Centre Hospitalier Régional Universitaire de Lille

FACULTE DE MEDECINE
Université de Lille
HENRI WAREMBOURG

Lactate de sodium dans le sepsis

Raphaël Favory

Université de Lille

Instituts thématiques

Inserm
Institut national de la santé et de la recherche médicale

Pourquoi parler d'apport de lactate ?

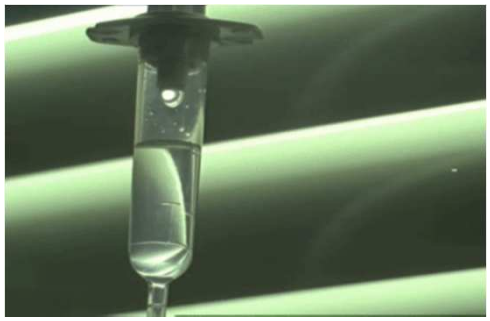
Même si c'est pas toxique, je ne vais pas en rajouter, il y en a déjà beaucoup…

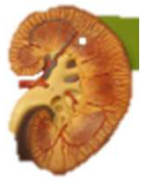
Il a fumé la moquette , le lactate c'est toxique !

A la fois on apporte du glucose même en cas d'hyperglycémie de stress, non ?

Pourquoi parler d’apport de lactate ?

- Il n’y a plus de produit de remplissage sans effet secondaire majeur





HEA

Albumine

Cristalloides

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Pourquoi parler d'apport de lactate ?

- Une balance hydrique très positive nuit à la santé

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Comparison of Two Fluid-Management Strategies in Acute Lung Injury

The National Heart, Lung, and Blood Institute Acute Respiratory Distress Syndrome (ARDS) Clinical Trials Network*

N Engl J Med 2006;354:2564-75.

Sepsis in European intensive care units: Results of the SOAP study*

Jean-Louis Vincent, MD, PhD, FCCM; Yasser Sakr, MB, BCh, MSc; Charles L. Sprung, MD; V. Marco Ranieri, MD; Konrad Reinhart, MD, PhD; Herwig Gerlach, MD, PhD; Rui Moreno, MD, PhD; Jean Carlet, MD, PhD; Jean-Roger Le Gall, MD; Didier Payen, MD; on behalf of the Sepsis Occurrence in Acutely Ill Patients Investigators

Crit Care Med 2006 Vol. 34, No. 2

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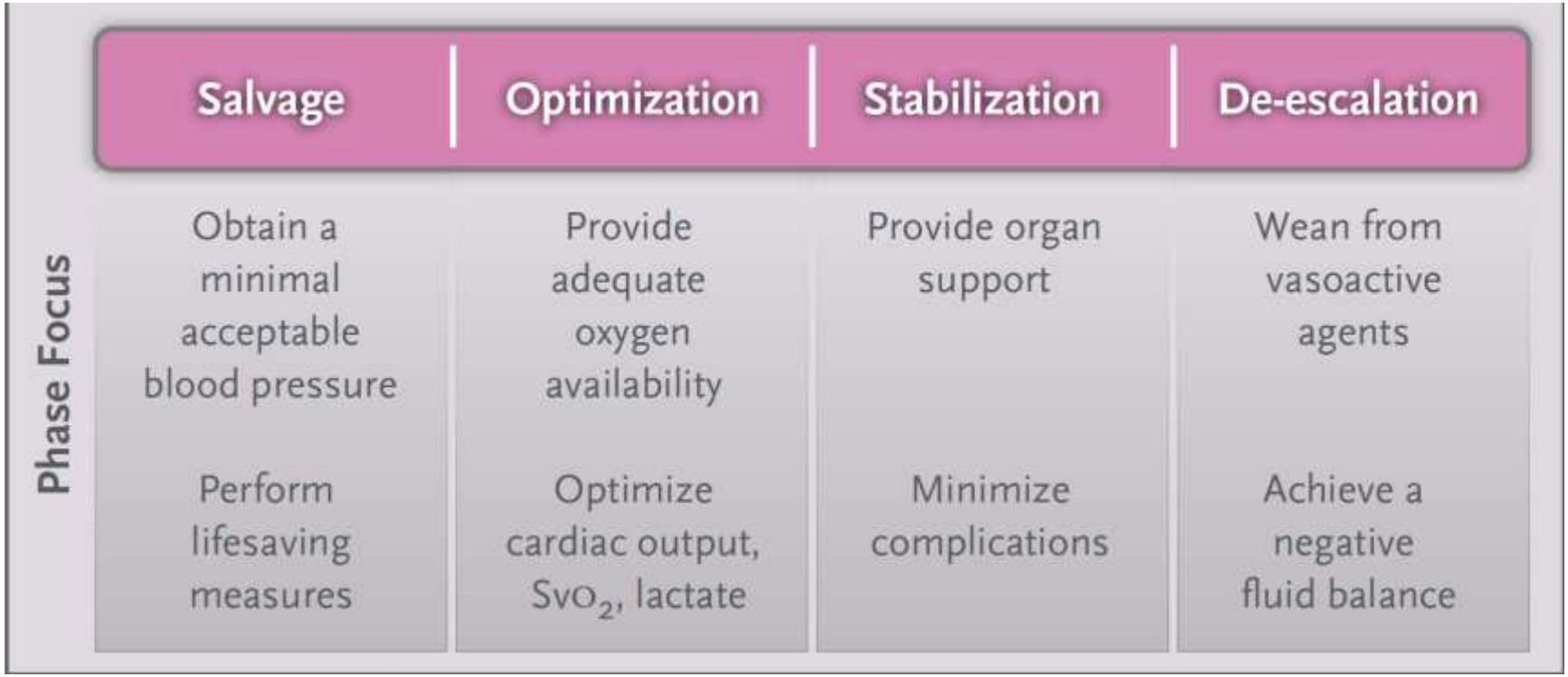


The NEW ENGLAND JOURNAL of MEDICINE

REVIEW ARTICLE

CRITICAL CARE MEDICINE

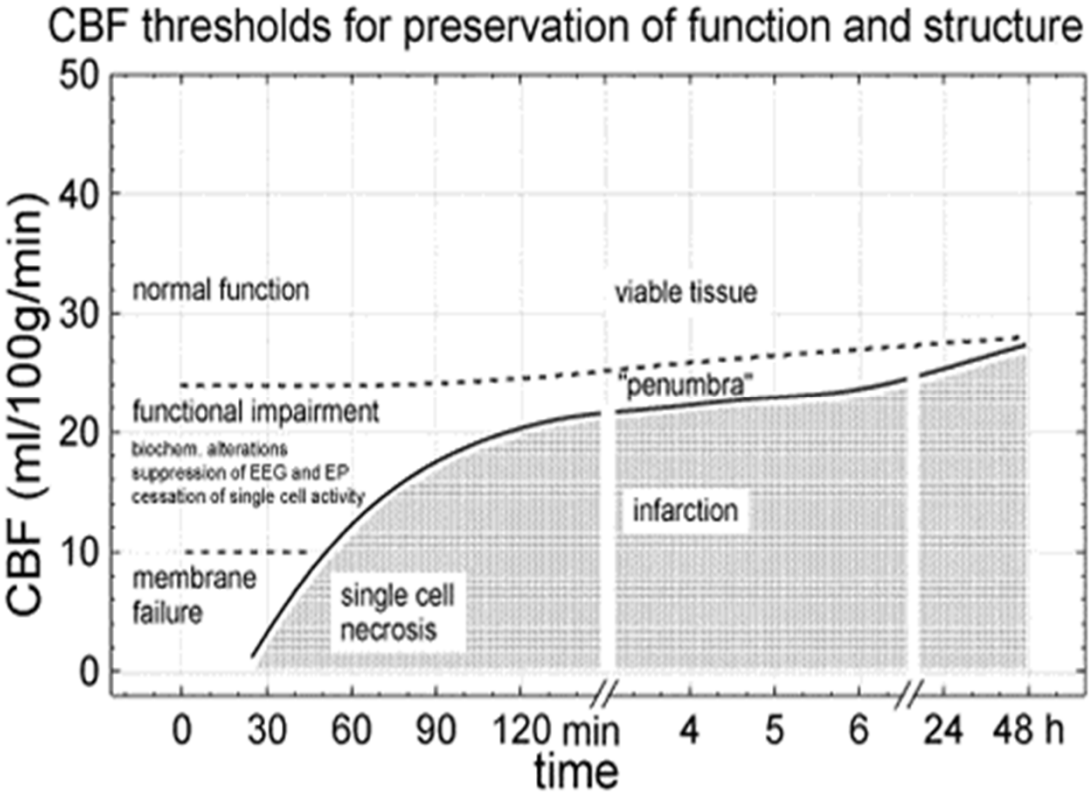
Simon R. Finfer, M.D., and Jean-Louis Vincent, M.D., Ph.D., *Editors*

Circulatory Shock

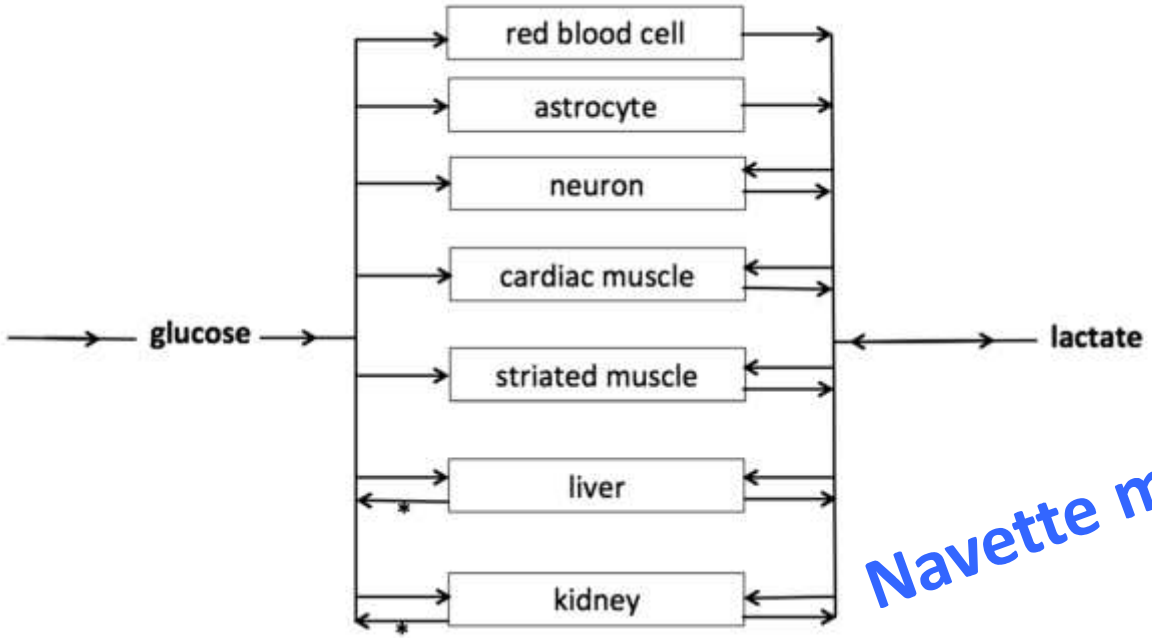
Jean-Louis Vincent, M.D., Ph.D., and Daniel De Backer, M.D., Ph.D.

Université de Lille

- Dans certains états pathologiques, les organes sont en zone de pénombre avec une hibernation/stuning..



métabolisme



Navette métabolique

Figure 2 Lactate at the physiological level. The flexible use of glucose and lactate as fuels on the cellular level is mirrored at the organism level. All living tissues can consume glucose. From the glucose/lactate point of view, three sorts of tissues/cells exist: 1) cells that must produce lactate because they lack mitochondria, e.g., red blood cells; 2) tissues or cells that either produce or consume lactate depending on circumstances, i.e., all mitochondria-containing cells; 3) tissues that can perform gluconeogenesis and export glucose that is resynthesized from lactate. The liver and the kidneys can only perform gluconeogenesis and export glucose. Only this so-called Cori cycle (denoted by *) carries an energy penalty, whereas the other shuttles do not lead to "waste" of energy.

Bakker, Annals of Intensive Care 2013

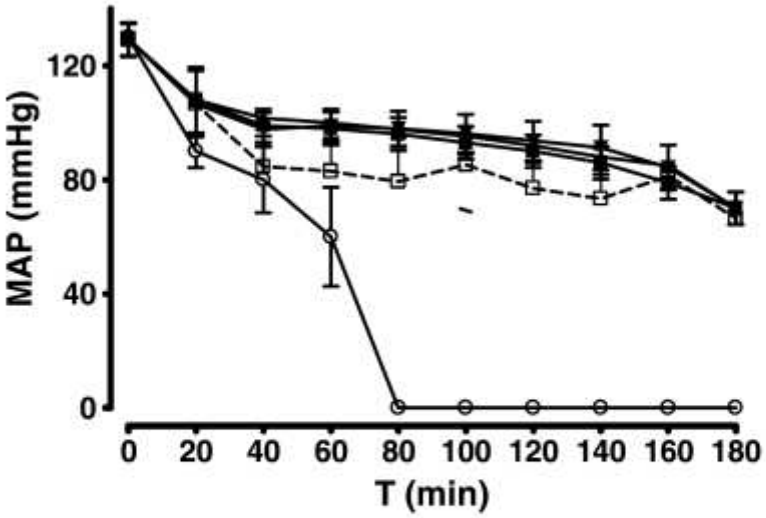
Intensive Care Med (2007) 33:495–502
DOI 10.1007/s00134-006-0523-9

EXPERIMENTAL

Bruno Levy
Arnauld Mansart
Chantal Montemont
Sebastien Gibot
Jean-Pierre Mallie
Veronique Regnault
Thomas Lecompte
Patrick Lacolley

Myocardial lactate deprivation is associated with decreased cardiovascular performance, decreased myocardial energetics, and early death in endotoxic shock

INSTALLING
MUSCLES
PLEASE WAIT



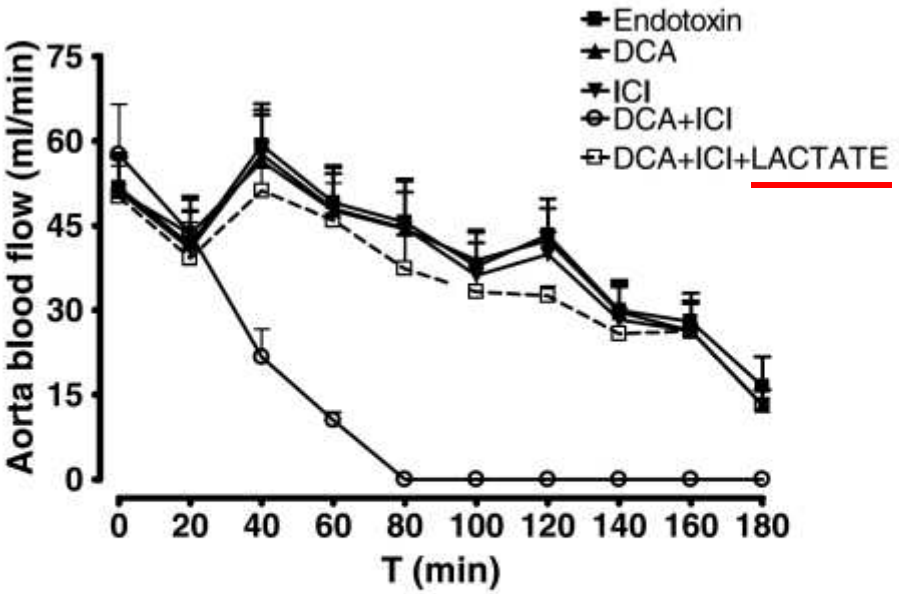
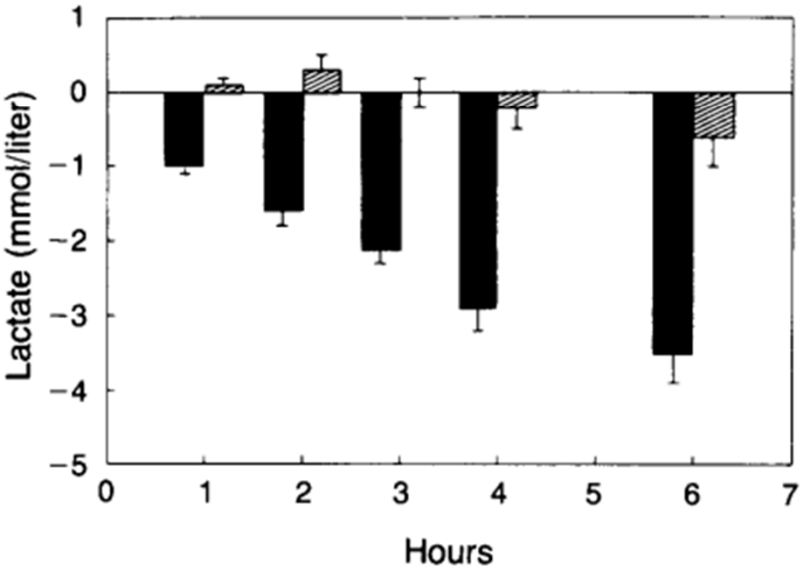


