Rapid Intravenous Rehydration Therapy in Children With Acute Gastroenteritis

A Systematic Review

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Background: Rapid intravenous (IV) rehydration is commonly used for the management of pediatric gastroenteritis in the emergency department. The current practice shows wide variation in the volume and rate of rapid IV hydration. The aim of this review was to assess the efficacy of rapid IV rehydration compared with standard method in children with gastroenteritis.
Method: MEDLINE (1946–2014), EMBASE (1974–2014), and CENTRAL via the Cochrane Library (Issue 8, 2014) were systematically searched to identify eligible studies. Inclusion criteria were randomized controlled trials of rapid IV rehydration in children with gastroenteritis.
Results: A total of 1513 articles were retrieved, and our inclusion criteria were met by 3 studies, with a total of 464 participants. The percentage of children who were successfully rehydrated and tolerated oral fluids at 2 to 4 hours after starting IV fluid therapy ranged from 69% to 100% in both rapid IV rehydration and standard method. Time to discharge ranged from 2 to 6 hours (rapid rehydration) versus 2 to 5 hours (standard rehydration). Emergency department revisits ranged from 3% to 16% (rapid rehydration) versus 5% to 14% (standard). Summarized results suggested that rapid IV rehydration may be associated with longer time-to-discharge and higher readmission rates. The new evidence fails to demonstrate superiority of large-volume (60 mL/kg/h) over standard (20 mL/kg/h) IV rehydration.
Conclusions: Standard volume IV rehydration for 1 to 4 hours followed by oral hydration or maintenance IV fluids seems sufficient for most children with gastroenteritis requiring IV fluid administration. However, more evidence is needed to establish an optimal IV rehydration regimen.

Key Words: gastroenteritis, intravenous, rapid, rehydration, dehydration

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Acute gastroenteritis in infants and children is a common reason for visiting the emergency department (ED). Among children younger than 5 years old in the United States, gastroenteritis has been accounting for greater than 1.5 million outpatient visits, 200,000 hospital admissions, and nearly 300 deaths each year.[1] Dehydration remains the most frequent and serious complication of gastroenteritis.[2] The severity of dehydration was classified by the World Health Organization into 3 clinical categories: no dehydration (<5% weight loss), mild-to-moderate dehydration (5%-10% weight loss), and severe dehydration (≥10% weight loss).[3] A recent advance in the management of gastroenteritis has been changed to rapid oral rehydration therapy (ORT) for a 4-hour period, which was introduced as the first-line treatment for all children with gastroenteritis.[4] When oral rehydration is not feasible, intravenous (IV) rehydration with 20 mL/kg/h of 0.9% saline solution for 2 to 4 hours, followed by resumption of oral rehydration or continuous infusion of dextrose-containing solution at maintenance rate, seems adequate for initial rehydration of most patients requiring IV fluid therapy.[5] The World Health Organization recommends IV rehydration for 3 to 6 hours for children with severe dehydration due to gastroenteritis.[3] Rapid IV rehydration has been gradually incorporated into clinical practice by many emergency physicians aiming for rapid recovery and decreased length of stay in the overcrowded ED.[6] The objective of this study was to assess the efficacy of rapid IV rehydration compared with standard IV rehydration scheme in children with mild-to-moderate dehydration secondary to acute gastroenteritis.

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METHODS

Search Strategies and Data Sources

Eligible studies were identified using electronic databases and manual searches of the reference lists of included papers for potentially relevant articles, in addition to direct communications with experts in the field. MEDLINE/OVID SP (1946-September 2014), EMBASE/OVID SP (1974-September 2014), and Cochrane Central Register of Controlled Trials (CENTRAL) through The Cochrane Library (Issue 8, August 2014) were searched. A search strategy including a combination of the following medical subject heading (MeSH) terms and key words was used: "(gastroenteritis OR diarrhea) AND (dehydration OR rehydration) AND intravenous AND (rapid OR ultra-rapid) AND (children OR pediatrics)." The search limits included age from birth to 18 years, and no language restrictions were used.

Study Selection

Inclusion criteria were (1) randomized controlled trials describing rapid IV rehydration in children with mild-to-moderate dehydration secondary to acute gastroenteritis, (2) children from birth to 18 years old, and (3) standard IV rehydration therapy as comparator. Exclusion criteria were (1) studies describing children with severe dehydration, (2) noncomparative or descriptive studies as they are susceptible to bias and confounding factors, (3) studies describing ORT or nasogastric rehydration therapy, (4) studies of adult population, (5) animal studies, and (6) disease states other than gastroenteritis. Articles were screened by 2 independent investigators for relevance and eligibility criteria. Differences in selection were resolved through discussions between the reviewers.

