

Incidence of Hyperchloremic Metabolic Acidosis in Use of Balanced Salt Crystalloid Group or 0.9% NaCl with Acetar® Group for General Anesthesia in Craniotomy to Remove Tumor

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Background: Intravenous fluids are used daily for general anesthesia. Normal saline (0.9% NaCl) is an isotonic solution. Excessive use of saline has been observed to result in hyperchloremic acidosis. Newer balanced solutions having fewer electrolytes composition different than plasma may avoid this effect. This study compared change in acid-base balance and serum electrolyte with use of 0.9% NaCl combined with Acetar® in 1:1 ratio group and Sterofundin group.

Methods: Twenty-eight adult patients with ASA 1-3 who were scheduled for craniotomy to remove tumor under general anesthesia were randomized into two groups. A balanced salt crystalloid group received sterofundin for intravenous fluids. A 0.9% NaCl plus Acetar® group received 0.9% NaCl and Acetar® in 1:1 ratio. Demographic data and anesthetic data were recorded. The amount of IV fluid given was guided with the goal directed to keep euvolemia by an anesthesiologist. Arterial blood gas, base

excess, and serum electrolytes were recorded at the beginning of surgery, postoperative 1 hour, and 1 day. Two patients were excluded due to incomplete records.

Results: Serum base excess and pH in baseline and postoperative in Sterofundin group had more alkalosis but was still in the normal range. A change in serum sodium and chloride did not yield a statistical difference in both groups. The amount of blood loss, urine output, operation time, PRC, and total crystalloid given were not statistically different. No patient developed acidosis.

Conclusion: Using Sterofundin® for IV fluids was not different in incidence of hyperchloremic metabolic acidosis, sodium and chloride than 0.9% NaCl plus Acetar® in 1:1 ratio for craniotomy to remove tumor. Using 0.9% NaCl plus Acetar® in 1:1 ratio was a good method to avoid acidosis from excessive intravenous 0.9% NaCl.

Keywords: Balanced salt crystalloid, Craniotomy, Normal Saline, Serum base excess

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Introduction

Crystalloids are required for intravenous fluid administration in anesthesia almost every day. Each crystalloid has different electrolytes composition. Normal saline (0.9% NaCl) is one of the most frequently used in resuscitation¹ and in neurosurgical patients because of its isotonic and isoosmolar property. However, an excessive amount of normal saline can cause hyperchloremic metabolic acidosis because of difference in electrolytes composition to plasma^{2,3,4}.

Mcfalane et al. showed that infusing 0.9% NaCl 15 ml/kg/h significantly increased chloride level and incidence of hyperchloremic metabolic acidosis comparing to plasmalyte 148 group⁵. Hyperchloremic metabolic acidosis may increase morbidity and mortality in some studies⁶. Newer crystalloids were invented to have electrolytes composition nearer to plasma to reduce the side effects⁷. Sterofundin® showed significantly better acid-base status when use intraoperatively in neurosurgery comparing to 0.9%NaCl⁸. In this study,

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we used Acetar[®], the common and widespread balanced salt solution in Thailand combined with 0.9% NaCl in 1:1 ratio and compared to Sterofundin[®] regarding incidence of hyperchloremic metabolic acidosis.

Objectives

Our study aimed to determine the difference in incidence of hyperchloremic metabolic acidosis after patients received Acetar[®] and 0.9% NaCl in 1:1 ratio compared with Sterofundin[®].

Population

We calculated sample size from a previous study by Krebbel et al.⁹ using difference in base excess in balanced crystalloid group and unbalanced crystalloid group. We used G Power 3.9.1.2 for calculation with standard deviation 1.185, type I error 0.05 and power of test 0.80 ($\sigma_1 = 0.425$, $\sigma_2 = 0.45$). The calculation resulted in 20 subjects, so we used a total of 28 subjects for this study.

Methods

The study is a prospective randomized controlled trial conducted at Ramathibodi Hospital, Bangkok, Thailand. After the trial had been approved by the Ramathibodi ethics committee, the trial was conducted from November 2015 to August 2016.

