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MINISTRY OF HEALTH
Control of Diarrheal Diseases Project
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A SINGLE POLY-ELECTROLYTE INTRAVENOUS FLUID FOR INFANTS WITH SEVERE DEHYDRATION FROM DIARRHEA.

Introduction

The rehydration centers of Abu El Reesh (Cairo University) and El-Shatby (Alexandria University) hospitals conducted a study to find a suitable formula for a poly-electrolyte intravenous fluid to rescusitate Egyptian children with severe dehydration. Various formulas have been in use for many years such as one-half Darrow's (in Africa), the "Dacca Solution" (in Bangladesh) and Lactated-Ringer's with Kadelex (in Egypt). While they vary in composition, all offer saline, potassium and a base in a single solution. Such poly-electrolyte fluids may be given rapidly with safety and most children may be moved to oral maintenance within 4-8 hours.

Materials, Methods, Patients

Between October 1983 and April 1984 100 infants (the majority at Abu El Reesh) with a history of diarrhea and severe dehydration (in coma, shock, or weak as to be unable to take oral fluid) were randomly (but not blindly) given one of three solutions whose contents are listed in Table 1.

Solution One is comparable to the W.H.O. oral rehydration solution formula; Solution Two is the intravenous fluid recommended by W.H.O.; Solution Three combines two fluids now given sequentially to children at Abu El Reesh Hospital. The fluids were prepared for the study by El Nasr pharmaceutical Company, Cairo.

One to three children with severe dehydration were admitted to the study on each study day. A history was taken; the degree of dehydration was measured by body weight and by a modified Fortin -Parent scale (appendix 1). Those with a scale score exceeding 8 were given one of the three solutions (chosen at random). The scores and weights were reassessed at 8 and 24 hours after admission, Blood chemistries were measured at 8 and 24 hours, and included sodium, potassium, Ph, PCO2, bicarbonate, osmolality, urea nitrogen and glucose. Hematocrits were also measured. 32 children were given Solution One; 36 got Solution Two; 32, Solution Three.

The children were given a dose of intravenous fluid of 120 milliliters per kilogram body weight over 6-8 hours. Those who were then responsive and able to drink were switched to oral rehydration solution (W.H.O. formula), and rice water; and soon after, milk formula at regular strength (or breast milk) was started.

Results

1. Clinical features: One hundred children (63 boys 37 girls) ranging in age from 1 to 18 months were entered into the study. 55% were 6 months old or less. The children were considerably malnourished: 45 % were below the Egyptian standard 3rd percentile. Only 6% exceeded the 50th percentile. The median hematocrit (after hydration) was 26, the range 16-36. All had watery diarrhea, 83% had vomiting by history and observation within the first few hours. Within 24 hours 69% no longer had watery stools (becoming loose or formed), 87% were not vomiting, and 84% were switched to oral fluids.

Nearly all were severely dehydrated on admission with shock, impending shock, coma or obtundation. Table 2 shows the mean dehydration scores as therapy progressed, and average weight gain. No differences between the solutions were signficant.

2. Deaths

Overall 14 children died within hours to a week after admission.

The death rate varied between the solution-groups: 2 in Solution One-group (6.3%), 8 in Solution Two-group (22.2%), 4 in Solution Three group (12.5%). The difference between the extremes was marginally significant (by standard error of differences, $0.1 > p > 0.05$). An analysis of the clinical stories indicates that those who died were among the sickest on admission and, by chance, more of these were given Solution Two.

Nine of 12 children with the data had hematocrits below the median for the whole study population. Half had high hypernatremia (> 170 meq/liter). Seven of 12 children with the data had elevated blood urea nitrogen over 50 mg% at or near the time of death. Six of the seven had high hypernatremia also. The probable contributing causes of death ranged as follows:

renal failure -3
shock not reversed -2
severe acidosis -1
CNS hemorrhage -1
hypoglycemia - 1
sepsis - 1
pneumomia - 1
adrenal failure - 1
too rapid fall in Na^+ with seizure - 1
unknown - 1

gangrene, DIC-1

3. Biochemical Results

54% were admitted with hypernatremia ranging from 150 to 197 meq/l (sodium values throughout were corrected upwards for blood glucose elevations at the time, 1.6 meq per each 100 mg% above 100).
Figure 1 shows that with each solution hypernatremic values tended to fall by 24 hours (the mean rate of fall was 0.85 mEq/hour $\pm$ 0.46 S.D. for initial values over 159 meq/l) and hyponatremic values to rise.
A few transient elevations to the hypernatremic range were seen, inconsequential in 7 patients; 1 patient, who also had renal failure and hyperkalemia, died.