Data Extraction

Data were extracted from each eligible study regarding the setting, design, study population, interventions, comparators, and outcomes. Outcome measures were defined a priori. The outcome measures were clinical rehydration, rate of hospitalization, ED length of stay, ED revisit, complications, and electrolyte imbalance.

TABLE 1. The Effective Public Health Practice Project Quality Assessment Tool[7]

Domains	Description
Selection bias	Representativeness of sample and participation rates is evaluated.
Study design (allocation bias)	Design is evaluated.
Confounders	Presence of confounders is evaluated.
Blinding (detection bias)	Blinding of outcomes is assessed.
Data collection methods	Validity and reliability of data collection tools are evaluated.
Completeness of follow-up, withdrawals/dropouts (attrition bias)	The percentage of participants completing the study is evaluated. Withdrawals and dropouts are evaluated in terms of numbers and/or reasons per group.

Critical Appraisal

The quality and risk of bias in the eligible studies were assessed using the quality assessment tool for quantitative studies developed by the Effective Public Health Practice Project, Canada (http://www.city.hamilton.on.ca/phcs/EPHPP/).[7] The criteria of the tool consist of 6 domains: selection bias, allocation bias, confounders, detection bias, data collection methods, and attrition bias (Table 1). The 6 components were rated as strong, moderate, or weak quality by 2 independent investigators, and the global quality ratings per study were totaled. The quality assignment for each study was rated as follows: strong (4 strong ratings with no weak ratings), moderate (less than 4 strong ratings and 1 weak rating), or weak (2 or more weak ratings). The interrater reliability for the raters was calculated for 3 studies using the κ statistic and was found to be excellent ($\kappa = 0.85$, $P < 0.001$).

Data Analysis

A meta-analysis of the randomized controlled trials was not feasible due to a paucity of eligible studies, heterogeneity of study design, variable outcome measures, and the risk of bias in the identified studies. The results of included studies have been summarized, tabulated, and evaluated for identified evidence. Quantitative variable mean values of serum electrolytes and blood sugar pretreatment and posttreatment were compared using the paired *t* test, and the results are presented together with 95% confidence intervals (CIs).

RESULTS

Figure 1 demonstrates the selection process of articles in the review. Three trials, with a total of 464 participants, met the inclusion criteria, and their results were analyzed. In addition, a further analysis of the electrolyte values in 1 of the 3 studies was reviewed (Table 2).

Nager and Wang[8] conducted a pilot study to evaluate the ability of large-volume rapid IV fluids to rehydrate children aged 3 to 36 months with gastroenteritis. The patients were randomized to receive 50 mL/kg of 0.9% normal saline through either

