RESEARCH

Rapid versus standard intravenous rehydration in paediatric gastroenteritis: pragmatic blinded randomised clinical trial

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Abstract

Objective To determine if rapid rather than standard intravenous rehydration results in improved hydration and clinical outcomes when administered to children with gastroenteritis.

Design Single centre, two arm, parallel randomised pragmatic controlled trial. Blocked randomisation stratified by site. Participants, caregivers, outcome assessors, investigators, and statisticians were blinded to the treatment assignment.

Setting Paediatric emergency department in a tertiary care centre in Toronto, Canada.

Participants 226 children aged 3 months to 11 years; complete follow-up was obtained on 223 (99%). Eligible children were aged over 90 days, had a diagnosis of dehydration secondary to gastroenteritis, had not responded to oral rehydration, and had been prescribed intravenous rehydration. Children were excluded if they weighed less than 5 kg or more than 33 kg, required fluid restriction, had a suspected surgical condition, or had an insurmountable language barrier. Children were also excluded if they had a history of a chronic systemic disease, abdominal surgery, bilious or bloody vomit, hypotension, or hypoglycaemia or hyperglycaemia.

Interventions Rapid (60 mL/kg) or standard (20 mL/kg) rehydration with 0.9% saline over an hour; subsequent fluids administered according to protocol.

Main outcome measures Primary outcome: clinical rehydration, assessed with a validated scale, two hours after the start of treatment. Secondary outcomes: prolonged treatment, mean clinical dehydration scores over the four hour study period, time to discharge, repeat visits

to emergency department, adequate oral intake, and physician's comfort with discharge. Data from all randomised patients were included in an intention to treat analysis.

Results 114 patients were randomised to rapid rehydration and 112 to standard. One child was withdrawn because of severe hyponatraemia at baseline. There was no evidence of a difference between the rapid and standard rehydration groups in the proportions of participants who were rehydrated at two hours (41/114 (36%) v 33/112 (30%); difference 6.5% (95% confidence interval -5.7% to 18.7%; P=0.32). The results did not change after adjustment for weight, baseline dehydration score, and baseline pH (odds ratio 1.8, 0.90 to 3.5; P=0.10). The rates of prolonged treatment were similar (52% rapid v 43% standard; difference 8.9%, 21% to -5%; P=0.19). Although dehydration scores were similar throughout the study period (P=0.96), the median time to discharge was longer in the rapid group (6.3 v 5.0 hours; P=0.03).

Conclusions There are no relevant clinical benefits from the administration of rapid rather than standard intravenous rehydration to haemodynamically stable children deemed to require intravenous rehydration.

Trial registration Clinical Trials NCT00392145.

Introduction

Gastroenteritis remains a disease of major importance in public health.¹ Although oral rehydration is appropriate for most children, many receive prolonged intravenous rehydration, which contributes to overcrowding in the emergency department.² Given the safety of replacing fluid deficits over 24 hours in

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Appendix: Tables of reasons for ineligibility and admissions

haemodynamically stable children, traditional teaching and the National Patient Safety Agency³ have advocated such an approach. Experts have noted, however, that there is a disparity between the slow restoration regimens recommended and the rapid rehydration regimens used by clinicians treating dehydration.⁴ The latter has the potential to reduce a child's level of agitation and clinical signs of dehydration, in addition to enhancing alertness and appetite.⁴ These potential benefits might enable clinicians to achieve earlier rehydration with subsequent reductions in length of stay and costs.⁵ A review of rapid intravenous rehydration studies concluded that evidence of efficacy is lacking.⁶ Thus gastroenteritis treatment guidelines aimed at developed countries, where severe dehydration is uncommon, rarely provide a detailed rapid rehydration strategy.^{1 7 8}

Because of its potential benefits, and despite a paucity of evidence, rapid intravenous rehydration has gradually become incorporated into clinical practice⁹ and is recommended in a leading textbook of emergency medicine.¹⁰ This procedure, however, is not without risks. A recent study of fluid bolus resuscitation in febrile African children had to be stopped early because of increased mortality in the bolus group.^{11 12} Moreover, advocates for rapid intravenous rehydration⁴ suggest that serum should be routinely tested to enable the detection of severe hyponatraemia or hypernatraemia, which necessitates specific therapeutic approaches to reduce the risk of central pontine myelinolysis and cerebral oedema, respectively. As only 30% of academic paediatric emergency medicine physicians routinely check electrolytes in the United States,⁹ the widespread use of rapid intravenous rehydration might place children at unnecessary risk. Given the established safety of standard rehydration in haemodynamically stable children, the lack of evidence of benefit, and the potential complications that might arise with the widespread use of rapid intravenous rehydration, a rigorous evaluation of this more aggressive approach is needed.¹