7 of 18 patients with high hypernatremia (over 170 meq/l) died: 2/10 getting Solutions One and Three (sodium = 90 meq/l), 5/8 getting Solution Two(sodium=119meq/l)The difference in these death rates was marginally significant: p= 0.0875 by Fisher exact probability (one - tail test). Three patients had seizures associated temporally with rapid lowering of serum sodium (within 8 hours, 190 to 166, 197 to 178, 190 to 177); two were in the Solution Two group.

Serum bicarbonate and potassium levels are shown in tables 3 and 4, respectively. Correction of acidosis was significantly more rapid the higher the concentration of base in the intravenous solution. Correction of acidosis then continued at about the same rate after the switch over to oral rehydration solution at 8 hours.

Serum potassium concentrations showed clear tendencies to normality with rehydration using any of the three poly-electrolyte solutions. Blood urea nitrogen tended to normal by 24 hours. The average 0,8, and 24 hour values(mg%) for the three groups were: 38,33,22 (Solution One); 38,33, 24 (Solution Two); 42,35, 25 (Solution Three).

68% of patients had hyperglycemia (over 125 mg%), and 19% had high hyperglycemia (equal to or over 300 mg%), the highest value 740 mg%. With rapid rehydration, despite the presence of glucose 10-20 grams per liter, in the solution, blood glucose fell rapidly. At 8 and 24 hours, respectively, 14% and 16% had hyperglycemia, 1% and 0 had high hyperglycemia.

Hyperglycemia and hypernatremia were not correlated, although 14/18 with high hyperglycemia also had hypernatremia. Those with high hyperglycemia on admission tended to be more acidotic than the others(in meq/l): 9.1± 3.6 SD compared tO 10.9 4.3 SD,$0.1 > p > 0.05$ by Student's t test.

Discussion and Recommendations

The study has demonstrated that a single poly-electrolyte intravenous solution may be given rapidly even to desperately ill children, with

hypertonic or hypotonic dehydration, with severe acidosis or abnormal serum potasium levels. The majority may be switched over to oral rehydration solution and liquid feeds within the first 6-12 hours of admission; vomiting and continued watery stools continued in a small minority.

The rate of convulsions associated with too rapid a fall in serum sodium (5%) is Guite low. Deaths occurred principally in those most desperately ill with high hypernatremia, acidosis, renal failure or late complications. The excess of deaths in Solution Two-group is due mostly to those with high hypernatremia.

We therefore recommend that Solutions One and Three be modified to form a single standard intravenous rehydration formula for children unable to take oral fluids. The formula would then be (in mM/l): Na^+ 90, K^+, 15,acetate 40, chloride 65, glucose 111. The formula should be used in established rehydration centers only in 1984, with further clinical and biochemical observations in large numbers of patients. Complete guide-lines to the use of the solution should accompany each bottle, and physicians be made familiar with them.

The cause of the high prevalence of hypernatremia must be further investigated. The misuse of "Rehydran". the commercial preparation of the W.H.O. solution, and predominance of artificial formula feeding are two probable causes.

