Effect of Intravenous Fluid Administration on Acid-Base Balance in Patients Undergoing Colonoscopy

Phongthara Vichitvejpaisal, M.D., Ph.D.*, Thawatchai Akaraviputh, M.D., Arpa Chutipongtanate, M.D.*, Benno von Bormann, M.D.*, Nuchanat Sakulpacharoen, B.N., M.Ed.*, Siriporn Kongphlay, B.N.*, Araya Ongiem, B.N.***

**Department of Anesthesiology, **Department of Surgery, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok 10700, Thailand.*

ABSTRACT

Objective: Common intravenous (IV) fluids to correct dehydration and acid-base derangement following bowel preparation are 0.9% Saline solution (SS), Lactate Ringer's solution (LRS) and Acetate Ringer's solution (ARS). Different IV fluids may have different effects on patient's acid-base status, defined as pH or base excess (BE) or strong ion difference (SID). We studied the effect of alternative IV crystalloids on acid-base balance in patients undergoing colonoscopy by using SID as parameter.

Methods: Ninety participants were randomized equally into three treatment groups (LRS, ARS and SS). At the gastrointestinal endoscopy center, the basic blood test (T1) was conducted. On the day of colonoscopy, the second blood sample (T2) was obtained in either forearm before an allocated intravenous fluid administered. At the end of colonoscopy, the IV fluid was off and the third blood sample (T3) was taken from the non-fluid administered arm.

Results: Compared to T1 and T2, SID at T3 was unchanged after LRS and ARS but significantly lowered in patients with SS. The only significant statistical differences could be observed for SID at T3 between SS and LRS (40.67 ± 3.01 vs. 42.55 ± 1.60; p = 0.004) as well as SS and ARS (40.67 ± 3.01 vs. 42.58 ± 2.03; p = 0.006). Univariate analysis showed that SS alone was significantly associated with the development of acidosis (OR 11.00, 95% CI of 2.77 - 43.64).

Conclusion: With respect to maintenance of acid-base balance, LRS and ARS are preferable to SS for fluid replacement in patients with colonoscopy.

(Registration number for the clinical trial: The trial was registered at ClinicalTrials.gov identifier NCT01250886 on 9 December 2012).

Keywords: Acid-base balance, strong ion difference, colonoscopy, crystalloid solutions, propofol-mediated anesthesia

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INTRODUCTION

Colonoscopy is a standard intervention for assessment of colonic mucosa, its diagnostic accuracy and therapeutic safety depending on the quality of bowel preparation[1], which is usually performed with polyethylene glycol (PEG) and sodium phosphate compounds. However, this preparative may lead to acid-base disturbance and dehydration. The incidence is still unclear as the symptoms are mostly subclinical in healthy individuals. There are some few reports though of serious complications such as hyponatremia leading

Correspondence to: Phongthara Vichitvejpaisal
E-mail: phongthara@gmail.com
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to seizure or hypokalemia causing cardiac arrhythmia.[2,3] Common intravenous (IV) fluids to correct dehydration and acid-base derangement following bowel preparation are 0.9% Saline solution (SS), Acetate Ringer's solution (ARS) (Thai Otsuka Pharmaceutical Co., Ltd. Samuthsakhon, Thailand) and Lactate Ringer's solution (LRS) (Thai Nakorn Patana Co., Ltd. Nonthaburi, Thailand).

Different IV fluids may have different effects on patient's acid-base status, usually defined as pH or base excess (BE). Alternatively Stewart[4] created the parameter 'strong ion difference (SID)', based on subtracting completely dissociated ('strong') anions from completely dissociated ('strong') cations. The idea was to provide therapists with a simple, immediately applicable method using routinely fast available lab data. The SS mistakenly named 'physiologic' has a SID of zero and can induce hyperchloremic acidosis.[5,6] In contrast, the SID of balanced crystalloids, such as LRS and ARS solution containing lactate or acetate instead of chloride is > 25 $mEq.L^{-1}$, thus being better compatible with human plasma[7]. Nonetheless, these differences between alternative solutions are estimated clinically important only, when large amounts of IV fluid are given.[7,8] Therefore, any crystalloids were considered to be adequate for patients with minor therapeutic or surgical procedures. Learning from Ho et al,[2] about severe electrolyte disturbances after bowel preparation, the aim of the present study was to find out which kind of IV crystalloid is best to achieve balance of acid base status in patients undergoing colonoscopy.