We carried out a pragmatic randomised, blinded, comparative effectiveness trial among haemodynamically stable children in whom oral rehydration had failed and who were deemed to require intravenous rehydration. Our primary objective was to determine whether treatment with rapid intravenous rehydration resulted in a clinically important increase in the number of children achieving rehydration compared with standard treatment.

Methods

Patients

Participants were recruited between December 2006 and April 2010 in the emergency department of The Hospital for Sick Children, Toronto, Canada. Eligibility was designed to enable the participation of typical children for whom intravenous rehydration is administered in North America. Eligible children were aged over 90 days, had a diagnosis of dehydration secondary to gastroenteritis, had not responded to oral rehydration,⁷ and had been prescribed intravenous rehydration. Dehydration was defined as a clinical dehydration scale score of >3 (table 1).¹³ This four item scale has previously been shown to have good inter-rater reliability (intraclass correlation coefficient=0.77, 95% confidence interval 0.68 to 0.86) and discriminatory power (Ferguson's δ =0.83, 0.77 to 0.88).¹³ Subsequent prospective validation has shown that it correlates with length of stay and the need for intravenous rehydration.¹⁴ It has also been validated independently in two emergency departments.¹⁵ We excluded children who weighed <5 kg or

>33 kg, required fluid restriction, had a suspected surgical condition, had a history of a severe chronic systemic disease, abdominal surgery, or bilious or bloody vomit, had hypotension, hypoglycaemia or hyperglycaemia. We also excluded children of parents/guardians in whom there was an insurmountable language barrier or who lacked a telephone for follow-up. Normal biochemical variables were not an entry requirement as they are not routinely available at the start of intravenous rehydration. A record of patients missed was kept to assess for enrolment bias.

Randomisation and masking

Patients were allocated in a 1:1 ratio to treatment with standard or rapid intravenous rehydration. The permuted block randomisation sequence was computer generated and stratified by severity of dehydration (clinical dehydration scale score 3-4 v 5-8). The sequence was concealed from the research nurses in sequentially numbered sealed opaque envelopes prepared by an independent coordinator. The envelopes were provided to the research nurse once consent had been obtained. They were opened sequentially after information on the participant was written on the appropriate envelope. The randomisation code remained secured until enrolment and data entry were complete.

The research nurse, attending physicians, and participants were blinded to treatment allocation. The bedside nurse, who was unblinded to set the intravenous rate, received instructions not to communicate any information about the infusion or the child's clinical status. Opaque covers were used to conceal the infusion bags and tubing, and soundproof (Quiet Barrier HD, Chambersburg, PA) boxes were constructed by the department of medical engineering to conceal the intravenous pumps. Attending physicians were blinded to the scores on the clinical dehydration scale assigned by the research nurse.

Intervention

Before randomisation, all potentially eligible children were given oral rehydration treatment. Caregivers were instructed to administer 5 mL of a flavoured oral rehydration solution through a syringe every five minutes.⁷ The rate was increased based on tolerance and the child's weight.⁷ For children with persistent vomiting, ondansetron was administered orally in an attempt to prevent the need for intravenous rehydration.¹⁶⁻¹⁸ A research nurse was present to recruit patients from 8 am to midnight; overnight coverage was provided by the principal investigator.

After insertion of an intravenous catheter and the performance of baseline biochemical tests, the bedside nurse set the intravenous rate in accordance with the randomisation assignment. The appearance of infusion pump set ups was identical in all children. Two 1 L bags of 0.9% saline were individually connected to 150 mL three injection PORT burette sets (Alaris Medical Systems, San Diego, CA). Imed Gemini PC-2TX infusion pumps (Alaris Medical Systems) controlled the infusion rate. The burette sets were attached first to a Y connector extension set (MedRx, Largo, FL; length 10 cm; volume 0.65 mL) and then to a T connector extension set (Baxter, Deerfield IL; length 15.2 cm; housing volume 0.20 mL; total volume 0.50 mL). The latter was connected to the intravenous catheter.