We recruited 28 patients undergoing elective craniotomy to remove tumors under general anesthesia. The inclusion criteria were patients aged 18-65 years old with ASA physical status 1 to 3. Exclusion criteria were patients with obesity ($BMI > 35 \text{ kg/m}^2$), those who received diuretic or mannitol or hypertonic saline before surgery, those who had congestive heart failure or renal failure, or diabetic insipidus, SIADH, cerebral salt wasting syndrome, emergency surgery, and patient refusal. After informed consent was obtained, patients were randomized into two groups by a computer-generated table; the first group received normal saline combined with Acetar[®] in 1:1 ratio (NA group), while the second group received Sterofundin[®] (ST group) as intraoperative fluids. For simplicity, all patients

underwent surgery and general anesthesia performed by neurosurgeons and anesthesiologists of Ramathibodi hospital. Before induction of anesthesia, all patients received standard monitoring and peripheral IV access. After induction of anesthesia with endotracheal tube and controlled ventilation, arterial catheter insertion was done for monitoring blood pressure and collecting blood samples. Blood samples were collected for arterial blood gas, electrolytes and sugar for three times after induction, 1 hour after surgery, and 1 day after surgery. Regarding the amount of crystalloids in both groups, we aimed to maintain euolemia by keeping pulse pressure variation less than 14, and urine output more than 0.5 ml/kg/hr. Other types of fluids such as colloids or blood components were not restricted, which could be given upon the anesthesiologists or surgeon's decision (Fig. 1).

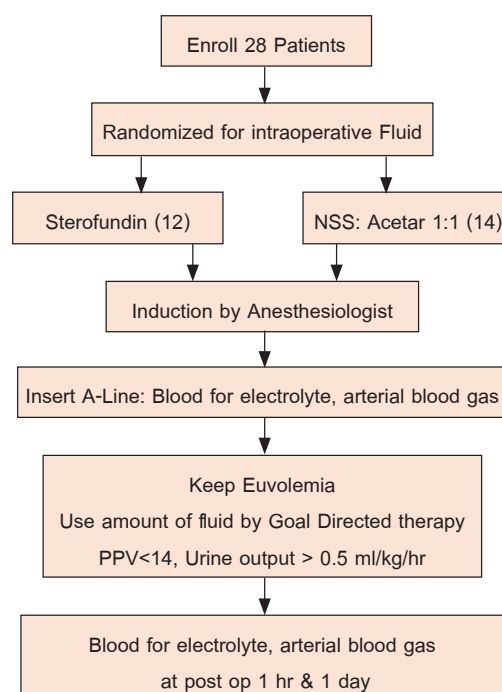


Figure 1 Flow chart of the study

Statistical analysis

Results are expressed as mean, median or frequencies. Distributions for normality were checked with Shapiro-Wilk's test for continuous data. Differences between two groups were tested using nonparametric

exact Mann-Whitney U tests for independent data or exact Wilcoxon tests for pairwise comparisons. Frequencies were compared using the exact Mantel-Haenszel test (ordered categories) or the exact χ^2 test in contingency tables. Repeated measures ANOVA test with Bonferroni adjustment was used for repeated data and multiple comparisons. All numerical calculations were performed using the SPSS® version 18.0. A two-tailed P-value<0.05 was considered statistically significant.

Results

Twenty-eight patients were included in this study, but two patients were not used in analysis due to incomplete data recorded. We randomized into two groups, 14 patients in the NA group, and 12 patients in the ST group. Demographic data were collected from all patients (Table 1).