MATERIALS AND METHODS

Ethical approval for this study (COA: Si.608/2010) was provided by the Siriraj Institutional Review Board (Si-IRB) of Siriraj Hospital, Mahidol University, Bangkok, Thailand on 10 November 2010. The written informed consent was obtained from all subjects, a legal surrogate, the parents or legal guardians for minor subjects, or the requirement for written informed consent was waived by the Institutional Review Board.

The study enrolled 90 outpatients older than 18 years with ASA risk score I - II undergoing bowel preparation and routine colonoscopy. They were scheduled for alternative fluid management (Table 1) during colonoscopy after random allocation to three groups, n = 30 each, receiving either SS, or LRS or ARS. Pregnant and breastfeeding women, patients with insulin-dependent diabetes, active gastrointestinal bleeding, ileus, acute bowel obstruction or perforation, presence of a colostomy or ileostomy, or history of a partial colon resection were excluded.

At the outpatient clinic

The co-researcher, an endoscopist recruited patients meeting the inclusion criteria. He explained the study design and gained informed consent. Then the first blood sample was obtained (T1). A registered nurse advised the patients regarding bowel preparation. They were instructed to restrict solid food intake including vegetables 2-3 days before the test, and to start the clear liquid diet with PEG plus 2-3 liters of clear liquids 24 h prior to their colonoscopy, stopping intake at midnight.

At the GI Endoscopy Center

After arrival on the day of procedure, the individual patient was randomly allocated to one of the treatment groups. The second blood sample (T2) was obtained before IV fluid supply started. The volume of IV fluid administration was calculated by means of Holliday and Segar formula,[10] which starts with 4 ml/kg for the first 10 kg, and continues with 2 ml/kg for 10-20 kg and 1 mL./kg for each kilogram over 20 kg.

During colonoscopy in light sedation with propofol and midazolam and supplemental oxygen, patients had standard vital signs monitored, including pulse oxymetry, noninvasive blood pressure, heart rate and ECG. At the end of colonoscopy patients were transferred to the recovery room, where the monitoring was

continued. After ceasing IV infusion the third blood sample (T3) was taken from the contralateral arm of IV fluid administration. Patients were discharged after being advised to follow the discharge instructions.

Lab tests – biochemical parameters

Three blood samples T1 (before bowel preparation), T2 (after bowel preparation) and T3 (after colonoscopy and completed fluid administration) were analyzed for hemoglobin concentration (cHb), hematocrit (Hct), blood urea nitrogen (BUN), creatinine (Cr), sodium (Na^+), potassium (K^+), chloride (Cl^-), bicarbonate (HCO_3^-), calcium (Ca^{2+}), magnesium (Mg^{2+}), and lactate.

Outcomes

Primary outcome was acid-base derangements linked to SID after alternative administration of SS, LRS or ARS in patients undergoing colonoscopy (n = 30 each group). SID is calculated by subtracting strong cations from strong anions as follows[3,4]:

$$SID = (Na^+ + K^+ + Ca^{2+} + Mg^{2+}) - (Cl^- + lactate)$$

As normal range is specified 40 - 44 $mEq.L^{-1}$ [4, 1], SID < 40 $mEq.L^{-1}$ has to be interpreted as acidosis, and SID > 44 $mEq.L^{-1}$ as alkalosis.

Secondary outcome was the correlation between presence of acidosis (SID < 40 $mEq.L^{-1}$) and type of IV fluid administration.