Children received either a 20 mL/kg (standard)^{9 19} or 60 mL/kg (rapid) 0.9% saline infusion over 60 minutes followed by 5% dextrose in 0.9% saline²⁰ at a maintenance rate.²¹ Potassium chloride was added based on the serum potassium concentration: 0 mEq/L if >5.0 mmol/L; 20 mEq/L if 4.0-5.0 mmol/L; 40 mEq/L if <4.0 mmol/L. Caregivers were instructed to continue

oral rehydration throughout the study period. Every 30 minutes the research nurse documented clinical outcomes, including the clinical dehydration score, vital signs, success of oral rehydration, and adverse events. The latter included the development of fluid overload represented by tachypnoea (increase greater than 20 breaths per minute from baseline), tachycardia (increase greater than 20 beats per minute from baseline, after adjustment for fever), peripheral oedema, and hypoxia (decrease in transcutaneous oximetry greater than 5% from baseline). If adverse events were suspected, the attending physician determined their presence and clinical relevance. Dysnatraemias, defined as a repeat serum sodium concentration <130 mmol/L or >150 mmol/L, or a value outside the range of normal (135–145 mmol/L) associated with a change of greater than 5 mmol/L from baseline, were also considered an adverse event. A data and safety monitoring board met twice to review data in a blinded manner and evaluated all adverse events. The protocol terminated four hours after the start of intravenous rehydration, at which time biochemical tests were repeated. Subsequent management decisions (discharge, observation, admission) were at the discretion of the attending physician.

We used a standardised telephone script to collect follow-up information on days three and seven after randomisation. Hospital records were reviewed to confirm caregivers' reports. If contact was not made on the designated day, attempts were continued daily for two weeks.

Outcome measurements

Primary outcome

The primary outcome was rehydration, defined as a score on the clinical dehydration scale of ≤ 1 ^{13 14} two hours after the start of treatment. This scale, which consists of four clinical variables, was used to improve diagnostic characteristics²² as individual measures, such as prolonged capillary refill, abnormal skin turgor, and abnormal respiratory pattern, have sensitivities of only 43–60% to detect 5% dehydration.²² In validation studies, the scale selected has been shown to correlate with length of stay and the use of intravenous rehydration and therefore seems to correlate with clinical decision making.^{14 15}

Secondary outcomes

Secondary outcomes included prolonged treatment—a composite measure defined as admission to an inpatient unit at the index visit or admission within 72 hours of randomisation or a stay in the emergency department longer than six hours after the start of treatment; score on the clinical dehydration scale; adequate oral intake, a common prerequisite for discharge,⁹ defined as consuming at least 5 mL/kg of liquid per two hour time period (only a small volume was prespecified as all children additionally received intravenous rehydration); time to discharge, determined by chart review—defined as the time between the start of treatment and discharge from the emergency department or inpatient unit; repeat emergency department visit within 72 hours; and attending physician's comfort with discharge at two and four hours as reported on a 5 point Likert scale. We found the latter correlated strongly with the outcome of hospital admission.

Sample size

We estimated that enrolling 226 children would provide 80% power to detect a 20 percentage point difference in the proportion of children rehydrated two hours after the start of treatment, given a two sided type I error probability of 0.05 and a 40% success rate in the standard group. This calculation

included a 5% adjustment for losses to follow-up, withdrawals, and missing data.²³

Statistical analysis

All analyses followed the intention to treat principle and included patients with protocol deviations. Analyses were performed with SAS software (version 9.1), with two sided significance tests at the 5% significance level for the primary outcome measure and, to adjust for multiple testing, the 1% significance level for secondary outcome measures. We also performed a sensitivity analysis excluding patients with deviations from the study protocol.

Primary and secondary analyses

We used Fisher's exact test to examine the difference in the primary outcome between groups and for the dichotomous secondary outcomes of prolonged treatment, adequate oral intake, and repeat visits to the emergency department. Rehydration at two hours and prolonged treatment were also analysed with multiple logistic regression models. Potential covariates identified a priori for rehydration at two hours were weight, administration of ondansetron, randomisation time, volumes of diarrhoea, vomiting, and oral rehydration consumed (mL/kg) as well as baseline bicarbonate concentration, pH, and score on clinical dehydration scale. For the outcome of prolonged treatment we additionally considered a history of previous intravenous rehydration during the current illness and bicarbonate concentration, pH, and score on clinical dehydration scale at four hours instead of baseline parameters. Because of sample size limitations and to avoid overfitting, the effect of these potential covariates was determined individually in univariate analysis. We considered those associated with the outcomes at a level of significance of <0.20 for inclusion in multiple logistic regression models provided they were not highly correlated with other variables.