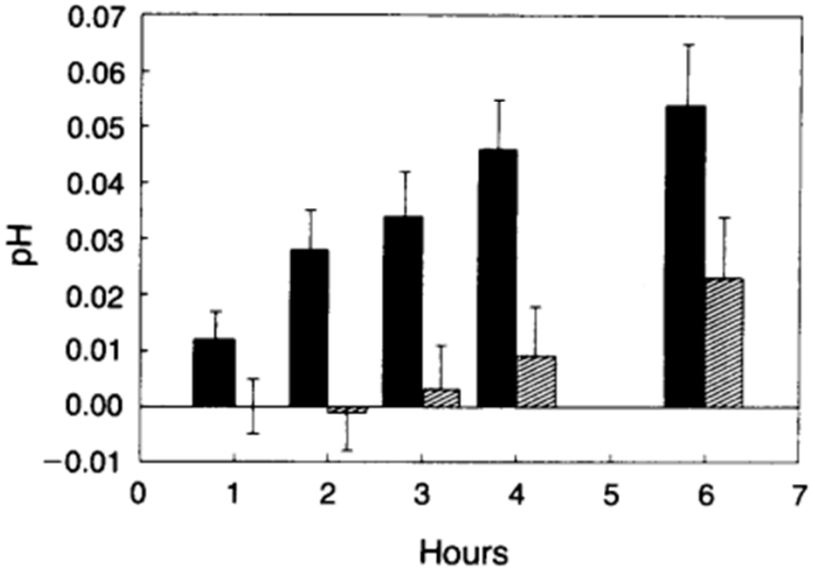
Fig. 3 Course of mean arterial pressure (*MAP*) and aorta blood flow in rats treated by either endotoxin, endotoxin plus ICI-118551, endotoxin plus dichloroacetate (*DCA*), endotoxin plus ICI-118551 plus DCA and endotoxin plus ICI-118551 plus DCA plus lactate. Neither DCA nor ICI-1185551, a selective β_2-blocker, changed MAP or aorta blood flow compared to endotoxin alone. The combination DCA and ICI-118551 dramatically decreased MAP and aorta blood flow and led to early death ($p < 0.01$). The addition of lactate blunted the effects of ICI plus DCA on hemodynamics ($p < 0.01$)

Levy, ICM 2007

A CONTROLLED CLINICAL TRIAL OF DICHLOROACETATE FOR TREATMENT OF LACTIC ACIDOSIS IN ADULTS

PETER W. STACPOOLE, PH.D., M.D., ELIZABETH C. WRIGHT, PH.D., THOMAS G. BAUMGARTNER, PHARM.D., ROBERT M. BERSIN, M.D., SCOTT BUCHALTER, M.D., STEPHEN H. CURRY, PH.D., CHARLES A. DUNCAN, M.D., ELOISE M. HARMAN, M.D., GEORGE N. HENDERSON, PH.D., STEVEN JENKINSON, M.D., JOHN M. LACHIN, SC.D., ANTHEA LORENZ, R.N., STEPHEN H. SCHNEIDER, M.D., JOHN H. SIEGEL, M.D., WARREN R. SUMMER, M.D., DOUGLAS THOMPSON, M.D., CHRISTOPHER L. WOLFE, M.D., BARBARA ZOROVICH, R.N., AND THE DICHLOROACETATE–LACTIC ACIDOSIS STUDY GROUP*





Stacpoole, NEJM 1992

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Table 3. Survival According to Treatment Group and Resolution of Lactic Acidosis.*

Subgroup	Dichloroacetate (N = 126)	Placebo (N = 126)
	no. (%)	
Died within 6 hr	30 (24)	21 (17)
Died within 7–72 hr		
No resolution of acidosis	37 (29)	49 (39)
Resolution of acidosis	17 (13)	4 (3)
Survived >72 hr		
No resolution of acidosis	3 (2)	11 (9)
Resolution of acidosis	39 (31)	41 (33)

*Resolution of lactic acidosis was defined as a decrease in the arterial-blood lactate concentration to less than 5 mmol per liter and an increase in the arterial-blood pH to more than 7.35. For patients whose pretreatment arterial-blood pH was greater than 7.35, a decrease in the base deficit to less than 6 mmol per liter was substituted as a criterion.

Stacpoole, NEJM 1992

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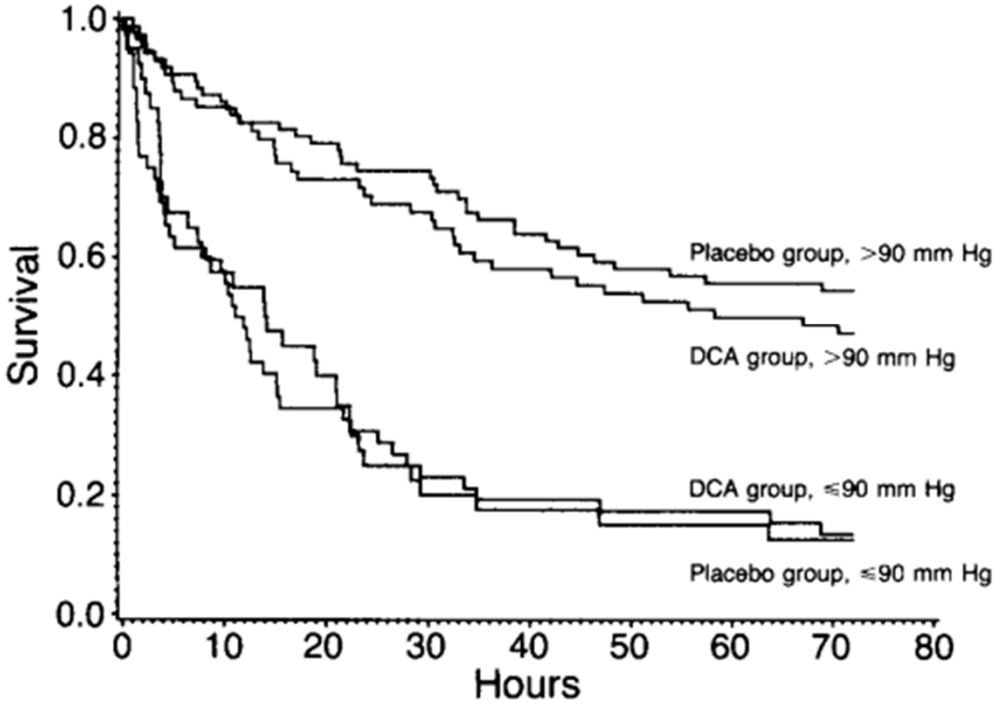

Figure 2. Kaplan–Meier Survival Curves for the 72 Hours after the First Treatment with Dichloroacetate (DCA) or Placebo in Patients with Pretreatment Systolic Blood Pressures ≤90 mm Hg and Patients with Pretreatment Systolic Blood Pressures >90 mm Hg.

The differences between the dichloroacetate group and the placebo group were not significant in either subgroup or for the subgroups combined.

Stacpoole, NEJM 1992

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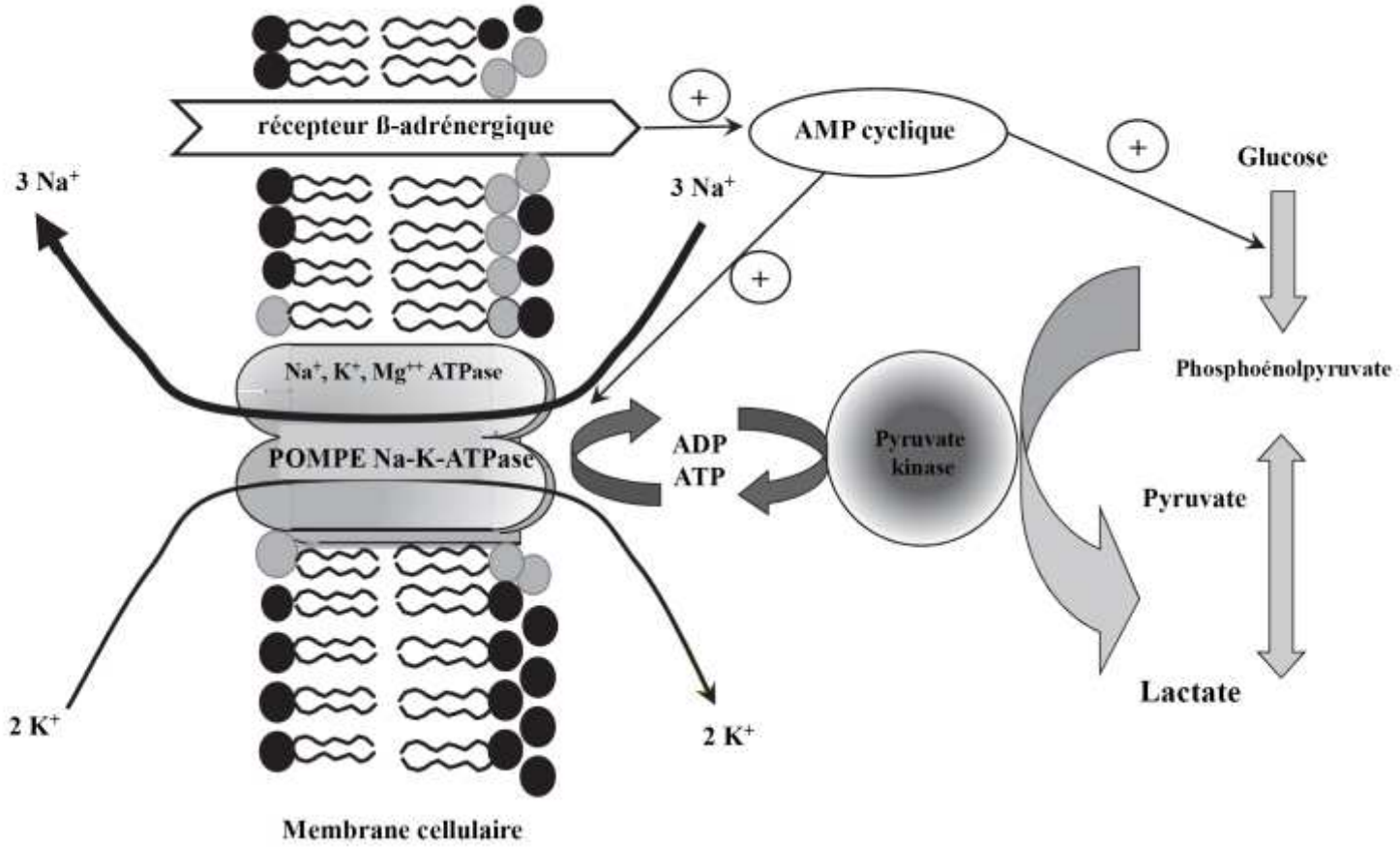
Effets métaboliques

- 3 carbones = ½ glucose
- En cas d'anaérobiose ou situation **de crise énergétique**:
- « Kick starter » du lactate
- Différence insuline (GLUT) et MCT
- **Navette métabolique**
- **Milieu intérieur**



Compartimentalisation énergétique: seul l'ATP fournit par la glycolyse permet de faire fonctionner la pompe Na/K ATPase

Ichaie SFAR 2014

Université de Lille

Crit Care Med 2000 Vol. 28, No. 12

Effects of cardiogenic shock on lactate and glucose metabolism after heart surgery

René L. Chioléro, MD; Jean-Pierre Revelly, MD; Xavier Leverve, MD; Philippe Gersbach, MD; Marie-Christine Cayeux, RN; Mette M. Berger, MD; Luc Tappy, MD

Table 2. Patients' hemodynamic characteristics and cardiovascular therapies

Patient	Inotropes Vasopressors	IABP	Lowest pHa	Lowest CI ($mL \cdot min^{-1} \cdot m^{-2}$)	CI at T0 ($mL \cdot min^{-1} \cdot m^{-2}$)	HR (bpm)	MAP (mm Hg)	MPAP (mm Hg)	PAOP (mm Hg)	SVRi ($dyne \cdot sec/cm^5 \cdot m^2$)
8	DOBU, NOR	+	7.19	1.25	1.97	103	69	22	15	3533
9	DOBU, ADRE	−	7.21	1.90	1.90	110	78	31	15	2800
10	DOBU, NOR	−	7.25	1.98	1.98	100	98	59	23	3022
11	DOBU, NOR	+	7.39	1.80	2.35	107	56	32	23	1305
12	DOBU, ADRE, NOR	−	7.19	2.15	2.19	101	54	32	14	1451
13	DOBU, ADRE, NOR	+	7.27	1.34	1.34	107	69	71	21	1947
14	DOBU, NOR	−	7.25	2.20	2.66	100	67	32	13	1624
Mean			7.25	1.80	2.06	105	70	32.7	17.7	2129
±SD			0.07	0.37	0.41	3.9	14.8	12.6	4.4	837

IABP, intra-aortic balloon pump; pHa, lowest arterial pH; CI, lowest cardiac index; T0, starting protocol; HR, heart rate; MAP, mean arterial pressure; MPAP, mean pulmonary arterial pressure; PAOP, pulmonary artery occlusion pressure; SVRi, indexed systemic vascular resistance; DOBU, dobutamine; NOR, noradrenaline; ADRE, adrenaline; +, present; −, absent.

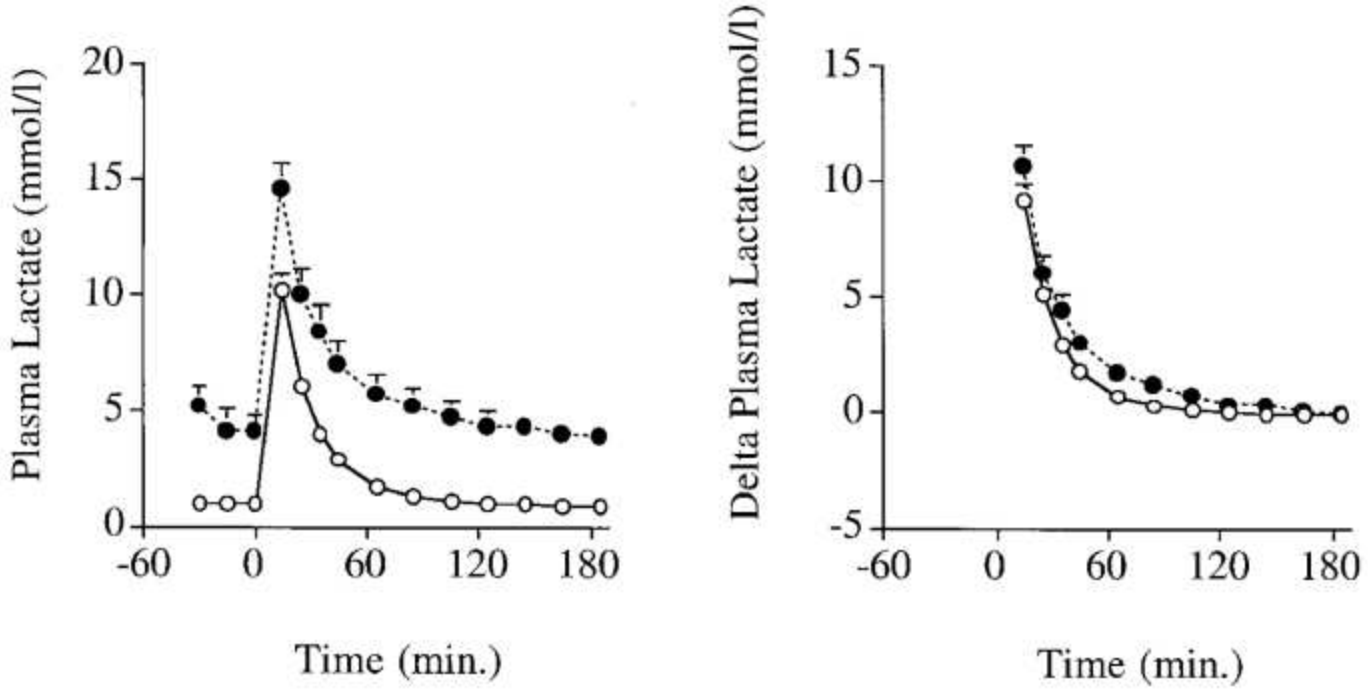


Figure 1. Evolution of plasma lactate concentration (*left*) or concentration changes from baseline level (T0; *right*) after 2.5 mol·kg^{-1}sodium lactate infused in 15 mins. *Open circles*, healthy subjects; *filled circles*, cardiogenic shock patients. SDs of healthy subjects are not all figured because of their minimal size.

