SAS Journal of Medicine
Abbreviated Key Title: SAS J Med
ISSN 2454-5112
Journal homepage: https://saspjournals.com/sasjm/

OPEN ACCESS

Comparison Between 6% Hydroxyethyl Starch 130/0.4 in A Balanced Solution (Volulyte®) And 6% Hydroxyethyl Starch 130/0.4 in A Saline (Voluven®) Regarding Acid-Base Status and Electrolytes in Burn Patients

Sungmin Joo[1], Hee Jeong Son[2], Jun Suck Lee[3], Eun Ji Youn[3], Jieun Park[3], Soo Kyung Lee[3*]

[1]Department of Medicine, Graduate School Kangwon National University, Chuncheon, Gangwon-do, Republic of Korea
[2]Department of Anesthesiology and Pain Medicine, Kangwon National University School of Medicine, Chuncheon, Gangwon-do, Republic of Korea
[3]Department of Anesthesiology and Pain Medicine, Hallym University College of Medicine, Chuncheon, Republic of Korea

DOI: 10.21276/sasjm.2019.5.7.2 | **Received:** 17.07.2019 | **Accepted:** 26.07.2019 | **Published:** 30.07.2019

***Corresponding author:** Soo Kyung Lee

Abstract **Original Research Article**

***Background*:** Because burn patients are accompanied by massive tissue destruction, adequate volume replacement is important. We studied the effects of 6% HES 130/0.4 in a balanced electrolyte solution (Volulyte) compared to 6% HES 130/0.4 in a saline (Voluven) regarding acid-base status and electrolytes in burn surgery. ***Methods*:** A total of 121 patients who underwent burn surgery were retrospectively reviewed using a medical record. Fifty-nine patients received Volulyte (Group B) and 62 patients received Voluven (Group S). We compared arterial pH, base excess, and serum chloride level using analysis of multivariate regression and pre- and postoperative changes of the two groups after controlling demographic and operational procedural factors. Each group was subdivided into three groups by the burned surface area as a percentage of total body surface area (TBSA) in order to see whether there are differences between the two groups regarding burn severity. ***Results*:** Preoperative arterial pH, base excess, and chloride level had no differences between two groups. Postoperative serum chloride level was significantly lower and arterial pH was significantly higher in group B than in group S. Postoperative base excess showed a significant difference between the two groups. There was a tendency of less increase in serum chloride level in patients with ≥ 50% TBSA in group B. ***Conclusions*:** Volulyte showed more beneficial effects on acid-base status and serum chloride level than Voluven in burn patients after surgery. Therefore, Volulyte could minimize the possibility of infusion related hyperchloremic acidosis in patients undergoing burn surgery.

Keywords: Acid base balance; Burn; Hydroxyethyl starch derivatives.

INTRODUCTION

Maintenance of adequate intravascular volume is very important in managing medical, surgical treatment especially for critically ill patients. During surgery, blood loss, peripheral vascular dilation and fluid shift induce a decrease in intravascular volume [1]. Deane and colleagues reported in 1988 that "A prospective study of patients who died in the hospital after admission for treatment of injuries showed that inadequate fluid resuscitation was the most common mismanagement."[2]. An adequate intravascular volume replacement therapy may help to improve organ function and reduce patient morbidity or even mortality: in approximately 50% of septic patients, adequate volume replacement alone can reverse hypotension and restore hemodynamics [3].

In burn patients, release of inflammatory mediators (e.g. histamine, prostaglandins, thromboxane, and nitric oxide), increase capillary permeability, and fluid shifts happen due to severe tissue destruction [4-6]. Furthermore, throughout burn wound evaporation, large amounts of fluid are lost from the damaged skin surfaces [7]. Burn patients' special pathophysiology makes maintenance of intravascular volume even more important than in other patients. However, a strategy for fluid resuscitation in burn patients has not been established yet [8].

Colloids contain large molecules and exert a high oncotic pressure, therefore remaining in the intravascular volume longer than crystalloids [9,10].

This makes colloids a more efficient tool for maintaining adequate intravascular volume, especially in patients with major trauma [11,12]. Recent studies suggest that colloid resuscitation may help patients to have a better postoperative recovery and experience less edema [6,13,14]. Since the infusion of large amounts of saline based solutions may contribute to the development of hyperchloremic metabolic acidosis, the use of a balanced carrier for colloid solution might improve postoperative acid-base status [15-17]. Currently used synthetic colloid solutions are gelatins, dextrans, and hydroxyethyl starches (HES) [18].

Voluven® (Fresenius Kabi, Bad Homburg, Germany) contains 6% HES 130/0.4 in normal saline and Volulyte® (Fresenius Kabi, Bad Homburg, Germany) contains 6% HES 130/0.4 in a balanced electrolyte solution. The newer carrier solution contains less chloride and is physiologically more similar to human plasma than Voluven [19]. In case of massive fluid resuscitation, HES in a balanced electrolyte solution may help to prevent hyperchloremic metabolic acidosis. An article reported that after administration of colloid solutions, the HES balanced group showed significantly lower serum chloride level and less acidosis compared with the conventional HES group [9].

There are many recent publications with HES balanced solutions, but published data on its use in burn patients is still limited. We therefore conducted a retrospective study to evaluate effects of 6% HES 130/0.4 in a balanced electrolyte solution (Volulyte) compared with 6% HES 130/0.4 in normal saline (Voluven) regarding acid-base status and electrolytes in burn surgery patients.

