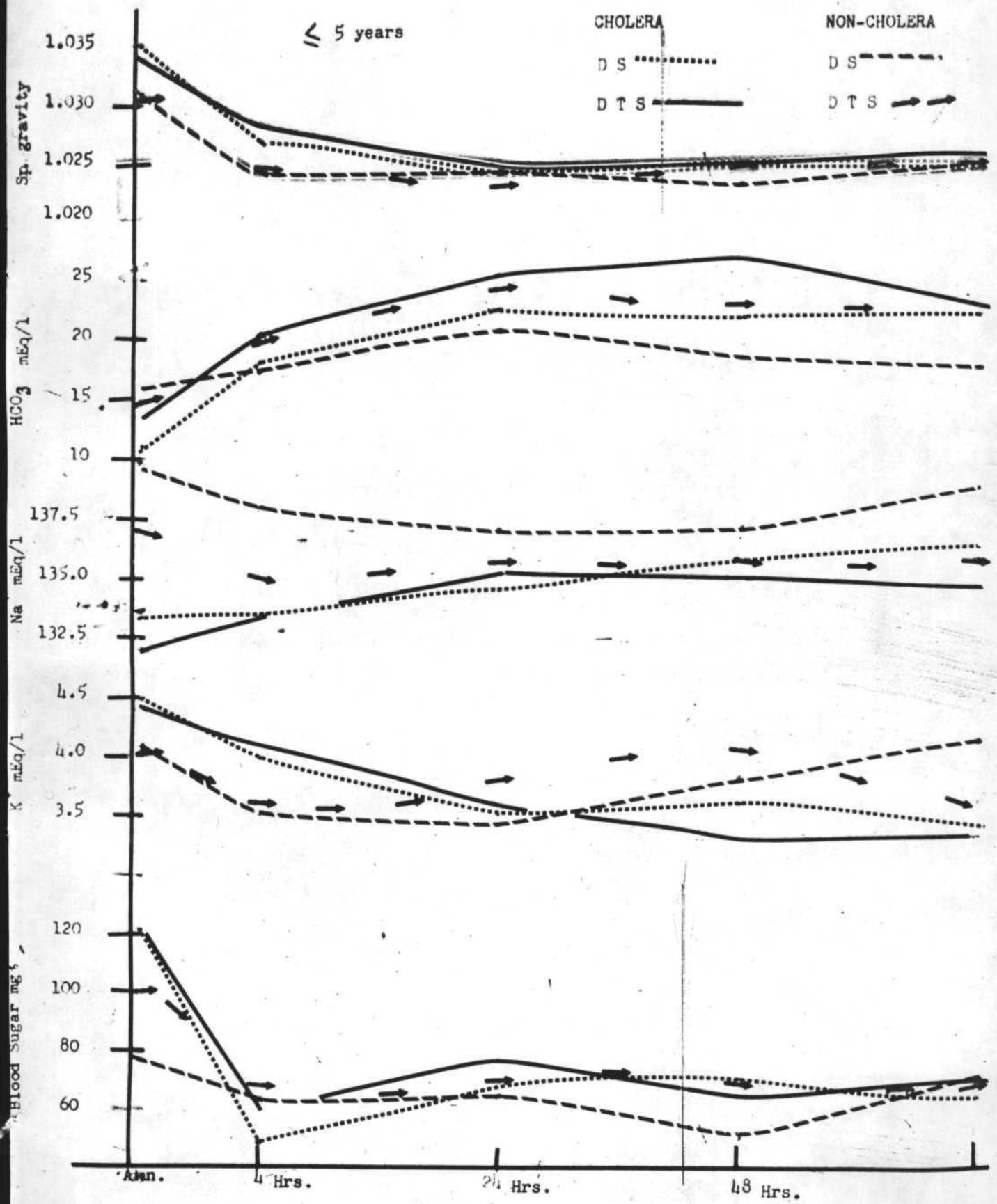
STOOL COMPOSITION - CO_2 (mEq/L)