Chiolero CCMed 2000

Crit Care Med 2003 Vol. 31, No. 3

Low exogenous lactate clearance as an early predictor of mortality in normolactatemic critically ill septic patients

Jacques Levraut, MD; Carole Ichai, MD, PhD; Isabelle Petit, MD; Jean-Pierre Ciebiera, MD; Olivier Perus, MD; Dominique Grimaud, MD

- Patients septiques peu hyperlactatémiques
- Mesure de la production et de l'élimination du lactate dans les 48 1^{ières} heures du sepsis après un test d'hyperlactatémie
- 56 patients : 64% origine pulmonaire, 27% digestive
- Mortalité à J28 : 30%

Table 2. Comparison of lactate metabolism variables between survivors and nonsurvivors

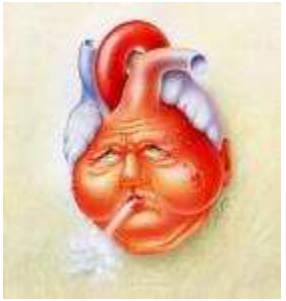
	Survivors (n = 39)	Nonsurvivors (n = 17)	Significance (p Value)
Baseline blood lactate, mmol·l^{-1}	1.4 ± 0.5	1.6 ± 0.7	.195
ΔLactate at T16, mmol·l^{-1}	2.8 ± 0.8	3.3 ± 0.5	.017
ΔLactate at T20, mmol·l^{-1}	1.8 ± 0.6	2.2 ± 0.5	.013
ΔLactate at T34, mmol·l^{-1}	0.7 ± 0.4	1.1 ± 0.4	.006
ΔLactate at T60, mmol·l^{-1}	0.3 ± 0.2	0.6 ± 0.3	.0005
T$_{\frac{1}{2}}$ of infused lactate, mins	19 ± 8	28 ± 14	.0038

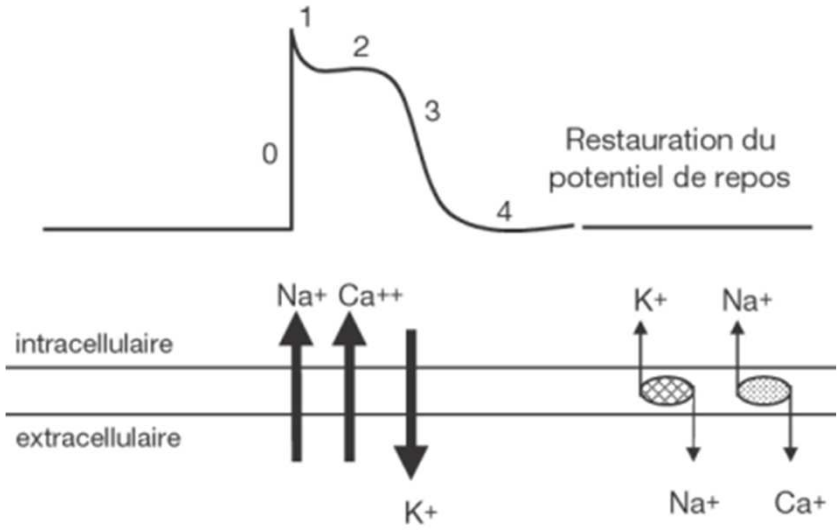
Baseline blood lactate, blood lactate concentration before lactate infusion; ΔLactate, increase in blood lactate induced by lactate infusion; calculated as the blood lactate concentration (at the time indicated) minus the baseline blood lactate value.

Levraut, CCMed 2003

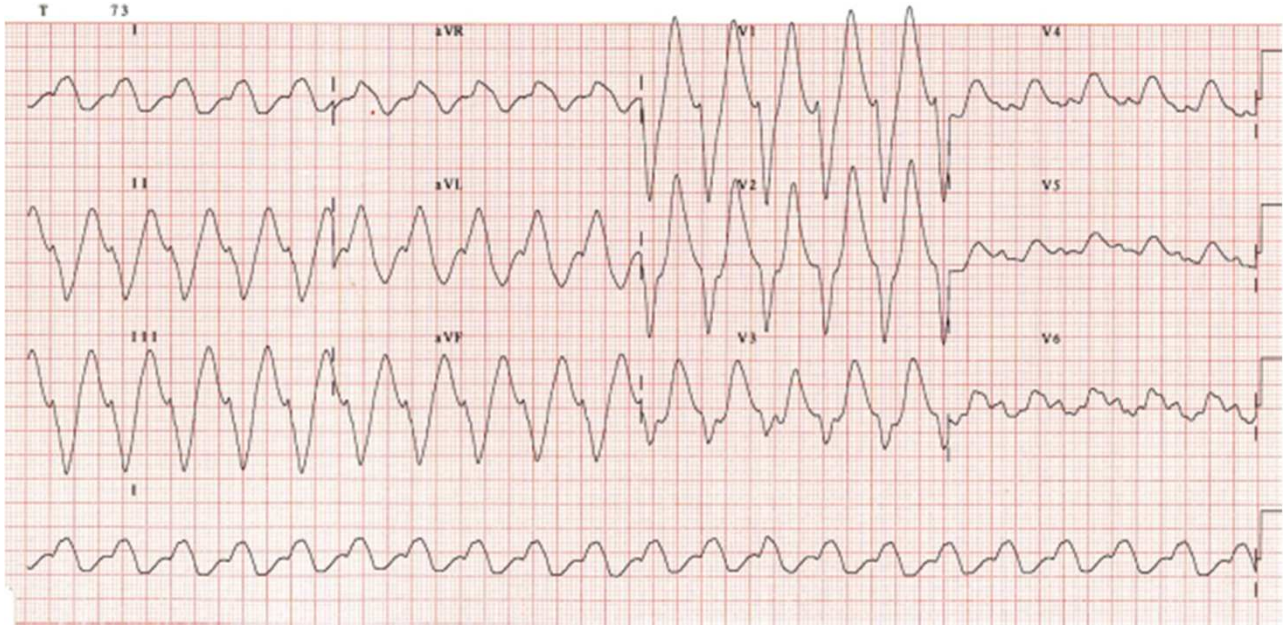
Lactate et myocarde

- Si VO_2 augmente : tachycardie, sepsis, catécholamines
- Si le transport en O_2 diminue: anémie, état de choc, infarctus
- Bêta-oxydation des Acides Gras → lactate
- L'inhibition de la production de lactate altère la contractilité choc endotoxinique ou hémorragique




1
2
3
0
4
Restauration du
potentiel de repos
Na+ Ca++
K+ Na+
intracellulaire
extracellulaire
K+
Na+ Ca+


LACTATE DE SODIUM AP-HP 11,2 %
solution pour perfusion
Apports :
Na + = 1 mmol/mL = 23 mg/mL
Lactate = 1 mmol/mL = 89 mg/mL
ATTENTION : SOLUTION HYPERTONIQUE

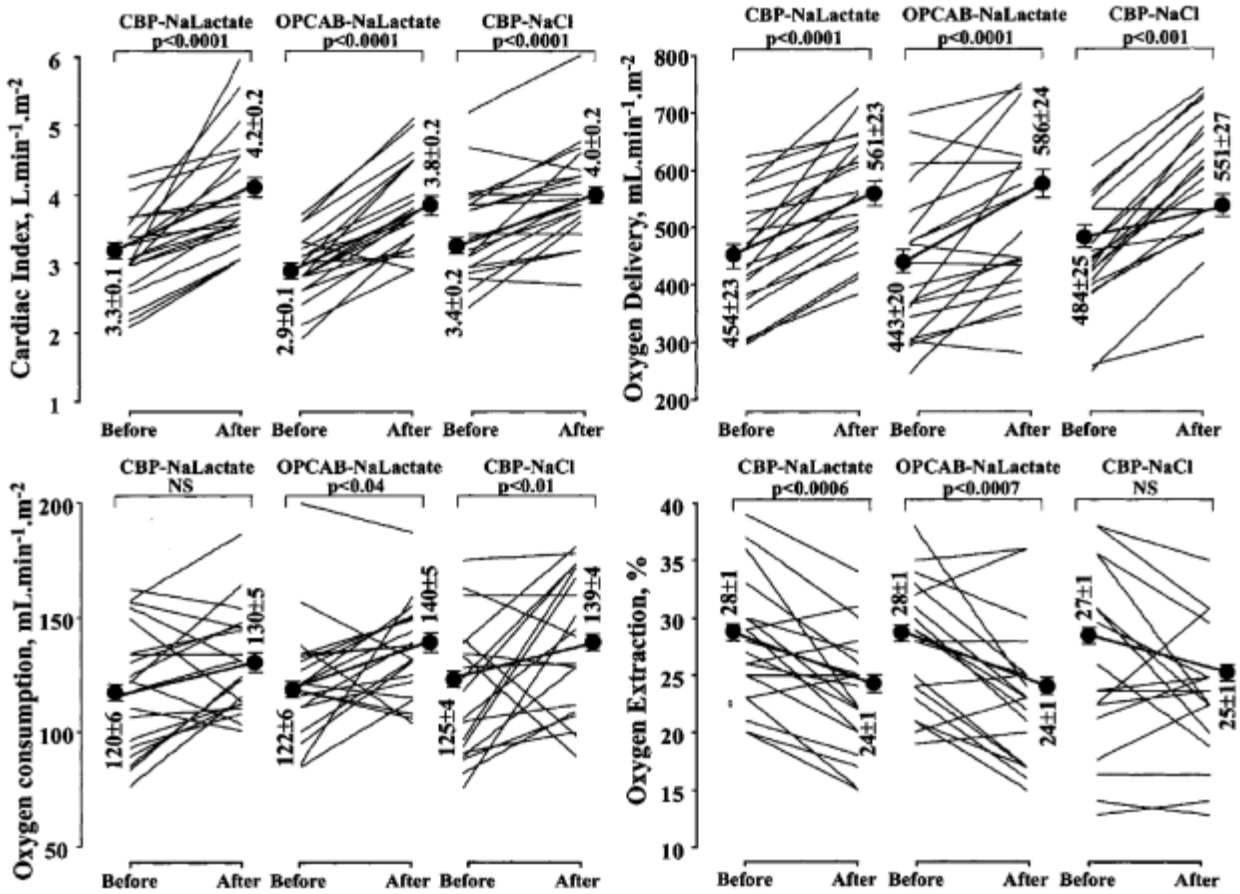

I
aVR
V1
V4
II
aVL
V2
V5
III
aVF
V3
V6

SHOCK, Vol. 18, No. 4, pp. 306–310, 2002

METABOLIC AND HEMODYNAMIC EFFECTS OF HYPERTONIC SOLUTIONS: SODIUM-LACTATE VERSUS SODIUM CHLORIDE INFUSION IN POSTOPERATIVE PATIENTS

Iqbal Mustafa* and Xavier M. Leverve†

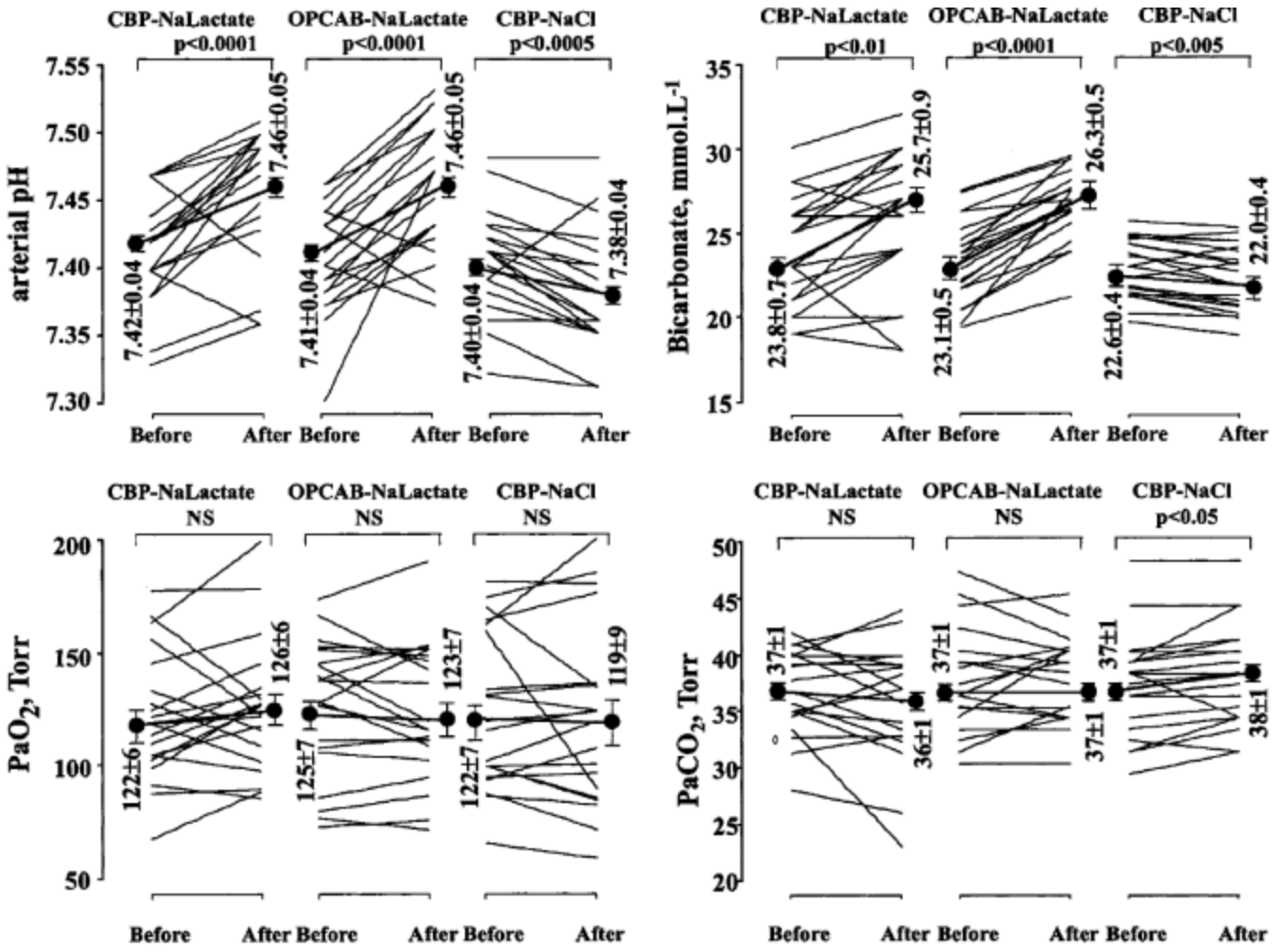
**Intensive Care Unit, Harapan Kita National Cardiovascular Center, Jakarta, Indonesia; and †Laboratoire de Bioénergétique Fondamentale et Appliquée, Université Joseph Fourier and Département de Médecine Aiguë Spécialisée, University Hospital, Grenoble, France*



Amélioration de l’index cardiaque comme avec SSH

Mustafa, Shock 2002

Université de Lille



Alcalinisant contrairement au SSH qui est acidifiant

Mustafa, Shock 2002

Université de Lille

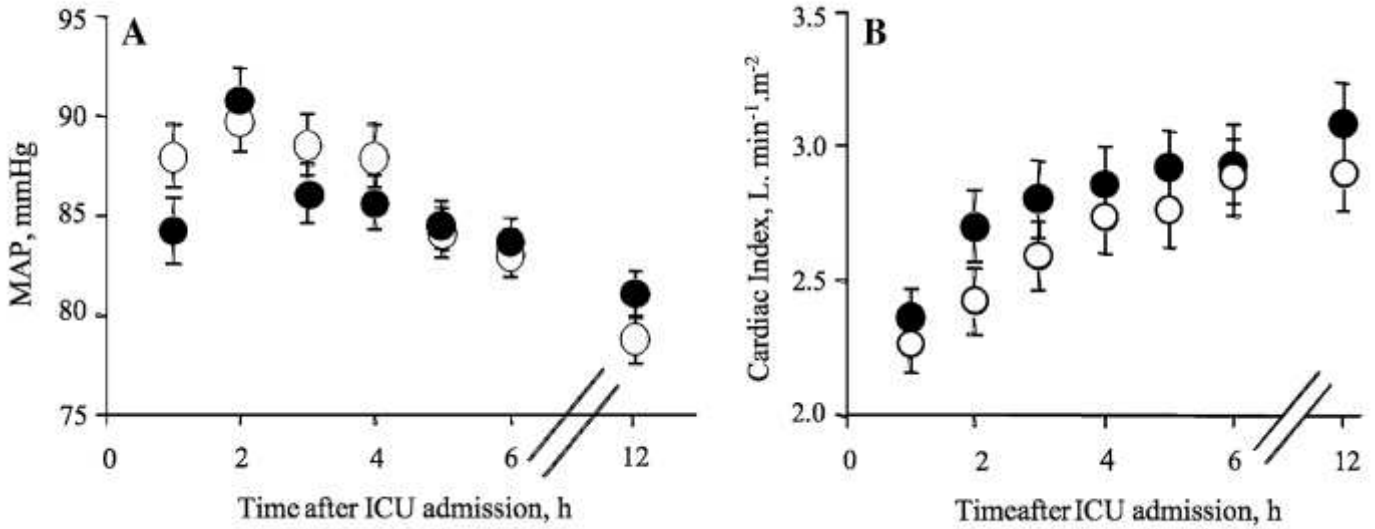
Intensive Care Med (2008) 34:1796–1803
DOI 10.1007/s00134-008-1165-x

ORIGINAL

Xavier M. Leverve
Cindy Boon
Tarmizi Hakim
Maizul Anwar
Erwin Siregar
Iqbal Mustafa

