## Crystalloids and the appeal for balanced solutions. What's the evidence and does it really matter?

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**Professor and Chief Cardiothoracic Anesthesiology Vanderbilt University Medical Center** 

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#### **Dr Robert Lewins**

DR. LEWINS ON INJECTION OF SALINE SALTS INTO THE VEINS. O

" Whenever the pulse fails, more fluid ought to be thrown in, without regard to quantity"

"The most wonderful and satisfactory effect is the immediate consequence of the injection."

"The quantity necessary to be injected will probably be found to depend upon the quantity of serum lost."

"The solution that was used consisted of two drachms of muriate, and two scruples of carbonate of soda to sixty ounces of water."

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Lewins: London Medical Gazette 1832

#### **Lancet editorial 1832**

#### THE CASES OF CHOLERA SUCCESSFULLY TREATED

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#### THE LANCET. don. Suturdov. June 2nd. 1931

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With respect to the quentity of warm amployed, two circumstance are to be borne in mind's first, that the spisious while the treat the quentity of blood is the solid boly are the content of the content

"A suitable clinical investigation is required... the mass of the profession is unable to decide; and thus, instead of any uniform mode of treatment, every town and village has its different

system or systems, while the daily lists of mortality proclaim the general inefficiency of the whole."

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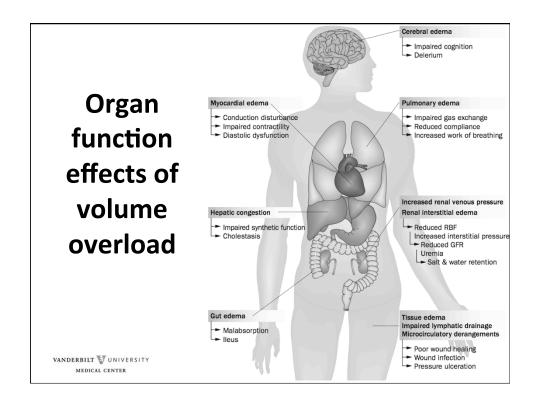
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Lancet 1832

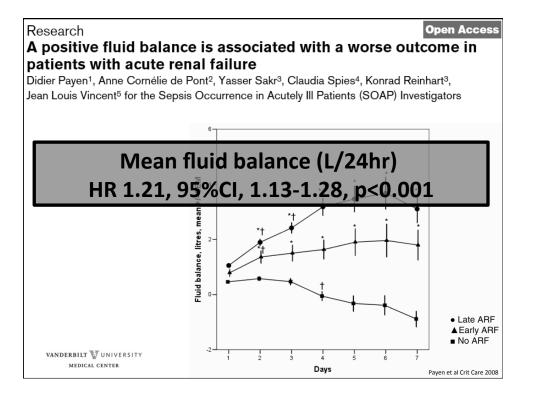
### Is fluid amount important?



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Reference	Study type	Population	n	Average fluid balance in less-positive group	Average fluid balance in more-positive group	Renal function measure	Renal outcome with more- restrictive fluid balance strategy	Principal outcome with more-restrictive fluid balance strategy
ARDS Clinical Trials Network (2006) <sup>88</sup>	Multicenter RCT	ARDS	1,000	–136 ml on day 7	+6,992 ml on day 7	Need for RRT; change in creatinine	No difference	Shorter duration of ventilation and ICU stay
Martin et al. (2005) <sup>86</sup>	Single-center RCT	Mixed ALI	40	-5,480 ml on day 5	-1,490 ml on day 5	Change in creatinine	No difference	Improved oxygenation
Martin et al. (2002)85	Single-center RCT	ALI after trauma	37	-3,300 ml on day 5	+500 ml on day 5	Change in creatinine	No difference	Improved oxygenation
Mitchell et al. (1992) <sup>127</sup>	Single-center RCT	Mixed ICU needing PAC	102	+142 ml	+2,239 ml	Change in creatinine	Small rise in creatinine	Shorter duration of ventilation and ICU stay
Bouchard et al. (2009) <sup>25</sup>	Retrospective observational	Mixed ICU with AKI	542	<10% rise	>10% rise	Dialysis independence	Improved	Decrease in mortality
Payen et al. (2008) <sup>6</sup>	Retrospective observational	Mixed ICU with or without AKI	3,147	-1,000 ml	+3,000 ml	Renal SOFA score	Improved	Decrease in mortality in patients with AKI
Vidal et al. (2008) <sup>72</sup>	Prospective observational	Mixed ICU with elevated or normal IAP	83	+5,000 ml	+9,000 ml	Renal SOFA score	Improved	Normal IAP associated with less organ failure and shorter ICU stay
Adesanya et al. (2008) <sup>128</sup>	Retrospective observational	Surgical ICU	41	+5 kg	+8.3 kg	Change in creatinine	No difference	Shorter duration of ventilation and ICU stay
McArdle et al. (2007) <sup>87</sup>	Retrospective observational	Surgical ICU	100	+7,500 ml	+10,000 ml	Change in creatinine	No difference	Decrease in postoperative complications
Arlati et al. (2007)99	Prospective observational	Burns ICU	24	+7,500 ml	+12,000 ml	Urine output	No difference	Decrease in organ dysfunction score