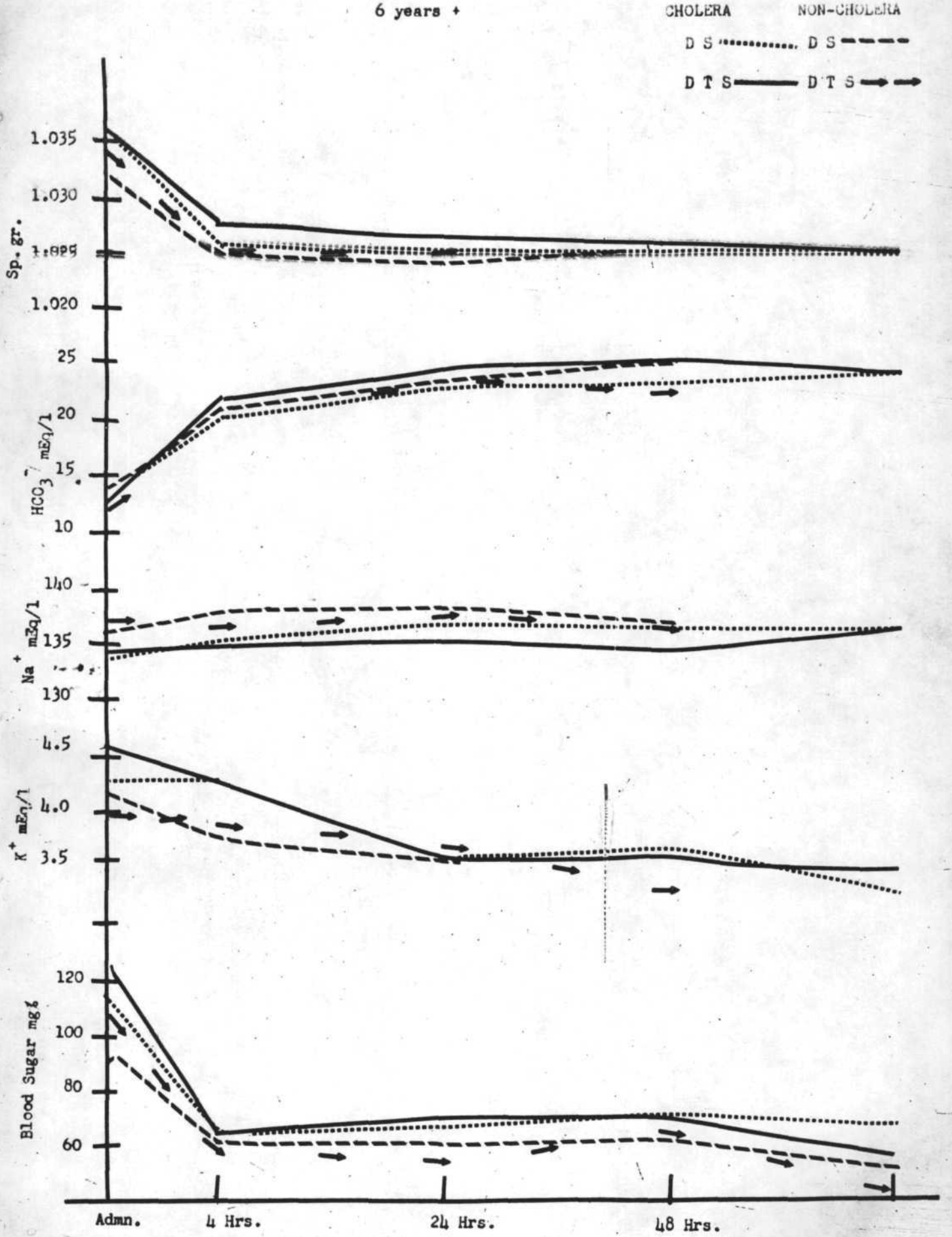
		Cholera				Non-cholera Diarrhoea			
		≤ 5 yrs.		6 yrs.+		≤ 5 yrs.		6 yrs.+	
		DS	DTS	DS	DTS	DS	DTS	DS	DTS
Time in hour	No.	17	10	17	17	4	5	9	9
0		29,2	30,1	37,1	37,3	16,6	20,5	29,9	27,2
		(10,8)	(10,7)	(13,4)	(10,1)	(18,4)	(2,3)	(15,9)	(8,3)
4		30,6	28,5	31,7	34,2	12,3	23,6	31,9	34,5
		(9,1)	(9,8)	(8,2)	(7,3)	(7,6)	(6,6)	(10,1)	(7,9)
24		26,7	29,4	27,1	26,0	9,3	34,6	29,7	25.4
		(8,9)	(11,5)	(9,1)	(9,8)	(3,7)	(12,5)	(9,9)	(14,7)
48		27,5	29,0	32,7	32,2	9,4	26,4		
		(8,3)	(14,6)	(11,1)	(8,9)	(3,6)	(5,4)		

TABLE 13

STOOL COMPOSITION K^+ (mEq/l)

	Cholera				Non-cholera Diarrhoea			
	≤ 5 yrs.		6 yrs.+		≤ 5 yrs.		6 yrs.+	
	DS	DTS	DS	DTS	DS	DTS	DS	DTS
Time in hour No.	17	10	17	17	4	3	8	9
0	32,5	23,5	32,8	30,3	22,2	45,9	41,6	32,8
	(14.1)	(9.5)	(16.2)	(12,4)	(4,0)	(13,4)	(20,4)	(12,0)
4	33,7	24,7	38,4	38,3			44,1	43,1
	(16.6)	(6,1)	(17.4)	(24,7)			(15,9)	(7,9)
24	26,5	21,7	25,7	28,8			42,6	52,9
	(17.1)	(10.9)	(10.0)	(20,2)			(12,9)	(35,8)
48	19,1	17,2	18,2	23,4				
	(10.0)	(6,1)	(6,4)	(16,3)				


≤ 5 years
CHOLERA
D S
D T S
NON-CHOLERA
D S
D T S
Sp. gravity
1.035
1.030
1.025
1.020
HCO_3 mEq/l
25
20
15
10
Na mEq/l
137.5
135.0
132.5
K mEq/l
4.5
4.0
3.5
Blood Sugar mg%
120
100
80
60
Adm.
4 Hrs.
24 Hrs.
48 Hrs.


6 years +
CHOLERA
NON-CHOLERA
D S
D S
D T S
D T S
Sp. gr.
1.035
1.030
1.025
1.020
HCO_3^- mEq/l
25
20
15
10
Na^+ mEq/l
140
135
130
K^+ mEq/l
4.5
4.0
3.5
Blood Sugar mg%
120
100
80
60
Admn.
4 Hrs.
24 Hrs.
48 Hrs.