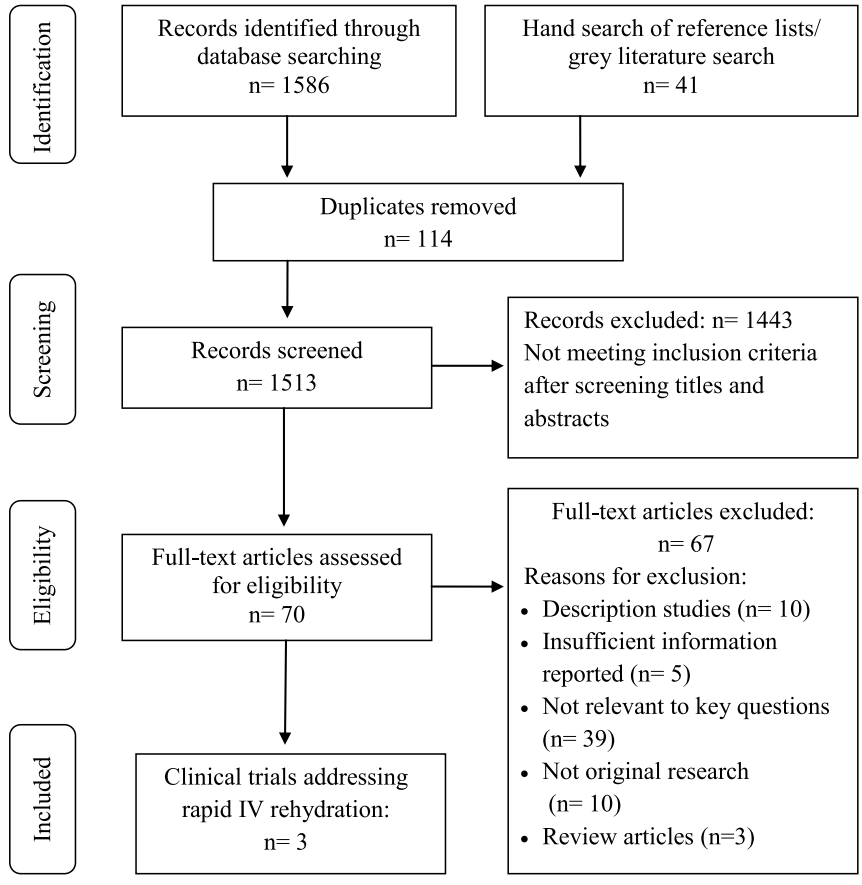

FIGURE 1. Flow diagram of study selection.

TABLE 2. Description of Randomized Clinical Trials Addressing Rapid IV Rehydration Therapy

Study, Year of Publication	Setting	Dehydration Severity	Sample Size	Fluid Volume, mL/kg	Solution and Concentration	Infusion Period, h	Quality Rating
Nager and Wang,[8] 2010	ED, United States	Moderate	45	50 (rapid)	0.9% saline	1	Moderate
			43	50 (standard)	0.9% saline	3	
Freedman and Geary,[9] 2011	ED, Canada	Moderate	112	60 (rapid)	0.9% saline	1	Strong
			114	20 (standard)	0.9% saline	1	
Azarfar et al,[11] 2014	ED, Iran	Moderate	75	20–30 (rapid)	Crystalloid solution	2	Weak
			75	30–35 (standard)	Crystalloid solution	4	

ED, Emergency Department

ultrarapid infusion for 1 hour or rapid infusion for 3 hours. The study was nonblinded and included only a small number of participants. Outcome measures were not clearly defined. Ultrarapid rehydration was well tolerated and similar to rapid hydration as suggested by the mean emesis volume (69 mL/h vs 63 mL/3 h, respectively), urine volume (93 mL/h vs 71 mL/3 h, respectively), and stool output (45 mL/h vs 75 mL/3 h, respectively; $P = 0.042$). The latter 2 results should be interpreted with caution because of the differences in the hydration time. The initial urine specific gravity (1.025) was the same in both treatment groups, with significantly different posthydration reduction in the ultrarapid method compared with standard hydration (1.015 vs 1.020, $P = 0.028$). Ultrarapid rehydration decreased the length of stay in the ED and allowed for earlier discharge from the ED than the standard rehydration method (2 vs 4 hours). No patients had serious complications, seizures, electrolyte disturbance, or overhydration related to fluid administration, although the study was not powered to assess potential safety concerns. One patient in each treatment group developed hypoglycemia in the postintervention phase. Of the ultrarapid patients discharged, 7 (15.6%) of 45 returned for additional treatment (six received oral fluids and one received IV fluids), and 6 (14.0%) of 43 of the standard patients returned (five treated with oral fluids and one treated with IV rehydration); all were improved.

A double-blind clinical trial was conducted in the ED of a tertiary children's hospital in Canada by Freedman et al,[9] comparing large-volume versus standard-volume IV rehydration in children, aged 3 months to 11 years, with dehydration secondary to gastroenteritis. The sample size was large (226 children), and the method of randomization was clearly described. Children in whom oral rehydration failed were randomized (1:1 allocation) to either large-volume (60 mL/kg) or standard-volume (20 mL/kg) IV rehydration for 1 hour. The time limit of the oral rehydration trial before randomization and definition of treatment failure were not clearly described. Severity of dehydration was defined on the basis of a validated 8-point clinical dehydration scale. Outcome measures were clearly defined. The primary outcome was clinical hydration, as defined by a score of 1 or lower after 2 hours from the beginning of therapy. At 2 hours of treatment, hydration was achieved in 36% of patients receiving large-volume infusions versus 29% of those receiving standard-volume infusions (difference of 6.5%; 95% CI, −5.7% to 18.7%). At 4 hours, clinical rehydration was achieved in 69% of patients receiving either treatment (difference of 0.5%; 95% CI, −12.6% to 11.5%). Prolonged treatment was observed in 52% of large-volume versus 43% of standard-volume rehydration patients (difference of 8.9%; 95% CI, −5.0% to 21.0%). No clinically significant difference was observed between large-volume and standard rehydration regarding ED length of stay greater than 6 hours (35% vs 33%) or ED revisits requiring admission (6% vs 5%). One child developed hyponatremia in each group. Overhydration in the form of edema was reported in 4 patients treated with the standard method and 2 patients by the large-volume approach, denoting inconsistent assessment of their dehydration severity. Subgroup analysis of children presenting with severe dehydration (baseline scores ≥ 5 on the clinical dehydration scale) and who achieved rehydration at 2 hours did not reveal greater clinical benefits of large-volume rehydration over standard rehydration. Children included in the large-volume fluid bolus arm had a longer median time-to-discharge compared with those treated with the standard method (6.3 vs 5.0 hours, $P = 0.03$). However, the significance level of P value was set to 0.01 for multiple testing. The frequency of ED revisits within 3 days was 14% in patients receiving large-volume rapid IV rehydration and 12% in those treated with the standard method ($P = 0.69$). Physician's comfort with discharge gave preference to the standard IV rehydration regimen. There was no evidence of clear clinical benefits of large-volume rapid rehydration, with the potential of worse outcome in patients receiving large-volume regimen.