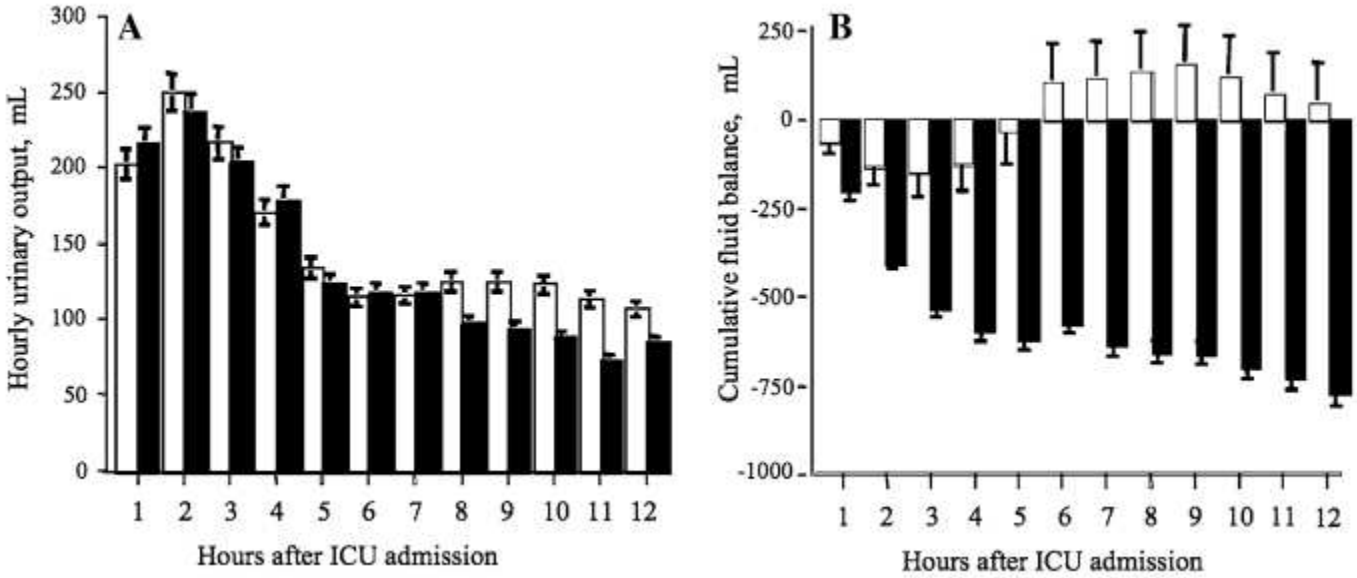
Half-molar sodium-lactate solution has a beneficial effect in patients after coronary artery bypass grafting

Fig. 1 Effect of RL versus HL on mean arterial pressure and cardiac index. *Open symbols*: RL, *closed symbols*: HL. **a** Mean arterial pressure (*MAP*), mm Hg, **b** Cardiac index (*CI*), L min^{-1} m^{-2}. Results are expressed as mean ± sem; statistical comparisons with ANOVA for repeated measures: MAP = NS; CI $P = 0.0242$ (unpaired student's post hoc analysis: 2 h $P = 0.004$; 3 h $P = 0.016$; 12 h $P = 0.037$)



Leverve ICM 2008

Fig. 2 Urinary output and body fluid balance in post-CABG patients treated with RL or HL. *White columns* patients treated with RL, *black columns* patients treated with HL. **a** hourly urinary output, mL. **b** cumulative body fluid balance, mL. Results are expressed as means ± sem, statistical comparisons between RL and HL with ANOVA for repeated measures: non-significant for urine output; $P < 0.0001$ for cumulative body fluid balance



Leverve ICM 2008

Table 4 Effect of RL or HL infusions on biological parameters

Time, h	1		6		12	
Group	RL	HL	RL	HL	RL	HL
Na[a, b]	137 ± 0.3	138 ± 0.4	136 ± 0.4[c]	140 ± 0.4[c,d]	136 ± 0.4[c]	140 ± 0.4[c,d]
Cl[a]	106 ± 0.5	106 ± 0.5	104 ± 0.5[c]	103 ± 0.5[c]	103 ± 0.5[c]	104 ± 0.5[c]
K[a, b]	3.6 ± 0.05	3.5 ± 0.04	3.9 ± 0.07[c]	3.7 ± 0.04[c,d]	4.2 ± 0.05[c]	3.9 ± 0.04[c,d]
Lactate[a, b]	2.4 ± 0.1	3.4 ± 0.2[d]	3.12 ± 0.2[c]	4.6 ± 0.2[c,d]	2.4 ± 0.2	3.0 ± 0.2[d]
pH[a, b]	7.46 ± 0.01	7.46 ± 0.01	7.38 ± 0.01[c]	7.45 ± 0.01[d]	7.40 ± 0.01[c]	7.44 ± 0.01[d]
Bicarbonate[a, b]	31.1 ± 0.8	31.2 ± 0.7	21.8 ± 0.3[c]	27.1 ± 0.4[d]	23.0 ± 0.3[c]	28.7 ± 0.3[c,d]

Sodium (Na), potassium (K), chloride (Cl), lactate and bicarbonate are in mmol L^{-1}. Data are mean ± sem. Statistical comparisons were carried out through a two-way ANOVA for repeated measures. When the difference was significant, a post hoc analysis was performed by either paired student's *t* test (vs. 1 h) or unpaired student's *t* test (vs. RL)

[a] Effect of time (ANOVA, $P < 0.02$)

[b] Effect of group (ANOVA, RL vs. RH, $P < 0.02$)

[c] Significantly different from time 1 (paired student's *t* test, $P < 0.02$)

[d] Significantly different from RL (unpaired student's *t* test, $P < 0.02$)

Leverve ICM 2008

Nalos *et al. Critical Care* 2014, **18**:R48
http://ccforum.com/content/18/2/R48

CRITICAL CARE

RESEARCH Open Access

Half-molar sodium lactate infusion improves cardiac performance in acute heart failure: a pilot randomised controlled clinical trial

Marek Nalos[1*], Xavier Maurice Leverve[2^], Stephen Joseph Huang[1], Leonie Weisbrodt[1], Ray Parkin[1], Ian Mark Seppelt[1], Iris Ting[1] and Anthony Stuart Mclean[1]

RCT : 20 patients dans chaque groupe

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Table 1 Baseline demographic variables, aetiology of acute heart failure and related chronic premorbid conditions[a]

Patient characteristics	Control group	Lactate group
Age (years)	69.9 ± 9.8	67.4 ± 14.6
Sex (male/female)	17/4	13/6
Weight (kg)	86.5 ± 19.6	79.2 ± 22.3
APACHE II score	18.5 ± 6.9	18.6 ± 5.3
LVEF (%)	27.1 ± 10.3	27.2 ± 8.1
Bilirubin (μmol/L)	15 ± 13	20 ± 25
ALT (IU/L)	489 ± 1,026	525 ± 928
Aetiology of AHF (*n*)[b]		
ADHF	4	2
NSTEMI	8	8
STEMI	5	5
Arrhythmia	1	1
Infection	6	4
Cardiac arrest	1	4
Other	1	1
Premorbid conditions (*n*)[b]		
IHD	14	11
CCF	10	6
HT	10	8
Diabetes	9	5

[a]ADHF = Acute decompensated heart failure; ALT = Alanine aminotransferase; APACHE II = Acute Physiology and Chronic Health Evaluation II; CCF = Chronic congestive heart failure; HT = Hypertension; IHD = Ischaemic heart disease; LVEF = Left ventricular ejection fraction; NSTEMI = Non-ST-segment elevation myocardial infarct; STEMI = ST-segment elevation myocardial infarct. [b]Some patients had more than one condition present. Data are expressed as mean ± SD unless indicated otherwise.

Nalos, Crit Care 2014

Université de Lille

Table 2 Evolution of haemodynamic and selected transthoracic echocardiography parameters during the study period[a]

Time points	MAP	HR	SV	TAPSE	SmTDI	*E/E'*
Baseline						
Control	78 ± 15	97 ± 23	50.6 ± 13.7	16.3 ± 5	6.0 ± 0.02	17.3 ± 8.3
Lactate	77 ± 16	95 ± 24	49 ± 19.4	14.7 ± 5.5	5.84 ± 0.02	14.4 ± 6.8
24 hours						
Control	78 ± 12	91 ± 14	53.3 ± 13.5	16 ± 5.5	6.53 ± 0.02	13.5 ± 4.7[a]
Lactate	79 ± 17	95 ± 15	59.6 ± 20[b]	18.3 ± 7[b]	7.0 ± 0.04	15.2 ± 7.6
48 hours						
Control	77 ± 15	91 ± 15	52.3 ± 16	17.1 ± 5.7	6.5 ± 0.02	13.8 ± 5.7[a]
Lactate	85 ± 18	89 ± 17	54.1 ± 26.5	18.1 ± 7.8[a]	6.2 ± 0.03	15.9 ± 9.7

[a]*E/E'* = Ratio of early peak diastolic transmitral Doppler flow velocity to early peak diastolic tissue Doppler velocity of the mitral annulus (averaged medial and lateral); HR = heart rate (beats/min); MAP = Mean arterial pressure (mmHg); SmTDI = Systolic motion of the mitral annulus (averaged medial and lateral) by tissue Doppler imaging (cm/s); SV = Stroke volume; TAPSE = Tricuspid annular plane systolic excursion (mm). [b]$P < 0.05$ and [c]$P < 0.01$ compared to baseline values. Data are expressed as mean ± SD.

Nalos, Crit Care 2014

Université de Lille

Diminution de la lactatémie

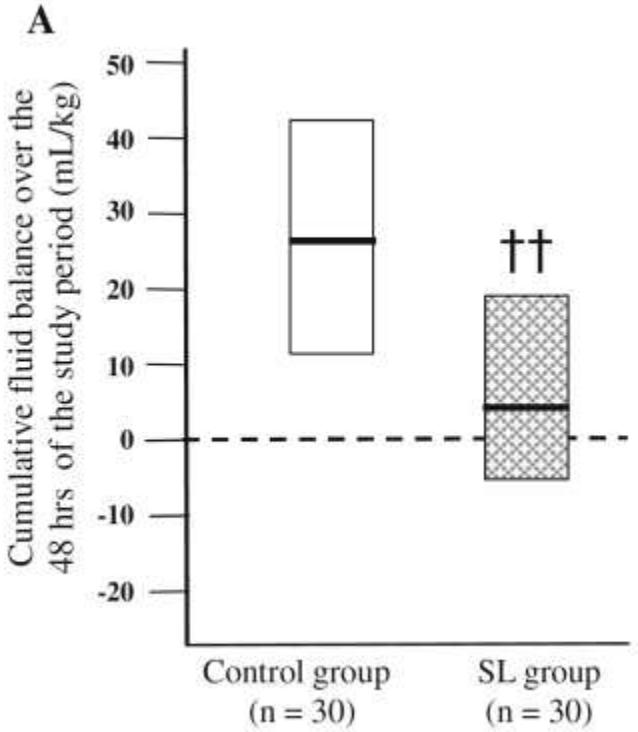
Baseline	pH	$paCO_2$	paO_2	HCO_3	BE	Lactate
C (n = 21)	7.37 ± 0.1	40 ± 13	98 ± 33	22.8 ± 4.9	−1.7 ± 5.6	1.4 ± 0.5
L (n = 19)	7.40 ± 0.06	36 ± 9	103 ± 28	23.3 ± 3.3	−0.3 ± 4.1	2.4 ± 2.3
post bolus						
C (n = 21)	7.37 ± 0.09	40 ± 9	91 ± 19	23.1 ± 5.1	−1.01 ± 5.7	2 ± 1.4
L (n = 19)	7.45 ± 0.05$^{**\#\#}$	38 ± 8	95 ± 30	25.9 ± 4.1**	2.7 ± 4.2	4.8 ± 2.0**
6 hours						
C (n = 20)	7.38 ± 0.06	42 ± 9	93 ± 27	24.1 ± 4.8	−0.7 ± 5.3	1.6 ± 1.2
L (n = 19)	7.49 ± 0.04$^{**\#\#}$	43 ± 5**	87 ± 24	32.5 ± 4.8$^{**\#\#}$	8.9 ± 4.5$^{**\#\#}$	2.9 ± 1.0$^{\#\#}$
12 hours						
C (n = 19)	7.38 ± 0.07	42 ± 10	95 ± 37	24.3 ± 4.7	−0.2 ± 5.2	1.4 ± 0.6
L (n = 19)	7.51 ± 0.04$^{**\#\#}$	47 ± 5**	82 ± 24	37.1 ± 5.3$^{**\#\#}$	12.9 ± 4.6	3.1 ± 1.6$^{\#\#}$
24 hours						
C (n = 19)	7.41 ± 0.07	38 ± 11	84 ± 20	23.9 ± 5.4	−0.9 ± 5.8	1.5 ± 1.0
L (n = 18)	7.53 ± 0.03$^{**\#\#}$	51 ± 7$^{**\#\#}$	81 ± 26	41.4 ± 6.3$^{**\#\#}$	16.8 ± 4.8$^{**\#\#}$	2.3 ± 0.8$^{\#\#}$
48 hours						
C (n = 18)	7.42 ± 0.03	42 ± 9	87 ± 28	26.9 ± 5.6**	2.8 ± 5.3**	1.6 ± 0.9
L (n = 18)	7.47 ± 0.03**	48 ± 4**	95 ± 42	34.2 ± 4.1$^{**\#\#}$	9.6 ± 4.2$^{**\#\#}$	1.2 ± 0.5**

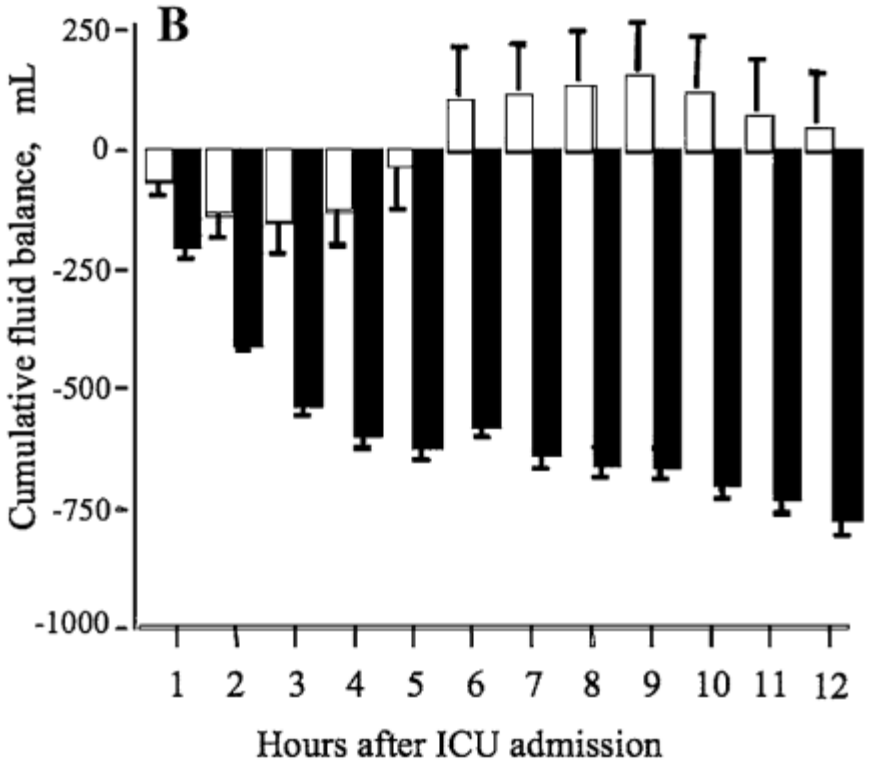
C = control group, L = lactate group, $paCO_2$ - partial pressure of carbon dioxide (mmHg), paO_2 - partial pressure of oxygen (mmHg), HCO_3 – bicarbonate (mmol/L) BE - base excess (mmol/l), ** $p < 0.01$ compared to baseline

Nalos Crit Care 2014

Université de Lille

Balance hydrique



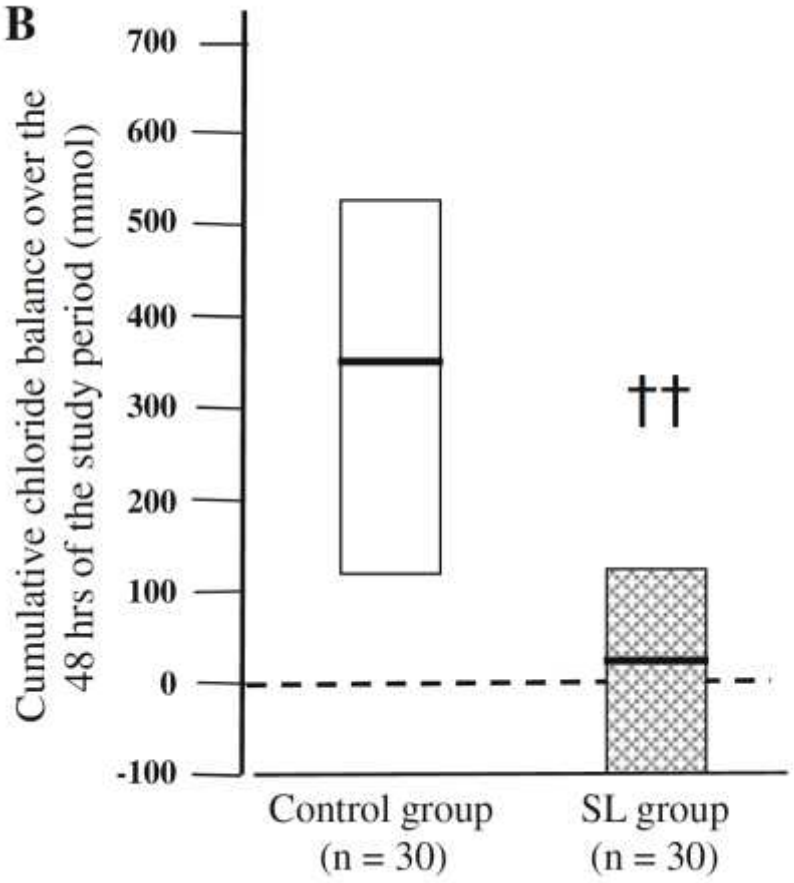


ICM Ichaie 2013

Leverve ICM 2008

Université de Lille

Balance chlorée



ICM Ichaie 2013

Université de Lille

Intensive Care Med (2009) 35:471–479
DOI 10.1007/s00134-008-1283-5

ORIGINAL

Carole Ichai
Guy Armando
Jean-Christophe Orban
Frederic Berthier
Laurent Rami
Corine Samat-Long
Dominique Grimaud
Xavier Leverve