Submitted to the National Control of
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TABLE I

Content (in mM/l) of intravenous Fluids

	Sodium	Potassium	Base*	Chloride	Glucose
Solution One	90	20	30	80	111
Solution Two	119	15	50	84	56
Solution Three	90	12	20	82	111

* As acetate

TABLE 2

Progression of Rehydration

(Mean Values, S.D. and Range)

	Rehydration Score			Weight Gain(%)*
HOUR:	0	8	24	
	(N)	(N)	(N)	(N)
Solution One	(32) 10.6 ± 2.0 (7-15)	(27) 3.1 ± 2.7 (0-11)	(30) 1.0 ± 2.4 (0-11)	(28) 9.7 ± 3.2 (4.1-20.0)
Solution Two	(36) 10.6 ± 2.7 (6-16)	(31) 2.3 ± 2.1 (0-6)	(31) 0.3 ± 1.3 (0-6)	(31) 10.4 ± 3.7 (0-16.7)
Solution Three	(32) 10.7 ± 2.5 (7-16)	(30) 3.1 ± 2.6 (0-10)	(29) 0.8 ± 2.1 (0-8)	(29) 9.9 ± 3.5 (0-18.8)

$$* \frac{\text{Weight at 24 hours} - \text{Weight at admission}}{\text{Weight at 24 hours}} \times 100$$

