

Smart Use of Balanced Crystalloid Solution in the Perioperative Period

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คณะแพทยศาสตร์ศิริราชพยาบาล

Balanced Crystalloid Solution

- Crystalloid should be the first fluid for resuscitation
- Non-balanced vs balanced crystalloid solution
- What is this issue?
- What the benefit of this balanced crystalloid solution in the perioperative period and critical care ?
- When we use, do we need to alternate bottle between balanced and non balanced crystalloid solution?

- Basic physiology and pharmacology of balanced crystalloid solution

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- Important clinical applications

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- Conclusion

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The Balanced Crystalloid Solution for the Critically and Non Critically Ill Patients

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Type of Fluid

Table 1. Electrolyte composition and osmolality of human plasma and widely available crystalloid solutions

	Human plasma	0.9% saline	Ringer's lactate ^a	Ringer's acetate ^b	Plasmalyte ^c	Jonosteril ^b	Sterofundin ^a
Sodium (mmol/l)	142	154	130	131	140	137	145
Potassium (mmol/l)	4.5		4	4	5	4	4
Calcium (mmol/l)	2.5		3	2		1.7	2.5
Magnesium (mmol/l)	1.25			1	1.5	1.3	1
Chloride (mmol/l)	103	154	110	110	98	110	127
Bicarbonate (mmol/l)	24						
Lactate (mmol/l)	1.5		28				
Acetate (mmol/l)				30	27	37	24
Gluconate (mmol/l)					23		
Malate (mmol/l)							5
Osmolality ^d (mosm/kg) H ₂ O	290	308	275	270	295	291	309

Balanced solution: different solutions with different electrolyte composition close to plasma composition

Electrolytes (mmol/ l)	Human Plasma	Sterofundin®ISO	NaCl 0.9%	Ringer's Lactate	Ringer's Acetate
Na ⁺	142	145	154	130	130
K ⁺	4.5	4	-	4	4
Ca ²⁺	2.5	2.5	-	1.5	1.4
Mg ²⁺	1.25	1.0	-	-	-
Cl ⁻	103	127	154	109	108.7
HCO ₃ ⁻	24	-	-	-	-
Lactate ⁻	1.5	-	-	28	-
Acetate ⁻	-	24	-	-	28
Maleate ²⁻	-	5	-	-	-
Real Osmolality (mOsmol/ kg H ₂ O)	287	287	286	256	256

Bicarb base balanced crystalloid solution

Original Article

Change in Serum Chloride Level after Loading Dose of Sterofundin Solution Compared with Normal Saline Solution

Sunthiti Morakul MD¹, Cherdkiat Karnjanarachata MD¹, Thanist Pravitharangul MD¹, Viratch Tangsujaritvijit MD²

J Med Assoc Thai 2018; 101 (2): 217-22

Conclusion: Sterofundin solution loading slightly increased serum chloride level, but delta change from baseline was significantly lower as compared with normal saline solution.

Malate improve survival

**RINGER'S MALATE SOLUTION PROTECTS AGAINST THE
MULTIPLE ORGAN INJURY AND DYSFUNCTION CAUSED
BY HEMORRHAGIC SHOCK IN RATS**

SHOCK, Vol. 38, No. 3, pp. 268–274, 2012

**L-Malate's Plasma and Excretion Profile in the Treatment of
Moderate and Severe Hemorrhagic Shock in Rats**

BioMed Research International
Volume 2016, Article ID 5237148, 9 pages

**Malate Protects the Kidneys From Hemorrhagic
Shock-Induced Injury in an Experimental Rat
Model**

JOURNAL OF SURGICAL RESEARCH • JANUARY 2020 (245) 225–233

Why Balanced Solution ?

- 0.9% NSS (high Na^+ , high Cl^-) non-balanced solution
- Dilutional acidosis when large amount was infused
- Any clinical effect?