We compared the clinical dehydration scores between groups at each 30 minute time point with the use of a mixed model repeated measures analysis of variance with adjustment for the baseline score. The median test was used to compare median times to discharge. The attending physician's comfort with discharge was analysed with a Cochrane test for linear trend.

Other analyses

We used Fisher's exact test for proportions or the *t* test for continuous variables, unless otherwise specified, to compare characteristics at four hours. The difference in biochemical parameters at four hours was evaluated with analysis of covariance with the baseline value serving as the covariate. Rehydration for children with moderate to severe dehydration (score ≥ 5) was analysed with Fisher's exact test.

Results

Participants

Between December 2006 and April 2010, we screened 785 children for participation; 278 met enrolment criteria, and 226 were enrolled, 114 to rapid rehydration and 112 to standard rehydration (fig 1). A total of 507 children did not meet the eligibility criteria (see table A in appendix on bmj.com). Protocol deviations were uncommon (14 patients) and equally distributed between groups. Baseline characteristics were similar across treatment groups (table 2). Only the primary (intention to treat) analysis is reported because the results were qualitatively similar to those of the sensitivity analysis.

Primary outcome

At two hours, 36% (41/114) of children given rapid intravenous rehydration and 29% (33/112) of those given standard rehydration were rehydrated (absolute difference for rapid *v* standard 6.5%, 95% confidence interval -5.7% to 18.7%; $P=0.32$). The point estimate of the absolute difference corresponds to 15 children needing to be treated for one child to achieve rehydration at two hours (number needed to treat). We repeated the primary analysis after controlling for baseline weight, score on clinical dehydration scale, and serum pH. Logistic regression analysis showed no significant association between treatment assignment and successful rehydration at two hours (odds ratio 1.8, 0.90 to 3.5; $P=0.10$, in favour of the rapid group).

Secondary outcomes

Tables 3 and 4 give details of the secondary outcomes. Overall, 52% (59/114) in the rapid rehydration group and 43% (48/112) in the standard group underwent prolonged treatment (absolute difference for rapid *v* standard, 8.9%, 21.0% to -5.0%; $P=0.19$). Logistic regression analysis showed no difference between the groups (odds ratio 0.81, 0.36 to 1.8; $P=0.61$, in favour of the standard group).

There were no significant differences in the mean scores on the clinical dehydration scale over time ($P=0.96$; fig 2) or in the proportions of children rehydrated at four hours (69% (79/114) and 69% (77/112) in the rapid and standard groups, respectively; absolute difference for rapid *v* standard 0.5%, -12.6% to 11.5%; $P>0.99$). Groups were similar in the proportions who achieved adequacy of oral intake (table 3) and the reasons for admission as stated by the attending physicians (see table B in appendix on bmj.com). More children in the rapid intravenous rehydration group were admitted to hospital at the index visit (33 *v* 19, $P=0.04$) (table 3). This difference persisted when we excluded from the analysis the children admitted to hospital because of their metabolic acidosis (number needed to harm = 9, 4 to 57).

Children admitted to hospital had similar unadjusted mean scores on the clinical dehydration scale in the rapid ($n=33$) and standard ($n=19$) groups at time 0 (4.9 (SD 1.2) *v* 4.9 (SD 1.2); $P=0.90$) and four hours (2.0 (SD 1.5) *v* 2.1 (SD 1.7); $P=0.82$), respectively. Although time to discharge was slightly higher in the rapid rehydration group, this did not achieve significance (6.3 hours *v* 5.0 hours; $P=0.03$). There was a trend in favour of standard rehydration in physician's comfort with discharge (table 3), and there were no differences between groups in the need for repeat visits (table 5).