Table 1 Demographic data

Patient characteristics	Sterofundin (12)	NSS: Acetar (14)	P-value
Male: Female	6:6	4:10	
Body weight	66.56±15.55	58.49±12.37	0.154
Height	161.5±12.12	156.26±9.09	0.22
BMI	25.31±4.24	23.78±3.12	0.299
Age (yr)	50.5±11.9	55.36±11.34	0.298
ASA 2, n (%)	4 (33.33%)	7 (50%)	0.391
3	8 (66.67%)	7 (50%)	0.391
Hypertension	4 (33.33%)	6 (42.86%)	0.701
Diabetes	4 (33.33%)	2 (14.29%)	0.365
Dyslipidemia	4 (33.33%)	5 (35.71%)	>0.999
Overweight	5 (41.67%)	2 (14.29%)	0.19
Anemia	4 (33.33%)	2 (14.29%)	0.365
Seizure	1 (8.33%)	1 (7.14%)	>0.999
On steroid	3 (25%)	3 (21.43%)	>0.999
Hx Radiotherapy	2 (16.67%)	2 (14.29%)	>0.999
Anesthetic drugs			
Thiopental	2 (16.67%)	4 (28.57%)	0.652
Propofol	11 (91.67%)	13 (92.86%)	>0.999
Fentanyl	12 (100%)	14 (100%)	-
Atracurium	5 (41.67%)	11 (78.57%)	0.105
Cisatracurium	7 (58.33%)	3 (21.43%)	0.105
Sevoflurane	7 (58.33%)	9 (64.29%)	>0.999
Desflurane	0 (0%)	2 (14.29%)	0.483
N ₂ O	2 (16.67%)	2 (14.29%)	>0.999

Data are expressed as mean±standard deviation and number (%) where appropriate. NNS=Normal saline

There was no difference in patient characteristics including age, height, body weight, body mass index (BMI), underlying diseases and also anesthetic agents between the two groups. The amount of crystalloid used was not statistically different. The ST group received Sterofundin® 3775 ml (1400, 6500) intraoperatively, and 4900 ml (2200, 7500) in 1 day. The NA group received 0.9% NaCl 1600 ml (500, 3600) plus Acetar 1125 ml

(600, 3000) intraoperatively and 0.9% NaCl 2850 ml (1880, 4800) plus Acetar® 1625 ml (1000, 3000) in 1 day. One patient in the NA group received Voluven 500 ml intraoperatively (Table 2). The amount of packed red blood cell (PRC) and mannitol received were not statistically different. Operation time, blood loss and urine output were not statistically different.

Table 2 Fluid received in both groups

Fluid (ml)		Sterofundin (12)	NSS: Acetar (14)	P-value
Sterofundin				
	intraoperation	3775 (1400, 6500)		
	total	4900 (2200, 7500)		
Normal saline intraoperation				
	total	325 (100, 1400)	1600 (500, 3600)	
Acetar				
	intraoperation		1125 (600, 3000)	
	total		1625 (1000, 3000)	
Voluven				
	intraoperation		500 (500, 500)	
	total		500 (500, 500)	
Packed red cell				
	intraoperation	355.5 (261, 1200)	548.5 (477, 793)	0.343
	total	405.5 (261, 1200)	548.5 (477, 1079)	0.686
Mannitol				
	intraoperation	208.33±72.17	250±0	0.571
	total	208.33±72.17	250±0	0.571
Urine output				
	intraoperation	850 (320, 2700)	750 (200, 3350)	>0.999
Blood loss				
		625 (150, 2500)	450 (100, 2500)	0.899
Operation time (min)				
		342.92±121.18	287.86±66.9	0.18

Data are expressed as mean±standard deviation and median (minimum, maximum) where appropriate.

There was a difference in serum base excess (BE) which was statistically different at baseline and post operative 1 hr. BE in ST group was -0.15 (-5.2, 5), -3.35 (-7.8, 0.5), -1.5 (-4.2, 9.6) at baseline, post op 1 hour, and 1 day, respectively. BE in NA group was -4.85 (-9, -1), -7.15 (-11.4, 0.8), -4.25 (-8.7, -0.5) at baseline, post op 1 hr, and 1 day, respectively. Serum pH was statistically different at post operative 1 hour. ST group

had serum pH 7.44 ± 0.04 , 7.44 ± 0.04 , 7.46 ± 0.04 at baseline, post op 1 hour, and 1 day, respectively. NA group had serum pH 7.42 ± 0.04 , 7.4 ± 0.04 , 7.43 ± 0.03 at baseline, post op 1 hour, and 1 day, respectively (Table 3). Serum sodium, chloride, potassium, bicarbonate (HCO_3), sugar, and hemoglobin level were not statistically different in both groups. No patients developed acidosis.