Table 1 Potentially deleterious effects of high Cl⁻-content secondary to administration of large volume of 0.9 % saline addressed in the literature

- Hyperchloremic metabolic acidosis (traditionally called dilution acidosis)
 - Acute kidney injury with reduced urine output and increase in interstitial fluid volume
 - Hyperkalemia (K⁺ mobilized from the intracellular space)
 - Damaged endothelial surface layer with increased vascular permeability and stiffness
 - Increase in proinflammatory mediators and tendency to infections
 - Detrimental effect on coagulation with tendency to blood loss
 - Detrimental gastrointestinal perfusion and function
 - Possible uneasiness at the bedside resulting in unnecessary administration of more fluids
-

CONCISE CLINICAL REVIEW



Balanced Crystalloid Solutions

Matthew W. Semler¹ and John A. Kellum²

¹Division of Allergy, Pulmonary and Critical Care Medicine, Vanderbilt University Medical Center, Nashville, Tennessee; and ²The Center for Critical Care Nephrology, Department of Critical Care Medicine, University of Pittsburgh, Pittsburgh, Pennsylvania

American Journal of Respiratory and Critical Care Medicine Volume 199 Number 8 | April 15 2019

- Balanced crystalloids have a sodium, potassium, and chloride content closer to that of extracellular fluid and, when given intravenously, have fewer adverse effects on acid–base balance.
- Preclinical research has demonstrated that saline may cause hyperchloremic metabolic acidosis, inflammation, hypotension, acute kidney injury, and death

Balanced Crystalloids Versus Saline in Critically Ill Adults: A Systematic Review and Meta-analysis

Annals of Pharmacotherapy
2020, Vol. 54(1) 5–13
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sagepub.com/journals-permissions
DOI: 10.1177/1060028019866420
journals.sagepub.com/home/aop


- **NON SEPSIS:**
 - Balanced crystalloids demonstrated lower hospital or 28-/30-day mortality
 - New acute kidney injury occurred less frequently with balanced crystalloids
- **SEPSIS**
 - major adverse kidney events occurring in the first 30 days were less with balanced crystalloids than saline
- **Balanced crystalloids should be provided preferentially to saline in most critically ill adult patients.**

Balanced Crystalloid Solutions

Matthew W. Semler¹ and John A. Kellum²

- Randomized trials in the operating room have demonstrated that using balanced crystalloids rather than saline prevents the development of hyperchloremic metabolic acidosis and may reduce the need for vasopressors
- Observational studies among critically ill adults have associated receipt of balanced crystalloids with lower rates of complications, including acute kidney injury and death
- Most recently, large randomized trials among critically ill adults have examined whether balanced crystalloids result in less death or severe renal dysfunction than saline

Balanced Fluid Versus Saline-Based Fluid in Post-operative Severe Traumatic Brain Injury Patients: Acid-Base and Electrolytes Assessment

Malays J Med Sci. 2017;**24**(5):83–93. 1

Methods: Sixty-six severe TBI patients who required emergency craniotomy or craniectomy and were planned for post-operative ventilation were randomised into NS ($n = 33$) and BF therapy groups ($n = 33$). The calculation of maintenance fluid given was based on the Holliday-Segar method. The electrolytes and acid–base parameters were assessed at an 8 h interval for 24 h. The data were analysed using repeated measures ANOVA.

Results: The NS group showed a significant lower base excess (-3.20 versus -1.35 , $P = 0.049$), lower bicarbonate level (22.03 versus 23.48 mmol/L, $P = 0.031$), and more hyperchloremia (115.12 versus 111.74 mmol/L, $P < 0.001$) and hypokalemia (3.36 versus 3.70 mmol/L, $P < 0.001$) than the BF group at 24 h of therapy. The BF group showed a significantly higher level of calcium (1.97 versus 1.79 mmol/L, $P = 0.003$) and magnesium (0.94 versus 0.80 mmol/L, $P < 0.001$) than the NS group at 24 h of fluid therapy. No significant differences were found in pH, $p\text{CO}_2$, lactate, and sodium level.

Conclusion: BF therapy showed better effects in maintaining higher electrolyte parameters and reducing the trend toward hyperchloremic metabolic acidosis than the NS therapy during prolonged fluid therapy for postoperative TBI patients.

Normal saline versus balanced-salt solution as intravenous fluid therapy during neurosurgery: effects on acid-base balance and electrolytes. *JNeurosurg Sci* 2017 Jun;61(3):263-270.

Method

- 30 adult patients who underwent craniotomy were randomly allocated into two groups of 15 patients each
- The non-balanced group received 0.9% normal saline while the balanced group received Sterofundin®ISO as the intraoperative fluid for maintenance

Results

- non-balanced group, significant changes were noted in the pH, base excess and bicarbonate values over time compared to its respective baseline values ($P < 0.01$)
- Both mean sodium and chloride levels were also significantly higher compared to its baseline values respectively (142.6 ± 2.4 versus 138 ± 2.7 mmol/L, $P < 0.01$ and 105.7 ± 4.1 versus 113.2 ± 3.0 mmol/L ($P < 0.01$))

Normal saline versus balanced-salt solution as intravenous fluid therapy during neurosurgery: effects on acid-base balance and electrolytes. *JNeurosurg Sci* 2017 Jun;61(3):263-270.