Other analyses

The most clinically important biochemical difference was the change in serum bicarbonate (0.56 (SD 1.9) *v* -0.31 (2.2) mmol/L; standard *v* rapid; $P=0.01$) (table 4). After adjustment for baseline values, the values at four hours differed by 1.1 mmol/L. Additional fluid boluses were administered to 16 (14%) children who received standard and 11 (10%) who received rapid intravenous rehydration ($P=0.31$). Subgroup analysis of children with baseline scores ≥ 5 on the clinical dehydration scale showed no difference between groups in the proportions who achieved rehydration at two hours (16% rapid *v* 15% standard; absolute difference for rapid *v* standard rehydration 0.7%, -14.3% to 15.9%; $P>0.99$).

One child in each group developed an interstitial displacement of the intravenous catheter, which resulted in the administered fluids entering the immediate surrounding tissue. Unblinding was performed for one child in the rapid intravenous rehydration

group whose baseline serum sodium concentration was 114 mmol/L. One child in each group developed a dysnatraemia: one child who received rapid rehydration had a decrease in serum sodium concentration from 138 mmol/L to 130 mmol/L and one child who received standard rehydration experienced a decrease in concentration from 130 mmol/L to 128 mmol/L. Oedema was reported in four children in the standard group and two in the rapid group ($P=0.44$). No other safety concerns were reported.

Discussion

There is no difference in clinical effectiveness with rapid or standard intravenous rehydration for the treatment of dehydration in children with gastroenteritis. Despite the increasing adoption of this intervention into routine clinical care,^{1 9} we found that two hours after the initiation of rapid intravenous rehydration, the resolution of dehydration was similar to that achieved with standard treatment. Of interest, and of borderline significance after adjustment for multiple comparisons, children administered rapid intravenous rehydration were more commonly admitted to hospital at the index visit and received longer periods of intravenous rehydration. None of the outcome measures favoured the use of rapid intravenous rehydration, and there was a trend toward worse outcomes in the rapid intravenous rehydration group, calling into question its use.

Comparison with other studies

The results of our study are important as the literature contains a paucity of high quality studies that show that rapid intravenous rehydration is effective. The most rigorous to date was an unblinded randomised clinical trial that compared outcomes in 45 children administered 50 mL/kg of 0.9% saline over one hour with 43 children given the same volume over three hours.⁵ While the authors concluded that rapid intravenous rehydration is "efficacious," this outcome measure was not clearly defined. As this was a pilot study, according to the authors, a post hoc power analysis was conducted that showed that it had only a 60% power for detecting a clinically relevant difference between groups. Lastly, while the rate of fluid administration was evaluated, the volume of fluid administered was the same in both groups, and as the study was unblinded the authors could not objectively evaluate the impact of rapid intravenous rehydration on clinical dehydration status or decision making.

While several non-randomised studies have described cohorts of children who underwent rapid rehydration, the participants either had severe dehydration²⁴⁻²⁷ or were administered fluid boluses similar to our standard group.²⁸⁻³⁰ A single study evaluated the ability of rapid intravenous and rapid nasogastric rehydration (50 mL/kg of 0.9% saline versus Pedialyte (Abbott Laboratories, Columbus, OH, over three hours) to successfully treat children with moderate dehydration.³¹ While both treatment protocols were found to be safe and efficacious, the serum bicarbonate concentration in the nasogastric rehydration arm increased by 1.8 mmol/L, while those administered intravenous rehydration experienced a decline of 0.2 mmol/L ($P<0.001$). Furthermore, the urine specific gravity dropped to a normal level faster in the nasogastric arm than in the rapid intravenous rehydration arm ($P=0.02$). Although the authors assumed that more children administered rapid intravenous rehydration would be ready for discharge at three hours, no difference was detected.

Although no standardised rapid intravenous rehydration strategy exists, a survey of North American physicians who specialise in paediatric emergency medicine found that various regimens

are used.⁹ Given that we found no benefit with our intervention, which is more aggressive than most rapid intravenous rehydration strategies, our findings can be generalised to those who use smaller fluid boluses (such as 40 mL/kg).³² There are several possible explanations as to why the use of rapid intravenous rehydration did not result in improved clinical outcomes. The most plausible physiological explanation could be the clinical impact of metabolic acidosis induced by large volume 0.9% saline administration. Although the development of a hyperchloraemic acidosis seems counterintuitive, it has previously been described in children with gastroenteritis^{5 26 31} and those undergoing general anaesthesia.^{33 34} The worsening acidosis, which is caused by a reduction in the anion gap from the excessive rise in plasma chloride and excessive renal elimination of bicarbonate,³⁵ has been associated with fatigue, impaired abstract thinking, and abdominal pain.³⁶

Other potential explanations could include the existence of a time lag between intravascular volume repletion and the resolution of clinical dehydration, or that the clinical dehydration scale overestimated the severity of dehydration in our study population. While no data are available to support the former hypothesis, the dehydration scale used has previously performed well in evaluating children similar to those enrolled in our study.¹³⁻¹⁵ The scale, however, might have overestimated the severity of dehydration in some children, as our standard rehydration protocol (20 mL/kg) was sufficient to rehydrate many of the study participants.

