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Randomised trial showed that rapid rehydration of severely malnourished children with dehydrating diarrhoea was as safe and effective as slow rehydration

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REGULAR ARTICLE

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Randomised trial showed that rapid rehydration of severely malnourished children with dehydrating diarrhoea was as safe and effective as slow rehydration

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Background

- The WHO recommendation for correction of dehydration in severely malnourished children especially severe acute malnutrition (SAM) includes oral rehydration and, if needed intravenous rehydration (IR), very slowly due to concern of over hydration and/or heart failure

- This recommendation was based on experience rather than evidence.

- Rapid rehydration on the other hand may help to achieve a faster improvement of renal function and correction of acidosis as well as reduce vomiting and subsequently reduce requirement of unscheduled IV.

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Safety of Rapid Intravenous Rehydration and Comparative Efficacy of 3 Oral Rehydration Solutions in the Treatment of Severely Malnourished Children With Dehydrating Cholera

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A recent uncontrolled study demonstrated that rapid IR (over 4 to 6 hours) of severely malnourished children with dehydrating cholera was safe and effective, 2009

icddr,b

To confirm this finding this controlled study comparing the rapid rehydration with that of slow rehydration in the management of dehydrating diarrhoea in severely malnourished children was carried out

Objectives

1. To evaluate the effectiveness and safety of rapid rehydration (RR) compared to slow rehydration (SR) in severely malnourished children with watery diarrhoea and severe dehydration

2. To assess the renal function at admission and after 24 hours

Methods

Study design: This was an open randomised controlled clinical trial carried out in severely malnourished children with dehydrating diarrhoea

Site: Dhaka Hospital of icddr,b in Bangladesh

Inclusion criteria

- Children of either sex age 6 months to 60 months
- Severely malnourished (weight for age < -3 Z score or weight for length/height <-3 z score or with bipedal edema
- Acute watery diarrhoea with severe dehydration
- Written informed consent given by the parents/legal guardian

Exclusion criteria

-The children with dysentery (blood in stool)
- Severe pneumonia, suspected severe sepsis/shock, meningitis etc.
- Those received antibiotics before presentation to the hospital for the current illness

Randomization

After enrolment the children were randomized to receive either:

a) IV rehydration rapidly over 6 hours (RR),

or

b) slow rehydration following the critical care pathway (CCP) recommended by WHO (SR) over a period of 12 hours

Case Management (Acute Phase)

After randomization, children were treated following the standardized protocol for the management of severely malnourished children with diarrhoea used at the icddr,b Dhaka Hospital differing only in the IV fluid therapy for dehydration.

Fluid Therapy

The children who were assigned to **RR** therapy, were given IV fluid 100 ml/kg over 6 hours

Ongoing stool losses were replaced with rice-ORS orally or through naso-gastric tube @ 5-10 ml/kg after each watery stool according to the volume of stool

The children assigned to **SR** therapy**,** were initiated rehydration following the critical care pathway according to the WHO treatment guidelines

Initially the children were infused with 15 ml/kg IV fluid over 1 hour and monitored every 10-15 minutes. If after one hour the respiratory and pulse rate slowed down IV fluid was repeated with 15 ml/kg for another 1 hour. After 2 hours IV fluid was stopped leaving the IV line open

Rice–ORS was started through a naso-gastric tube at a rate of 5-10 ml/kg and additionally ongoing stool loss was replaced with the same ORS

Other treatments

Supplementary food (Milk, rice powder, sugar oil mixture), vitamins and minerals and antibiotics treatments were similar in both groups

Measurements

Body weight of the children were measured on admission and every 6 hours.
Intakes (ORS, food, water) and output (stool, urine and vomit) were measured every 6 hours until discharged

CRITICAL CARE PATHWAY (CCP) — SEVERE MALNUTRITION WARD

NAME Cara M (F) DATE OF BIRTH OR AGE 18 mos DATE OF ADMISSION 10 Dec '01 TIME 10:00a.m. HOSP. ID NUMBER 464

INITIAL MANAGEMENT Comments on pre-referral and/or emergency treatment already given: referred by health centre

SIGNS OF SEVERE MALNUTRITION Severe wasting? (Yes) No

Oedema? (0) + ++ +++

Dermatosis? (0) + ++ +++ (raw skin, fissures)

Weight(kg): 6.3 kg Height/length (cm): 72 cm

SD score: < -3 or % of median:

TEMPERATURE 36 °C (rectal) axillary

If rectal < 35.5°C (95.9°F), or axillary < 35°C (95°F), actively warm child. Check temperature every 30 minutes.

