Acute kidney injury (AKI) in Pre and post treatment of 0.9% Sodium Chloride solution in pediatric shock in tertiary center

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Abstract

Background: Pediatric Advanced Life Support (PALS) guideline was recommended administration of large volume intravenous crystalloid solution for treatment of pediatric shock. From other study[1] found that incidence of acute kidney injury (AKI) and hyperchloremic metabolic acidosis after received 0.9%NaCl, it has been used as the isotonic crystalloid of choice in treating pediatric shock for a long time due to its availability.

Objective: Primary outcome to evaluate the prevalence of AKI in pediatric shock patients that received large volume of 0.9%NaCl within 48 h. **Secondary outcomes** to evaluate the prevalence of electrolytes imbalance in pediatric shock patients that received large volume of 0.9%NaCl and mortality rate.

Materials and Methods: Thirty pediatric shock patients age 3 months to 15 years old, which received large volume of 0.9%NaCl since 2015 to December 2021, were included in our study. Baseline characteristics and laboratory data: electrolytes data and renal function test at 0, 24 and 48 h after resuscitation were recorded.

Results: The prevalence of AKI was statistically significant decreased from 0 h (60%), 24h (23.3%)($p=0.003$) and 48 h (16.7%)($p<0.001$).The prevalence of hypokalemia and hyperchloremia at 24 h was significantly increased ($p=0.008$), ($p<0.001$) respectively. The mortality rate was 16.7%, four were diagnosed septic shock with three had hematologic malignancy as an underlying disease.

Conclusion: The prevalence of AKI in pediatric shock patients decreased after receiving 0.9% NaCl iv resuscitation at 24 and 48 h. Electrolytes imbalance such as hyperchloremia and hypokalemia could be found. Patients with underlying hematologic malignancy had higher mortality rate than other pediatric patients.

Keyword: Acute Kidney injury (AKI), Normal Saline Solution (NSS), Pediatric Shock

Introduction

Pediatric shock is a life-threatening condition resulting in high mortality and morbidity. Shock was defined as poor tissue perfusion and/or hypotension. Common sequelae was acute kidney injury (AKI), defined as increasing in serum creatinine by 50% from baseline within 7 days, or 0.3 mg/dl (26.5 mmol/l) within two days, or oliguria[2].

American College of Critical Care (ACCM)/Pediatric Advanced Life Support (PALS) guidelines for sepsis resuscitation in the first hour recommended goal for administration of intravenous fluids, antibiotics, and vasoactive agents[3].

Large intravenous crystalloid infusion is a key component in the treatment of pediatric

shock[3]. It is aimed to restore intravascular volume, maintain cardiac output, and reestablish tissue oxygenation

Three different solutions comprise isotonic crystalloid by definition, namely 0.9% sodium chloride solution, lactate ringer solution and acetated ringer solution. 0.9% NaCl has 154 mmol/L of sodium and chloride compared to 140 and 109 mmol/L of sodium and chloride in the extracellular fluid respectively. On the contrary, electrolyte in lactate and acetated ringer solutions are the same as in the content of extracellular fluid.

Pathophysiology of AKI is multifactorial and complex. Physiological adaptations of patient with shock resulted in the reduction of blood flow as well as the lowering of oxygen and metabolic substrates concentration. The resulting cellular injury from the shock leads to AKI[5].

The use of 0.9% NaCl in shock patients resulted in AKI and hyperchloremic metabolic acidosis[1] but 0.9% NaCl has been used as the isotonic crystalloid of choice in treating pediatric shock for a long time due to its availability.

The aim of this study was to investigate the prevalence of AKI before and after 0.9% NaCl resuscitation in pediatric shock.

Primary objective was to study the prevalence of AKI in pediatric patients who were under shock condition. The secondary objective was the prevalence of electrolytes imbalance and mortality rate.

Materials and Methods

This retrospective study was conducted at the department of pediatrics, Bhumibol Adulyadej Hospital (BAH), Bangkok, Thailand. Approval for the study was granted by the BAH ethics committees (IRB No.49/63). Period of study was between August 2019 and December 2021.