MATERIALS and METHODS

Study design

All patients who had burn surgery at the Department of Burn Surgery for three months were reviewed in this study. The information was obtained by manual searching of electronic medical records. We reviewed the preoperative orders, anesthesia records and intensive care unit (ICU) records for preoperative medications orders as well as intraoperative and postoperative adverse events. All patients received a normal saline and Ringer's lactate solution infusion supplemented with colloids and blood products such as packed red blood cells (PRBC) and fresh frozen plasma (FFP) for intraoperative hemodynamic stabilization. All patients received either Volulyte or Voluven for colloids used during the surgery.

Inclusion criteria were: 1) adults above 20 years old, 2) under general anesthesia 3) with third-degree burns undergoing either elective cadaveric allograft, split thickness skin graft (STSG) or both, 4) a body mass index (BMI) between 17 and 31 kg/m^2, 5) data from the first operation, if a patient had several surgeries, 6) urine output > 0.5 ml/kg/h, 7) serum potassium level between 3.3 and 5.5 mmol/L. Exclusion criteria were: 1) hemoglobin concentration <12 g/dl and >17 g/dl before operation, 2) a known allergy to HES, 3) renal insufficiency (serum creatinine > 2.5 mg/dl), significant hepatic disease (liver function tests > 3 times upper limit of normal), a history of coagulation disorders, 4) use of sodium bicarbonate or diuretics, 5) pregnancy, 6) total fluid infusion amount over 100 ml/kg, 7) body temperature during surgery below 33°C.

A total of 121 cases were sorted from anesthesia records. In 59 cases, patients treated with Volulyte (Group B), and in 62 cases, patients treated with Voluven (Group S). Additional crystalloid (normal saline and Ringer's lactate solution) and blood products (PRBC and FFP) were used concomitantly for fluid maintenance and hemodynamic stability in both groups. PRBC transfusion is targeted to a hemoglobin to >8 g/dl (>9 g/dl in patients with significant heart disease). In all patients, anesthesia was induced with propofol (1.0-2.0 mg/kg), fentanyl (0.5-1.0 μg/kg), rocuronium bromide (1 mg/kg), and maintained with 2.5-3.0% sevoflurane and air in oxygen (fraction of inspired oxygen, 0.5). Unless patient has a facial burn including the forehead, all patients were monitored with a bispectral index monitor (BIS VISTA^{TM} Monitoring System; Aspect Medical Systems, Norwood, MA, USA). The concentration of sevoflurane was modulated to maintain the heart rate and blood pressure within 20% above or below baseline values and the BIS value between 40 and 60. Mechanical ventilation was modulated to maintain an end-tidal carbon dioxide partial pressure of 32-38 mmHg throughout the procedure. Body temperature was maintained by a forced air warming device, circulating-water mattress, intravenous fluid warming device, and the heating room air itself.

Variables analyzed were arterial pH, base excess, and serum chloride level. All three variables were sorted from the first arterial blood gas analysis just after induction and the first arterial blood gas analysis after transfer to the ICU postoperatively. All blood gas analysis values were measured at 37°C.

We studied the effects of Volulyte on arterial pH, base excess, and serum chloride level by comparing them to the effects of Voluven after controlling the relevant factors. To explore effects of burn severity, each group was divided into three sub-groups by the burned surface area as a percentage of total body surface area (TBSA) (subgroup 1; < 20% TBSA, subgroup 2; ≥ 20% and < 50% TBSA, subgroup 3; ≥ 50% TBSA) and compared between two study groups. Additionally, we compared between preoperative value and postoperative value in each study groups to examine the changes in pH, base excess, serum chloride level between before and after fluid administration. We also compared 30 day mortality between group B and group S to study effects of HES on patient outcome.

Statistical analyses

In the baseline analysis, continuous variables are presented as mean, standard deviation, range and categorical variables are presented as frequency count and percent. To detect the difference between the two groups, we used t-test, Chi-squared test. To analyze the effects of treatment, the preoperative index (the arterial pH, base excess, and serum chloride level) and the postoperative index were compared using t-test. In addition, a paired t-test was used for comparison of the same patients before and after surgery.

The study was performed using analysis of multivariate regression. The effect of treatment is checked after controlling the influence of co-variates. In this study, demographic characteristics of patients (sex, age, BMI) and operational procedural factors were considered as co-variates that could affect the results of the trial. Thus, we investigated the effect of treatment by controlling demographic factors and % TBSA (model 1), further controlling the operational procedural factors (model 2), controlling the amount of administered Ringer's lactate solution and PRBC (model 3) and controlling the amount of administered Ringer's lactate solution, PRBC, the demographic variables, and % TBSA (model 4). Statistical adjustment is to determine the magnitude of the effect that we are observing after removing the interference from other relevant factors. Multivariate regression adopted in this study is one of the general methods of statistical adjustment. The effect of adjustment for the interference is presented by a partial regression coefficient.

For more rigorous study, in the final analysis model, we examined whether treatment was effective after controlling covariates. The level of significance was set at 0.05. This study was performed using SAS® ver. 9.3 (SAS, Cary, CA).

RESULTS

A total of 121 cases were sorted from anesthesia records. Patient demographics and clinical data, including age, sex, weight, height, body mass index, cerebrovascular prior surgery, and concomitant diseases are presented in Table 1. There were no significant differences in the most of demographic factors and major diseases except a number of patients with previous history of cardiovascular accident between group B (N=59) and group S (N=62). There were more patients with previous history of cardiovascular accident in group B (5 vs. 0).

Table 2 shows variables related to operation and anesthetic management. Similar volumes of Volulyte and Voluven were administered during the surgery. The mean doses were 1145.9 ± 379.9 ml and 1259.7 ± 353.1 ml in group B and group S, respectively. However, there was a difference in the amount of administered Ringer's lactate solution and PRBC. The mean doses of Ringer's lactate solution were 539.8 ± 313.2 ml and 390.6 ± 338.6 ml in group B and group S. There were more units of PRBC transfused in group B (5.1 ± 3.7 vs. 3.9 ± 2.4). Intraoperative infusion volumes grouped by components are presented in Table 2.