BLOOD GLUCOSE (mmol/l): 2-4 mmol/l

If < 3mmol/l and (alert), give 50 ml bolus of 10% glucose or sucrose (oral or NG). If < 3 mmol/l and lethargic, unconscious, or convulsing, give sterile 10% glucose IV: 5 ml x ___ kg (child's wt) = ___ ml *Then give 50 ml bolus NG.*

Time glucose given: 10:15 (Oral) NG IV

HAEMOGLOBIN (Hb) (g/l): 90 or Packed cell vol (PCV): Blood type: A+

If Hb < 40 g/l or PCV < 12%, transfuse 10 ml/kg whole fresh blood (or 5-7 ml/kg packed cells) slowly over 3 hours. Amount: Time started: Ended:

EYE SIGNS None (Left) Right **MEASLES** Yes (No)

Bitot's spots (Pus)/inflammation Corneal clouding Corneal ulceration

If ulceration, give vitamin A & atropine immediately. Record on Daily Care page.

Oral doses vitamin A:	< 6 months	50 000 IU
	6 - 12 months	100 000 IU
	> 12 months	200 000 IU

FEEDING *Begin feeding with F-75 as soon as possible. (If child is rehydrated, reweigh before determining amount to feed. New weight: ___ kg)*

Amount for 2-hourly feedings: 70 **ml F-75*** **Time first fed:** 10:45

** If hypoglycaemic, feed ¼ of this amount every half hour for first 2 hours; continue until blood glucose reaches 3 mmol/l.*

Record all feeds on 24-hour Food Intake Chart.

SIGNS OF SHOCK (None) Lethargic/unconsious Cold hand Slow capillary refill(> 3 seconds) Weak/fast pulse

If lethargic or unconscious, plus cold hand, plus either slow capillary refill or weak/fast pulse, *give oxygen. Give IV glucose as described under Blood Glucose (left). Then give IV fluids:*

Amount IV fluids per hour: 15 ml x ___ kg (child's wt) = ___ ml

	Start:	Monitor every 10 minutes					*2nd hr:	Monitor every 10 minutes				
Time							*					
Resp. rate							*					
Pulse rate							*					

**If respiratory & pulse rates are slower after 1 hour, repeat same amount IV fluids for 2nd hour; then alternate ReSoMal and F-75 for up to 10 hours as in right part of chart below. If no improvement on IV fluids, transfuse whole fresh blood. (See left, Haemoglobin.)*

DIARRHOEA Watery diarrhoea? Yes (No) → *If diarrhoea, circle signs present:* Skin pinch goes back slowly

Blood in stool? Yes (No) Restless/irritable Lethargic Thirsty

Vomiting? Yes (No) Sunken eyes Dry mouth/tongue No tears

If diarrhoea and/or vomiting, give ReSoMal. Every 30 minutes for first 2 hours, monitor and give:*

5 ml x ___ kg (child's wt) = ___ ml ReSoMal

For up to 10 hours, give ReSoMal and F-75 in alternate hours. Monitor every hour. Amount of ReSoMal to offer:*

5 to 10 ml x ___ kg (child's wt) = ___ to ___ ml ReSoMal

Time	Start:														
Resp. rate															
Pulse rate															
Passed urine? Y N															
Number stools															
Number vomits															
Hydration signs															
Amount taken (ml)						F-75		F-75		F-75		F-75		F-75	

Stop ReSoMal if: Increase in pulse & resp. rates Jugular veins engorged Increasing oedema, e.g., puffy eyelids

ANTIBIOTICS *(All receive)* **Drug / Route**	**Dose / Frequency / Duration**	**Time of 1st dose**
Cotrimoxazole - oral	4ml syrup, every 12 hours, for 5 days	10:30 am

Laboratory tests

After admission, blood samples for the determination of Hct, total protein, serum albumin, glucose, and serum electrolytes and creatinine. Serum electrolytes, creatinine and serum albumin

Repeated after 24 hours of therapy

Stool tests for microscopy and culture for *Shigella, Salmonella and Vibrio cholerae*. Stool dark-field microscopy within 1 hour of enrolment to identify *V. cholerae* for antibiotic treatment

Outcome Variables

Unscheduled IV therapy (ORS failure) was considered when intravenous fluid had to be restarted if severe dehydration re-apeared as a result of high purging and/or vomiting

Teatment failure was defined as not achieving complete rehydration (no sign of dehydration) after 6 hours for rapid and 12 hours for slow rehydration group.