#### Is fluid amount important?

- Excess fluid leads to adverse outcomes
- When fluid given is blinded the ratio of crystalloid : colloid is generally 1.3 : 1
- NOT 3:1 as is widely believed
- Why are fluids not afforded the same respect as other intravenous drugs?

## Is crystalloid type important?



ays



9g NaCl = 36 bags of chips, or 1 bag of saline

ays

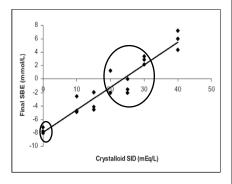


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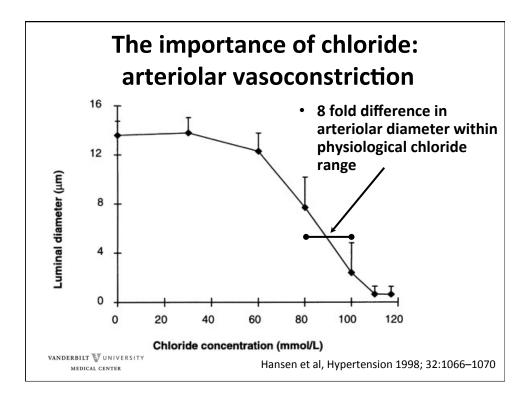
## **Fluid Therapy Basics**

Not all IV Fluids are created equal...

- A "balanced" fluid has the physiological electrolyte composition of plasma
- Balanced fluids do not cause the hyperchloremic acidosis associated with 0.9% saline



- •Base excess after infusion is determined by the strong ion difference (SID) of the fluid infused.
- •The red circle represents 0.9% NaCl, the blue circle represents balanced crystalloid



#### **Abnormal Saline**

- 0.9% saline contains Na and Cl in equal amounts (154 meq/l)
- Unlike plasma
- Adding NaCl to plasma increases the relative Cl concentration more than that of Na
- 0.9% saline reduces plasma SID and leads to hyperchloremic metabolic acidosis

#### The Abuse of Normal Salt Solution

George H. Evans, JAMA 1911

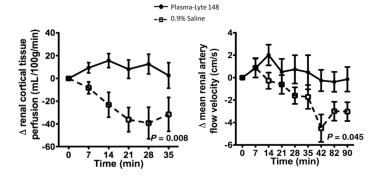
"One cannot fail to be impressed with the danger...(of) the utter recklessness with which salt solution is frequently prescribed, particularly in the postoperative period..."

"...the disastrous role played by the salt solution is often lost in light of the serious conditions that call forth its use."

