



HAL
open science

A novel isotonic balanced electrolyte solution with 1% glucose for perioperative fluid management in children- an animal experimental pre- authorisation study

Running title: A novel balanced electrolyte solution

Lars Witt, Wilhelm Alexander Osthaus, Christoph Buente, Natascha Teich, Elvis Hermann, Martin Kaske, Wolfgang Koppert, Robert Sümpelmann

► **To cite this version:**

Lars Witt, Wilhelm Alexander Osthaus, Christoph Buente, Natascha Teich, Elvis Hermann, et al.. A novel isotonic balanced electrolyte solution with 1% glucose for perioperative fluid management in children- an animal experimental pre- authorisation study Running title: A novel balanced electrolyte solution. *Pediatric Anesthesia*, 2010, 20 (8), pp.734. 10.1111/j.1460-9592.2010.03349.x . hal-00560696

HAL Id: hal-00560696

<https://hal.science/hal-00560696>

Submitted on 29 Jan 2011

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

Pediatric Anesthesia

A novel isotonic balanced electrolyte solution with 1% glucose for perioperative fluid management in children- an animal experimental pre- authorisation study

Running title: A novel balanced electrolyte solution

Journal:	<i>Pediatric Anesthesia</i>
Manuscript ID:	PAN-2010-0027.R2
Manuscript Type:	Original Paper
Date Submitted by the Author:	09-May-2010
Complete List of Authors:	Witt, Lars; Medizinische Hochschule Hannover, Klinik für Anästhesiologie und Intensivmedizin Osthaus, Wilhelm Alexander; Medizinische Hochschule Hannover, Klinik für Anästhesiologie und Intensivmedizin Buente, Christoph; Medizinische Hochschule Hannover, Klinik für Anästhesiologie und Intensivmedizin Teich, Natascha; Medizinische Hochschule Hannover, Klinik für Anästhesiologie und Intensivmedizin Hermann, Elvis; Medizinische Hochschule Hannover, Klinik für Neurochirurgie Kaske, Martin; Tierärztliche Hochschule Hannover, Klinik für Rinder Koppert, Wolfgang; Medizinische Hochschule Hannover, Klinik für Anästhesiologie und Intensivmedizin Sümpelmann, Robert; Medizinische Hochschule Hannover, Klinik für Anästhesiologie und Intensivmedizin
Key Words:	balanced electrolyte solution, normal saline, children, margin of safety, acid-base, fluid management

1
2
3 Address for correspondence:
4

5 Dr. Lars Witt, Klinik für Anästhesiologie und Intensivmedizin,
6

7
8 Medizinische Hochschule Hannover, Carl-Neuberg-Str.1, D-30625 Hannover, Germany
9

10 Fax +49 511 532 9048, email: Witt.Lars-Henrik@MH-Hannover.de
11
12
13
14
15
16
17
18

19 A novel isotonic balanced electrolyte solution with 1% glucose for perioperative
20
21 fluid management in children- an animal experimental pre- authorisation study
22
23
24
25

26 L. Witt¹, W.A. Osthaus¹, C. Bünte¹, N.Teich¹,
27

28 E. J. Hermann², M. Kaske³, W. Koppert¹ and R. Sümpelmann¹
29
30
31
32

33 ¹ Klinik für Anästhesiologie und Intensivmedizin, Medizinische Hochschule Hannover,
34
35 Hannover, Deutschland
36
37

38 ² Klinik für Neurochirurgie, Medizinische Hochschule Hannover, Hannover, Deutschland
39
40

41 ³ Klinik für Rinder, Tierärztliche Hochschule Hannover, Hannover, Deutschland
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58

59 Running title: A novel balanced electrolyte solution
60

Abstract

Background: The recommendations for perioperative maintenance fluid in children have been adapted from hypotonic to isotonic electrolyte solutions with lower glucose concentrations (1-2.5% instead of 5%) in order to avoid hyponatraemia or hyperglycaemia.

Objective: The objective of this prospective animal study was to determine the margin of safety of a novel isotonic balanced electrolyte solution with 1% glucose (BS-G1) in comparison to normal saline with 1% glucose (NS-G1) in case of accidental hyperhydration with a focus on acid- base- electrolyte balance, glucose concentration, osmolality and intracranial pressure in piglets.