Fluid Overload: Early signs of fluid overload was considered in presence of puffy face or peri-orbital oedema with at least 5% weight gain over the rehydration weight

Heart failure was defined by the occurrence increased respiratory rate (>60/minute) in absence of pneumonia and/or increased heart rate (>160/minute) in absence of fever, enlarged liver, prominent neck veins and respiratory distress at any time during hospitalisation

Sample size:

210 (105 in each group)

Estimated on the expectation of 15% less chance of requiring unscheduled IV fluid with rapid rehydration compared with slow rehydration, 5% level of significance with 80% power

Data analyses

The baseline and outcome variables were compared between the groups using the Student's *t*-test for continuous data and Chi-squared test for categorical data.

Figure 1

Trial Profile

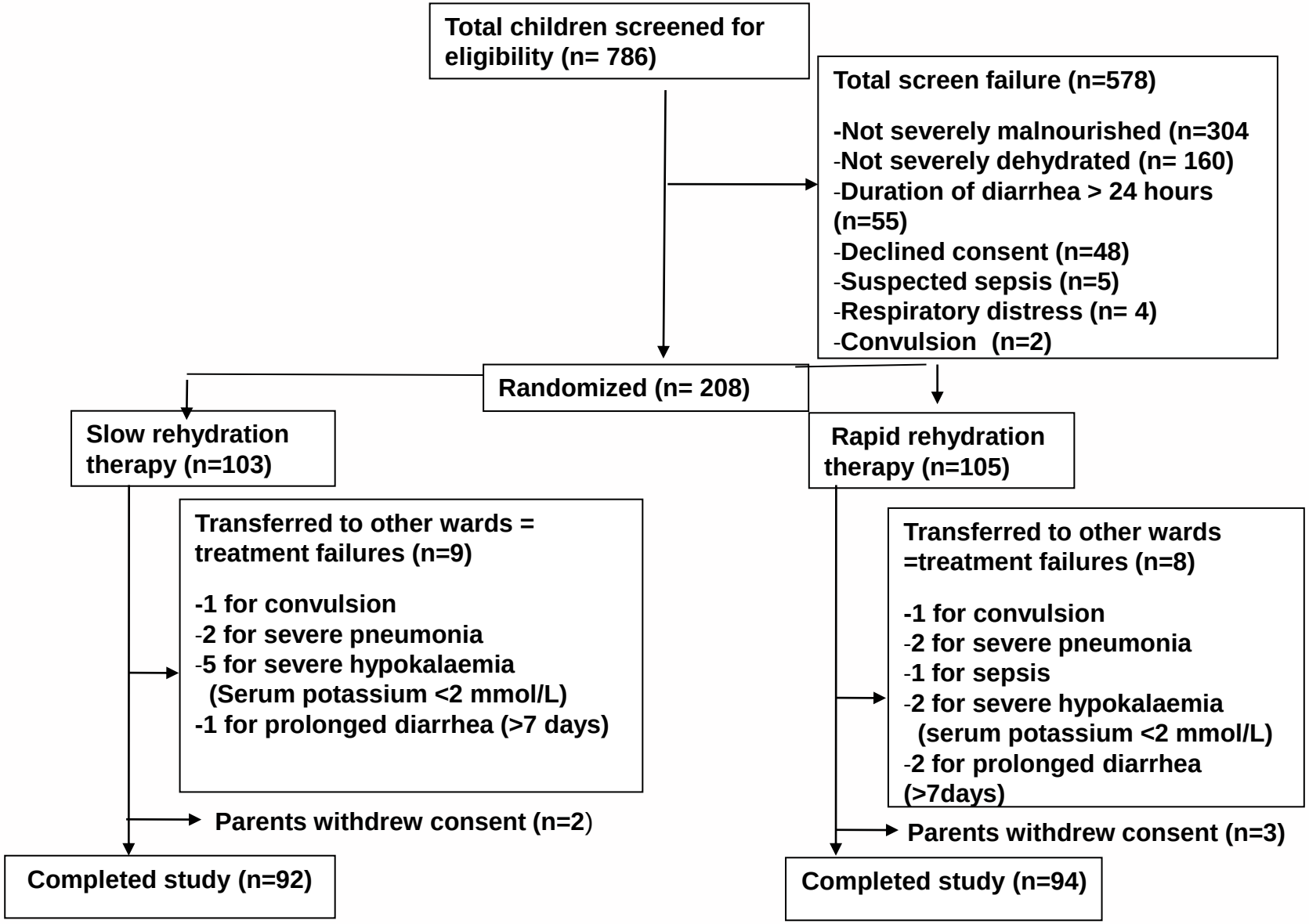

Table 3. Baseline characteristics of children at admission and randomization

Characteristics Data are mean ± SD or number (%)	Slow rehydration n=103	Rapid rehydration n=105
Age (months)	32.0 ± 16.6	30.7 ± 15.7
Sex (Male/Female)	54(52.4%)/49(47.6%)	60(57.1%)/45(42.9%)
Body weight on admission (kg)	8.4 ± 2.1	8.3 ± 2.0
Body weight at 24 hours (kg)	9.1 ± 2.2	9.1 ± 2.2
Percent weight gain at 24 hours	8.5 ± 4.5	9.0 ± 5.7
Weight for age Z- score	-4.0 ±1.1	-3.8 ± 0.8
Weight for length Z –score	-3.5 ±1.4	-3.6 ± 0.9
Number (%) of children with weight for length <-3 Z-score	87/103 (84)	85/105 (81)
Number (%) of children with pedal oedema	23/103 (22)	26/105 (25)
Diarrhoea duration before admission, hours	15.1 ± 6.2	14.1 ± 6.2
Number (%) of children with serum Na <130 mmol/L	28/103 (27.2)	20/105 (19.0)
Number (%) of children with serum K <3.5 mmol/L	52/103 (50.5)	40/105 (38.1)
Number(%) of children with TCO_2 <15 mmol/L	59/103 (57.3)	58/105 (55.2)
Vibrio cholerae ogawa eltor, number (%)	58/103 (56)	66/105 (63)

Table 4. Comparison of outcome variables between the two groups (Intention to treat analysis)

Variables Data are mean ± SD or number (%)	Slow rehydration n=103	Rapid rehydration n=105	Difference between mean (95%CI)	Odds ratio (95% confidence interval)	p-value
Number of children developing fluid overload	0/103	0/105			-