In addition to lacking evidence of effectiveness, the routine use of intravenous fluid bolus treatment should be reconsidered as children initially diagnosed with gastroenteritis might have alternative or coexistent disease processes that, when treated with rapid intravenous rehydration, might result in important complications. Examples include patients with myocarditis who, if given excessive volumes of intravenous fluids, can suddenly decompensate³⁷⁻⁴⁰ and those with diabetic ketoacidosis³⁹ and diabetes insipidus⁴⁰ who can develop cerebral oedema.

Strengths and limitations

The strengths of this study include the rigorous measures used to ensure blinding and minimise the risk of bias. Moreover, this was a large pragmatic study that included patients typical of those who receive intravenous rehydration in developed countries, thus supporting the generalisability and external validity of our findings. Because of the diagnostic imprecision of available clinical characteristics used in assessing dehydration and the poor sensitivity of individual features such as capillary refill time (lower 95% confidence limit 29%),²² we used a four item clinical scale to maximise the probability of enrolling moderately dehydrated children. This resulted in the exclusion of 131 children who were given intravenous rehydration but did not meet the criteria for severity of dehydration. Nevertheless, we probably enrolled some children with mild dehydration. The inclusion of this group enhances the pragmatic nature of this trial as our study population is similar to those included in other intravenous rehydration studies in developed countries,⁴¹⁻⁴⁴ and hence are candidates for rapid intravenous rehydration. Furthermore, subgroup analysis did not show a trend towards increased benefit in children with more severe dehydration.

Although, in certain regions, alternative rehydration strategies such as persistence with oral rehydration or the use of nasogastric fluid treatment might be more commonly used, we aimed to conduct a pragmatic trial in keeping with current practice patterns.⁹ Because of ethical and logistical reasons we did not study children with compromised cardiovascular stability

so our results cannot be generalised to such children. Lastly, we did not blind the attending physicians to the repeat electrolyte results, which could have influenced the final outcome. The attending physician's level of comfort with discharge at four hours, however, was assigned before the availability of the repeat laboratory results and no difference between groups was detected. Moreover, the same numbers of children (n=3) were admitted in each study arm primarily because of the severity of their metabolic acidosis.

Conclusions and policy implications

In summary, our study of haemodynamically stable children with gastroenteritis who were deemed to require intravenous rehydration found no beneficial clinical effects from the administration of rapid intravenous rehydration. Given the potential risks associated with this approach, its routine use in such children should be reconsidered.

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Contributors: SBF acquired the data, supervised the study, drafted the manuscript, and is guarantor. SBF, PCP, SS were responsible for study concept and design. SBF, ARW, and Derek Stephens were responsible for statistical analysis. SBF and SS provided administrative, technical, or material support. All authors obtained funding, analysed and interpreted data, critically revised the manuscript for important intellectual content, and had full access to all of the data in the study and can take responsibility for the integrity of the data and the accuracy of the data analysis.

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Competing interests: All authors have completed the ICMJE uniform disclosure form at www.icmje.org/coi_disclosure.pdf (available on request from the corresponding author) and declare: no support from any organisation for the submitted work; SBF has previously served as a consultant for Baxter Healthcare, which might have an interest in the submitted work; no other relationships or activities that could appear to have influenced the submitted work.

Ethical approval: The study was approved by The Hospital for Sick Children's research ethics board. Written informed consent was obtained from caregivers, and participant assent was obtained when appropriate.

Data sharing: No additional data available.