The risk of developing hyponatremia when large-volume bolus fluid therapy was used for rehydrating children with gastroenteritis was evaluated by Freedman and Geary.[10] It was based on the same population as the study conducted by Freedman et al in 2011.[11] Children in whom ORT failed were randomized to either large-volume

TABLE 3. Clinical and Laboratory Outcome Measures of Rapid IV Rehydration Studies

Outcome Measures		Successful Rehydration at 2 to 4 h	Tolerance of Oral Fluid at 2 to 4 h	Electrolyte Disturbances	Complications	ED Revisits
Nager and Wang,[8] 2010	Rapid	100% (45/45)	100% (45/45)	0% (0/45)	0% (0/45)	16% (7/45)
	Standard	100% (43/43)	100% (43/43)	0% (0/43)	0% (0/43)	14% (6/43)
Freedman and Geary,[9] 2011	Rapid	69% (79/114)	69% (79/114)	0.9% (1/114)	1.8% (2/114)	14% (16/114)
	Standard	69% (77/112)	73% (82/112)	0.9% (1/112)	3.6% (4/112)	12% (13/111)
Azarfar et al,[11] 2014	Rapid	84% (63/75)	84% (63/75)	0% (0/75)	0% (0/75)	3% (2/63)
	Standard	82% (62/75)	82% (62/75)	0% (0/75)	0% (0/75)	5% (3/62)

(60 mL/kg) or standard (20 mL/kg) IV rehydration using bolus 0.9% saline for 1 hour, followed by 0.9% saline for 3 hours at a maintenance rate. Outcome measures were clearly defined in the methodology, although it was a secondary analysis of previously collected data. Development of hyponatremia at 4 hours of treatment was the primary outcome measure. In both groups, similar numbers of children were hyponatremic at 4 hours of treatment (large volume, 21% [23/112]; standard, 20% [21/105]; $P = 0.92$). Among children with hyponatremia before the start of treatment, 63% (30/48) in the large-volume group and 44% (15/34) in the standard-volume group had improvement of their hyponatremia at 4 hours ($P = 0.10$). Children who received large-volume IV rehydration experienced a mean serum sodium increase of 2 mEq/L or greater (59/112 vs 39/105, $P = 0.02$) and were less likely to experience a sodium decrease of 2 mEq/L or greater (8/112 vs 17/105, $P = 0.04$) than those rehydrated with the standard method. At 4 hours of treatment, there was no difference in the number of children who developed hypernatremia (standard, 1/105; large, 3/112; $P = 0.62$).

The most recent trial by Azarfar et al[11] compared rapid IV rehydration with standard 24-hour IV rehydration in children with moderate dehydration due to gastroenteritis. One hundred fifty children were randomized (1:1 ratio) to receive crystalloid solution either 20 to 30 mL/kg for 2 hours or 30 to 35 mL/kg for 4 hours. Outcome measures were not clearly defined. At 2 hours from starting IV fluids, 84% of patients in the rapid rehydration group were successfully rehydrated, vomiting resolved, and discharged. Two of 63 discharged patients had vomiting and readmitted to ED. In the standard rehydration group, 83% recovered from dehydration by the end of 4-hour infusion period, and three of them had persistent vomiting for more than 12 hours. No adverse events or complications were reported in both treatment groups.