Variables analyzed are the pre- and postoperative arterial pH, base excess, and serum chloride level (Table 3). The serum chloride level (mmol/L) from the postoperative blood gas analysis was significantly lower in group B (105.44 ±3.79 vs. 109.31 ± 4.29) (Fig. 1). The postoperative arterial pH was significantly higher in group B than in group S (7.41 ± 0.07 vs. 7.37 ± 0.06) (Fig. 2). The postoperative base excess showed significant difference between the two groups as well (-0.96 ± 3.26 vs. -3.51 ± 2.84) (Fig. 3).

Table 4 shows the results of subgroups. In subgroup 2 (20-49% TBSA), there were significant differences in postoperative base excess and serum chloride level between the two groups. In subgroup 3 (≥ 50% TBSA), there was a significant difference in postoperative chloride level between the study groups. However, not every variable had significant differences between the study groups by burn severity due to the small sizes of samples.

For more rigorous study, we examined whether treatment was effective after controlling other variables (Table 5). As a result of the analysis model 1, which controlled the demographic variables and % TBSA, coefficients of base excess difference and arterial pH difference were positive (β = 2.303, $p<.0001$; β = 0.037, p =0.0019, respectively) and coefficient of serum chloride level was negative (β =-2.411, p=0.0026). In model 2, which controlled the demographic variables, % TBSA and the operational procedural variables, the difference in base excess, arterial pH, and serum chloride level showed significant coefficients in the expected hypothesis (β= 2.365, $p<.0001$; β = 0.031, p = 0.0084; β = -1.681, p = 0.0345, respectively). In model 3, we controlled the amount of administered Ringer's lactate solution and PRBC which were significantly different in two study groups. The difference in base excess, arterial pH, and serum chloride level showed significant coefficients in the expected hypothesis (β= 2.727, $p<.0001$; β = 0.033, p = 0.005; β = -2.661, p = 0.001, respectively). In model 4, which controlled the amount of administered Ringer's lactate solution, PRBC, the demographic variables, and % TBSA, the difference in base excess, arterial pH, and serum chloride level showed significant coefficients in the expected hypothesis (β= 2.481, $p<.0001$; β = 0.036, p = 0.003; β = -2.240, p = 0.005, respectively). Therefore, all differences between pre- and postoperative values of base excess, arterial pH, and

serum chloride level showed more stable results in group B than in group S.

For each group, we analyzed the differences in pre- and postoperative values of arterial pH, base excess, and serum chloride level using paired t-test (Table 6). The arterial pH and base excess had statistically significant changes in group S, however, both remained stable in group B. The change of serum chloride level was significant in both groups, but the mean difference between pre- and postoperative values in group B was smaller (-1.14 ± 3.68 vs -3.66 ± 4.66). In subgroup 3, there were significant changes in all three laboratory values in group S, while laboratory values remained stable in group B (Table 7). There was a tendency for Volulyte to give less chloride loading especially in patients with more than 20% TBSA (Table 8, Fig. 4).

Additionally, there was no statistically significant difference in 30-day mortality rate between the two groups (Table 9).

Table-1: Patient Characteristics

	Group B (n=59)			Group S (n=62)			P-value
	n (%)	Mean (SD)	Range	n (%)	mean (SD)	Range	
Demographics							
Male	50(84.8)			51(82.3)			0.7127
Female	9(15.3)			11(17.7)			
Age		46.2(15.4)	20-80		47.2(11.2)	22-68	0.6611
20-29	9(15.3)			5(8.1)			0.6500
30-39	9(15.3)			9(14.5)			
40-49	14(23.7)			21(33.9)			
50-59	18(30.5)			18(29.0)			
60+	9(15.3)			9(14.5)			
Weight (kg)		65.9(10.4)	44-97		68.1(11.3)	44-92	0.2753
Height (cm)		169.1(7.8)	150-185		169.0(8.3)	150-185	0.9513
BMI (kg/m2)		23.0(2.6)	18.9-29.9		23.7(2.9)	17.6-30.8	0.1280
Pre-existing medical conditions at admission							
Previous MI	2(3.4)			0(0)			0.1438
Cardiovascular accident	5(8.5)			0(0)			0.0192
Heart Failure	1(1.7)			0(0)			0.3033
Diabetes Mellitus	2(3.4)			3(4.6)			0.6890
Hypertension	3(5.1)			7(10.8)			0.2153
Previous CABG	1(1.7)			0(0)			0.3033
Previous PCI	0(0)			1(1.5)			0.3273
Burn severity							
TBSA0-19 (%)	22(37.3)			14(22.6)			0.1202
TBSA 20-49 (%)	25(42.4)			27(43.6)			
TBSA 50+ (%)	12(20.3)			21(33.9)			

Group B: 6% HES 130/0.4 in a balanced electrolyte solution (Volulyte), Group S: 6% HES 130/0.4 in a saline (Voluven), MI: myocardial infarction, CABG: coronary artery bypass graft, PCI: percutaneous coronary intervention, TBSA: total body surface area