Conclusion

A balanced solution (Sterofundin®ISO) provided significantly better control over acid-base balance, sodium and chloride levels when used as intraoperative fluid maintenance and replacement during elective neurosurgery.

MODERN APPROACHES TO CORRECTION OF HYPERNATREMIA IN NEUROSURGICAL PATIENTS

Georgian Med News 2016 Nov;(Issue):12-16

- The use of Sterofundin in complex therapy of electrolyte disturbances, particularly of hypernatremia in neurosurgical patients after removal of brain tumors, is reflected in the form of significant regression of increased sodium concentration in plasma compared with the method of use "hypotonic" hemodilution, saluretics and potassium-sparing diuretics.



Randomized, Double-Blind Trial of the Effect of Fluid Composition on Electrolyte, Acid–Base, and Fluid Homeostasis in Patients Early After Subarachnoid Hemorrhage

Laura Lehmann · Stepani Bendel · Dominik E. Uehlinger ·
Jukka Takala · Margaret Schafer · Michael Reinert ·
Stephan M. Jakob

Conclusions Treatment with saline-based fluids resulted in a greater number of patients with hyperchloremia, hyperosmolality, and positive fluid balance $>1,500$ mL early after SAH, while administration of balanced solutions did not cause more frequent hyponatremia or hypo-osmolality. These results should be confirmed in larger studies.

The Effects of Colloid Solutions on Renal Proximal Tubular Cells In Vitro

Winfried Neuhaus, PhD,*† Martin A. Schick, MD,* Raphael R. Bruno,* Bianca Schneiker,*
Carola Y. Förster, PhD, Prof.,*‡ Norbert Roewer, MD, Prof.,* and Christian Wunder, MD, Prof.*

In lower concentrations,

- human albumin and the crystalloid solution Sterofundin ISO were cytoprotective in comparison with the NaCl control.

Martin Alexander Schick
Tobias Jobst Isbary
Nicolas Schlegel
Juergen Brugger
Jens Waschke
Ralf Muellenbach
Norbert Roewer
Christian Wunder

The impact of crystalloid and colloid infusion on the kidney in rodent sepsis

Animals infused with balanced crystalloid Sterolso exhibited the least effects on kidney function

A novel balanced isotonic sodium solution vs normal saline during major surgery in children up to 36 months: a multicenter RCT

Pediatric Anesthesia **24** (2014) 980–986

Results: A total of 240 patients were included in the two study sites and randomized to receive Sterofundin plus 1% glucose or normal saline plus 1% glucose, in a open fashion (229 were finally analyzed). Δ of Cl^- and Mg^{++} was statistically less relevant in patients who received intraoperative Sterofundin, and Δ of the other electrolytes was comparable between the two study groups. Relative risk of hyperchloremia was significantly higher when large volumes were infused (over than $46.7 \text{ ml} \cdot \text{kg}^{-1}$), regardless of type of crystalloid infused. Hypoglycemia occurred in two of 229 patients.

Conclusions: Sterofundin is safer than normal saline in protecting young children undergoing major surgery against the risk of increasing plasma chlorides and the subsequent metabolic acidosis.

A Comparison of Sterofundin and Ringer's Lactate on Intraoperative Acid Base and Electrolytes Status in Children: A Randomized Controlled Trial

Volume 3 Issue 1

Received Date: March 26, 2018

Published Date: April 20, 2018

Anaesth Critic Care Med J

Conclusion: The use of Sterofundin is better to Ringer's Lactate in the management of Intraoperative acid base, electrolyte and hemodynamic parameters in pediatric patient undergoing major surgery.

Effect of Early Balanced Crystalloids Before ICU Admission on Sepsis Outcomes

Karen E. Jackson, MD; Li Wang, MS; Jonathan D. Casey, MD; Gordon R. Bernard, MD; Wesley H. Self, MD, MPH;

*Todd W. Rice, MD; and Matthew W. Semler, MD; on behalf of the SMART Investigators and the Pragmatic Critical Care Research Group**

CHEST 2020;

Among patients with sepsis, the effect of balanced crystalloids vs saline on mortality was greater among patients for whom fluid choice was controlled starting in the ED compared with starting in the ICU.