Statistical analysis

Sample size calculation was performed using data obtained during the initial phase of this study (n = 10 in each group). A difference in SID between SS- and non-SS groups of 1.842 with a standard deviation of 3.288 was used for the calculation. With 90% power and a statistical significance level of 0.05, the sample size per group was 26. We determined 30 patients per group for compensation for drop out.

Continuous data were presented as mean ± SD and were evaluated for statistical significance using SPSS 13.0. Gender within the groups and ASA risk score were compared by the Chi-square test. Comparisons of SID were performed by one-way ANOVA. Fisher's exact test was used to determine the correlation between development of acidosis and type of IV fluid; because SID of LRS and ARS are similar (Table 1). We compared SS (N = 30) vs. non-SS (N = 60). Odds ratio (OR) with 95% confidence interval (CI) was calculated to measure the strength of association. Statistical significance was defined as $p < 0.05$.

RESULTS

All ninety patients finished the study. Demographic data demonstrated no significant differences between the groups (Table 2). As a result of the fluid regimen described above, average amounts of SS, LRS and ARS administered were 1,070 ± 165 mL, 1,140 ± 169 mL and 1,046 ± 167 mL respectively (p = 0.099), again with no significant differences between the groups. There were no differences of baseline lab test and calculated SID between the three groups. In addition all parameters were within normal range (Table 3).

Patients baseline SID at T1 (before bowel preparation) in SS-, LRS- and ARS-group was 43.07 ± 1.99, 42.95 ± 2.10 and 43.02 ± 2.52 $mEq.L^{-1}$ respectively, and at T2 (after bowel preparation, before IV fluid) 43.65 ± 2.45, 44.18 ± 1.72 and 44.05 ± 2.41 $mEq.L^{-1}$ respectively. At T3, after colonoscopy and complete fluid intake, SID was 40.67 ± 3.01, 42.55 ± 1.60, and 42.58 ± 2.03 $mEq.L^{-1}$, respectively. Between T1 and T2 there were no statistically significant differences regarding group and measurement time. At T3 after complete IV fluid intake the SID in SS- patients dropped significantly to 40.67 ± 3.01 $mEq.L^{-1}$, but not within the two other groups (42.55 ± 1.60 and 42.58 ± 2.03 mEq/L resp., $p = 0.952$). The differences of SID between SS and LRS (40.67 ± 3.01 vs. 42.55 ± 1.60 $mEq.L^{-1}$; $p = 0.004$) and SS and ARS (40.67 ± 3.01 vs. 42.58 ± 2.03 $mEq.L^{-1}$; $p = 0.006$) at T3 were statistically significant (Fig 1).

TABLE 1. Concentration of cations, anions and strong ion differences ($mEq.L^{-1}$) in different fluids.

Type of solution	Na^+	K^+	Cl^-	Ca^{+2}	Acetate	Lactate	SID
SS	154	-	154	-	-	-	0
LRS	130.4	4	109.4	2.7	-	27.7	27.7
ARS	130	4	108.7	2.7	28	-	28

ARS = Acetated Ringer's solution, LRS = Lactated Ringer's solution, SS = Saline solution, SID = strong ion difference

TABLE 2. Demographic characteristics of patients with colonoscopy and the average Intravenous intake of alternative fluids.

	SS (n=30)	LRS (n=30)	ARS (n=30)	*p*
Sex (n, %)				
M	8 (26.67)	14 (46.67)	13 (43.33)	0.235
F	22 (73.33)	16 (53.33)	17 (56.67)	
Age (yr)	57.20 (9.03)	54.87 (7.72)	55.87 (9.34)	0.567
Weight (kg)	58.24 (10.05)	63.06 (12.03)	58.11 (09.00)	0.099
Height (cm)	158.90 (7.30)	162.57 (7.51)	160.23 (8.03)	0.216
BMI (kg/m^2)	23.1 (3.4)	23.7 (3.6)	22.7 (2.9)	0.558
ASA (n, %)				
1	20 (66.7)	21 (70.0)	21 (70.0)	0.949
2	10 (33.3)	9 (30.0)	9 (30.0)	
Total fluid (mL)	1,070 (165)	1,140 (169)	1,046 (167)	0.099

Data are means (SD) or numbers (%), * $p < .05$
ARS = Acetated Ringer's solution, LRS = Lactated Ringer's solution, SS = Saline solution

TABLE 3. Baseline lab test results and the calculated strong ion difference.