Methods: Ten piglets (bodyweight 11.8 ± 1.8 kg) were randomly assigned to receive either 100 ml·kg⁻¹ of BS-G1 or NS-G1 within one hour. Before, during and after fluid administration electrolytes, lactate, haemoglobin, haematocrit, glucose, osmolality and acid-base parameters were measured.

Results: Unlike BS-G1, administration of NS-G1 produced mild hyperchloraemic acidosis (base excess BS-G1 vs. NS-G1, baseline 1.9 ± 1.7 vs. 2.9 ± 0.9 mmol l⁻¹, study end 0.2 ± 1.7 vs. -2.7 ± 0.5 mmol l⁻¹, $p < 0.05$, chloride BS-G1 vs. NS-G1 baseline 102.4 ± 3.4 vs. 102.0 ± 0.7 mmol l⁻¹, study end 103.4 ± 1.8 vs. 109.0 ± 1.4 mmol l⁻¹ $p < 0.05$).

The addition of 1% glucose led to moderate hyperglycaemia ($p < 0.05$) with a concomitant increase in serum osmolality in both groups ($p < 0.05$).

Conclusion: Both solutions showed a wide margin of safety in the case of accidental hyperhydration with less acid-base-electrolyte changes when using BS-G1. This novel solution could therefore enhance patient's safety within the scope of perioperative volume management.

Keywords: balanced electrolyte solution, normal saline, children, margin of safety, acid-base, fluid management

Introduction

Maintenance fluid therapy in children has been based for half a century on Holiday and Segar's recommendations suggesting the use of hypotonic fluids with 5% glucose added (1). After several reports of serious hyponatraemia or hyperglycaemia (2, 3), guidelines of several associations of paediatric anaesthesiologists now recommend the perioperative use of isotonic electrolyte solutions, i.e. normal saline or balanced electrolyte solutions with or without 1-2.5% glucose in order to avoid perioperative electrolyte and glucose imbalances (4, 5). Unfortunately these solutions were not commercially available on the German market (6, 7). Therefore in 2005, the association of German paediatric anaesthesiologists filed an application for approval of a balanced electrolyte solution with 1% glucose (BS-G1) with the German regulatory agency. In October 2009, this solution achieved a national approval and was introduced on the German market. In order to determine the margin of safety of BS-G1 in comparison to normal saline with 1% glucose (NS-G1) in case of accidental hyperhydration, we conducted a prospective animal experimental pre-authorisation study with focus on acid- base- electrolyte balance, glucose concentrations, serum osmolality and intracranial pressure.

We formulated the hypothesis that BS-G1 has less influence on the acid- base- electrolyte balance, when compared to NS-G1, while the other outcome parameters will not differ significantly between the groups.

Material and Methods

After approval of the study by the local animal experimentation committee, ten female German landrace piglets, four weeks of age, were included in the study. After a water- only overnight fast, they received intramuscular premedication with azaperone and atropine. The piglets were then anaesthetised with intravenous propofol and fentanyl, orotracheally intubated and mechanically ventilated with 1.5% isoflurane in oxygen/air ($F_i O_2$ 0.5). The tidal volume was adjusted to maintain an end-tidal carbon dioxide tension of 40mmHg. All

1
2
3 animals received $20\mu\text{g}\cdot\text{kg}^{-1}\cdot\text{h}^{-1}$ fentanyl and $0.5\text{mg}\cdot\text{kg}^{-1}\cdot\text{h}^{-1}$ rocuronium during the surgical
4
5 interventions. Body temperature was maintained by using an infrared lamp (LP1, Lister,
6
7 Germany) and a circulating water mattress (HICO Aquatherm 650, Hirtz, Cologne,
8
9 Germany). Heart rate, body temperature, and end-tidal carbon dioxide were measured using a
10
11 patient monitoring system (Cardiocap 5, Datex-Ohmeda, Freiburg, Germany). Using standard
12
13 cut down techniques, 5 F percutaneous sheath introducer sets (Arrow, Reading, USA) were
14
15 inserted in the right jugular vein and the right common carotid artery. Through the venous
16
17 introducer set, a 4 F two-lumen central venous catheter (Arrow, Reading, USA) was placed in
18
19 the superior vena cava for central venous pressure (CVP) recording. Additionally, a 20-G
20
21 cannula was placed in the right saphenous vein for fluid administration. Arterial pressure and
22
23 CVP were recorded from a calibrated pressure transducer. Thereafter all animals underwent
24
25 burr hole craniotomy (9mm) 1cm paramedian to the sagittal suture over the right cortex in
26
27 order to fix a 1.65mm precision pressure catheter (Neurovent P, Raumedic, Helmbrechts,
28
29 Germany) for intracranial pressure (ICP) measurements. Continuous ICP was monitored by
30
31 transduction of the cortex tissue with pressure lines set to zero at the external auditory
32
33 meatus.
34
35