Effect of 0.9% saline versus balanced salt solution resuscitation on kidney function in shock patients: A randomized, open-labeled, controlled study

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Critical care Division, Department of medicine, Siriraj Hospital.

Background: Fluid therapy is the most common medical intervention in the critically ill. While fluid resuscitation to hemodynamic goals showed evidences of benefit, recent literature demonstrates that there are evidences of acute kidney injury (AKI) associated with chloride-rich fluid administration in animal and human studies. There was no randomized study comparing use of chloride-rich versus balanced salt solution in shock patients.

Objectives: This study aimed to compare effect between 0.9% saline and physiologically balanced crystalloid solution (Sterofundin®) resuscitation on development of AKI in shock patients.

Materials and Methods:

We conducted prospective randomized study and enrolled 22 critically ill patients with shock to receive the resuscitation with either 0.9% saline or balanced crystalloid solution (Sterofundin®) during the first 72-h after shock diagnosis. All patients were treated with the standard guidelines according to type of shock. We compared development of AKI using KDIGO criteria between both treatments. Organ support and biochemical variables were also collected.

Results:

Eleven received 0.9% saline and 11 patients were treated with balanced crystalloid solution. The mean age was 59.1 ± 19.1 year, and 15 of 22 were male. Mean APACHE II scores were comparable (21 ± 4 in the balanced solution group, 20 ± 4 in 0.9% saline, $P=0.43$). There were no significant differences in baseline demographic, hemodynamic and metabolic data between two groups at enrollment. During 72 h of therapy, there were no significant differences in electrolyte disturbances between the two groups, but serum bicarbonate trended to be lower in the 0.9% saline group. One of 11 in the balanced solution group and 6 of 11 patients in the 0.9% saline group developed AKI defined by KDIGO criteria ($p=0.05$). Of all, 2 cases in the 0.9% saline group but none in the balanced solution required renal replacement therapy ($p=0.47$). There was no difference in 28-d mortality, ICU stay, hospital stay, and uses of organ support.

Conclusion: The use of a balanced crystalloid as resuscitation fluid in shocked patients is safe and trends to associate with less AKI development than resuscitation by 0.9% saline. However, this benefit and advantages in other clinical outcomes should be further demonstrated with a larger number of populations.

0.9% Saline versus Sterofundin® in
shock patient

Single center, RCT (Siriraj Hospital)

N = 220

Primary Outcome: AKI per KDIGO
criteria in 7 days

Secondary Outcome: Need for RRT,
28-day mortality, LOS, Number of
organ support, Metabolic
derangements

Outcomes	Balanced Crystalloid (n = 111)	Saline (n = 109)	RR (95%CI)	P Value
Primary outcome				
<u>Cumulative incidence of AKI during 7 day (by KDIGO), n (%)</u>	85 (76.6%)	88 (80.7%)	0.95 (0.83-1.09)	0.45
Stage, n (%)				0.34
- KDIGO1	31 (27.9%)	32 (29.4%)	0.95 (0.63-1.44)	0.82
- KDIGO2	24 (21.6%)	18 (16.5%)	1.31 (0.75-2.27)	0.34
- KDIGO3	30 (27.0%)	38 (34.9%)	0.78 (0.52-1.16)	0.21
Secondary outcome				
<u>AKI incident at day 7th (by KDIGO), n (%)</u>	24 (21.6%)	32 (29.4%)	0.74 (0.47-1.16)	0.19
Stage, n (%)				
- KDIGO1	8 (7.2%)	8 (7.3%)	0.98 (0.38-2.52)	0.97
- KDIGO2	7 (6.3%)	4 (3.7%)	1.72 (0.52-5.7)	0.37
- KDIGO3	9 (8.1%)	20 (18.3%)	0.44 (0.21-0.93)	0.03*

Secondary outcomes	Balanced Crystalloid (n = 111)	Saline (n = 109)	RR (95%CI)	P Value
RRT, n (%)	7 (6.3%)	16 (14.7%)	0.43 (0.18-1.00)	0.04
Mortality, n (%)				
- Death in ICU	10/72 (13.9%)	17/77 (22.1%)	0.63 (0.31-1.28)	0.28
- Death at day 28	21 (18.9%)	25 (22.9%)	0.82 (0.49-1.38)	0.46
- Death in hospital	24 (21.6%)	29 (26.6%)	0.81 (0.51-1.30)	0.39