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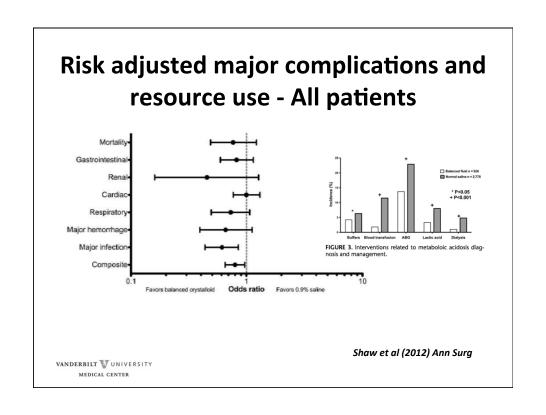
## 2L of Saline versus Balanced Crystalloid in Healthy Volunteers



Chowdhury et al (2012) Ann Surg

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#### **FEATURE** Major Complications, Mortality, and Resource Utilization After **Open Abdominal Surgery** 0.9% Saline Compared to Plasma-Lyte Andrew D. Shaw, MB, FRCA, FCCM,\* Sean M. Bagshaw, MD,† Stuart L. Goldstein, MD,‡ Lynette A. Scherer, MD,§ Michael Duan, MS, || Carol R. Schermer, MD,¶ and John A. Kellum, MD# MAJOR OPEN ABDOMINAL SURGERY 467,131 CASES Retrospective analysis of a RECEIVED BALANCED prospectively collected data RECEIVED 0.9% SALINE DURING HOSPITALIZATION 346,901 CASES FLUID (PLASMA-LYTE) DURING HOSPITALIZATION 9,905 CASES asset (Premier database) Major (non cardiac) surgery RECEIVED BALANCED FLUID ON PROCEDURE DATE 8,285 CASES RECEIVED 0.9% SALINE ON PROCEDURE DATE 262,904 CASES >30,000 patients who received 0.9% saline or balanced ONLY 0.9% SALINE ON PROCEDURE DATE 30,994 CASES ONLY BALANCED FLUID ON PROCEDURE DATE 926 CASES crystalloid alone on day of surgery BALANCED FLUID COHORT 926 CASES VANDERBILT WUNIVERSITY (Ann Surg 2012;00:1-9) MEDICAL CENTER



# Risk adjusted outcomes non-elective surgery

(NNT 29)

Outcome	Balanced	Saline	P value
n	296	20,047	-
All cause mortality (%)	3.7	7.2	0.019
Major morbidity (%)	36	41	0.01
Minor morbidity (%)	35	42	0.01
Post op ventilation (%)	13.2	18.7	0.02
Discharged home (%)	86	78	7 x 10 <sup>-6</sup>
30 day readmit rate (%)	30	31	NS

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Shaw et al (2012) Ann Surg

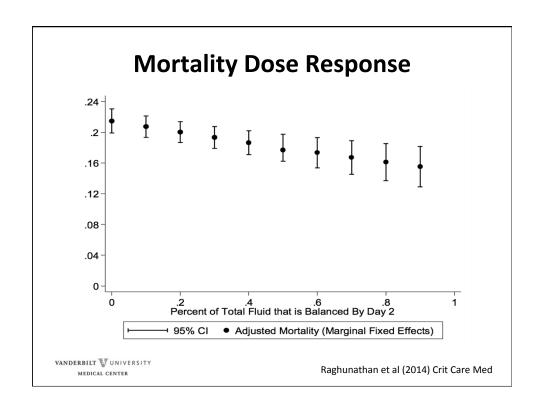


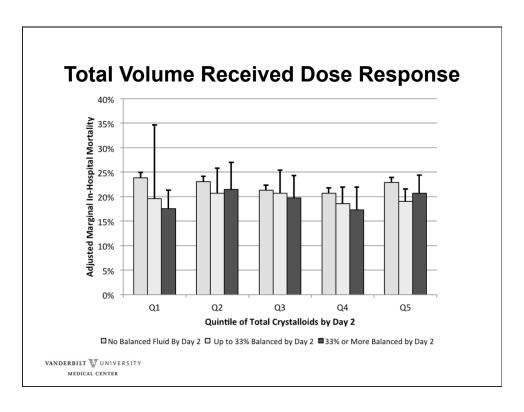
# Association Between the Choice of IV Crystalloid and In-Hospital Mortality Among Critically III Adults With Sepsis