36
37 After catheter placement and burr hole craniotomy, the first blood samples for blood gas
38
39 analysis using a standard blood gas oximetry system (ABL 735, Radiometer, Copenhagen,
40
41 Denmark) were collected into heparinised syringes. In each sample, pH, $p_a\text{O}_2$, $p_a\text{CO}_2$, actual
42
43 base excess, actual bicarbonate, sodium, chloride, potassium, lactate, haemoglobin and
44
45 haematocrit were measured. Additionally, a further blood sample was drawn to measure
46
47 serum phosphate (PO_4), serum albumin and serum osmolality using standard laboratory
48
49 techniques. The piglets were then randomly assigned to receive either $100\text{ml}\cdot\text{kg}^{-1}$ NS-G1
50
51 (Table 1, Central Pharmacy Department, Hanover Medical School, Hanover, Germany) or
52
53 $100\text{ml}\cdot\text{kg}^{-1}$ BS-G1 (Table 1, E148 G1 PÄD, Serumwerk Bernburg, Bernburg, Germany),
54
55 within one hour. During fluid administration, blood samples were collected every 15 minutes.
56
57
58
59
60

1
2
3 When the infusion was stopped, the last blood sample was collected and the piglets were
4
5 euthanized by intravenous injection of pentobarbital.
6
7

8 For calculation of strong ion difference (SID), the sum of chloride and lactate concentrations
9
10 was subtracted from the sum of sodium and potassium concentrations. The total of weak acids
11
12 (A^-) was calculated using the equation of Fencl *et al.*(8)
13

$$14 [A^-] = [\text{albumin } [g\cdot l^{-1}] \cdot (0.123 \cdot \text{pH} - 0.631)] + [\text{phosphate } [mmol\cdot l^{-1}] \cdot (0.309 \cdot \text{pH} - 0.469)]$$

15
16
17 The power calculation was carried out using the nQuery Advisor software 6.0 (Statistical
18 solutions, Cork, Ireland) with a power of 90% and a significance level (α) of 0.05. This
19
20 showed that a sample size of 5 piglets per group would allow detection of a difference of 10%
21
22 in the sodium, chloride and osmolality values in each infusion group. As all measured and
23
24 calculated data described above were normally distributed (as tested by Kolmogorov-Smirnov
25
26 tests), these are presented as mean values with standard deviations. For demographic data and
27
28 measured values before and after fluid administration two-way ANOVA test were performed.
29
30
31 Significance was accepted at $p < 0.05$. Recorded data were analysed using the SPSS 15.0
32
33 software for Windows (SPSS Software, Munich, Germany).
34
35
36
37

38 **Results**

39
40 All ten piglets used in the study received their intended treatment, completed the study
41
42 protocol and were analysed as reported. The two groups were comparable for weight (BS-G1
43
44 group $11.7 \pm 2.0\text{kg}$, NS-G1 group $11.9 \pm 1.6\text{kg}$) and length (BS-G1 group $73.4 \pm 3.5\text{cm}$, NS-
45
46 G1 group $73.5 \pm 3.5\text{cm}$). At baseline, there were no between-group differences in acid-base
47
48 variables, concentrations of serum electrolytes, albumin and glucose, serum osmolality,
49
50 haemoglobin, haematocrit, CVP or ICP (Tables 2 and 3). However, mean arterial pressure
51
52 differed significantly between the groups at the start of the study, with the higher values in the
53
54 NS-G1 group. During the experiment, haemoglobin, haematocrit, albumin and phosphate
55
56 decreased and CVP increased significantly in both groups, while the mean arterial pressure
57
58 remained almost stable, preserving the primarily significant between-group difference (Table
59
60