Sodium lactate versus mannitol in the treatment of intracranial hypertensive episodes in severe traumatic brain-injured patients

Intensive Care Med 2013
DOI 10.1007/s00134-013-2978-9

ORIGINAL

Carole Ichai
Jean-François Payen
Jean-Christophe Orban
Hervé Quintard
Hubert Roth
Robin Legrand
Gilles Francony
Xavier M. Leverve

Half-molar sodium lactate infusion to prevent intracranial hypertensive episodes in severe traumatic brain injured patients: a randomized controlled trial

Intensive Care Med (2014) 40:412–421
DOI 10.1007/s00134-013-3203-6

ORIGINAL

Pierre Bouzat
Nathalie Sala
Tamarah Suys
Jean-Baptiste Zerlauth
Pedro Marques-Vidal
François Feihl
Jocelyne Bloch
Mahmoud Messerer
Marc Levivier
Reto Meuli
Pierre J. Magistretti
Mauro Oddo

Cerebral metabolic effects of exogenous lactate supplementation on the injured human brain

Etude de phase II 15 patients avec TC isolé

Table 1 Patient characteristics

Patient no.	Age (years)	Gender	Admission GCS	Marshall score	Injury type	Time from TBI to intracranial monitoring (hours)	Time from TBI to sodium lactate therapy (hours)	Duration of intracranial monitoring (days)	GOS (at 6 months)
1	54	F	3	2	Diffuse	13	21	4	4
2	39	M	8	2	Focal	52	57	3	4
3	19	M	6	2	Diffuse	7	24	4	5
4	55	M	8	3	Diffuse	6	20	11	5
5	30	M	7	5	Diffuse	8	30	10	3
6	24	M	6	2	Diffuse	6	34	6	2
7	46	M	8	2	Diffuse	7	66	3	4
8	60	M	8	3	Focal	23	64	5	1
9	24	F	6	2	Diffuse	6	24	3	4
10	41	M	3	2	Diffuse	6	24	8	1
11	24	M	8	2	Diffuse	17	23	3	4
12	52	F	7	2	Diffuse	26	38	4	4
13	24	M	7	3	Diffuse	5	21	4	1
14	60	M	6	2	Diffuse	7	24	4	4
15	55	M	8	6	Diffuse	13	27	11	3

F female, *GCS* Glasgow Coma Scale, *GOS* Glasgow Outcome Score, *M* male, *TBI* traumatic brain injury

Bouzat ICM 2014

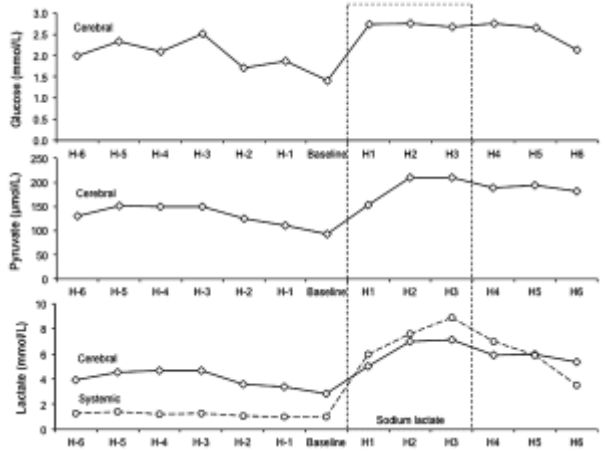


Table 2 Changes of main cerebral and systemic variables during sodium lactate therapy

	Coefficient ± SE	95 % Confidence interval	*p* value
Cerebral variables			
CMD lactate (mmol/L)	0.47 ± 0.08	0.31 to 0.63	<0.01
CMD pyruvate (µmol/L)	13.10 ± 2.20	8.78 to 17.40	<0.01
CMD glucose (mmol/L)	0.10 ± 0.04	0.04 to 0.16	<0.01
CMD glutamate (mmol/L)	−0.95 ± 0.51	−1.94 to 0.06	0.06
$PbtO_2$ (mmHg)	−0.58 ± 0.29	−1.14 to −0.01	0.04
Intracranial pressure (mmHg)	−0.86 ± 0.32	−1.47 to −0.24	<0.01
Systemic variables			
Glucose (mmol/L)	0.08 ± 0.09	−0.11 to 0.28	0.39
Sodium (mmol/L)	1.96 ± 0.25	1.48 to 2.44	<0.01
Chloride (mmol/L)	−0.08 ± 0.25	−0.57 to 0.42	0.76
pH	0.04 ± 0.01	0.00 to 0.02	<0.01
Osmolarity (mosm/L)	3.57 ± 0.44	2.71 to 4.43	<0.01

Analysis was conducted using mixed-effects multilevel regression with time as an independent variable and allowing it to have a random intercept and a random slope according to patient
CMD cerebral microdialysis, *$PbtO_2$* brain tissue oxygen tension

Baisse du glutamate

Bouzat ICM 2014

Reperfusion / Sepsis

- Accès au cycle de Krebs bloqué
- Rapport ATP/ADP bas
- La glycolyse ne peut pas débuter car nécessite de l'ATP dans sa phase initiale
- L'oxygène ne va pas être utilisé et former des radicaux libres
- Les complexes I et IV sont inhibés mais pas le II donc le lactate peut amorcer la pompe…

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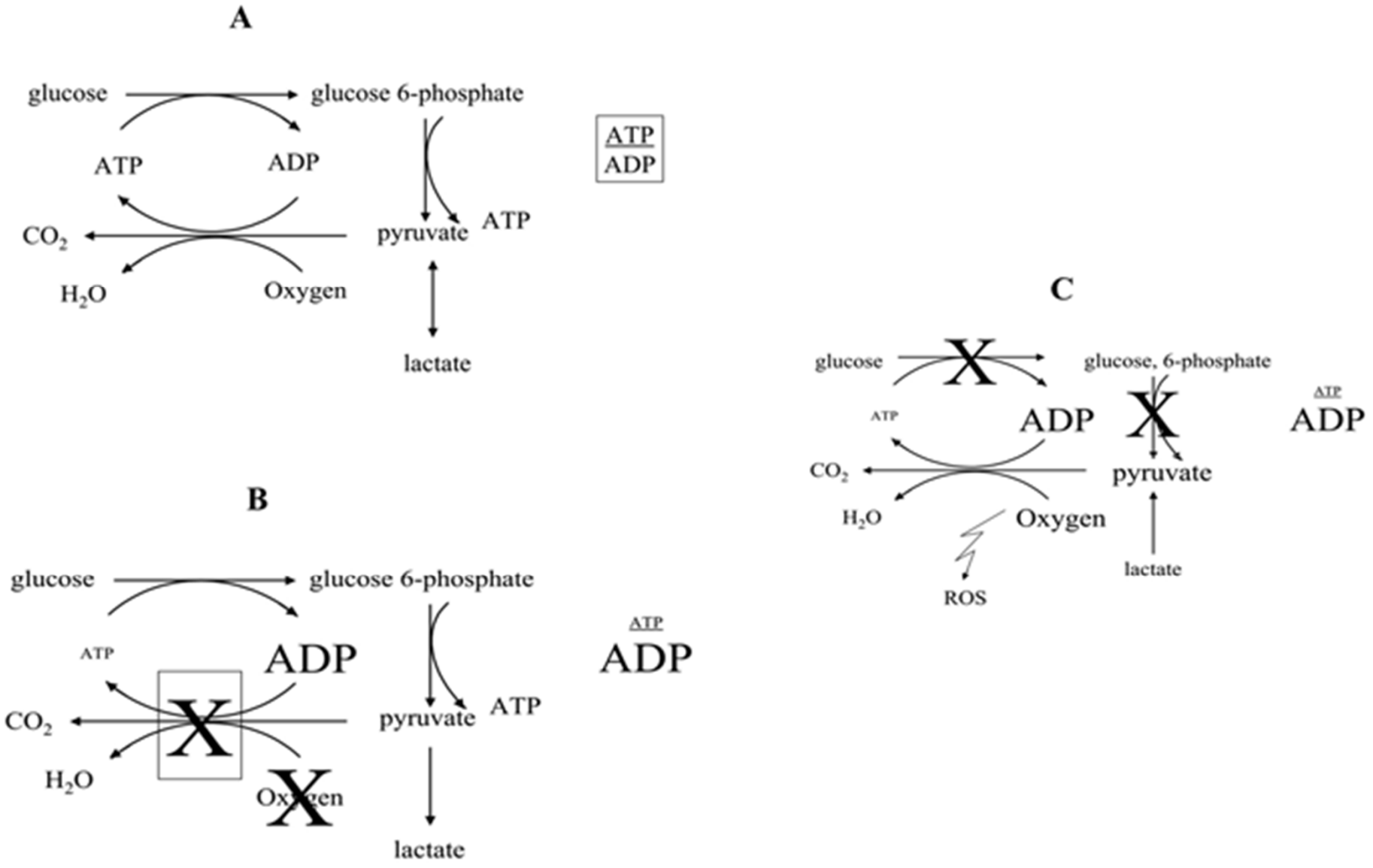
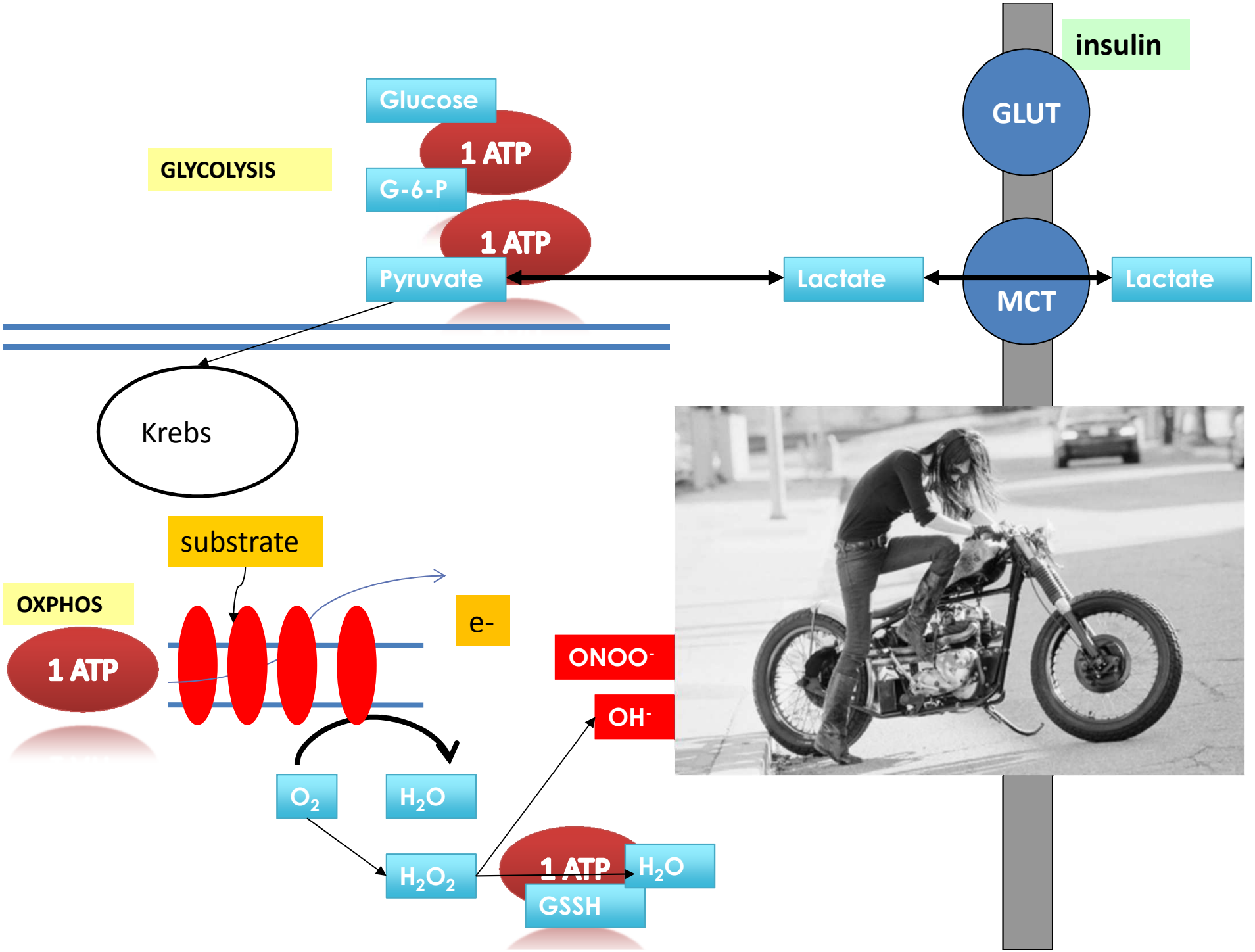
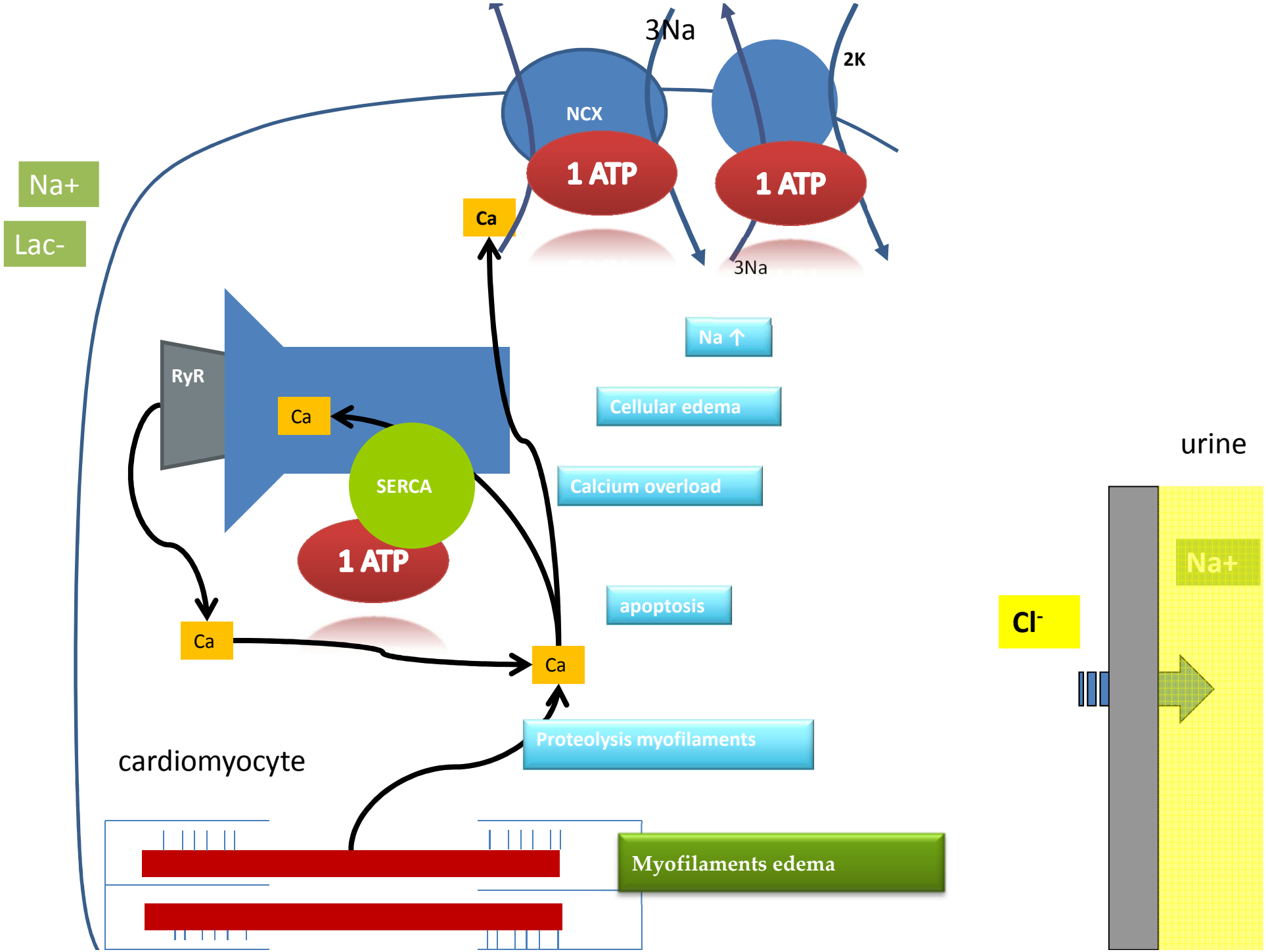

A
glucose
glucose 6-phosphate
ATP
ADP
ATP
ADP
CO_2
pyruvate
ATP
H_2O
Oxygen
lactate
B
glucose
glucose 6-phosphate
ATP
ADP
ATP
ADP
CO_2
pyruvate
ATP
H_2O
Oxygen
lactate
C
glucose
glucose, 6-phosphate
ATP
ADP
ATP
ADP
CO_2
pyruvate
H_2O
Oxygen
lactate
ROS


insulin
GLUT
Glucose
1 ATP
GLYCOLYSIS
G-6-P
1 ATP
Pyruvate
Lactate
MCT
Lactate
Krebs
substrate
OXPHOS
1 ATP
e-
ONOO-
OH-
O2
H2O
H2O2
1 ATP
H2O
GSSH