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What is already known on this topic

There is a lack of good quality evidence from clinical trials to make a clinical recommendation on the optimal rate of administration of intravenous fluid in children

What this study adds

Our study found no clinical benefits from the use of rapid intravenous rehydration in children with mild to moderate dehydration secondary to gastroenteritis

Given the absence of evidence to support the use of rapid intravenous rehydration and the potential side effects that can occur, it seems prudent to avoid the routine use of rapid rehydration in children with gastroenteritis

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Tables

Table 1 | Clinical dehydration scale* used in children with gastroenteritis

Characteristic	Score category		
	0	1	2
General appearance†	Normal	Thirsty, restless, or lethargic but irritable when touched	Drowsy, limp, cold or sweaty, comatose
Eyes	Normal	Slightly sunken	Very sunken
Mucous membranes‡	Moist	Sticky	Dry
Tears	Present	Decreased	Absent

*Higher scores indicate more severe dehydration. Scores range from 0 to 8. Scores 0= $\leq$ 3% dehydration (positive likelihood ratio 2.2, 95% confidence interval 0.9 to 5.3), scores 1-4=some (3-6%) dehydration (1.3, 0.9 to 1.7), and scores 5-8=moderate to severe ($\geq$ 6%) dehydration (5.2, 2.1 to 12.8).⁴⁵

†“Normal” includes children who might be sleeping but are easily aroused to normal level of consciousness. Takes into account time of day and child's usual pattern as described by child's parent/guardian.

‡Assessed on buccal mucosa and tongue, and not lips.

Table 2 Baseline characteristics in children with gastroenteritis according to different methods of intravenous rehydration.* Figures are means (SD) unless stated otherwise

Characteristic	Rapid intravenous rehydration (n=114)	Standard intravenous rehydration (n=112)
Median (IQR) age (years)†	2.2 (1.4-3.8)	2.4 (1.3-4.2)
Weight (kg)	13.4 (4.9)	14.2 (5.4)
Serum values at catheterisation:		
Sodium (mmol/L)	136.3 (4.2)	136.7 (3.8)
Potassium (mmol/L)	4.2 (0.7)	4.3 (0.6)
Bicarbonate (mmol/L)	18.0 (3.9)	18.1 (3.5)
No (%) with bicarbonate ≤15 mmol/L	31 (27)	23 (21)
Blood urea nitrogen (mmol/L)	5.7 (3.1)	5.4 (2.2)
Creatinine (µmol/L)	36.3 (11.2)	35.0 (8.5)
Glucose (mmol/L)	4.6 (1.3)	4.5 (1.4)
pH	7.36 (0.06)	7.37 (0.06)
Clinical characteristics:		
Temperature (°C)	38.1 (0.6)	38.1 (0.7)
Respiratory rate (breaths/min)	28 (6)	27 (6)
Heart rate (beats/min)	127 (20)	127 (20)
Oxygen saturation (%)	99 (1)	98 (1)
Clinical dehydration scale score‡	4.5 (1.2)	4.5 (1.2)
No (%) with clinical dehydration scale score ≥5	45 (40)	47 (42)
Capillary refill time (sec)	0.86 (0.42)	0.82 (0.42)
No (%) with previous visit to emergency department	41 (36)	43 (38)
No (%) who received ondansetron in emergency department	43 (38)	44 (39)

IQR=interquartile range.

*No significant differences between groups.

†Age distribution non-parametric; compared with median test.

‡Higher values indicate more severe dehydration.

Table 3| Secondary outcomes over time according to different methods of rehydration in children with gastroenteritis. Figures are numbers (percentage) of children unless stated otherwise

	Rapid intravenous rehydration group (n=114)	Standard intravenous rehydration group (n=112)	P value*
Prolonged treatment†	59 (52)	48 (43)	0.18
Hospital admission at initial visit	33 (29)	19 (17)	0.04
Emergency department length of stay >6 hours	40 (35)	37 (33)	0.78
Revisit resulting in admission	7 (6)	5 (5)	0.77
Adequacy of oral intake‡:			
5 mL/kg at 2 hours	29 (25)	36 (32)	0.31
5 mL/kg at 4 hours	50 (44)	46 (41)	0.69
10 mL/kg at 2 hours	13 (11)	15 (13)	0.54
10 mL/kg at 4 hours	25 (22)	24 (21)	0.87
Mean (SD) volume consumed (mL/kg), 0-2 hours	4.0 (6.3)	4.1 (4.5)	0.86
Mean (SD) volume consumed (mL/kg), 0-4 hours	7.2 (9.8)	5.9 (6.2)	0.23
Vomited during 4 hour study period	22 (19)	14 (13)	0.20
Physician was comfortable with discharge§:			
2 hours	30 (26)	42 (38)	0.07
4 hours	61 (54)	74 (66)	0.06
Emergency department revisits¶:			
Within 3 days	16 (14)	13 (12)	0.69
Within 7 days	17 (15)	19 (17)	0.72

*For comparisons of standard with rapid intravenous rehydration.