Overall Result

Successful rehydration and ability to take oral fluids were achieved in 69% to 100% of both rapid and standard IV rehydration. Emergency department time to discharge ranged from 2 to 6 hours (rapid rehydration) versus 2 to 5 hours (standard method). The rates of electrolyte alterations ranged from 0.0% to 0.9% of both rapid and standard IV rehydration (Table 3). The frequency of ED revisits ranged from 3% to 16% (rapid rehydration) versus 5% to 14% (standard). The measurements of serum electrolytes in some studies showed significant changes in potassium, sodium, and blood sugar at 4 hours of treatment (Table 4). None of the studies were sufficiently powered to assess safety concerns.

DISCUSSION

Despite superiority of oral rehydration, IV rehydration therapy for pediatric gastroenteritis is frequently practiced by emergency physicians.[12] Intravenous rehydration should be reserved for patients who fail ORT (insufficient intake, persistent vomiting, worsening diarrhea, or dehydration) or those with severe dehydration.[13] The possibility of electrolyte disturbance and the effects of fluid shift between intracellular and extracellular spaces with rapid fluid resuscitation remain potential safety concerns. The conditions that could be worsened by administration of large amount of fluids, such as hyponatremia/hypernatremia, are not common and might be not enrolled in available studies. The changes in serum electrolytes and blood sugar during IV rehydration were trivial or not clinically relevant during the short term of treatment. A recent trial by Levy et al[14] reported no clear evidence supporting dextrose administration during rapid IV rehydration. The new evidence of large-volume (60 mL/kg/h) bolus fluid

TABLE 4. Prerehydration and Postrehydration Measurements of Serum Electrolytes and Blood Sugar Has Been Demonstrated by 2 Rapid IV Rehydration Trials

Study, Year of Publication	Sodium, mmol/L				Potassium, mmol/L				Bicarbonate, mmol/L				Glucose, mmol/L			
	Pre	Post	Difference (95% CI)	P	Pre	Post	Difference (95% CI)	P	Pre	Post	Difference (95% CI)	P	Pre	Post	Difference (95% CI)	P
Nager and Wang,[8] 2010 (rapid)	140 ± 4.4	141 ± 3.7	−1 (−2.70 to 0.70)	0.246	4.3 ± 0.53	4.0 ± 0.56	0.3 (0.07–0.53)	0.010	16.8 ± 3.5	15.1 ± 2.7	1.7 (0.39–3.01)	0.012	5.3 ± 1.3	4.4 ± 1.0	0.9 (0.41–1.39)	<0.001
Nager and Wang,[8] 2010 (standard)	141 ± 4.1	142 ± 3.9	−1 (−2.72 to 0.72)	0.250	4.4 ± 0.64	4.1 ± 0.57	0.3 (0.04–0.56)	0.024	16.5 ± 2.6	16.0 ± 3.1	0.5 (−0.73 to 1.73)	0.420	5.4 ± 1.1	4.4 ± 0.7	1 (0.61–1.40)	<0.001
Freedman and Geary,[9] 2011 (rapid)	136.3 ± 4.2	138.0 ± 2.0	−1.7 (−2.57 to −0.83)	<0.001	4.2 ± 0.7	3.8 ± 0.48	0.4 (0.24–0.56)	<0.001	18.0 ± 3.9	17.4 ± 2.1	0.6 (−0.23 to 1.43)	0.153	4.6 ± 1.3	5.4 ± 1.6	−0.8 (−1.18 to −0.42)	<0.001
Freedman et al,[9] 2011 (standard)	136.7 ± 3.8	137.5 ± 2.0	−0.8 (−1.59 to −0.01)	0.048	4.3 ± 0.6	3.9 ± 0.48	0.4 (0.26–0.54)	<0 .001	18.1 ± 3.5	18.5 ± 2.1	−0.4 (−1.15 to 0.35)	0.297	4.5 ± 1.4	5.1 ± 1.2	−0.6 (−0.94 to −0.26)	<0.001

therapy is inconsistent and fails to show any superiority over standard (20 mL/kg/h) IV rehydration. The possible explanation for failure of large-volume IV hydration to provide better clinical outcome is the hyperchloremic acidosis produced by large volumes of 0.9% normal saline, resulting in delay in recovery from dehydration.[15]

Limitations of this Study

(1) Standard methods of IV rehydration schemes are not well defined. (2) No evidence of large-volume vs standard IV rehydration. (3) There is debate about how to best measure degree of dehydration and the appropriate use of dehydration scales. (4) Wide variation in rehydration regimens limits the ability to make significant and generalizable conclusions. (5) This study has small sample size.