3Na
2K
NCX
1 ATP
1 ATP
Ca
3Na
Na+
Lac-
Na ↑
RyR
Ca
Cellular edema
SERCA
Calcium overload
1 ATP
apoptosis
Ca
Ca
Proteolysis myofilaments
cardiomyocyte
Myofilaments edema
urine
Cl-
Na+

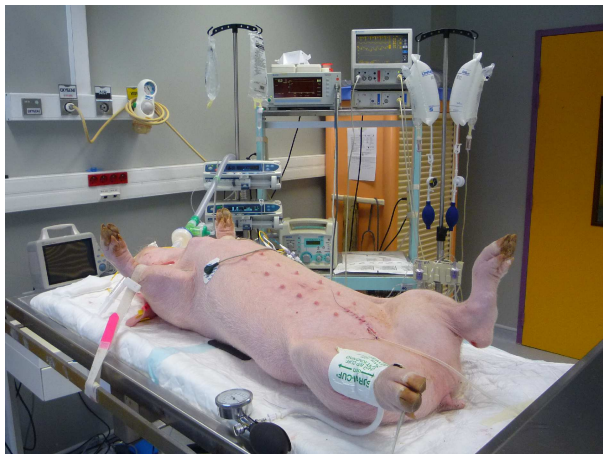
Duburcq *et al. Critical Care* 2014, **18**:467
http://ccforum.com/content/18/4/467

CRITICAL CARE

RESEARCH Open Access

Hypertonic sodium lactate improves fluid balance and hemodynamics in porcine endotoxic shock

Thibault Duburcq[1,2,3,4], Raphaël Favory[3,4], Daniel Mathieu[3,4], Thomas Hubert[1,2,3], Jacques Mangalaboyi[3,4], Valery Gmyr[1,2,3], Laurence Quintane[1,2,3], Patrice Maboudou[3,5], François Pattou[1,2,3] and Mercé Jourdain[1,2,3,4*]



NaCl 0.9%
500 mL

100 mL/h of NaCl 0,9% or Hypertonic Sodium Lactate 11,2% or
Hypertonic Sodium Bicarbonate 8,4% (= 450 mL from T30 to T300)
± 2,5mL/kg of NaCl 0,9% every 15 min to maintain MAP ≥ 60 mmHg

LPS infusion (5 γ/kg/min)

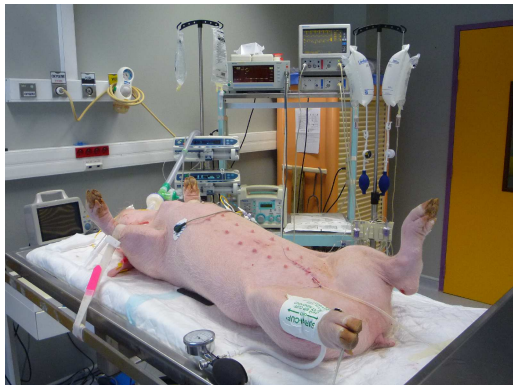
T | T0 | T30 | T60 | T120 | T210 | T300

Preparation | Stabilisation

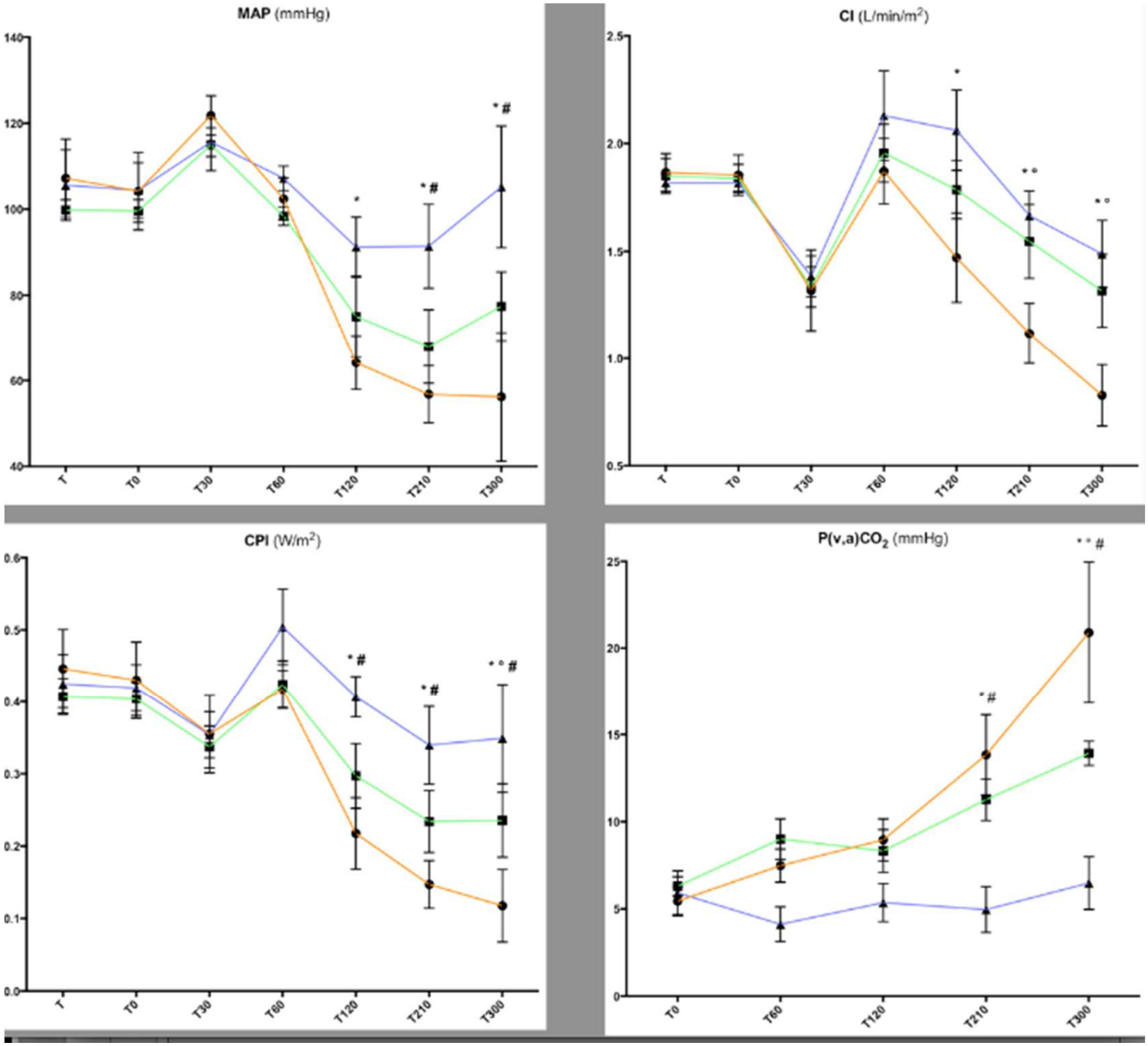
HR, BP, PBP, PCWP, SvO2, CI measurements from T to T300

Laser Doppler flowmetry measurements from T0 to T300

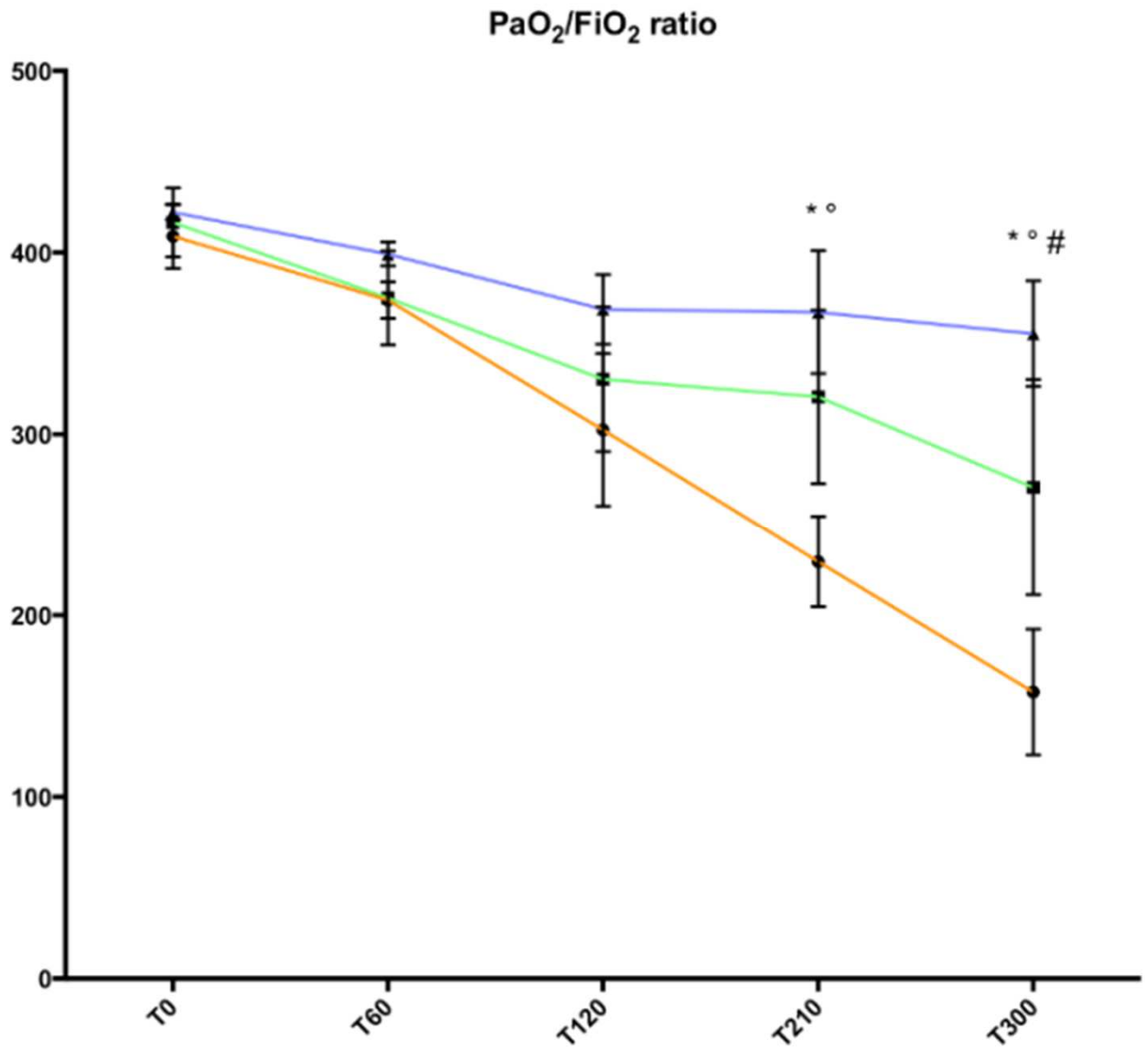
A-VBG, lactate and glucose levels + urine output at T0, T60, T120, T210 and T300



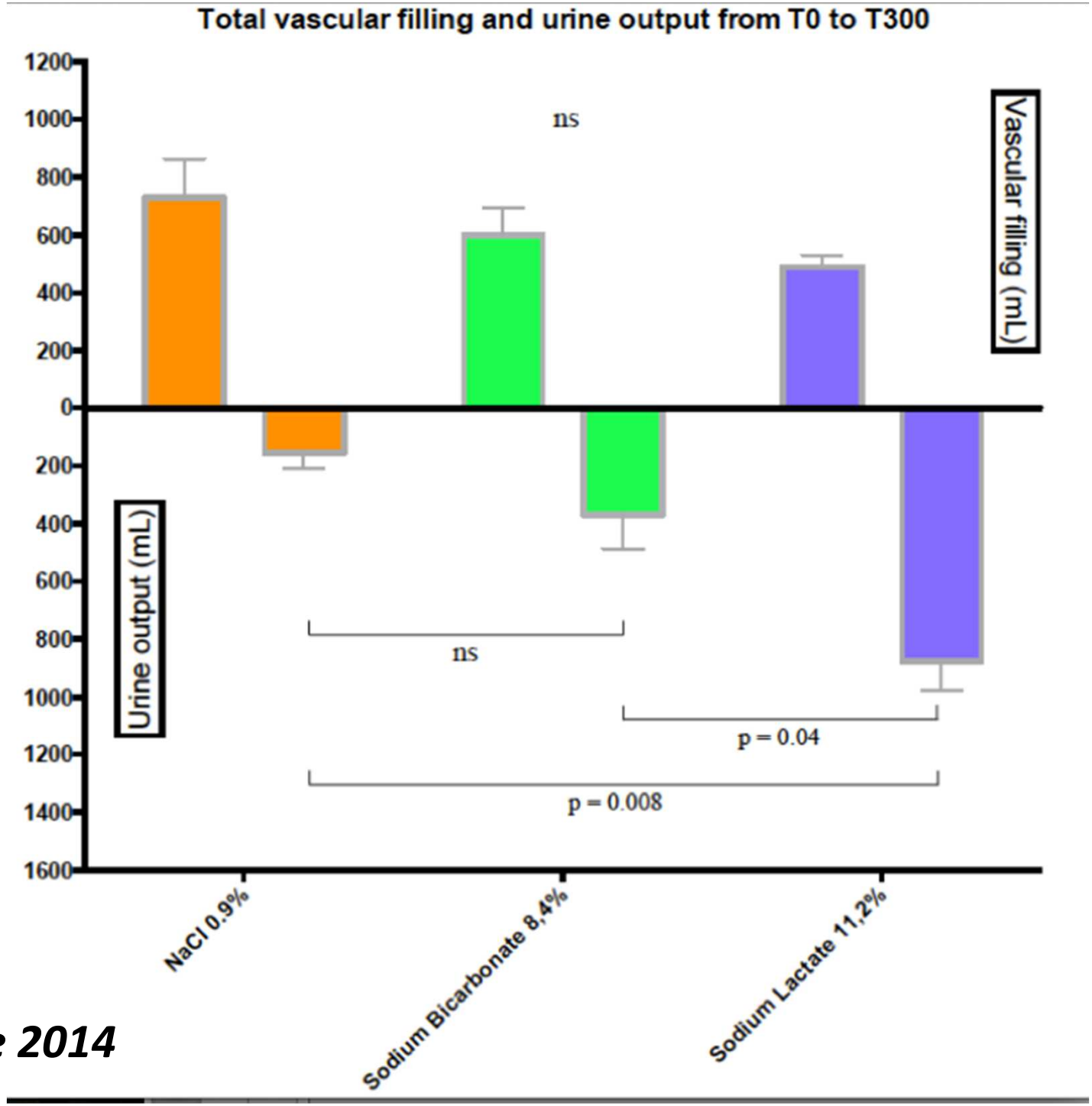
Duburcq, Crit Care 2014



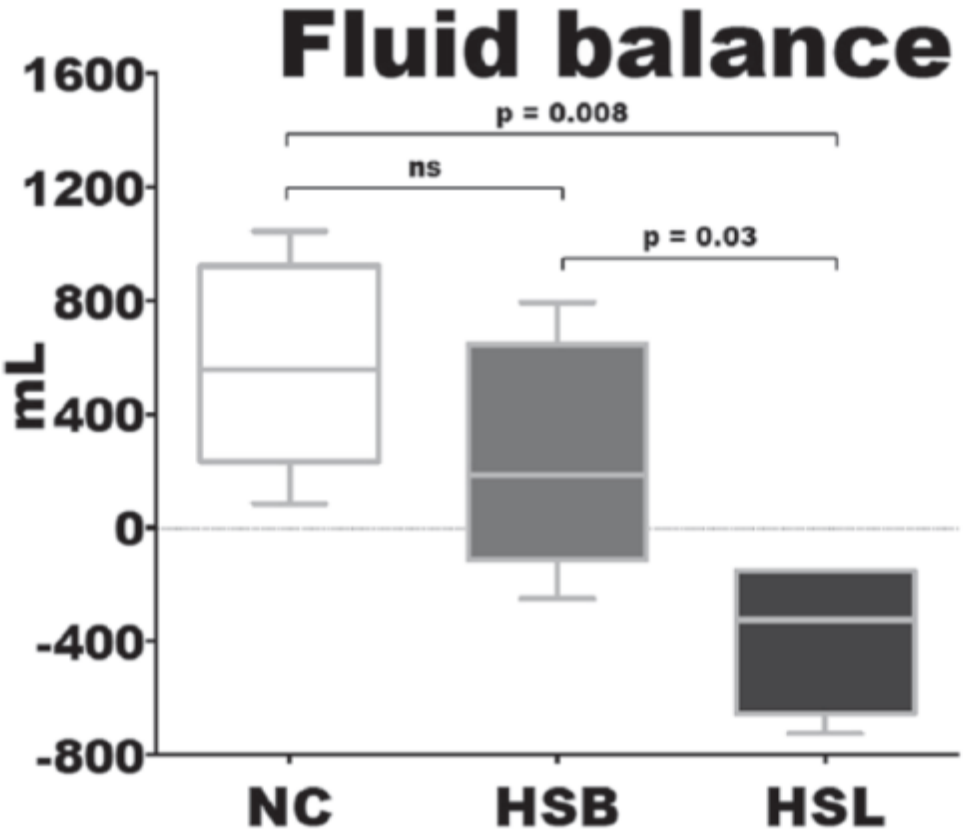
Duburcq, Crit Care 2014



Duburcq, Crit Care 2014



Duburcq, Crit Care 2014



Duburcq, Crit Care 2014

Somasetia et al. Critical Care 2014, 18:466
http://ccforum.com/content/18/5/466

CRITICAL CARE

RESEARCH Open Access

Early resuscitation of dengue shock syndrome in children with hyperosmolar sodium-lactate: a randomized single-blind clinical trial of efficacy and safety