1
2
3 2). ICP increased significantly in both groups, but remained within physiological ranges
4 (Table 2). The increase in chloride concentrations was significantly higher in the NS-G1
5
6 group. Actual bicarbonate and actual base excess decreased in both groups and were
7
8 significantly lower in the NS-G1 group at study end (Figure 1, Table 3). Regarding further
9
10 acid-base variables, significant decreases in SID and A^- were found in both groups.
11
12 Osmolality and glucose concentrations increased with both BS-G1 and NS-G1 infusion.
13
14 Sodium levels in the NS-G1 group increased significantly, while the potassium and lactate
15
16 concentrations decreased at the same time. The infusion of balanced electrolyte solution
17
18 caused no significant changes in sodium, potassium and lactate levels.
19
20
21
22
23
24
25
26

27 Discussion

28
29 The objective of this prospective animal study was to determine the margin of safety of a
30
31 novel isotonic balanced electrolyte solution (BS-G1) in comparison to the likewise
32
33 recommended isotonic normal saline solution (NS-G1) both with 1% glucose. The
34
35 experimental study design was chosen to illustrate an accidental hyperhydration. Key findings
36
37 were mild hyperchloraemic acidosis after administration of NS-G1 and stable acid-base
38
39 parameters after BS-G1 application. The development of moderate hyperglycaemia resulting
40
41 in increased serum osmolality in both groups, while the intracranial pressures remained stable
42
43 within the physiological range.
44
45
46

47
48 Intravenous fluid administration influences the composition of serum electrolytes, osmolality,
49
50 acid-base balance and glucose concentration due to the composition of the administered fluid.
51

52
53 Incidents due to parenteral infusion in infants and children are mainly caused by changes in
54
55 one of these parameters (3, 9-11). In case of a high volume load, these effects are more
56
57 pronounced and may include fatal complications, as reported in several case reports (3).
58

59
60 A balanced volume replacement strategy is a well established concept for perioperative fluid
management using plasma adapted isotonic crystalloid solutions with a physiological

1
2
3 electrolyte pattern and acetate as bicarbonate precursor in order to prevent iatrogenic acid-
4
5 base imbalances (12, 13). Acetate may be preferable to lactate because it is metabolised
6
7 significantly faster, more independently of hepatic function, with a lower increase in oxygen
8
9 consumption and no interference with the diagnostic use of lactate as a marker of low tissue
10
11 perfusion (14, 15). Rapid administration of high acetate doses (e.g. during haemodialysis)
12
13 may lead to metabolic disturbances like a transient elevated blood glucose level or the release
14
15 of cytokines (16) with a potential decrease in mean arterial pressure. However, in our study
16
17 blood glucose levels increased comparable in both groups and mean arterial blood pressures
18
19 and acid-base- electrolyte parameters were stable during hyperhydration with the acetate
20
21 containing BS-G1 solution.
22
23
24
25

26
27 When compared to extracellular fluid or plasma normal saline contains unphysiological large
28
29 amounts of sodium (154 mmol l^{-1}) and chloride (154 mmol l^{-1}). The potential acidifying effect
30
31 of large volumes of normal saline solutions on plasma has been recognised in several
32
33 controlled trials (17, 18), but controversy has surrounded the aetiology of this phenomenon. In
34
35 traditional terms, according to Hendersson-Hasselbalch, acidosis from fluid administration
36
37 implies that plasma expansion and the consecutive dilutional reduction of plasma bicarbonate
38
39 are the underlying mechanisms (19). Based on these findings, we demonstrated a decrease in
40
41 actual bicarbonate and mild hyperchloraemic acidosis with normal saline infusion and almost
42
43 stable acid-base conditions after BS-G1 application.
44
45
46
47

48
49 In contrast to Hendersson-Hasselbalch, the Stewart approach, which is discussed in detail
50
51 elsewhere (20), defines $p_a\text{CO}_2$, SID and the sum of all anionic charges of weak plasma acids
52
53 (mainly albumin and phosphate) as independent pH-regulating variables, whereas pH and
54
55 bicarbonate are dependent variables (21). Assuming a constant $p_a\text{CO}_2$, the Stewart approach
56
57 provides an alternative to simple dilution as an explanation for acidosis and postulates that a
58
59 decrease in SID or an increase in A^- will result in a decrease in pH, or vice versa an increase
60
in SID or a fall in A^- will cause a pH increase (21). Morgan *et al.* (22) previously