Our systematic review is more rigorous and helps to address the gap in the literature regarding rapid IV rehydration volume compared with the review by Gorelick[16] in 2002. The evidence for standard IV rehydration scheme as a treatment strategy for children with gastroenteritis has been strengthened by the findings of new studies, with higher quality ratings, published in the last few years.

CONCLUSIONS

Overall, the new evidence regarding IV rehydration is not consistent. The discharge and readmission rates showed no consistent, statistically significant difference between the standard and rapid or ultrarapid rehydration approaches for children with dehydration due to gastroenteritis. When oral rehydration is not feasible, standard IV rehydration (20 mL/kg/h) for 1 to 4 hours followed by oral or maintenance IV fluids is adequate for most patients with uncomplicated gastroenteritis. Furthermore, large multicenter randomized trials are needed to achieve the optimal IV rehydration approach for pediatric gastroenteritis.

REFERENCES

1. King CK, Glass R, Bresee JS, et al. Managing acute gastroenteritis among children: oral rehydration, maintenance, and nutritional therapy. In: *MMWR Recomm Rep*. vol. 52. 2003:1–16.
2. Tanaka G, Faruque AS, Luby SP, et al. Deaths from rotavirus disease in Bangladeshi children: estimates from hospital-based surveillance. *Pediatr Infect Dis J*. 2007;26:1014–1018.
3. World Health Organization. *The Treatment of Diarrhoea. A Manual for Physicians and Other Senior Health Workers*. 4th rev. ed. Geneva, Switzerland: World Health Organization; 2005.
4. National Collaborating Centre for Women's and Children's Health (UK). *Diarrhoea and Vomiting Caused by Gastroenteritis: Diagnosis, Assessment and Management in Children Younger than 5 Years*. London: RCOG Press; 2009. Available at: http://www.ncbi.nlm.nih.gov/books/NBK63844/.
5. Guarino A, Ashkenazi S, Gendrel D, et al. European Society for Paediatric Gastroenterology, Hepatology, and Nutrition/European Society for Paediatric Infectious Diseases Evidence-based Guidelines for the Management of Acute Gastroenteritis in Children in Europe: update 2014. *J Pediatr Gastroenterol Nutr*. 2014;59:132–152.
6. Simpson JN, Teach SJ. Pediatric rapid fluid resuscitation. *Curr Opin Pediatr*. 2011;23:286–292.
7. Thomas BH, Ciliska D, Dobbins M, et al. A process for systematically reviewing the literature: providing the research evidence for public health nursing interventions. *Worldviews Evid Based Nurs*. 2004;1:176–184.
8. Nager AL, Wang VJ. Comparison of ultrarapid and rapid IV hydration in pediatric patients with dehydration. *Am J Emerg Med*. 2010;28:123–129.
9. Freedman SB, Parkin PC, Willan AR, et al. Rapid versus standard IV rehydration in paediatric gastroenteritis: pragmatic blinded randomised clinical trial. *BMJ*. 2011;343:d6976.
10. Freedman SB, Geary DF. Bolus fluid therapy and sodium homeostasis in paediatric gastroenteritis. *J Paediatr Child Health*. 2013;49:215–222.
11. Azarfar A, Ravanshad Y, Keykhosravi A, et al. Rapid intravenous rehydration to correct dehydration and resolve vomiting in children with acute gastroenteritis. *Turk J Emerg Med*. 2014;14:111–114.
12. Freedman SB, Sivabalasundaram V, Bohn V, et al. The treatment of pediatric gastroenteritis: a comparative analysis of pediatric emergency physicians' practice patterns. *Acad Emerg Med*. 2011;18:38–45.
13. Niescierenko M, Bachur R. Advances in pediatric dehydration therapy. *Curr Opin Pediatr*. 2013;25:304–309.
14. Levy JA, Bachur RG, Monuteaux MC, et al. Intravenous dextrose for children with gastroenteritis and dehydration: a double-blind randomized controlled trial. *Ann Emerg Med*. 2013;61:281–288.
15. Handy JM, Soni N. Physiological effects of hyperchloraemia and acidosis. *Br J Anaesth*. 2008;101:141–150.
16. Gorelick MH. Rapid intravenous rehydration in the emergency department: a systematic review. *Pediatr Emerg Med Database*. 2002. Available at: http://www.pemdatabase.org/files/rapid_iv_hydration_23.07.doc. Accessed September 4, 2014.