Use of 0.9% saline as a resuscitation fluid in shock patients, as compared with a balanced crystalloid was significantly increased the number of cases who still had AKI stage 3 at day 7, and need of renal replacement therapy (RRT)

Effect of lactate versus acetate-based intravenous fluids on acid-base balance in patients undergoing free flap reconstructive surgeries

2018 Journal of Anaesthesiology Clinical Pharmacology

Sunil Rajan, Soumya Srikumar, Pulak Tosh, Lakshmi Kumar

Department of Anaesthesiology, Amrita Institute of Medical Sciences, Amrita University, Kochi, Kerala, India

Results: Intraoperative lactate levels were significantly high in RL group at 2, 4, 6, and 8 h. The pH was comparable between groups except at 8 h where RL group had a significantly lower pH than SF group (7.42 ± 0.1 vs. 7.4 ± 0.1). Sodium, potassium, chloride, bicarbonate, and $p\text{CO}_2$ did not show any significant difference between the groups.

Conclusion: Use of acetate-based intravenous solutions reduced levels of lactate in comparison with RL in patients undergoing free flap reconstructive surgeries.

A comparative study of Sterofundin and Ringer lactate based infusion protocol in scoliosis correction surgery

Ashima Sharma, Monu Yadav, B. Rajesh Kumar, P. Sai Lakshman, Raju Iyenger¹, Gopinath Ramchandran [December 14, 2020, IP: 202.28.177.42\]](#) **Anesthesia: Essays and Researches**

Results: There was no statistically significant difference in the volume of infused fluid (2400 ± 512 ml in Group RL and 2200 ± 640 ml in Group SF). There were no significant changes in pH of patients infused with SF. Statistically, significant higher lactate levels were seen in RL-infused group. The strong ion difference was decreased in both groups, but it normalized earlier with SF.

Conclusions: SF-infused patients had nonremarkable changes in acid–base physiology in scoliosis surgery.

Metabolic profile in right lobe living donor hepatectomy: Comparison of lactated Ringer's solution and normal saline versus acetate based balanced salt solution - a pilot study

© 2016 Indian Journal of Anaesthesia | Published by Wolters Kluwer - Medknow

Conclusion: Acetated fluids were associated with higher levels of bicarbonate, lesser base deficit, glucose and chloride but no difference in lactate levels in comparison with Ringer's lactate and normal saline in living donor hepatectomy.

**A COMPARATIVE STUDY OF ACETATED ISOTONIC ELECTROLYTE
SOLUTION, NORMAL SALINE SOLUTION, AND LACTATED RINGER'S
SOLUTION IN THE INITIAL FLUID RESUSCITATION OF CHILDREN
1 MONTH TO 18 YEARS OLD WITH SEVERE DENGUE AT THE
PHILIPPINE CHILDREN'S MEDICAL CENTER** The PCMC Journal, Vol. 14 No. 1

CONCLUSION AND RECOMMENDATION: Acetated isotonic electrolyte solution is more effective than normal saline and lactated Ringer's solutions in initial fluid resuscitation among severe dengue patients. It should be the fluid of choice in the initial resuscitation among severe dengue patients. It is recommended that a randomized control study with more patients be conducted.

Review

Balanced crystalloids vs 0.9% saline for adult patients undergoing non-renal surgery: A meta-analysis

International Journal of Surgery 51 (2018) 1–9

Lili Huang, Xiaoshuang Zhou, Hai Yu*

Department of Anesthesiology, West China Hospital of Sichuan University, Chengdu, Sichuan, 610041, PR China

Conclusion: Comparing to normal saline, balanced crystalloids are more beneficial in keeping postoperative electrolytes and acid-base balance among adult patients undergoing non-renal surgery. Future researches should pay more attention to meaningful clinical outcomes concerning the safety of balanced crystalloids and normal saline.