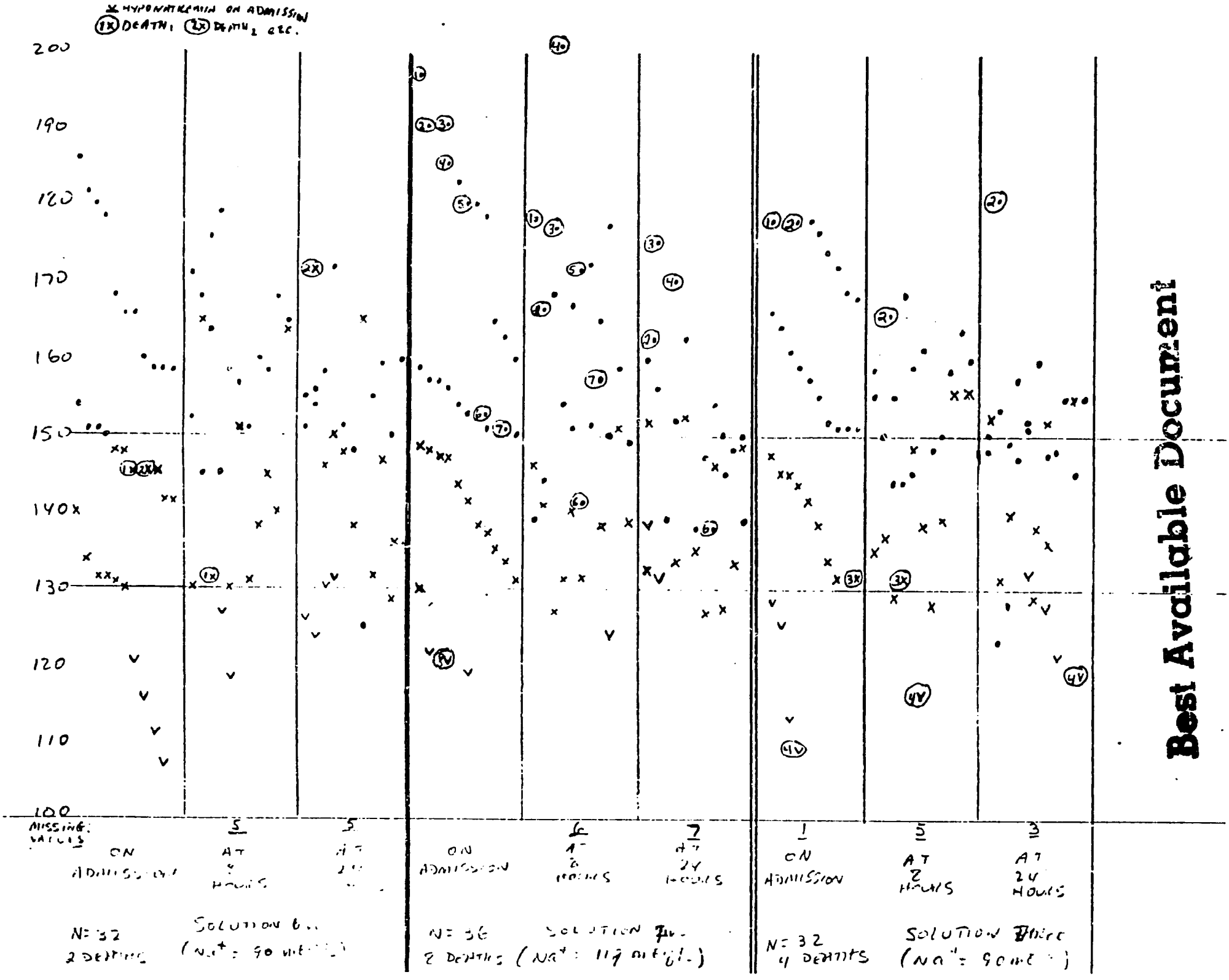

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Table - 3

Progression of Acidosis with Therapy - Serum Bicarbonate concentration(meq

HOUR :	0	8	24	Paired differenc 0-8 Hours
Solution Three (Base=20 meq/l)	11.1 ± 4.8	12.3 ± 4.6	15.2 ± 3.7	1.4 ± 2.1
(N)	(28)	(27)	(26)	(26)
Solution One (Base=30 meq/l)	11.2 ± 4.6	14.5 ± 5.0	17.1 ± 5.3	3.2 ± 2.1
(N)	(28)	(27)	(24)	(27)
Solution Two (Base=50 meq/l)	9.5 ± 3.1	15.1 ± 4.2	18.7 ± 5.1	5.6 ± 3.6
(N)	(34)	(30)	(25)	(30)

* P Values (Student t test):

One VS. Two $P < 0.01$

Two VS. Three $P < 0.001$

One VS. Three $P < 0.01$

TABLE 4

Progression of Serum Potassium with Therapy (mEq/ l , Means and Range) by Concentration on Admission

Admission:	Hypokalemia (<3.5)			Isokalemia (3.5 - 5.0)			Hyperkalemia (>5.0)		
Hour :	0	8	24	0	8	24	0	8	24
.ution One =20mEq/l)									
$\bar{X}$	2.7	4.2	3.7	4.0	4.7	4.5	6.2	6.3	4.4
N	9	9	9	18	13	14	5	5	5
Range	(2.4-3.1)	(2.2-6.2)	(2.5-5.4)	(3.6-4.9)	(3.3-5.7)	(3.4-6.5)	(5.1-7.2)	(4.9-7.3)	(2.6-6.4)
ıtion Two =15 mEq/l)									
$\bar{X}$	3.0	3.5	3.7	4.1	4.4	3.9	7.1	5.7	5.7
N	12	11	10	18	15	15	4	-	4
Range	(2.4-3.4)	(2.5-4.7)	(3.0-4.4)	(3.5-4.9)	(2.6-6.6)	(3.0-6.1)	(5.3-9.2)	(2.9-7.1)	(4.5-7.
ıtion Three =12 mEq/l)									
$\bar{X}$	2.8	3.2	3.5	4.1	3.9	4.2	7.1	5.2	4.6
N	13	11	12	7	5	7	10	10	9
Range	(1.9-3.4)	(2.0-4.0)	(2.4-4.1)	(3.5-5.0)	(3.1-4.5)	(3.2-5.3)	(5.1-10-1)	(3.4-9.3)	(2.7-7.0

APPENDIX ONE

DEHYDRATION SCORE

	2	1	0	SCORE
A. TONGUE	DRY	SLIGHTLY DRY	WET	A=
B. SKIN FOLD	STAYS TENTED	SLIGHT TENTED	ABSENT	B=
C. EYES BALLS	DEEP SUNKEN	SLIGHT SUNKEN	NORMAL	C=
D. FONTANELLE	DEEP SUNKEN	SLIGHT SUNKEN	FLAT	D=
E. EXTREMITIES	COLD & BLUE	COLD	WARM	E=
F. MENTAL STATE	APATH., IRRIT.	LESS ACTIVE	NORMAL	F=
G. BREATHING	DEEP, FAST	FAST	QUIET	G=

IF THE CHILD IS SEMICOMATOSE OR VERY IRRITABLE WITH PITCHED CRY, ADD 3 TO THE TOTAL DEHYDRATION SCORE. TOTAL=

THE TOTAL SCORE IS THE RESULT OF THE ADDITION OF THE VALUES (2,1,0) GIVEN TO THE CLINICAL CRITERIA (A-G).