†Composite outcome measure defined as any of: admission to hospital at initial visit, stay of >6 hours after start of intravenous treatment, or revisit resulting in admission within 72 hours of start of treatment.

‡Defined a priori as consuming at least 5 mL/kg of liquid per 2 hour time period.

§Physicians determined to be comfortable with discharge if they either "strongly agreed" or "agreed," on 5 point Likert scale, that child was ready for discharge at indicated time points. P values represent analysis of responses with Cochrane test for linear trend.

¶No of children contacted on day 3: 114 in rapid rehydration group; 111 in standard rehydration group. No of children contacted on day 7: 114 and 109, respectively.

Table 4| Clinical and biochemical characteristics over time according to different methods of rehydration in children with gastroenteritis*. Figures are means (SD) unless stated otherwise

	Rapid intravenous rehydration (n=114)	Standard intravenous rehydration (n=112)	P value*
Serum values, time 4 hours (least squares means)†:			
Sodium (mmol/L)	138.0 (2.0)	137.5 (2.0)	0.06
Potassium (mmol/L)	3.8 (0.48)	3.9 (0.48)	0.01
Bicarbonate (mmol/L)	17.4 (2.1)	18.5 (2.1)	<0.001
Blood urea nitrogen (mmol/L)	3.8 (2.0)	4.1 (1.7)	<0.001
Creatinine (μmol/L)	32.3 (8.2)	33.1 (8.1)	0.003
Glucose (mmol/L)	5.4 (1.6)	5.1 (1.2)	0.20
pH	7.34 (0.04)	7.35 (0.04)	0.10
Clinical characteristics:			
Respiratory rate (breaths/min):			
120	27 (6)	25 (5)	0.14
240	26 (5)	25 (5)	0.09
Heart rate (beats/min):			
120	122 (19)	125 (19)	0.17
240	121 (16)	118 (17)	0.13
% Weight change between time 0 and 4 hrs	3.9 (3.9)	1.9 (3.2)	<0.001

*For comparisons of standard with rapid intravenous rehydration.

†Obtained in 219 children for sodium; 218 for potassium; 214 for bicarbonate; 216 for blood urea nitrogen; 218 for creatinine; 211 for glucose; 172 for pH.

Table 5| Follow-up data* according to different methods of rehydration in children with gastroenteritis. Figures are numbers (percentage) of children unless stated otherwise

Variable	Rapid intravenous rehydration (n=114)	Standard intravenous rehydration (n=112)
Follow-up on day 3		
Completed follow-up	114/114 (100)	111/112 (99)
Mean interval between enrolment and follow-up (days)	4.1	3.7
Return visit to emergency department	16/114 (14)	13/111 (12)
Intravenous rehydration	10/114 (9)	5/111 (5)
Hospital admission	7/114 (6)	5/111 (5)
Follow-up on day 7		
Completed follow-up	114/114 (100)	109/112 (97)
Mean interval between enrolment and follow-up (days)	8.2	8.3
Return visit to emergency department	1/114 (1)	7/109 (6)
Intravenous rehydration	1/114 (1)	5/109 (5)
Hospital admission	0/114 (0)	3/109 (3)
Follow-up on both days		
Any return visit to emergency department	16/114 (14)	19/109 (17)
Any intravenous rehydration	11/114 (10)	10/109 (9)

*There were no significant ($P<0.01$) differences between groups.

Figures

Fig 1 Eligibility, randomisation, and follow-up of study participants. Data were available for all 226 infants for primary outcome of rehydration at two hours

Fig 2 Score on clinical dehydration scale as continuous variable analysed with repeated measures analysis of variance (ANOVA) adjusted for baseline score in children allocated to standard or rapid intravenous rehydration. Time 0 represents all children at the start of rehydration protocol. Data for each time point represent mean score with 95% confidence intervals, as recorded by research nurse every 30 minutes until completion of protocol at 240 minutes (four hours). No significant difference between groups in scores through study period ($P=0.96$)