Major Complications, Mortality, and Resource Utilization After Open Abdominal Surgery

0.9% Saline Compared to Plasma-Lyte (Ann Surg 2012;255:821–829)

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#

- Retrospective cohort (30,994 patients) using 0.9% NSS compared with Premier perspective comparative database (926) balanced crystalloids solution on the day of surgery
- **The primary outcome was major morbidity**
- **The secondary outcomes included minor complications and acidosis related interventions.**

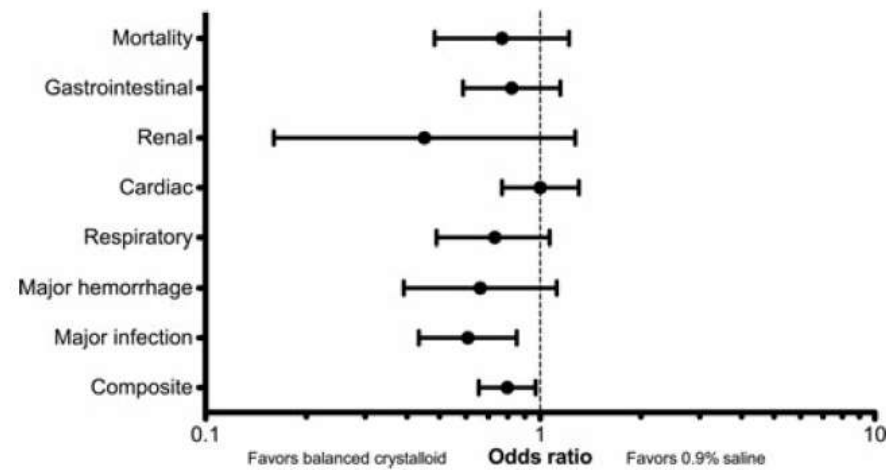


FIGURE 2. Odds ratios and 95% confidence intervals for pre-specified clinical outcomes.

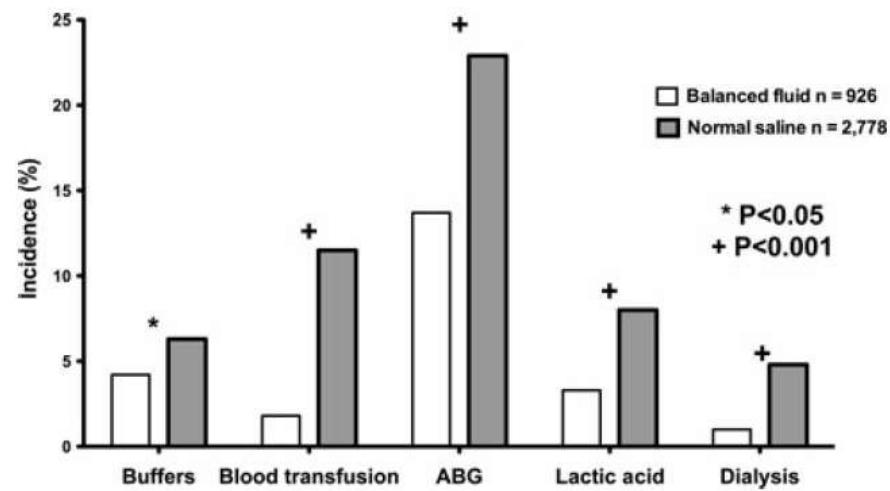


FIGURE 3. Interventions related to metabolic acidosis diagnosis and management.

Results: For the entire cohort, the in-hospital mortality was 5.6% in the saline group and 2.9% in the balanced group ($P < 0.001$). One or more major complications occurred in 33.7% of the saline group and 23% of the balanced group ($P < 0.001$). In the 3:1 propensity-matched sample, treatment with balanced fluid was associated with fewer complications (odds ratio 0.79; 95% confidence interval 0.66–0.97). Postoperative infection ($P = 0.006$), renal failure requiring dialysis ($P < 0.001$), blood transfusion ($P < 0.001$), electrolyte disturbance ($P = 0.046$), acidosis investigation ($P < 0.001$), and intervention ($P = 0.02$) were all more frequent in patients receiving 0.9% saline.

Conclusions: Among hospitals in the Premier Perspective Database, the use of a calcium-free balanced crystalloid for replacement of fluid losses on the day of major surgery was associated with less postoperative morbidity than 0.9% saline.

Conclusion

- Benefit of Balanced Crystalloid solution for crystalloid resuscitation
- Critical care: compare to NSS
 - Better renal function
 - Less ICU and hospital stay
 - Better outcome in ICU
- Non critical care
 - Better electrolyte
 - Better gut function
 - Lesser complications
- Acetate base is better
- Sterofundin ...malate ...good conversion more and more data of outcome improving