1
2
3 demonstrated a linear relationship between crystalloid SID and post-dilutional metabolic acid-
4 base status. They proved that a crystalloid infusion with a SID of 24 mmol l^{-1} preserves
5 base status. They proved that a crystalloid infusion with a SID of 24 mmol l^{-1} preserves
6 normal acid-base status (22). According to these findings, in the present study the change in
7
8 SID was significantly lower in the group with the novel isotonic balanced electrolyte solution
9
10 (chloride 118 mmol l^{-1} , SID 26 mmol l^{-1}) when compared to normal saline (chloride 154
11
12 mmol l^{-1} , SID 0 mmol l^{-1}). The simultaneous decreases in A^- , caused by the dilution of serum
13
14 albumin, prevent severe metabolic acidosis (22). In other words, according to Stewart, the
15
16 hyperchloraemic acidosis in both groups is completely (BS-G1 group) or mostly (NS-G1
17
18 group) neutralised by hypoalbuminaemic alkalosis.
19
20
21
22
23

24 The choice of glucose concentration in perioperative solutions in paediatric anaesthesia is a
25
26 compromise between avoiding hypoglycaemia and hyperglycaemia (23). Several clinical
27
28 trials comparing the perioperative use of infusion solutions containing no glucose, 1% glucose
29
30 or 5% glucose showed that the use of 1% glucose prevents hypoglycaemia and lipid
31
32 mobilisation and is associated with blood glucose concentrations in the normal range (24, 25).
33
34 The present study showed that in the case of accidental hyperhydration 1% glucose
35
36 concentration may lead to moderate hyperglycaemia (study end: BS-G1 $12.6 \pm 1.8 \text{ mmol l}^{-1}$,
37
38 NS-G1 $13.0 \pm 2.0 \text{ mmol l}^{-1}$) but the plasma glucose concentrations did not reach levels where
39
40 severe health threatening events were likely. Actually, in a recent study of de Ferranti *et al.*
41
42 (26), evaluating long- term neurological development of neonates and infants after correction
43
44 of transposition of the great arteries, patients who presented low blood glucose concentrations
45
46 had an increased risk of electroencephalic seizures whereas high glucose concentrations were
47
48 not associated with worse neurodevelopmental outcomes.
49
50
51
52

53 However, rapid infusion with normal saline and balanced electrolyte solution with 1% glucose
54
55 leads to a significant increase of serum osmolality. Serum osmolality is primarily determined
56
57 by sodium, glucose and urea concentrations. Urea concentrations were not measured in this
58
59 study setting, but hyperhydration with urea-free solutions makes stable to decreased urea
60

1
2
3 concentrations likely. The simultaneous decrease (BS-G1 group) or only modest increase in
4
5 sodium concentrations (NS-G1 group) suggests that the increase in glucose concentrations is
6
7 the main reason for the rise in serum osmolality in both groups. In any case, serum osmolality
8
9 remained within the physiological range; therefore, severe effects on the osmotic balance did
10
11 not occur. The significant increase of central venous pressure (CVP) in both groups, was most
12
13 likely due to the volume load and may contribute to the likewise moderate increase in ICP.
14
15 Nevertheless, although the increases in CVP and ICP were statistically significant, the values
16
17 remained in physiological ranges, so that the clinical impact is negligible.
18
19

20
21
22 In conclusion, both solutions showed a wide margin of safety in the case of accidental
23
24 hyperhydration with less acid-base-electrolyte changes when using the novel isotonic
25
26 balanced electrolyte solution. The addition of 1% glucose led to moderate hyperglycaemia
27
28 with a concomitant increase in serum osmolality in both groups, while CVP and ICP remained
29
30 in physiological ranges. Therefore, this novel solution can be regarded, even in the case of
31
32 accidental hyperhydration, as being almost `foolproofed` (6) and should enhance patients
33
34 safety.
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