Table-2: Operational Characteristics

	Group B (n=59)			Group S (n=62)			P-value
	n (%)	mean (SD)	Range	n (%)	mean (SD)	Range	
Type of procedure							
Caderveric allograft	27(45.8)			30(48.4)			0.7725
STSG	32(54.2)			33(58.2)			0.9112
Surgery details							
Elapsed day (day)		14.0(13.0)	1-54		12.7(10.9)	1-57	0.5601
Blood loss (mL)		1586.4(1124.9)	500-6000		1354.0(744.4)	250-3500	0.1807
HES(mL)		1145.9(379.9)	700-2700		1259.7(353.1)	500-2300	0.0904
Saline (mL)		1368.6(794.3)	0-3650		1227.4(697.3)	0-3400	0.3002
RL solution (mL)		539.8(313.2)	0-1600		390.6(338.6)	0-1300	0.0133
PRBC (unit)		5.1(3.7)	0-18		3.9(2.4)	0-11	0.0421
FFP (unit)		1.9(2.4)	0-16		1.3(1.3)	0-6	0.0746
Operation time (min)		128.7(46.4)	50-240		142.5(66.4)	30-385	0.1000
Outcome							
Mortality	8(13.6)			12(19.4)			0.3910

Group B: 6% HES 130/0.4 in a balanced electrolyte solution (Volulyte), Group S: 6% HES 130/0.4 in a saline (Voluven), STSG: split thickness skin graft, RL solution: Ringer's lactate solution, PRBC: packed red blood cells, FFP: fresh frozen plasma

Table-3: Preoperative and Postoperative Laboratory Values in Two HES Groups

	Group B (n=59)		Group S(n=62)		P-value
	mean (SD)	Range	mean (SD)	Range	
Preoperative					
BE	-0.04(3.16)	-7.0~6.7	-0.15(2.78)	-6.2~6.3	0.8373
pH	7.42(0.07)	7.26~7.56	7.42(0.06)	7.26~7.60	0.7932
Cl	104.31(4.52)	93~113	105.65(5.80)	89~127	0.1603
Postoperative					
BE	-0.96(3.26)	-10.9~6.4	-3.51(2.84)	-11.6~2	<.0001
pH	7.41(0.07)	7.20~7.62	7.37(0.06)	7.13~7.47	0.0021
Cl	105.44(3.79)	97~113	109.31(4.29)	102~127	<.0001
Group B: 6% HES 130/0.4 in a balanced electrolyte solution (Volulyte), Group S: 6% HES 130/0.4 in a saline (Voluven), BE: base excess (mmol/L), Cl: serum chloride level (mmol/L)					

Table-4: Preoperative and Postoperative Laboratory Values in Two HES Groups (Subgroup Analysis by TBSA)

	Group B(n=22)		Group S(n=14)		
TBSA (0~19)	mean (SD)	Range	mean (SD)	Range	P-value
Preoperative					
BE	0.79(2.32)	-3.7~6.2	0.46(1.80)	-2.1~4.2	0.6586
pH	7.46(0.04)	7.36~7.53	7.45(0.05)	7.36~7.60	0.6045
Cl	104.55(3.73)	96~110	107.29(2.79)	101~112	0.0242
Postoperative					
BE	0.70(2.29)	-4.9~5.0	-1.49(1.70)	-4.0~2.0	0.0067
pH	7.44(0.07)	7.34~7.62	7.40(0.03)	7.30~7.40	0.0080
Cl	105.64(4.20)	97~113	108.50(2.41)	104~113	0.0139
	Group B (n=25)		Group S (n=27)		
TBSA (20~49)	mean (SD)	Range	mean (SD)	Range	P-value
Preoperative					
BE	0.05(3.32)	-7.0~6.7	0.63(3.18)	-4.8~6.3	0.5217
pH	7.43(0.06)	7.28~7.56	7.43(0.05)	7.30~7.54	0.9881
Cl	103.92(5.00)	93~113	102.70(4.09)	92~108	0.3397
Postoperative					
BE	-1.67(3.34)	-8.8~6.4	-3.69(2.70)	-9.0~1.3	0.0200
pH	7.40(0.06)	7.27~7.50	7.38(0.05)	7.26~7.47	0.1402
Cl	104.72(3.14)	99~110	107.48(3.03)	102~114	0.0022
	Group B (n=12)		Group S (n=21)		
TBSA (50+)	mean (SD)	Range	mean (SD)	Range	P-value
Preoperative					
BE	-1.74(3.68)	-6.3~4.2	-1.56(2.26)	-6.2~1.7	0.8627
pH	7.35(0.05)	7.26~7.43	7.39(0.06)	7.26~7.47	0.0561
Cl	104.67(5.10)	95~111	108.33(7.40)	89~127	0.1392
Postoperative					
BE	-2.52(3.25)	-10.9~1.7	-4.64(3.00)	-11.6~0.1	0.0682
pH	7.36(0.07)	7.20~7.47	7.35(0.07)	7.13~7.46	0.6470
Cl	106.58(4.23)	100~112	112.19(5.17)	106~127	0.0033
Group B: 6% HES 130/0.4 in a balanced electrolyte solution (Volulyte), Group S: 6% HES 130/0.4 in a saline (Voluven), TBSA: Total body surface area, BE: base excess (mmol/L), Cl: serum chloride level (mmol/L)					

Table-5: The Effect of Volulyte on the Change of Laboratory Values after Covariate Control