The subjects were pediatric patients age between three months to 15 years old who had been diagnosed of shock. All cases received massive intravenous 0.9%NaCl (>20 ml/kg in 10-15 minutes). Patients with underlying chronic kidney disease (CKD) were excluded in this study.

All cases underwent resuscitation treatment according to AACM and PALS guideline[2]. Specific investigation namely hemogram, electrolyte, renal function test and hemoculture with clinical application were applied. Endotracheal intubation, respiratory support, inotrope administration, adjustment of total volume of initial fluid resuscitation and type of the maintenance fluid were applied to patients according to their clinical status under the judgment of certified attending pediatric staff. Vital sign and laboratory monitoring were closely observed for at least 48 h.

Baseline characteristics were recorded, including age, gender, underlying diseases and source of infection. Laboratory data were recorded, including electrolytes data, renal function test, urine output at 0, 24, and 48 h after resuscitation by large volume of 0.9% NaCl.

Sample size was calculated by n4 study program (Prince of Songkla University, Songkla, Thailand). Alpha and Beta were set at level of 0.05 and 0.2, respectively.

Prevalence of AKI according to Martínez-García's study was applied to sample size calculation[7].The sample size was at least 29 cases from the calculation at power 80%.

SPSS software (version 23.0; IBM, Armonk, NY, US) was used for statistical analysis. Patient demographics and clinical outcomes were reported using mean and SD for continuous data. Number (percent) and frequencies were used for categorical data. McNemar's test was used for calculation of AKI different during treatments. Friedman test was used for the calculation of electrolyte imbalance during shock treatment.

Result

The baseline characteristic was shown in **Table 1.**A total of 33 children were eligible to our study, from whom three patients were excluded as **Figure 1.** Thirty cases, including 18 (60%) male and 12 (40%) female with a median age of 9.82 years. Nearly one quarter of cases (7/30)had no underlying disease. Hematology, neurology and other underlying disease such as gastrointestinal, allergy, musculoskeletal and rheumatology were found at 26.6, 33.3 and 16.6 percent respectively.

Table 1 Baseline Characteristics of pediatric shocks subject (n=30)

	n (%)
Age(years)*	9.82±4.82
3 months-1 years old	3 (9.7)
1-15 years old	28 (90.3)
BW (kg)*	29.72±22.1
HT (cm)*	127.72±31.2
Male	18 (60)
Underlying disease	
No	7 (23)
Hematology*	8 (26.6)
Neurology*	10 (33.3)
Others*	5 (16.6)
Type of shock	
Septic shock	24 (80)
Hypovolemic shock	4 (13)
Dengue shock syndrome	1 (3.3)
Anaphylactic shock	1 (3.3)
Positive Hemoculture	9 (30)
Source of infection	
Respiratory system	9 (30.0)
Gastrointestinal	11 (36.6)
Skin	3 (10)

BW: body weight, Ht: height
Underlying disease: Hematology: ALL, AML, osteosarcoma, G6PD deficiency, thalassemia Neurology: epilepsy, Others: asthma, SLE

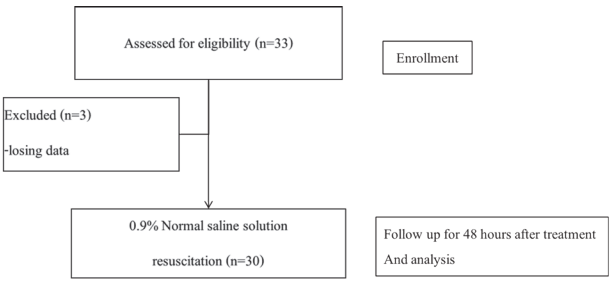


Figure 1 Flow chart of this study

Septic shock was the most common diagnosis among children. All cases of shock were received iv board spectrum antibiotic therapy. About the cause of infection, one-third of cases had respiratory infection (9/30) and gastrointestinal infection (11/30). Adjustment of total volume of initial fluid adjusted to their clinical status. Intravenous rate of 20, 40 and 60 ml/kg of initial fluid resuscitation were reported at percentage of 33.3 (10/30), 16.7 (5/30) and 50 (15/30), respectively