Dadang H Somasetia[1], Tatty E Setiati[2*], Azhali M Sjahrodji[1], Ponpon S Idjradinata[1], Djatnika Setiabudi[1], Hubert Roth[3], Carole Ichai[4], Eric Fontaine[3*] and Xavier M Leverve[3*]

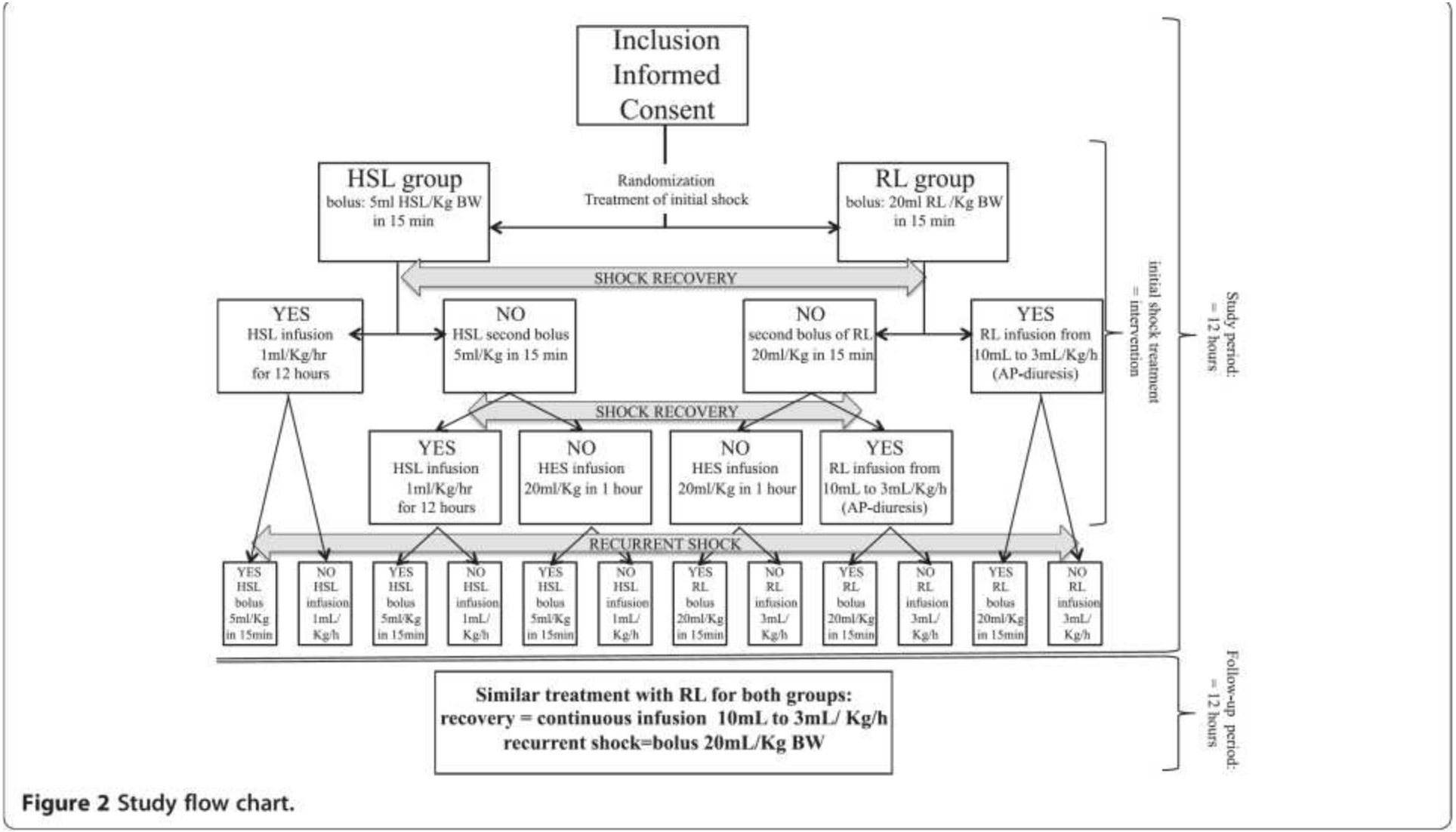


Figure 2 Study flow chart.

Somasetia Crit Care 2014

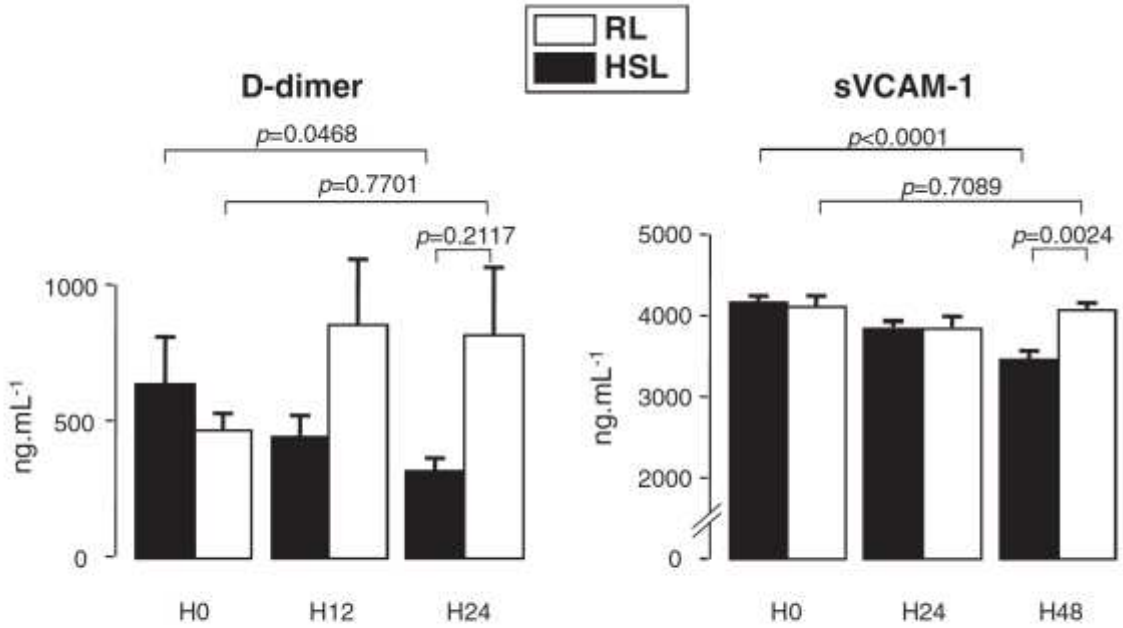


Figure 5 Effect of treatments on homeostasis (D-dimer) and endothelial cell dysfunction (sVCAM-1). Open bars, RL; solid bars, HSL. Comparisons were performed by using Wilcoxon tests for paired data (effect of time) and Mann–Whitney tests for unpaired data (difference between the two groups).

Somasetia Crit Care 2014

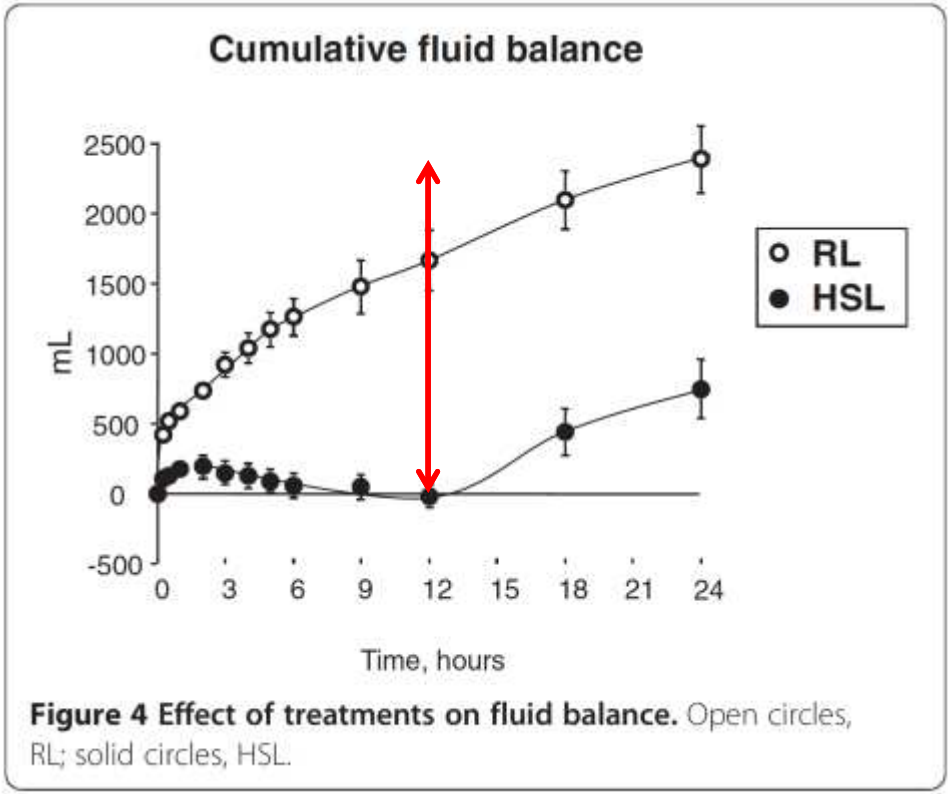


Figure 4 Effect of treatments on fluid balance. Open circles, RL; solid circles, HSL.

Somasetia Crit Care 2014

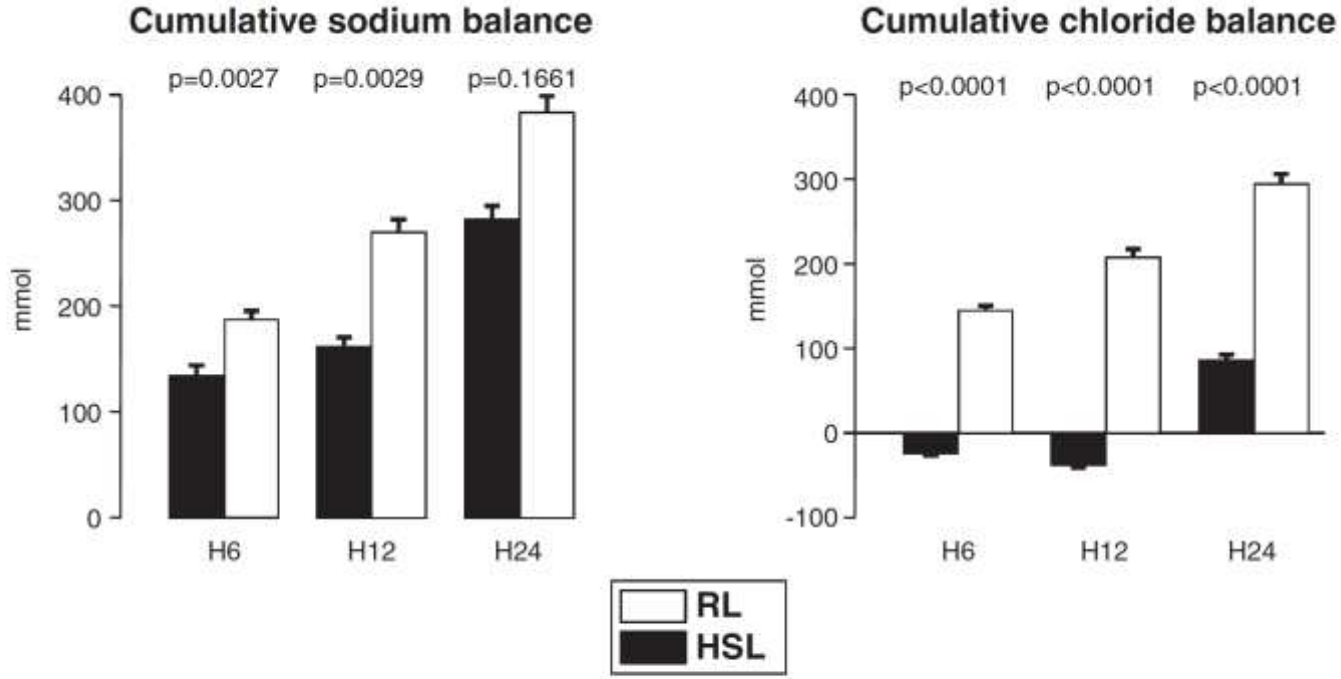


Figure 6 Effect of treatments on sodium and chloride balance. Open bars, RL; solid bars, HSL. Comparisons were performed by using Mann–Whitney tests.

Outcome			
Recovery	22	20	0.70
Forced discharge	2	2	>0.99
Death	1	3	0.60

Somasetia Crit Care 2014

American Journal of Epidemiology and Infectious Disease, 2015, Vol. 3, No. 4, 76-79
Available online at http://pubs.sciepub.com/ajeid/3/4/1

DOI:10.12691/ajeid-3-4-1

Impact of Hyperosmolar Sodium-Lactate Resuscitation on Lactate Clearance in Pediatric Severe Sepsis

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Received July 20, 2015; Revised August 20, 2015; Accepted September 07, 2015

Table 2. Impact of Fluid Resuscitation on Lactate Clearance

Parameter			p value
	HSL Group (n=17)	NS Group (n=17)	
1 Hour Lactate Clearance (%)	20.5 (-228.5–80.3)	-15.5 (-185.7–44.4)	<0.05*
6 Hour Lactate Clearance (%)	33.3 (-71.4–90.9)	-16.7 (-1350–62.5)	<0.01*

Note : *) Mann-Whitney test, decrement was calculated based on the formula :
100*(value before – value after)/value before.

5ml/kg

Balance hydrique

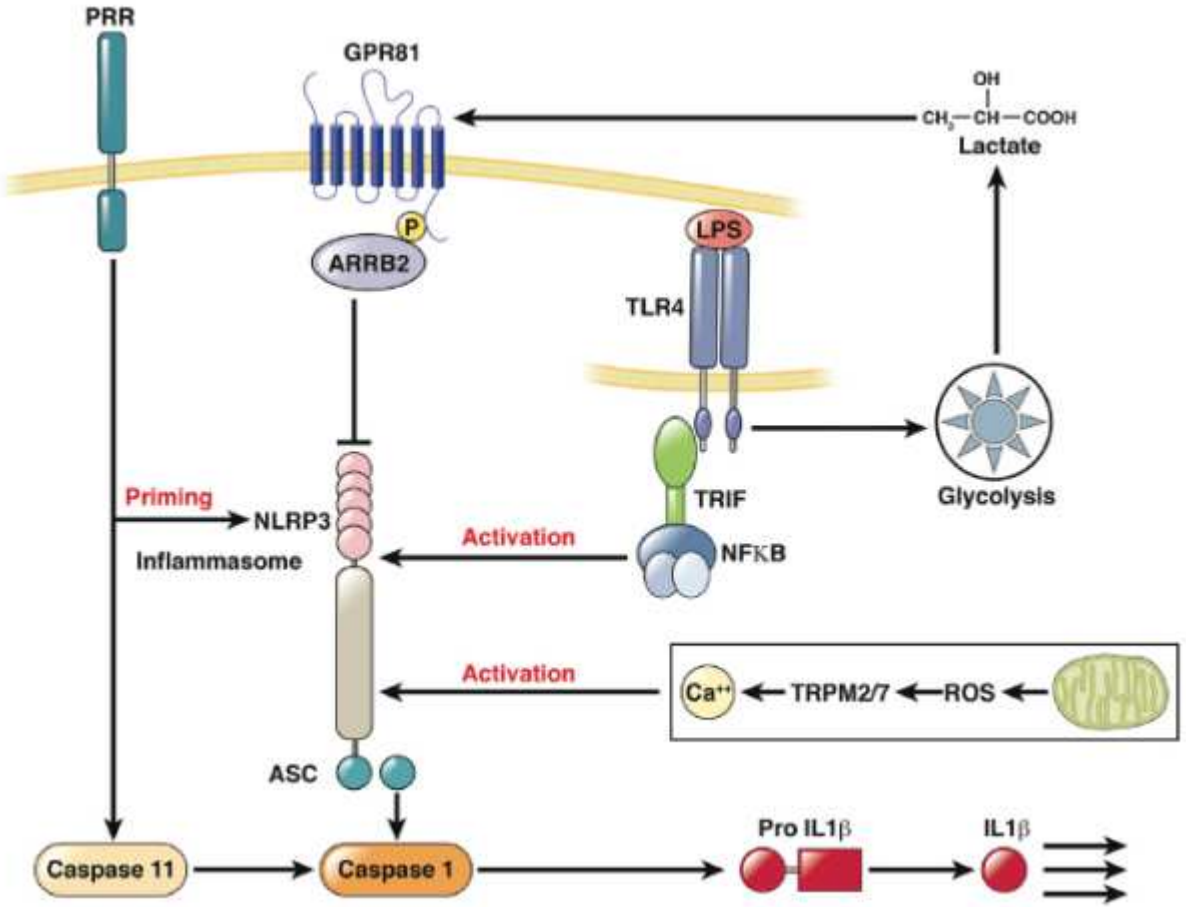
- Effet calorique
- Effet sur le chlore
- Effet antiinflammatoire (endothélium…)