		Model 1			Model 2		
		Estimate	SE	P-value	Estimate	SE	P-value
Dependent variable	*Treatment*						
BE difference	Group S(Voluven)	0			0		
	Group B (Volulyte)	2.303	0.489	<.0001	2.365	0.514	<.0001
pH difference	Group S(Voluven)	0			0		
	Group B (Volulyte)	0.037	0.011	0.0019	0.031	0.012	0.0084
Cl difference	Group S(Voluven)	0			0		
	Group B (Volulyte)	-2.411	0.768	0.0026	-1.681	0.785	0.0345
		Model 3			Model 4		
		Estimate	SE	p-value	Estimate	SE	p-value
Dependent variable	*Treatment*						
BE difference	Group S(Voluven)	0			0		
	Group B (Volulyte)	2.727	0.494	<.0001	2.481	0.501	<.0001
pH difference	Group S(Voluven)	0			0		
	Group B (Volulyte)	0.033	0.011	0.005	0.036	0.012	0.003
Cl difference	Group S(Voluven)	0			0		
	Group B (Volulyte)	-2.661	0.769	0.001	-2.240	0.779	0.005
Model 1: adjusted for age, sex, BMI, and TBSA, Model 2: adjusted for age, sex, BMI, TBSA, blood loss, HES, Saline, Ringer's lactate solution, packed red blood cells, fresh frozen plasma, and operation time, Model 3: adjusted for Ringer's lactate solution and packed red blood cells, Model 4: adjusted for age, sex, BMI, TBSA, Ringer's lactate solution, and packed red blood cells, Group B: 6% HES 130/0.4 in a balanced electrolyte solution (Volulyte), Group S: 6% HES 130/0.4 in a saline (Voluven), BE: base excess (mmol/L, Cl: serum chloride level (mmol/L)							

Table-6: Comparison between Preoperative and Postoperative Laboratory Values Using Paired t-test

	Preoperative		Postoperative		Paired t-test: difference (pre-post)		
	mean (SD)	Range	mean (SD)	Range	mean(SD)	t value	P-value
Group B (n=59)							
BE	-0.04(3.16)	-7.0~6.7	-0.96(3.26)	-10.9~6.4	0.92(2.63)	2.70	0.092
pH	7.42(0.07)	7.26~7.56	7.41(0.07)	7.20~7.62	0.01(0.06)	1.61	0.113
Cl	104.31(4.52)	93~113	105.44(3.79)	97~113	-1.14(3.68)	-2.37	0.021
Group S (n=62)							
BE	-0.15(2.78)	-6.2~6.3	-3.51(2.84)	-11.6~2.0	3.36(2.72)	9.74	<.0001
pH	7.42(0.06)	7.26~7.60	7.37(0.06)	7.13~7.47	0.05(0.06)	6.74	<.0001
Cl	105.65(5.80)	89~127	109.31(4.29)	102~127	-3.66(4.66)	-6.19	<.0001
Group B: 6% HES 130/0.4 in a balanced electrolyte solution (Volulyte), Group S: 6% HES 130/0.4 in a saline (Voluven), BE: base excess (mmol/L), Cl: serum chloride level (mmol/L)							

Table-7: Comparison between Preoperative and Postoperative Laboratory Values Using Paired t-test (Subgroup Analysis by TBSA)

	Preoperative		Postoperative		Paired t-test: difference (pre-post)		
	mean (SD)	Range	mean (SD)	Range	mean (SD)	t value	P-value
TBSA (0~19%)							
Group B (n=22)							
BE	0.79(2.32)	-3.7~6.2	0.70(2.29)	-4.9~5.0	0.09(1.49)	0.27	0.789
pH	7.46(0.04)	7.36~7.53	7.44(0.07)	7.34~7.62	0.01(0.05)	0.85	0.403
Cl	104.55(3.73)	96~110	105.64(4.20)	97~113	-1.09(2.35)	-2.18	0.041
Group S (n=14)							
BE	0.46(1.81)	-2.1~4.2	-1.49(1.70)	-4.0~2.0	1.95(1.09)	6.70	<.0001
pH	7.45(0.05)	7.36~7.60	7.40(0.03)	7.34~7.44	0.05(0.05)	3.6	0.003
Cl	107.29(2.79)	101~112	108.5(2.41)	104~113	-1.21(3.51)	-1.29	0.218
TBSA (20~49%)							
Group B (n=25)							
BE	0.05(3.32)	-7.0~6.7	-1.67(3.34)	-8.8~6.4	1.72(2.85)	3.02	0.006
pH	7.43(0.06)	7.28~7.56	7.40(0.06)	7.27~7.50	0.03(0.07)	2.03	0.053
Cl	103.92(5.00)	93~113	104.72(3.14)	99~110	-0.80(4.59)	-0.87	0.392
Group S (n=27)							
BE	0.63(3.18)	-4.8~6.3	-3.69(2.70)	-9.0~1.3	4.32(3.47)	6.48	<.0001
pH	7.43(0.05)	7.30~7.54	7.38(0.05)	7.26~7.47	0.05(0.06)	4.51	<.0001
Cl	102.70(4.09)	92~108	107.48(3.03)	102~114	-4.78(5.00)	-4.96	<.0001
TBSA (50%+)							
Group B (n=12)							
BE	-1.74(3.68)	-6.3~4.2	-2.52(3.25)	-10.9~1.7	0.78(3.40)	0.8	0.442
pH	7.35(0.05)	7.26~7.43	7.36(0.07)	7.20~7.47	-0.01(0.07)	-0.49	0.632
Cl	104.67(5.10)	95~111	106.58(4.23)	100~112	-1.92(3.75)	-1.77	0.105
Group S (n=21)							
BE	-1.56(2.26)	-6.2~1.7	-4.64(3.00)	-11.6~0.1	3.08(1.85)	7.62	<.0001
pH	7.39(0.06)	7.26~7.47	7.35(0.07)	7.13~7.46	0.043(0.06)	3.45	0.003
Cl	108.33(7.40)	89~127	112.19(5.17	106~127	-3.86(4.44)	-3.98	0.001
Group B: 6% HES 130/0.4 in a balanced electrolyte solution (Volulyte), Group S: 6% HES 130/0.4 in a saline (Voluven), TBSA: Total body surface area, BE: base excess (mmol/L), Cl: serum chloride level (mmol/L)							