Table 3 Results

	Sterofundin (12)	NSS: Acetar (14)	P-value
pH Baseline	7.44±0.04	7.42±0.04	0.016*
1 hr	7.44±0.04	7.4±0.04	0.03*
1 day	7.46±0.04	7.43±0.03	0.012*
Na Baseline	139.42±2.31	140.07±2.02	0.338
1 hr	140.17±2.33	138.29±2.23	
1 day	139.25±3.25	138.21±2.55	
Cl Baseline	105.58±3.6	106.21±2.36	0.606
1 hr	108.58±3.48	108.57±1.99	
1 day	106.83±4.57	107.79±3.21	
K Baseline	3.78±0.3	3.74±0.38	0.725
1 hr	3.84±0.31	3.86±0.41	
1 day	3.9±0.29	4.03±0.53	
HCO ₃ Baseline	24.84±4.07	22.19±3.02	0.066
1 hr	20.51±3.98	19.03±2.99	
1 day	22±2.21	20.34±2.88	
BE Baseline	-0.15 (-5.2, 5)	-4.85 (-9, -1)	0.001*
1 hr	-3.35 (-7.8, 0.5)	-7.15 (-11.4, 0.8)	0.001*
1 day	-1.5 (-4.2, 9.6)	-4.25 (-8.7, -0.5)	0.007*
Hb Baseline	11.63±1.61	12.48±1.36	0.136
1 hr	11.59±1.26	11.89±1.07	
1 day	10.77±1.59	11.81±1.28	
Sugar Baseline	145±45.23	120.18±38.08	0.712
1 hr	167.27±38.7	157.82±46.98	
1 day	139.64±26.99	157.27±44.39	

Data are expressed as mean±standard deviation and median (minimum, maximum) where appropriate.

*P-value < 0.05, statistically significant. Na=sodium, Cl=chloride, K=potassium, BE=Base excess, Hb= hemoglobin

Discussion

Normal saline is commonly used in neurosurgery. A large amount of fluid must be administered due to long hours of surgery. Data from randomized controlled study in patients undergoing major surgery, 67% of patients who receive 0.9% NaCl but none of patients who received balanced electrolyte solution developed hyperchloremic metabolic acidosis. Volume of 0.9% NaCl infusion that can cause hyperchloremic metabolic acidosis is 15 ml/kg/h up to 3 hours⁵.

Hyperchloremic metabolic acidosis may cause negative impact on patient outcome⁹. McCluskey et al.

showed that hyperchloremia was an independent predictor of 30-day mortality⁶. Moreover, hyperchloremia can induce renal vasoconstriction in response to tubuloglomerular feedback¹¹ and may cause acute kidney injury¹²⁻¹⁴. Sterofundin® is a new balanced salt solution showing better acid-base balance when used as maintenance fluid in neurosurgical anesthesia compared to 0.9% normal saline, lower chloride level (105.7 ± 4.1 versus 113.2 ± 3.0 mmol/L ($P < 0.01$))⁸.

Our study showed that combining 0.9% normal saline with Acetar® in 1:1 ratio can produce similar acid-base status, chloride level comparing to

Sterofundin®. Even though the NA group caused more base deficit and lower pH than the ST group at baseline, postoperative 1 hour, and 1 day, nevertheless, they were still in normal range. Incidence of hyperchloremic metabolic acidosis was the same among the two groups.

There were some limitations that some patients retained endotracheal tube and used a mechanical ventilator post-operative during the first day. We did not record PaCO₂ that might affect acid-base balance, but we adjusted all patients to keep normocarbica during perioperative period.

Conclusion

Using 0.9% NaCl plus Acetar in 1:1 ratio was a good alternative to avoid acidosis from excessive intravenous 0.9% NaCl.

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