Karthik Raghunathan, MD, MPH¹²; Andrew Shaw, MB, FRCA, FFICM, FCCM¹; Brian Nathanson, PhD³; Til Stürmer, MD, PhD⁴; Alan Brookhart, PhD⁴; Mihaela S. Stefan, MD⁵; Soko Setoguchi, MD, DrPH⁶; Chris Beadles, MD, PhD²; Peter K. Lindenauer, MD, MSc⁻

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Raghunathan et al (2014) Crit Care Med





#### Yunos et al 2012

PRELIMINARY COMMUNICATION

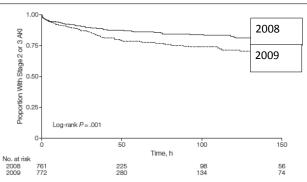
Association Between a Chloride-Liberal vs Chloride-Restrictive Intravenous Fluid Administration Strategy and Kidney Injury in Critically III Adults

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Yunos et al (2012) JAMA

#### **KDIGO 2&3**

Figure 1. Development of Stage 2 or 3 Acute Kidney Injury (AKI) While in the Intensive Care Unit (ICU)



Stage 2 or 3 defined according to the Kidney Disease: Improving Global Outcomes clinical practice guideline.

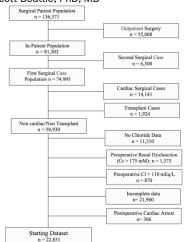
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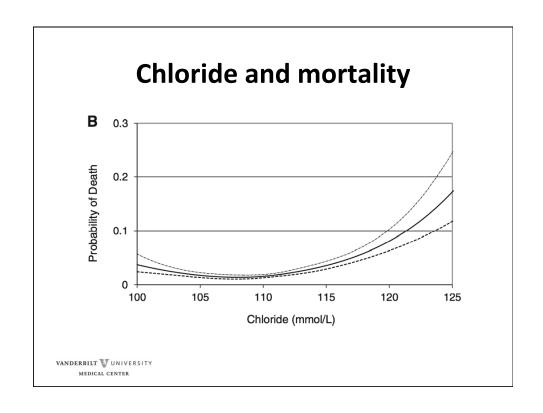
Yunos et al (2012) JAMA

#### Hyperchloremia After Noncardiac Surgery Is Independently Associated with Increased Morbidity and Mortality: A Propensity-Matched Cohort Study

Stuart A. McCluskey, PhD, MD,\* Keyvan Karkouti, MSc, MD,\*† Duminda Wijeysundera, PhD, MD,\* Leonid Minkovich, PhD, MD,\* Gordon Tait, PhD,\* and W. Scott Beattie, PhD, MD\*

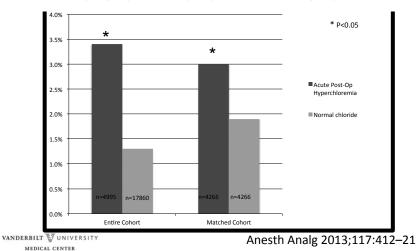
- Observational cohort study
- · Major (non cardiac) surgery
- 23000 patients
- 4266 of 4955 who developed high serum chloride propensity matched to patients who did not





# Independently Associated with Increased Morbidity and Mortality: A Propensity-Matched Cohort Study

Stuart A. McCluskey, PhD, MD,\* Keyvan Karkouti, MSc, MD,\*† Duminda Wijeysundera, PhD, MD,\* Leonid Minkovich, PhD, MD,\* Gordon Tait, PhD,\* and W. Scott Beattie, PhD, MD\*