Rehydration success at 12 and 6 hours respectively	101/103	102/105		1.5 (0.24, 8.98)	0.67
Number (%) of children requiring unscheduled intravenous therapy/ORS failure	19/103 (18.4)	18/105 (17.2)		1.1 (0.53, 2.20)	0.83
Number (%) of children with serum sodium <130 mmol/L, 24 hours after admission	16/98 (16.3)	14/98 (14.3)		1.2 (0.53, 2.55)	0.84
Number (%) of children with potassium <3.5 mmol/L, 24 hours after admission	52/98 (53)	58/98 (59)		0.7 (0.44, 1.3)	0.47
Number (%) of children with serum TCO_2 level <15 mmol/L, 24 hours after admission	14/98 (14.3)	10/97 (10.3)		1.5 (0.66, 3.66)	0.51
Number (%) of children with serum creatinine above normal range	6/93 (6.5)	8/96(8.3)		1.5(0.43, 5.42)	0.49
Number (%) of children passed urine >1mL/kg/hour after 24 hours	13/98 (87)	11/100 (89)		0.8 (0.34, 1.9)	0.62

Table 5. Comparison of outcome variables between two treatment groups among children with severe acute malnutrition

Variables Data are mean ± SD or number (%)	Slow rehydration n=87	Rapid rehydration n=85	Difference between mean (95% CI) or indicated otherwise	Odds ratio (95% confidence interval)	p-value
Number (%) of children received unscheduled intravenous fluid	17 (19.5)	14 (16.5)		0.8 (0.37, 1.77)	0.60
Number (%) of children with serum sodium <130 mmol/L, 24 hours after admission	12/82 (15)	10/80 (12.5)		1.2 (0.48, 2.95)	0.69
Number (%) of children with potassium <3.5 mmol/L, 24 hours after admission	45/82 (55)	48/80 (60)		0.8 (0.43, 1.51)	0.50
Number (%) of children with serum TCO_2 level <15 mmol/L at 24 hours	9/82 (10.9)	8/80 (10.0)		1.1 (0.40, 3.0)	0.83
Number (%) of children with serum creatinine above normal range in different age groups, 24 hours after admission	9/85(10)	4/79(5.0)		1.9 (0.34, 12.64)	0.44

Conclusion

The results of this study demonstrate that both rapid and slow rehydration of severely malnourished children including those with SAM suffering from severe dehydration due to acute diarrhoea was effective and safe.

Rapid rehydration was simple and saved time for rehydration.

So, rapid rehydration may be an preferred option especially in children with severe dehydration due to cholera and severe malnutrition

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