	SS (n=30)	LRS (n=30)	ARS (n=30)	*p*
Na^+ ($mEq.L^{-1}$)	141.60 (1.63)	141.97 (1.65)	141.20 (2.16)	0.27
K^+ ($mEq.L^{-1}$)	4.12 (0.36)	3.98 (0.35)	4.09 (0.49)	0.37
Ca^{2+} ($mEq.L^{-1}$)	2.28 (0.14)	2.26 (0.09)	2.27 (0.08)	0.79
Mg^{2+} ($mEq.L^{-1}$)	0.86 (0.06)	0.86 (0.07)	0.84 (0.05)	0.23
Cl^- ($mEq.L^{-1}$)	104.37 (2.36)	104.67 (2.55)	103.93 (2.74)	0.54
HCO_3^- ($mEq.L^{-1}$)	27.40 (2.19)	27.40 (1.77)	27.00 (2.08)	0.68
Lactate ($mEq.L^{-1}$)	1.42 (0.73)	1.45 (0.64)	1.44 (0.41)	0.98
Albumin ($g.dL^{-1}$)	4.46 (0.26)	4.57 (0.36)	4.53 (0.20)	0.31
BUN ($mg.dL^{-1}$)	12.97 (3.94)	13.81 (4.18)	13.44 (4.36)	0.74
Cr ($mg.dL^{-1}$)	0.80 (0.14)	0.90 (0.26)	0.91 (0.30)	0.13
SID ($mEq.L^{-1}$)	43.07 (1.99)	42.95 (2.10)	43.02 (2.52)	0.98

ARS = Acetated Ringer's solution, LRS = Lactated Ringer's solution, SS = Saline solution, SID = strong ion difference, Data are means (SD) * $p < .05$

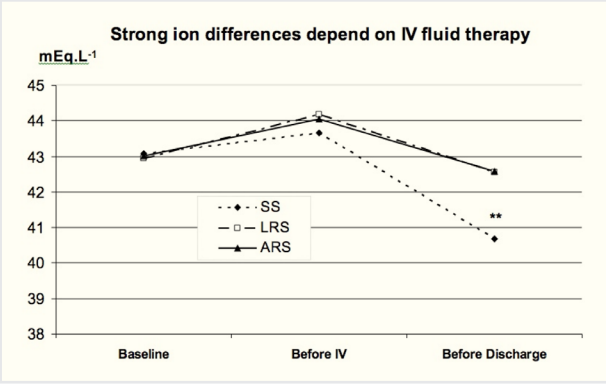

Fig 1. Comparison of SID at baseline (T1), after bowel preparation (T2) and after colonoscopy (T3) between groups.

Note: ARS = acetated Ringer's solution, LRS = lactated Ringer's solution, SS = saline solution, SID = strong ion difference, Data are means (SD)

** $p < .001$

Correlation between acid base disturbance, defined as SID moving to < 40 $mEq.L^{-1}$ and type of IV fluid has been demonstrated in Table 4. Saline solution was significantly associated with the development of acidosis as compared to the non-SS group ($p < 0.001$) with OR of 11.00 and 95% CI of 2.77 - 43.64.

DISCUSSION

The main finding of this study was that 0.9% Saline solution contrary to Lactate- and Acetate-Ringer Solution led to development of acidosis established by significant decrease of SID. The amount of fluid given to our patients followed accepted recommendations[10], thus not contributing to the findings. Summarizing the LRS- and ARS-group into one group for comparison with SS was statistically adequate as there were no differences at all in any parameter within these two groups.