Intensive Care Med DOI 10.1007/s00134-014-3505-3

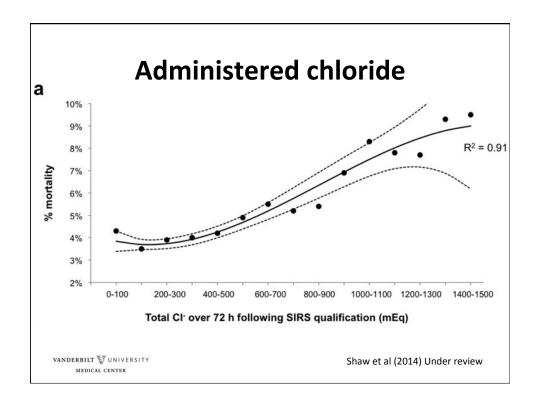
ORIGINAL

Andrew D. Shaw Karthik Raghunathan Fred W. Peyerl Sibyl H. Munson Scott M. Paluszkiewicz Carol R. Schermer Association between intravenous chloride load during resuscitation and in-hospital mortality among patients with SIRS

- 109,836 adult patients with SIRS from Cerner health facts database
- Baseline risk adjustment as well as APS included in outcomes model
- Effect of volume adjusted chloride load on mortality

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Shaw et al (2014) Int Care Med





#### Systematic review

#### Meta-analysis of high- versus low-chloride content in perioperative and critical care fluid resuscitation

M. L. Krajewski<sup>1</sup>, K. Raghunathan<sup>1,2</sup>, S. M. Paluszkiewicz<sup>3</sup>, C. R. Schermer<sup>4</sup> and A. D. Shaw<sup>5</sup>

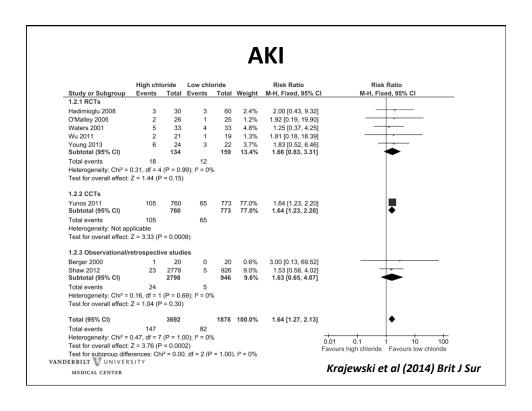
<sup>1</sup>Department of Anesthesiology, Duke University Medical Center, and <sup>2</sup>Anesthesiology Service, Durham VA Medical Center, Durham, North Carolina, <sup>3</sup>Boston Strategic Partners, Boston, Massachusetts, <sup>4</sup>Baxter Healthcare Corporation, Deerfield, Illinois, and <sup>5</sup>Department of Anesthesiology, Vanderbilt University Medical Center, Nashville, Tennessee, USA

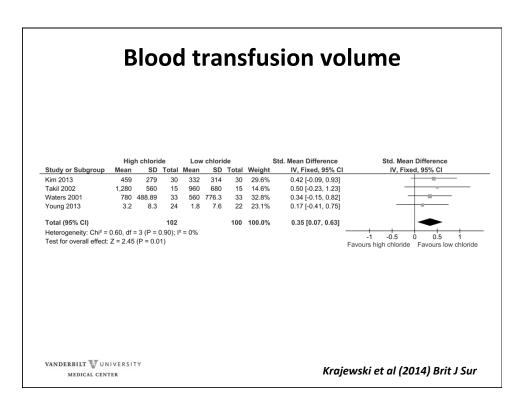
Correspondence to: Professor A. D. Shaw, Division of Cardiothoracic Anesthesiology, Vanderbilt University Medical Center, Nashville, Tennessee

37232-8274, USA (e-mail: andrew.shaw@vanderbilt.edu)

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Krajewski et al (2014) Brit J Sur