Table-8: Differences between Preoperative and Postoperative serum Chloride Values in Two HES Groups

	Group B		Group S		P-value
	mean (SD)	Range	mean (SD)	Range	
Cl difference					
Total	-1.14 (3.68)	-9 ~ 13	-3.66 (4.66)	-20 ~ 4	0.001
TBSA 0~19%	-1.09 (2.35)	-6 ~ 3	-1.21 (3.51)	-8 ~ 4	0.900
TBSA 20~49%	-0.80 (4.59)	-7 ~ 13	-4.78 (5.00)	-14 ~ 3	0.004
TBSA 50%+	-1.92 (3.75)	-9 ~ 5	-3.86 (4.44)	-20 ~ 2	0.212
Group B: 6% HES 130/0.4 in a balanced electrolyte solution (Volulyte), Group S: 6% HES 130/0.4 in a saline (Voluven),TBSA: Total body surface area, Cl: serum chloride level (mmol/L)					

Table-9: The Effect of Volulyte on 30-day Mortality (Logistic Regression)

		Model 1				Model 2	
		OR	95% CI	p-value	OR	95% CI	p-value
Dependent variable	*Treatment*						
Death	Group S	1			1		
	Group B	1.475	0.381-5.712	0.5740	3.431	0.505-23.311	0.2072
Model 1: adjusted for age, sex, BMI, and TBSA, Model 2: adjusted for age, sex, BMI, TBSA, blood loss, HES, Saline, Ringer's lactate solution, PRBC, FFP, and operation time, Group B: 6% HES 130/0.4 in a balanced electrolyte solution (Volulyte), Group S: 6% HES 130/0.4 in a saline (Voluven)							

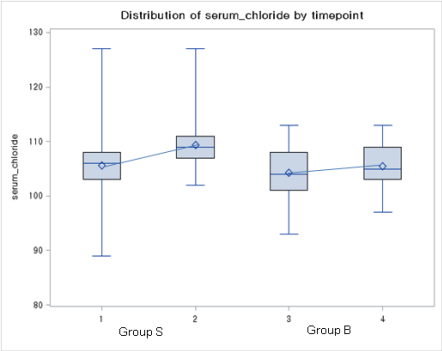

Fig-1: Change of serum chloride level (mmol/L) in two HES groups (Group B: 6% HES 130/0.4 in a balanced electrolyte solution (Volulyte), Group S: 6% HES 130/0.4 in a saline (Voluven), Pre-OP: preoperative, Post-OP: postoperative), 1,3: preoperative, 2,4: postoperative)

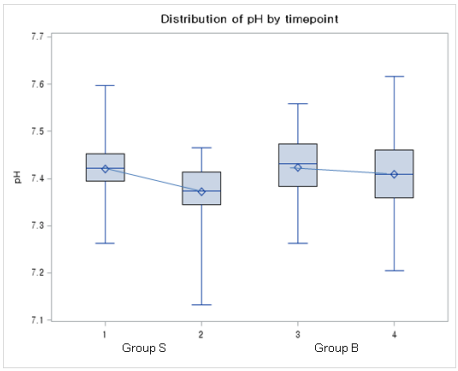

Fig-2: Change of pH level in two HES groups (Group B: 6% HES 130/0.4 in a balanced electrolyte solution (Volulyte), Group S: 6% HES 130/0.4 in a saline (Voluven), 1,3: preoperative, 2,4: postoperative)

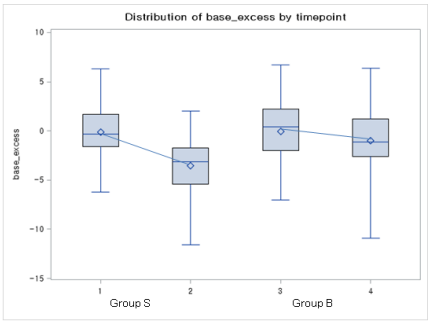

Fig-3: Change of base excess in two HES groups (Group B: 6% HES 130/0.4 in a balanced electrolyte solution (Volulyte), Group S: 6% HES 130/0.4 in a saline (Voluven), 1,3: preoperative, 2,4: postoperative)

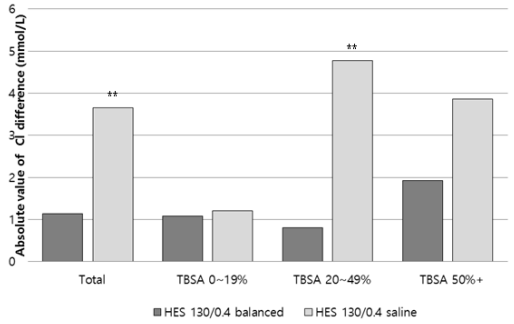

Fig-4: Differences between preoperative and postoperative serum chloride level in two HES groups (P<0.01)**

DISCUSSION

In this study, we evaluated the effects of Volulyte compared with Voluven regarding acid-base status and electrolytes. Although patients in group B had disadvantages such as having more PRBC transfusion and more patients with previous myocardial infarction or cerebrovascular accident, the postoperative base excess and arterial pH were significantly higher in group B. In order to overcome the heterogeneity of data, we analyzed the effect of treatment after controlling other variables in four ways.