Strong ion difference as a parameter to detect plasma acidosis is well established and has been used in several studies with different approaches,[7, 12-17] especially to estimate the effect of alternative crystalloid infusions on acid base balance. In addition the parameter has been used as a mortality predictor. Durward and co-workers[18] investigated 85 children after surgery for congenital heart defect, finding that an elevated SID after cardiopulmonary bypass is quite common, but also that its extent correlates with mortality appearing to be even more reliable with lactate.

Several research groups have demonstrated that administration of large volumes of SS is associated with hyperchloremic acidosis.[9,19,20] Scheingraber et al,[6] prospectively studied two randomized groups of patients undergoing major gynecologic surgery: Infusion of 30 $mL.kg^{-1}$ of SS (1,800 ml in a 60 kg individual) within one hour resulted in relevant hyperchloremic metabolic acidosis, whereas infusing an identical amount of LRS had no such complication. Morgan and co-workers performed hemodilution from basic cHb 14.2 $g.dl^{-1}$ to 4.4 $g.dl^{-1}$ in Sprague-Dawley rats investigating the effect of 7 different solutions with SID ranging from 0 to 40. They concluded that a crystalloid needs a SID of about 24 $mEq.L^{-1}$ to leave the acid base balance unaffected after infusion. Omron and Omron[5] infused up to 10

TABLE 4. Correlation (odd ratio, OR) between different types of intravenous fluid and strong ion difference.

	SID ≥ 40 $mEq.L^{-1}$ n (%)	SID < 40 $mEq.L^{-1}$ n (%)	OR (95% CI)	*p*
ALL, n = 90	76 (84)	14 (16)		
Lactate-, Acetate-Ringer Solution, n = 60	57 (95)	3 (5)	1	
Saline Solution n = 30	19 (63)	11 (37)	11 (2.8 – 43.6)	0.0002

SID = strong ion difference

*Data are means (SD) * $p < .05$, ** $p < .001$*

litres of different crystalloids to a test person, the SID of the solutions ranging from 0 to 150 $mEq.L^{-1}$. They found the SID-threshold to either create alkalosis or acidosis to be 24.5 $mEq.L^{-1}$. Sodium (Saline) solution is the oldest, still widely used crystalloid solution in medicine. The name 'physiologic saline solution' is due to its physiologic osmolality of 280 – 300 $mOsm.kg^{-1}$ which is similar to plasma (295 $mOsm.kg^{-1}$). However, its pH is 7.2 as a consequence of high chloride content of 154 $mEq.L^{-1}$ [21]. Indeed, the key abnormality of saline solution is chloride gain. Therefore saline solution should no longer be characterized as 'physiologic'.

Our data are different to the literature cited as metabolic acidosis (SID < 40 $mEq.L^{-1}$) already occurred after relative small amounts of IV fluid (approximately 1 L). The insignificant results in patients receiving either LRS or ARS clearly demonstrate the acid base disturbances after SS are substance specific. This is additionally substantiated by statistical analysis: The correlation between the developed acidosis and SS administration was high (OR 11.00, 95% CI 2.77-43.64, p<0.001) (Table 4).

There were limitations of this study. First, blood pH which is the gold standard to reveal acid-base imbalance was not measured, because it needs an invasive approach, which is not included in the routine monitoring for patients undergoing colonoscopy. However, the tight correlation between blood pH and SID was previously published.[20] Additionally, we believe with others that Stewart's approach compared to pH is more appropriate to detect small changes of acid-base status in a quantitative manner. Second, the sample size was not calculated from the beginning, but after 3 x 10 patients. However, our data showed enough statistical significance to support the presented conclusions with adequate power.

CONCLUSION

Saline Solution (SS) - SID zero - has an adverse effect on acid base balance even after amounts adequate for minor diagnostic procedures, such as colonoscopy. To prevent potential disturbances of acid-base-metabolism, Lactate- or Acetate-Ringer's solution - SID approximately 25 $mEq.L^{-1}$ - are superior to SS for all kinds of fluid replacements.

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