The prevalence of AKI at o h was 60 percent (18/30). After large volume of 0.9% NaCl iv administration, the prevalence of AKI at 24 h (23.3%) and 48 h (16.7%) which statistically significant lower than at 0 h. (p=0.003), (p<0.001) respectively, as shown in **Table 2.**

Table 2 Prevalence of AKI at 0, 24 and 48 hours of intravenous 0.9% Sodium Chloride solution treatment (n=30)

	AKI*	No AKI*	p value
Hour			
0	18(60.0)	12(40.0)	
24	7(23.3)	23(76.7)	0.003
48	5(16.7)	25(83.3)	< 0.001

Glomerular filtration rate (GFR) was increased at 0, 24, 48 h of intravenous 0.9% NaCl solution treatment in pediatric shock patients as reported in **Figure 2.**

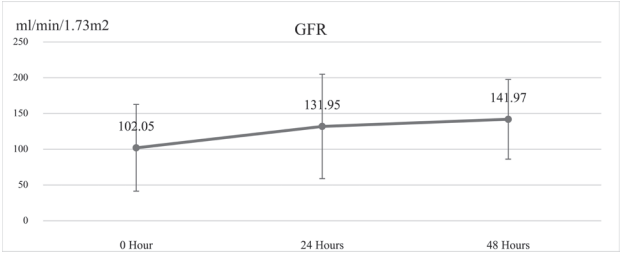
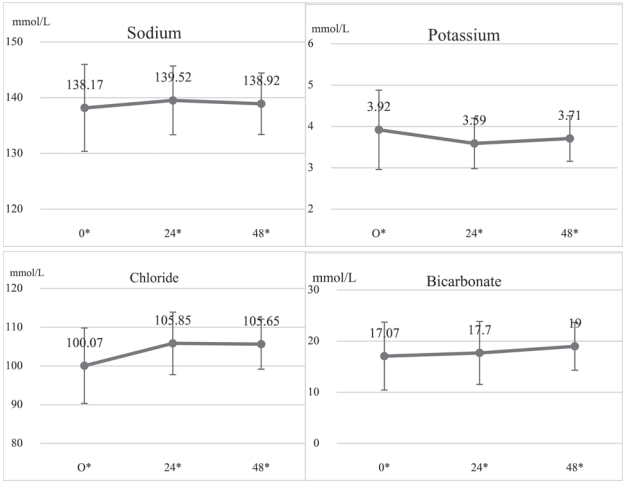


Figure 2 Glomerular filtration rate (GFR) at 0, 24, 48 hours of intravenous 0.9% Sodium Chloride solution treatment in Pediatric shock

Serum electrolytes at 0, 24, 48 h of 0.9% NaCl IV solution treatment in pediatric shock patients were reported in **Figure 3.**

At initial treatment 56.7% (17/30) and 53.3% (16/30) of patients had normokalaemia and normochloremia. The prevalence of hypokalemia and hyperchloremia were significantly increased at 24 h after received large volume of intravenous 0.9%NACl and returned back to normokalaemia and normochloremiaat 48 h (p=0.008),(p<0.001) respectively. as reported in **Table 3.**



*Hours

Figure 3 Serum electrolytes at 0, 24, 48 hours of intravenous 0.9% Sodium Chloride solution treatment in Pediatric shock

The mortality rate of the patients was 16.7% (5/30). Most of them were diagnosed with septic shock. Three (60%) patients had hematologic malignancy as an underlying disease.

The mortality rate was 16.7% (5/30), four were diagnosed septic shock with three had hematologic malignancy as an underlying disease such as acute lymphoblastic leukemia and osteosarcoma, one was diagnosed hypovolemic shock.