#### ORIGINAL ARTICLE

## Saline Versus Plasma-Lyte A in Initial Resuscitation of Trauma Patients

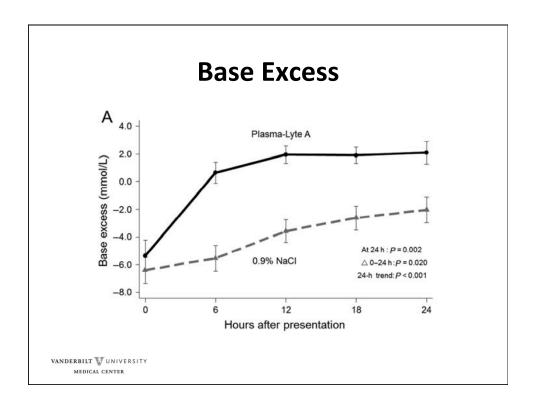
#### A Randomized Trial

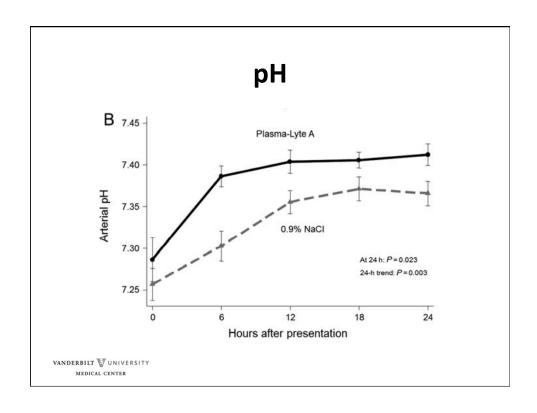
Jason B. Young, MD, PharmD, Garth H. Utter, MSc, MD, Carol R. Schermer, MD, MPH, Joseph M. Galante, MD, Ho H. Phan, MD, Yifan Yang, MD, Brock A. Anderson, MD, and Lynette A. Scherer, MD

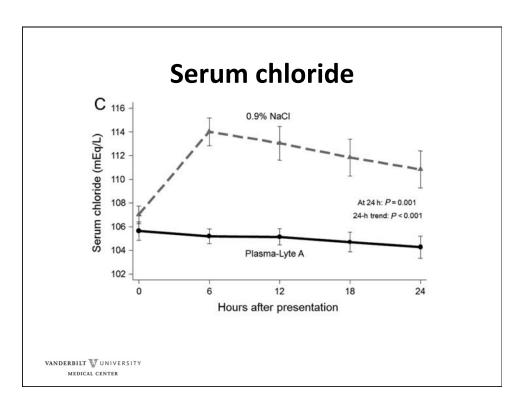
- DBRCT of 65 trauma patients
- Plasma Lyte vs 0.9% saline
- Primary EP change in Base Excess first 24 hrs
- Deferred consent to allow immediate inclusion

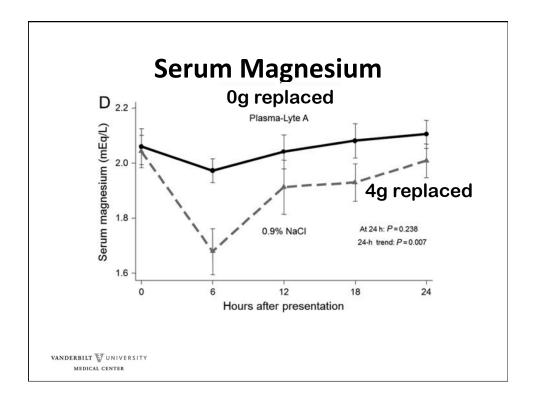
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(Ann Surg 2013;00:1-8)









## Mg supplementation

A thorough cost analysis is beyond the scope of this article, but based on information from our center, a 1-L bag of 0.9% NaCl costs \$0.86/L and Plasma-Lyte A costs \$1.62/L, a cost difference of 76 cents. The cost of standard IV magnesium replacement is \$5.19 per 2 g and does not include the cost for nursing care to administer the infusion.

# Cost-minimization analysis of two fluid products for resuscitation of critically injured trauma patients

CAITLIN A. SMITH, JEREMIAH J. DUBY, GARTH H. UTTER, JOSEPH M. GALANTE, LYNETTE A. SCHERER, AND CAROL R. SCHERMER

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Am J Health-Syst Pharm—Vol 71 Mar 15, 2014