Generally, base excess and arterial pH were decreased and serum chloride level was increased after the fluid infusion. The increase in serum chloride level was expected to be less in group B than in group S. The differences between pre- and postoperative values in base excess and arterial pH were expected to be smaller by the infusion of Volulyte, and the postoperative values were expected to be higher than that of group S. Therefore, a larger regression coefficient value was more effective. In serum chloride level, the difference was expected to be smaller in group B, and a larger negative regression coefficient value indicated a greater effect of treatment.

After controlling demographic variables and operative characteristics, the result was still significant. In models 1 - 4, which had different control variables, group B showed better results than group S. The positive coefficient for 'base excess difference' means that the degree of drop from preoperative to postoperative base excess was lower in group B than in group S. The coefficient for the arterial pH difference can also be interpreted as the base excess difference.

The negative coefficient for 'serum chloride level difference' means that the preoperative to postoperative increase in serum chloride level was less in group B than in group S. The results of our study demonstrated that the use of Volulyte gives positive effects tothe serum chloride level and acid-base status in burn surgery patients.

Third-generation hydroxyethyl starch (HES 130/0.4 balanced; Volulyte) is used widely because of its improved safety profile [20]. Volulyte has less sodium (137 vs. 154), chloride (110 vs. 154), and osmolality (283 mOsm/kg vs. 304 mOsm/kg) compared with Voluven. The difference in composition between Volulyte and Voluven could have different effects on the human body when administered to patients.

Previous studies have compared Volulyte and Voluven. In a study in cardiac surgery, Base et al. compared balanced and saline-based HES solutions [21]. In a similar comparison of concepts in major abdominal surgery, Boldt et al. examined a total balanced volume replacement strategy using balanced HES solutions [22]. Both studies showed higher serum chloride level postoperatively and larger base excess difference in the Voluven groups. Also a similar study has been conducted in children reported that bicarbonate and base excess decreased only with Voluven and remained stable with Volulyte [23]. Similar to previous studies, the postoperative serum chloride level was significantly higher in the Voluven group. These findings are consistent with the results of our study.

Fluid resuscitation affects acid-base status and electrolytes such as hyperchloremic acidosis which may contribute to many other complications [24]. Major burn patients need more fluid resuscitation during burn surgery which makes the choice of fluid even more important. One study reported that major burn patients who received larger volumes of resuscitation fluid were at higher risk for injury complications and death [25]. There were animal studies suggest that hyperchloremia causes renal vasoconstriction [26,27], and hyperchloremic acidosis has been often associated with reduced gastric mucosal perfusion on gastric tonometry, vasoconstriction and reduction of the glomerular filtration rate in patients as well [28]. In another animal study with burned rats, the burned and infected group developed septic shock with hypernatremia, hyperchloremia, and hyperosmolality [29]. Burn injury can cause fluid and electrolyte disturbances due to fluid shift. Therefore, prevention of hyperchloremic acidosis may be more important in major burn patients. Walker et al. [30] compared effects of balanced electrolyte solution and normal saline on bicarbonate and base deficit in major burn patients during burn surgery. The result showed that bicarbonate and total buffering capacity in balanced electrolyte solution group were significantly higher than in normal saline group.

The current study had several limitations. Since it was a retrospective study, we could not control many things before we conduct a study. First, administered mean dose of Ringer's lactate solution and transfused units of packed red blood cells had differences between the study groups. Therefore, we used analysis of multivariate regression in order to adjust and control these different factors. Second, we did not compare the effect for hemodynamic stability or outcome measures such as lengths of ICU and hospital stay. Third, regarding metabolism of the fluid, future research should perform consecutive postoperative measurements throughout time course. This is because our data was obtained from routine medical records and laboratory investigations. Therefore, further clinical investigations to determine the effects of Volulyte should be performed.

The present study showed that Volulyte, compared to Voluven, had more beneficial effects on acid-base status and serum chloride level in burn patients. In addition, more severe burn patients had a more distinct change in blood gas analysis according to the type of HES solution. This finding can be interpreted that Volulyte contributes to the stability of acid-base status and electrolytes during burn surgery in more severe burn patients. In massive burn patients, there should be a concern in choice of colloid solution. In conclusion, Volulyte could minimize the possibility of infusion related hyperchloremic acidosis in burn patients undergoing surgery.

REFERENCES

1. Boldt J, Suttner S. Plasma substitutes. Minerva ane stesiologica. 2005 Dec;71(12):741-58..
2. Deane SA, Gawky PL, Woods P, Cass D, Hollands MJ, Cook RJ, Read C. The management of injuries –a review of deaths in hospital. Australian and New Zealand Journal of Surgery. 1988 Jun;58(6):463-9.
3. American Academy of Pediatrics. American colleg e of critical care medicine. Society of critical care medicine Consensus report for rationalization of se rvices for critically ill or injured children. Pediatric s. 2000;105:152-5.
4. Tiwari VK. Burn wound: How it differs from other wounds?. Indian journal of plastic surgery: official publication of the Association of Plastic Surgeons o f India. 2012 May;45(2):364.
5. Nguyen TT, Gilpin DA, Meyer NA, Herndon DN. Current treatment of severely burned patients. Ann als of surgery. 1996 Jan;223(1):14.
6. Haberal M, Abali AE, Karakayali H. Fluid manage ment in major burn injuries. Indian journal of plasti c surgery: official publication of the Association of Plastic Surgeons of India. 2010 Sep;43(Suppl):S29.
7. Harbin KR, Norris TE. Anesthetic management of patients with major burn injury. AANA J. 2012 De c 1;80(6):430-9.
8. Boldt J, Papsdorf M. Fluid management in burn pat