References

- 1 Holliday M, Segar W. The maintenance need for water in parenteral fluid therapy. *Pediatrics* 1957; **19**: 823-832.
- 2 Arieff A. Postoperative hyponatraemic encephalopathy following elective surgery in children. *Paediatr Anaesth* 1998; **8**: 1-4.
- 3 Arieff A, Ayus J, Fraser C. Hyponatraemia and death or permanent brain damage in healthy children. *BMJ* 1992; **304**: 1218-1222.
- 4 APA. Consensus guideline on perioperative fluid management in children. .2007. www.apagbi.org.uk
- 5 Sumpelmann R, Hollnberger H, Schmidt J *et al.* Recommendations for perioperative iv fluid management in neonates, infants and toddlers. *Anästh Intensivmed* 2006; **47**: 616-619.
- 6 Lonnqvist PA. Inappropriate perioperative fluid management in children: time for a solution?! *Paediatr Anaesth* 2007; **17**: 203-205.
- 7 Sumpelmann R, Hollnberger H, Schmidt J *et al.* Inappropriate perioperative fluid management in children: time for an isotonic solution?! *Paediatr Anaesth* 2008; **18**: 191.
- 8 Fencel V, Jabor A, Kazda A *et al.* Diagnosis of metabolic acid-base disturbances in critically ill patients. *Am J Respir Crit Care Med* 2000; **162**: 2246-2251.
- 9 Paut O, Remond C, Lagier P *et al.* Severe hyponatremic encephalopathy after pediatric surgery: report of seven cases and recommendations for management and prevention. *Ann Fr Anesth Reanim* 2000; **19**: 467-473.
- 10 Skellett S, Mayer A, Durward A *et al.* Chasing the base deficit: hyperchloraemic acidosis following 0.9% saline fluid resuscitation. *Arch Dis Child* 2000; **83**: 514-516.
- 11 Steward D. Hyperglycaemia, something to worry about ! *Paediatr Anaesth* 1992; **2**: 81-83.
- 12 Boldt J. The balanced concept of fluid resuscitation. *Br J Anaesth* 2007; **99**: 312-315.

- 1
2
3 13 Zander R. Infusion fluids: Why should they be balanced solutions? *EJHP Practice*
4
5 2006; **12**: 60-62.
6
7
8 14 Hamada T, Yamamoto M, Nakamaru K *et al.* [The pharmacokinetics of D-lactate, L-
9
10 lactate and acetate in humans]. *Masui* 1997; **46**: 229-236.
11
12
13 15 Knowles SE, Jarrett IG, OH F. Production and utilization of acetate in mammals.
14
15 *Biochem J* 1974; **142**: 401-411.
16
17
18 16 Veech R, Gitomer W. The medical and metabolic consequences of administration of
19
20 sodium acetate. *Adv Enzyme Regul* 1988; **27**: 313-343.
21
22
23 17 McFarlane C, Lee A. A comparison of Plasmalyte 148 and 0.9% saline for intra-
24
25 operative fluid replacement. *Anaesthesia* 1994; **49**: 779-781.
26
27
28 18 Scheingraber S, Rehm M, Sehmisch C *et al.* Rapid saline infusion produces
29
30 hyperchloremic acidosis in patients undergoing gynecologic surgery. *Anesthesiology* 1999;
31
32 **90**: 1265-1270.
33
34
35 19 Asano S, Kato E, Yamauchi M *et al.* The mechanism of acidosis caused by infusion of
36
37 saline solution. *Lancet* 1966; **1**: 1245-1246.
38
39
40 20 Rinaldi S, De Gaudio A. Strong ion difference and strong ion gap: the Stewart
41
42 approach to acid base disturbances. *Curr Anaesth and Crit Care* 2005; **16**: 395-402.
43
44
45 21 Stewart PA. Independent and dependent variables of acid-base control. *Respir Physiol*
46
47 1978; **33**: 9-26.
48
49
50 22 Morgan TJ, Venkatesh B, Hall J. Crystalloid strong ion difference determines
51
52 metabolic acid-base change during acute normovolaemic haemodilution. *Intensive Care Med*
53
54 2004; **30**: 1432-1437.
55
56
57 23 Berleur MP, Dahan A, Murat I *et al.* Perioperative infusions in paediatric patients:
58
59 rationale for using Ringer-lactate solution with low dextrose concentration. *J Clin Pharm*
60
Ther 2003; **28**: 31-40.