## Cost-minimization analysis of two fluid products for resuscitation of critically injured trauma patients

Variable	0.9% Sodium Chloride Injection (n = 24)	Plasma-Lyte A (n = 22)	p <sup>b</sup>
Mean ± S.D. concentration	•		
Magnesium, mg/dL			
6 hr	$1.7 \pm 0.40$	$2.0 \pm 0.20$	0.004
24 hr	$2.0 \pm 0.30$	$2.1 \pm 0.24$	0.24
Potassium, meg/L			
6 hr	$4.0 \pm 0.62$	$3.8 \pm 0.49$	0.22
24 hr	4.1 ± 0.52	4.2 ± 0.63	0.34
Calcium, mg/dL			
6 hr	$7.9 \pm 0.95$	$7.9 \pm 1.28$	0.82
24 hr	8.1 ± 0.54	$8.3 \pm 0.60$	0.28
Phosphate, mg/dL			
6 hr	3.7 ± 1.01	$3.0 \pm 0.88$	0.03
24 hr	3.2 ± 0.92	$3.4 \pm 0.96$	0.59
Amount replaced within 24 hr, median (IQR)			
Magnesium, g	4.0 (2.5-4.0)	0 (0-2.0)	< 0.00
Potassium, meq	0 (0–20)	5 (0-20)	0.49
Calcium, g	0.5 (0-3.0)	1.50 (0-5.25)	0.46
Phosphate, mmol	0	0	0.52
Patients receiving electrolyte replacement			
within 24 hr, no. (%)			
Magnesium	21 (87.5)	6 (27.3)	<0.00
Potassium	9 (37.5)	12 (54.5)	0.25
Calcium	12 (50)	12 (54.5)	0.76
Phosphate	1 (4.2)	2 (9.1)	0.60

#### Cost-minimization analysis of two fluid products for resuscitation of critically injured trauma patients

	0.9%				
	Cost (\$) Inc	luding Labor	Cost (\$) Excluding Labor		
Expense Item	Administration of 2 g Magnesium	Administration of 4 g Magnesium	Administration of 4 g Magnesium	Plasma-Lyte A (n = 22)	
Mean ± S.D. resuscitation fluid					
cost (per 24 hr) <sup>a</sup>	$7.65 \pm 4.92$	$7.65 \pm 4.92$	$7.65 \pm 4.92$	$20.46 \pm 12.94^{b}$	
Safety syringe with attached					
needle (1 unit)	0.72 <sup>b</sup>	0.72 <sup>b</sup>	0.72 <sup>b</sup>	0.00	
0.9% sodium chloride i.v. flush,					
10 mL	1.34 <sup>b</sup>	1.34 <sup>b</sup>	1.34 <sup>b</sup>	0.00	
Surgical gloves (pair)	0.17 <sup>b</sup>	0.17 <sup>b</sup>	0.17 <sup>b</sup>	0.00	
Tubing (single tubing)	1.82 <sup>b</sup>	1.82 <sup>b</sup>	1.82 <sup>b</sup>	0.00	
Alcohol wipes (per swab)	0.01 <sup>b</sup>	0.01 <sup>b</sup>	0.01 <sup>b</sup>	0.00	
Drug acquisition cost	6.77 <sup>b</sup>	13.54	13.54 <sup>b</sup>	0.00	
Labor cost (for average)d	7.56 <sup>b,c</sup>	7.56 <sup>b,c</sup>	<sup>d</sup>		
Total (per 24 hr)	26.04	32.81	25.25	20.46	

\*Based on obfuscated threshold cost of \$0.85/L for 0.9% sodium chloride injection and \$2/L for Plasma-Lyte A.

\*Cost reflects administration of two 2-g doses of magnesium sulfate, which is the common practice for magnesium replacement at the study site.

\*Calculated using U.S. Bureau of Labor Statistics data on mean nurse compensation in California; assumes mean nursing time of 9.2 minutes (4.6 minutes per infusion). dNot applicable.

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#### When should we give abnormal saline?

- Rarely
- Traumatic brain injury
- HCl loss (severe vomiting)

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#### **Conclusions**

- The circumstantial evidence that high chloride solutions are harmful continues to mount
- There are no data suggesting 0.9% saline is beneficial
- New multicenter cardiac surgical data suggest balanced crystalloids are the fluids of choice for both cardiac surgery and in SIRS patients.

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#### **Thank You**