ients: results from a European survey—more questi ons than answers. Burns. 2008 May 1;34(3):328-38 .
9. Base EM, Standl T, Lassnigg A, Skhirtladze K, Jun gheinrich C, Gayko D, Hiesmayr M. Efficacy and s afety of hydroxyethyl starch 6% 130/0.4 in a balanc ed electrolyte solution (Volulyte) during cardiac su rgery. Journal of cardiothoracic and vascular anesth esia. 2011 Jun 1;25(3):407-14.
10. Lee JJ, Kim JH. Plasma volume expanders: classifi cation and characteristics of colloids. Journal of the Korean Medical Association/Taehan Uisa Hyophoe Chi. 2013 Oct 1;56(10).
11. Van Haren F, Zacharowski K. What's new in volu me therapy in the intensive care unit?. Best Practice & Research Clinical Anaesthesiology. 2014 Sep 1; 28(3):275-83.
12. Hiltebrand LB, Kimberger O, Arnberger M, Brandt S, Kurz A, Sigurdsson GH. Crystalloids versus coll oids for goal-directed fluid therapy in major surger y. *Crit Care* 2009; 13: R40.
13. Moretti EW, Robertson KM, El-Moalem H, Gan TJ . Intraoperative colloid administration reduces post operative nausea and vomiting and improves posto perative outcomes compared with crystalloid admin istration. Anesthesia & Analgesia. 2003 Feb 1;96(2):611-7.
14. Lawrence A, Faraklas I, Watkins H, Allen A, Coch ran A, Morris S, Saffle J. Colloid administration no rmalizes resuscitation ratio and ameliorates "fluid c reep". Journal of Burn Care & Research. 2010 Jan 1;31(1):40-7.
15. Gan TJ, Bennet-Guerrero E, Phillips-Bute B, Wake ling H, Moskowitz DM, Olufolabi Y, Konstadt SN, Bradford C, Glass PS, Machin SJ, Mythen MG. He xtend, a physiologically balanced plasma expander for large volume use in major surgery. a randomize d phase III clinical trial.:88.
16. Allen SJ. Fluid therapy and outcome: balance is bes t. The journal of extra-corporeal technology. 2014 Mar;46(1):28.
17. Westphal M, James MF, Kozek-Langenecker S, St ocker R, Guidet B, Van Aken H. Hydroxyethyl Star chesDifferent Products–Different Effects. Anesthes iology: The Journal of the American Society of An esthesiologists. 2009 Jul 1;111(1):187-202.
18. Grocott MP, Mythen MG, Gan TJ. Perioperative fl uid management and clinical outcomes in adults. A nesthesia & Analgesia. 2005 Apr 1;100(4):1093-10 6.
19. Boldt J, Schöllhorn T, Münchbach J, Pabsdorf M. A total balanced volume replacement strategy usin g a new balanced hydoxyethyl starch preparation (6 % HES 130/0.42) in patients undergoing major abd ominal surgery. European journal of anaesthesiolog y. 2007 Mar;24(3):267-75.
20. Jungheinrich C, Neff TA. Pharmacokinetics of hyd roxyethyl starch. Clinical pharmacokinetics. 2005 J ul 1;44(7):681-99.
21. Base EM, Standl T, Lassnigg A, Skhirtladze K, Jun gheinrich C, Gayko D, Hiesmayr M. Efficacy and s afety of hydroxyethyl starch 6% 130/0.4 in a balanc ed electrolyte solution (Volulyte) during cardiac su rgery. Journal of cardiothoracic and vascular anesth esia. 2011 Jun 1;25(3):407-14.
22. Boldt J, Schöllhorn T, Münchbach J, Pabsdorf M. A total balanced volume replacement strategy usin g a new balanced hydoxyethyl starch preparation (6 % HES 130/0.42) in patients undergoing major abd ominal surgery. European journal of anaesthesiolog y. 2007 Mar;24(3):267-75.
23. Suempelmann R, Witt L, Bruett M, Osterkorn D, K oppert W, Osthaus WA. Changes in acid- base, ele ctrolyte and hemoglobin concentrations during infu sion of hydroxyethyl starch 130/0.42/6: 1 in normal saline or in balanced electrolyte solution in children . Pediatric Anesthesia. 2010 Jan;20(1):100-4.
24. Dorje P, Adhikary G, Tempe DK. Avoiding iatroge nic hyperchloremic acidosis—call for a new crystal loid fluid. Anesthesiology: The Journal of the Ame rican Society of Anesthesiologists. 2000 Feb 1;92(2):625-.
25. Klein MB, Hayden D, Elson C, Nathens AB, Game lli RL, Gibran NS, Herndon DN, Arnoldo B, Silver G, Schoenfeld D, Tompkins RG. The association b etween fluid administration and outcome following major burn: a multicenter study. Annals of surgery. 2007 Apr;245(4):622.
26. Wilcox CS, Peart WS. Release of renin and angiote nsin II into plasma and lymph during hyperchlorem ia. American Journal of Physiology-Renal Physiolo gy. 1987 Oct 1;253(4):F734-41.
27. Wilcox CS. Regulation of renal blood flow by plas ma chloride. The Journal of clinical investigation. 1 983 Mar 1;71(3):726-35.
28. Eisenhut M. Causes and effects of hyperchloremic acidosis. Critical Care. 2006 Jun;10(3):413.
29. Chiao JJ, Barber AE, Shires GT. Effect of sepsis on intracellular sodium activity, sodium concentration, and water content in thermal injured rat. Circulator y shock. 1992 Sep;38(1):42-9.
30. Walker SC, Hoover L, Shepherd J, Cancio L, Good win C. Balanced Electrolyte Solution Reduces Acid osis as Compared to Normal Saline in the Resuscita tion of Perioperative Burn Patients. Anesthesiology . 2001 Oct 1;95:A375.