- 1
2
3 24 Dubois MC, Gouyet L, Murat I. Lactated ringer with 1% dextrose: an appropriate
4 solution for peri-operative fluid therapy in children. *Paediatr Anaesth* 1992; **2**: 99-104.
5
6
7
8 25 Geib I, Dubois MC, Gouyet L *et al.* Perioperative perfusion in children: evaluation of
9 a new perfusion solution. *Ann Fr Anesth Reanim* 1993; **12**: 6-10.
10
11
12 26 de Ferranti S, Gauvreau K, Hickey P *et al.* Intraoperative Hyperglycemia during Infant
13 Cardiac Surgery Is Not Associated with Adverse Neurodevelopmental Outcomes at 1,4, and 8
14 Years. *Anesthesiology* 2004; **100**: 1345-1352.
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

For Peer Review

Table 1

	Serum at baseline (n=10)	BS-G1	NS-G1
Sodium (mmol·l ⁻¹)	136.6 ± 3.1	140.0	154.0
Potassium (mmol·l ⁻¹)	3.7 ± 0.3	4.0	-
Calcium (mmol·l ⁻¹)	1.4 ± 0.1	2.0	-
Chloride (mmol·l ⁻¹)	102.2 ± 2.3	118.0	154.0
Actual bicarbonate (mmol·l ⁻¹)	26.5 ± 1.3	-	-
Acetate (mmol·l ⁻¹)	-	30.0	-
Lactate (mmol·l ⁻¹)	1.1 ± 0.4	-	-
Glucose (mmol·l ⁻¹)	3.4 ± 0.9	55.0	55.0

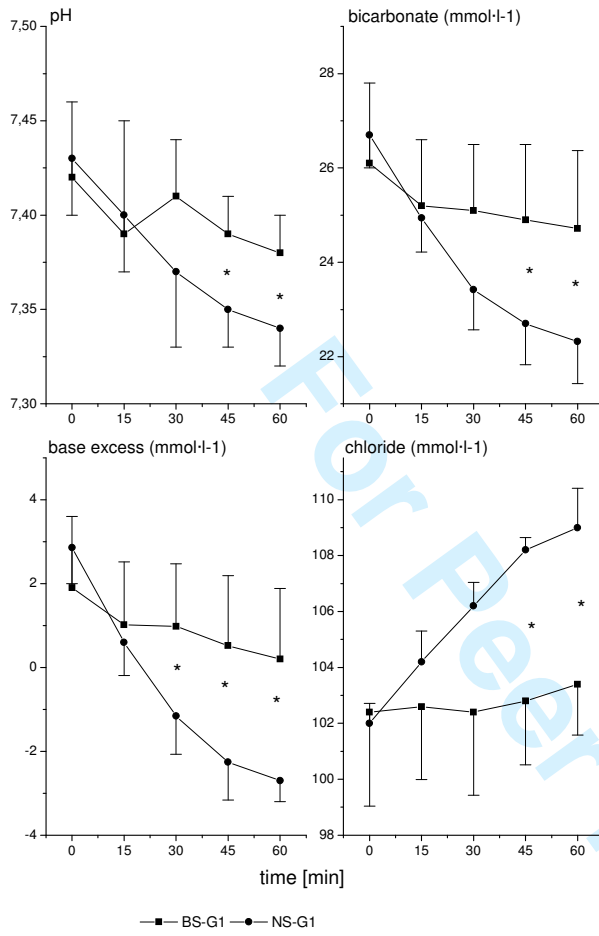
Table 2

Variable	Baseline		¹ p	Study end		² p
	BS-G1	NS-G1		BS-G1	NS-G1	
Haemoglobin (g·dl ⁻¹)	8.7 ± 0.3	9.2 ± 0.7	ns	6.6 ± 0.1*	7.0 ± 0.7*	ns
Haematocrit (%)	27.2 ± 0.8	28.4 ± 2.0	ns	20.7 ± 0.4*	22.0 ± 2.0*	ns
Mean arterial pressure (mmHg)	71.8 ± 3.3	88.2 ± 7.5	<0.05	75.6 ± 1.1	94.0 ± 13.7	<0.05
Central venous pressure (mmHg)	4.2 ± 2.1	5.0 ± 2.2	ns	12.4 ± 2.0*	10.4 ± 3.1*	ns
Intracranial pressure (mmHg)	4.2 ± 1.8	5.4 ± 6.1	ns	8.0 ± 2.0*	8.8 ± 6.3*	ns