Table 3 Electrolyte at 0, 24 and 48 hours of intravenous 0.9% Sodium Chloride solution treatment (n=30)

Hour	0	24	48	P Value
Sodium, n (%)				
Hypo	3 (10)	0 (0)	2 (6.7)	0.524
Normal	23(76.7)	26 (86.6)	23 (76.7)	
Hyper	4 (13.3)	4 (13.3)	5 (16.7)	
*	138.17±7.80	139.52±6.17	138.92±5.51	
Potassium, n (%)				
Hypo	10 (33)	19 (63.3)	9 (30)	0.008 *
Normal	17 (56.7)	11 (36.6)	21 (70)	
Hyper	3 (10)	-	-	
*	3.92±0.96	3.59±0.65	3.68±0.55	
Chloride, n (%)				
Hypo	8 (26.7)	1 (3.3)	1 (3.2)	< 0.001 *
Normal	16 (53.3)	11 (36.6)	20 (66.7)	
Hyper	6 (20)	18 (60)	9 (30)	
*	100.07±9.74	105.85±8.07	105.65±6.46	
Bicarbonate, n (%)				
Acidosis	25 (83.3)	25 (83.3)	25 (83.3)	1.000
Normal	5 (16.7)	5 (16.7)	5 (16.7)	
*	17.07±6.64	17.70±6.15	19.00±4.67	

*Mean±SD

Discussion

The outcomes of this retrospective study were the prevalence of AKI after the resuscitation in pediatric shock patients with the large volume of 0.9%NaCl at 24 and 48 h was lower than 0 h.

0.9%NaCl is a chloride-rich and potassium-free solution. As the consequence of large volume 0.9%NaCladministration, hyperchloremia and hypokalemia were found in the patients at 24 h after resuscitation. Therefore attending pediatric staff had chosen the maintenance fluid (0.45%NaCl) and potassium supplement used to correct electrolyte imbalances, hypercholemia and hypokalemia were trended to normal at 48 h.

Brown et al.conducted a SMART trial study compared 0.9% NaCltobalance isotonic crystalloid solution to resuscitation adult patient with septic shock[1]. The outcome in this study was the incidence of acute kidney injury in 30 days. Among 0.9%NaCl group the incidence of AKI was 40.1% while balance crystalloid group was 35.4%. The incidence of AKI in our study was different from Brown et al. study which

incidence of AKI at 48 h after resuscitation was 16.7% because of our study performed in pediatric population, patient with chronic disease were excluded from this study and we still need to follow up the incidence of AKI at 30 days.

Trepatchayakorn S et al. conducted RCT study concerning types of crystalloid fluid-related complication on resuscitation outcomes in pediatric sepsis patients admitted at PICU King Chulalongkorn Memorial Hospital[8]. The prevalence of AKI after 0.9% NaCl bolus at 24 h was 9.1% (1/11) and headed towards more serum chloride at two hours. From our study the incidence of AKI at 24 h was 23.3% which higher than Trepatchayakorn S et al. study may be because from the difference of tool The prevalence of AKI and hyperchloremia at 24 h was 23.3and 60% in our study. The incidence of AKI in his study was lower than our study. There was different tool to predict the incidence of AKI. In this study used serum creatinine to evaluate of AKI and GFR but in Trepatchayakorn S et al. study use urinary neutrophil gelatinase-associated lipocalin (uNGAL).

Shime N et al. conducted a prospective, multicenter study, Incidence and risk factors for mortality in pediatric sever sepsis in PICU, one hundred twenty-two patient s were included in this study, This study found that patient with hematologic disorder had highest mortality rate from other diseases pediatric patients (OR 8.97, 95%CI 1.56-51.60)[9] . The mortality rate in this study was 17.7% while in our study was 16.7%. Eighty percent of the dead patients were diagnosed hematologic malignancy. Shime N et al. mortality outcome was likely to our outcomes.

Conclusion

The prevalence of AKI in pediatric shock patients decreased after receiving 0.9% NaCl iv resuscitation at 24 and 48 h. Electrolytes imbalance such as hyperchloremia and hypokalemia could be found.

Patients with underlying hematologic malignancy had higher mortality rate than other pediatric patients.