Table 3

Variable	Baseline			Study end		
	BS-G1	NS-G1	¹ p	BS-G1	NS-G1	² p
pH	7.42 ± 0.0	7.43 ± 0.0	ns	7.38 ± 0.0	7.34 ± 0.0*	<0.05
p _a CO ₂ (mmHg)	41.6 ± 5.0	41.6 ± 4.0	ns	42.6 ± 2.6	42.9 ± 3.9	ns
Actual base excess (mmol·l ⁻¹)	1.9 ± 1.7	2.9 ± 0.9	ns	0.2 ± 1.7*	-2.7 ± 0.5*	<0.05
Osmolality (mosmol·kg ⁻¹)	289.4 ± 5.4	291.6 ± 3.7	ns	299.2 ± 4.9*	303.2 ± 6.2*	ns
Glucose (mmol·l ⁻¹)	3.4 ± 1.3	3.4 ± 0.5	ns	12.6 ± 1.8*	13.0 ± 2.0*	ns
Sodium (mmol·l ⁻¹)	136.8 ± 4.2	136.4 ± 2.1	ns	135.4 ± 2.8	138.8 ± 2.1*	ns
Potassium (mmol·l ⁻¹)	3.7 ± 0.3	3.8 ± 0.4	ns	3.4 ± 0.2	3.1 ± 0.3*	ns
Chloride (mmol·l ⁻¹)	102.4 ± 3.4	102.0 ± 0.7	ns	103.4 ± 1.8	109.0 ± 1.4*	<0.05
Actual bicarbonate (mmol·l ⁻¹)	26.1 ± 1.7	26.9 ± 0.7	ns	24.7 ± 1.7*	22.3 ± 0.9*	<0.05
Lactate (mmol·l ⁻¹)	1.1 ± 0.5	1.0 ± 0.2	ns	1.3 ± 0.2	0.8 ± 0.2*	<0.05
Phosphate (mmol·l ⁻¹)	2.5 ± 0.6	2.4 ± 0.7	ns	2.0 ± 0.5*	1.98 ± 0.46*	ns
Albumin (g·l ⁻¹)	27.3 ± 2.8	28.0 ± 0.9	ns	19.1 ± 2.4*	19.2 ± 0.8*	ns
Strong ion difference (mmol·l ⁻¹)	37.0 ± 3.0	37.1 ± 1.9	ns	34.1 ± 2.5*	32.1 ± 1.6*	ns
Weak acids (mmol·l ⁻¹)	12.3 ± 1.8	12.3 ± 1.5	ns	8.9 ± 2.0*	8.7 ± 1.0*	ns

Figure 1



1
2
3 **Table 1** Composition of piglets' serum at baseline (expressed as means \pm SD), balanced
4 electrolyte solution with 1% glucose (BS-G1) and normal saline with 1% glucose (NS-G1).
5
6
7
8
9

10 **Table 2** Comparison of haemoglobin, haematocrit, mean arterial pressure, central venous
11 pressure and intracranial pressure at baseline and at the end of the study after infusion of
12 100 ml·kg⁻¹ of either balanced electrolyte solution with 1% glucose (BS-G1) or normal saline
13 with 1% glucose (NS-G1), within one hour.
14
15
16
17
18
19

20 Data are expressed as means \pm SD, ¹p value at baseline, BS-G1 vs. NS-G1, ²p value at end of
21 study, BS-G1 vs. NS-G1, * p<0.05, end of study vs. baseline
22
23
24
25
26
27

28 **Table 3** Comparison of acid-base, electrolyte parameters, osmolality, glucose and albumin at
29 baseline and at the end of the study after infusion of 100 ml·kg⁻¹ of either balanced electrolyte
30 solution with 1% glucose (BS-G1) or normal saline with 1% glucose (NS-G1), within one
31 hour.
32
33
34
35
36
37

38 Data are expressed as means \pm SD, ¹p value at baseline, BS-G1 vs. NS-G1, ²p value at end of
39 study, BS-G1 vs. NS-G1, * p<0.05, end of study vs. baseline
40
41
42
43
44
45
46

47 **Figure 1** Changes in pH, bicarbonate, base excess and chloride concentrations after infusion
48 of 100ml·kg⁻¹ of either balanced electrolyte solution with 1% glucose (BS-G1) or normal
49 saline with 1% glucose (NS-G1), within one hour.
50
51
52
53
54

55 Data are expressed as means \pm SD, * p<0.05, BS-G1 vs. NS-G1
56
57
58
59
60

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

For Peer Review