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Potential conflicts of interest

The authors declare no conflict of interest

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การศึกษาเปรียบเทียบการบาดเจ็บของไต ก่อนและหลังการรักษาภาวะช็อกในเด็ก ด้วยสารละลาย 0.9% โซเดียมคลอไรด์

รติมา พันธ์ไชยศรี, วิศรุต การุญบุญญานันท์, สธนา เสริมศรี

ภูมิหลัง: แนวทางการรักษาภาวะช็อกในเด็ก คือการให้สารน้ำชนิดคริสตัลลอยด์ปริมาณมาก (มากกว่า 10-20 ซีซี/กก.ภายใน 10-15 นาที) ทำให้เกิดการบาดเจ็บไตและภาวะเลือดเป็นกรด ปัจจุบันยังมีการใช้ 0.9%โซเดียมคลอไรด์เพื่อรักษาภาวะช็อกในเด็กเนื่องจากความสะดวกในเข้าถึงในโรงพยาบาลมากกว่าสารละลายอื่น

วัตถุประสงค์: เปรียบเทียบอุบัติการณ์การเกิดการบาดเจ็บของไต และความผิดปกติของเกลือแร่ในผู้ป่วยเด็กที่มีภาวะช็อกก่อนและหลังได้รับการรักษาด้วยสารละลาย 0.9%โซเดียมคลอไรด์ภายใน 48 ชั่วโมง และอัตราการเสียชีวิต

วัสดุและวิธีการ: การศึกษาเก็บข้อมูลย้อนหลังตั้งแต่ปี พ.ศ. 2558 ถึง ปี 2564 เก็บข้อมูลผู้ป่วยเด็กที่ได้รับการวินิจฉัยและรักษาภาวะช็อกด้วย 0.9% โซเดียมคลอดไรด์ (มากกว่า 10-20 ซีซี/กก. ภายใน 10-15 นาที) จำนวน 30 คน ข้อมูลพื้นฐาน ชนิดของภาวะช็อกและข้อมูลติดตามผลค่ากรองไต ค่าเกลือแร่ ตั้งแต่ก่อนรักษา, 24 และ 48 ชั่วโมงหลังรักษา และข้อมูลอัตราการเสียชีวิตระหว่างนอนโรงพยาบาล

ผลการศึกษา: อุบัติการณ์การเกิดการบาดเจ็บของไตก่อนทำการรักษา, 24 ชั่วโมงและ 48 ชั่วโมงหลังการรักษาด้วยสารละลาย 0.9% โซเดียมคลอไรด์คือ 60, 23.3 และ 16.7 เปอร์เซ็นต์ตามลำดับ ลดลงอย่างมีนัยสำคัญทางสถิติ เมื่อเปรียบเทียบก่อนทำการรักษากับ 24ชั่วโมง ($p=0.003$) และ 48 ชั่วโมง ($p<0.001$) อุบัติการณ์การเกิดโพแทสเซียมต่ำที่ 24ชั่วโมงหลังทำการรักษาเพิ่มขึ้นเมื่อเปรียบเทียบกับก่อนรักษา และลดลงที่ 48 ชั่วโมงอย่างมีนัยสำคัญทางสถิติ ($p=0.008$) ในขณะที่อุบัติการณ์การเกิดคลอไรด์สูงที่ 24 ชั่วโมงหลังทำการรักษาเพิ่มขึ้นเมื่อเปรียบเทียบกับก่อนรักษา และลดลงที่ 48 ชั่วโมงอย่างมีนัยสำคัญทางสถิติ ($p<0.001$) อัตราการเสียชีวิตในผู้ป่วยเด็กที่มีภาวะช็อกคือ 16.7 เปอร์เซ็นต์ โดย 60 เปอร์เซ็นต์ของผู้ป่วยที่เสียชีวิตมีโรคประจำตัวเกี่ยวกับมะเร็งระบบเลือด

สรุป: อุบัติการณ์การเกิดการบาดเจ็บของไตในผู้ป่วยเด็กที่มีภาวะช็อกลดลงที่ 24 และ 48 ชั่วโมงหลังการรักษาด้วยสารละลาย 0.9% โซเดียมคลอไรด์ พบภาวะโพแทสเซียมต่ำและคลอไรด์สูงได้หลังได้รับสารละลาย 0.9% โซเดียมคลอไรด์ พบอัตราการตายที่สูงในโรคประจำตัวเกี่ยวกับมะเร็งระบบเลือดในผู้ป่วยเด็กที่มีภาวะช็อก