Gastroenterology 2014;146:1763–1774

BASIC & TRANSLATIONAL—LIVER & PANCREAS

Lactate Reduces Liver and Pancreatic Injury in Toll-Like Receptor– and Inflammasome-Mediated Inflammation via GPR81-Mediated Suppression of Innate Immunity

Rafaz Hoque,[1] Ahmad Farooq,[1] Ayaz Ghani,[1] Fred Gorelick,[1,2] and Wajahat Zafar Mehal[1,2]



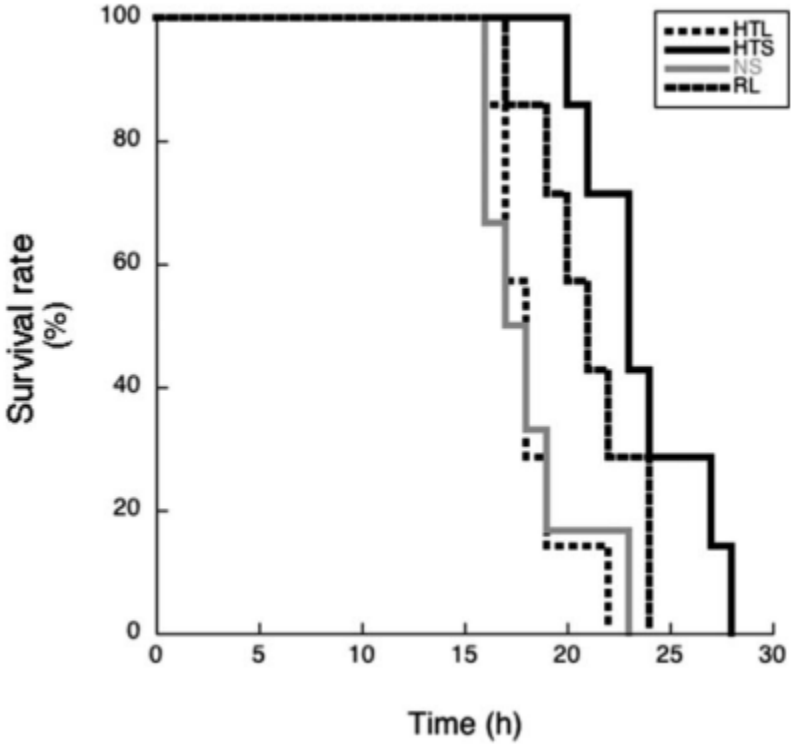
SHOCK, Vol. 46, No. 6, pp. 663–671, 2016

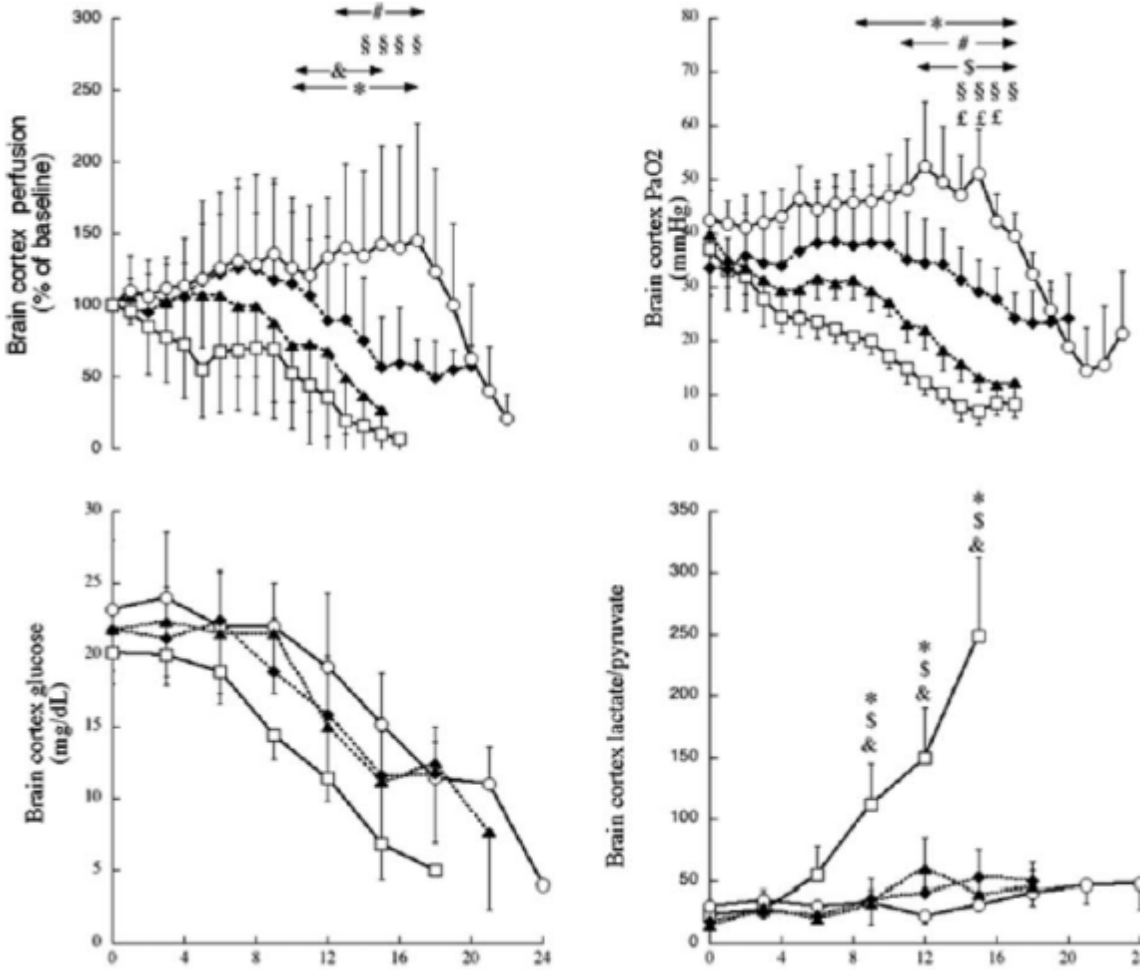
THE HARMFUL EFFECTS OF HYPERTONIC SODIUM LACTATE ADMINISTRATION IN HYPERDYNAMIC SEPTIC SHOCK

Fuhong Su,* Keliang Xie,*† Xinrong He,*‡ Diego Orbegozo,* Koji Hosokawa,* Emiel Hendrik Post,* Katia Donadello,* Fabio Silvio Taccone,* Jacques Creteur,* and Jean-Louis Vincent*

**Department of Intensive Care, Erasme University Hospital, Université Libre de Bruxelles, Brussels, Belgium; †Department of Anesthesiology, Tianjin Institute of Anesthesiology, Tianjin Medical University General Hospital, Tianjin, China; and ‡Department of Intensive Care, Sun Yat-sen University Cancer Center, Guangzhou, China*

Received 18 Apr 2016; first review completed 9 May 2016; accepted in final form 27 Jun 2016





Fuhong Su Shock 2016

Fluids infused

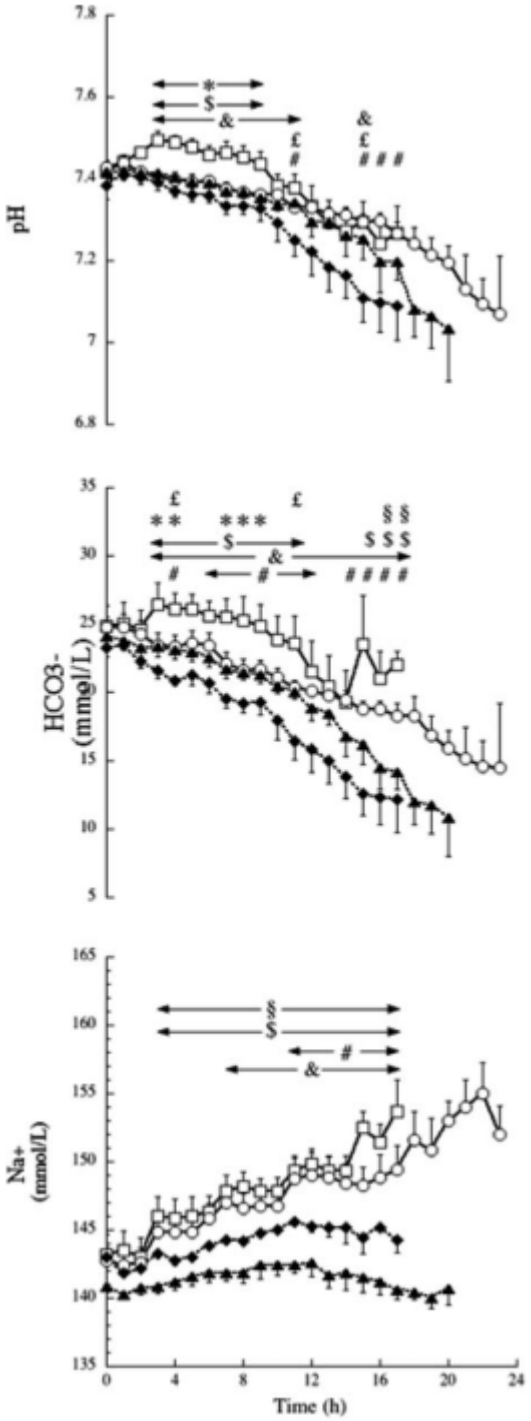
A total of 200 mEq to 253 mEq of sodium was infused in the different groups; 200 mEq of lactate was administered in the HTL group and 44 mEq in the RL group (Table 1). The total fluid intakes in the HTL, HTS, RL, and NS groups were 5.1 ± 0.1 L, 7.1 ± 0.8 L, 7.5 ± 0.3 L, and 8.4 ± 0.7 L, respectively.

Modèle hypovolémique ?

around the abdomen. Throughout the experiment, a 1:1 mixture of RL (Hartman, Baxter International, Deerfield, Ill) and 6% hydroxyethyl starch (HES; Voluven, Fresenius Kabi, Bad Homburg, Germany) solutions was infused to maintain the pulmonary artery occlusion pressure (PAOP) at baseline levels.

Cible pragmatique ?

Fuhong Su Shock 2016



Une des hypothèses des auteurs est l'effet délétère de l'alcalinisation

Mais ils n'ont pas de groupe contrôle de l'alcalinisation…

Fuhong Su Shock 2016

Duburcq et al. Critical Care (2017) 21:113
DOI 10.1186/s13054-017-1694-1

Critical Care

RESEARCH Open Access

Comparison of fluid balance and hemodynamic and metabolic effects of sodium lactate versus sodium bicarbonate versus 0.9% NaCl in porcine endotoxic shock: a randomized, open-label, controlled study

Thibault Duburcq[1*], Arthur Durand[1,6], Anne-Frédérique Dessein[3], Joseph Vamecq[3], Jean-Claude Vienne[3], Dries Dobbelaere[4], Karine Mention[4], Claire Douillard[4], Patrice Maboudou[3], Valery Gmyr[2], François Pattou[2], Mercé Jourdain[1,2], Fabienne Tamion[5], Julien Poissy[1], Daniel Mathieu[1] and Raphaël Favory[1,6]

(3.61 kcal/g). Conversely to our previous study [19], the NC and SB groups received 39 g glucose (3.75 kcal/g) as 780 mL 5% glucose solution (Baxter SAS, Guyancourt, France) from T30 to T300 in order to infuse an equivalent energy supply as in the SL group. Finally, in order to maintain the same fluid intake in the three groups, the SL group received 780 mL sterile water for injection (Baxter SAS, Guyancourt, France) in place of the 5% glucose solution from T30 to T300.

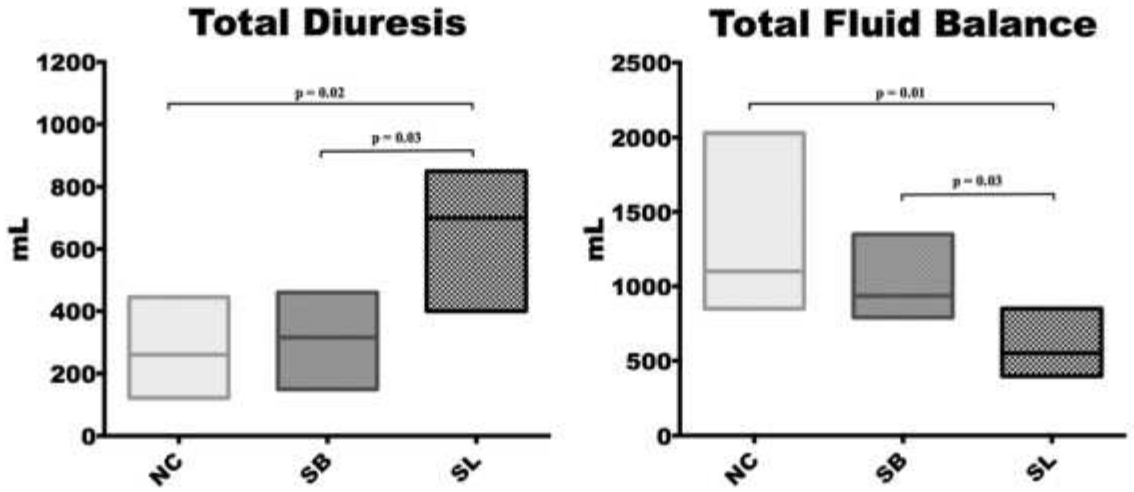


Fig. 1 Total diuresis and total fluid balance. Results are expressed as median with interquartile ranges. *NC* isotonic control group receiving NaCl ($n = 5$), *SB* hypertonic control group receiving sodium bicarbonate ($n = 5$), *SL* treatment group receiving hypertonic sodium lactate ($n = 5$)

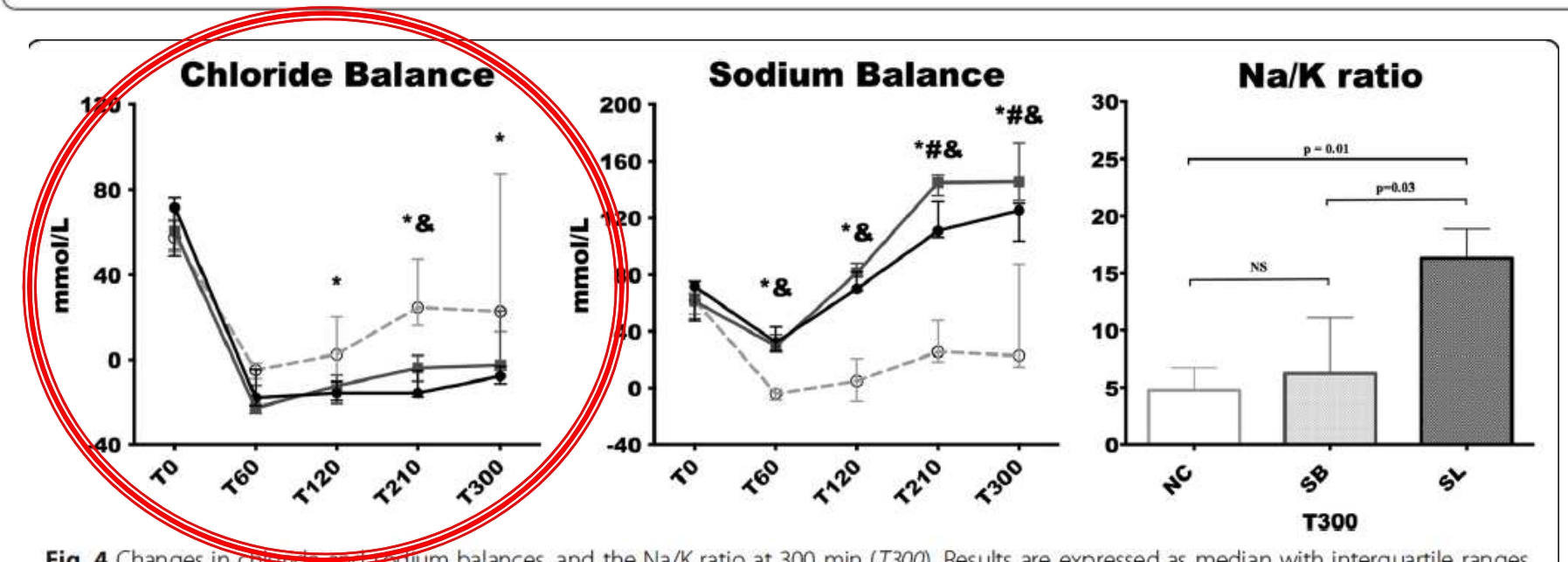


Fig. 4 Changes in chloride and sodium balances, and the Na/K ratio at 300 min (*T300*). Results are expressed as median with interquartile ranges. *$p < 0.05$, NC versus SL; #$p < 0.05$, SB versus SL; &$p < 0.05$, NC versus SB. *Open circles and dotted line*: *NC* isotonic control group receiving NaCl ($n = 5$); *squares and grey line*: *SB* hypertonic control group receiving sodium bicarbonate ($n = 5$); *closed circles and black line*: *SL* treatment group receiving hypertonic sodium lactate ($n = 5$)

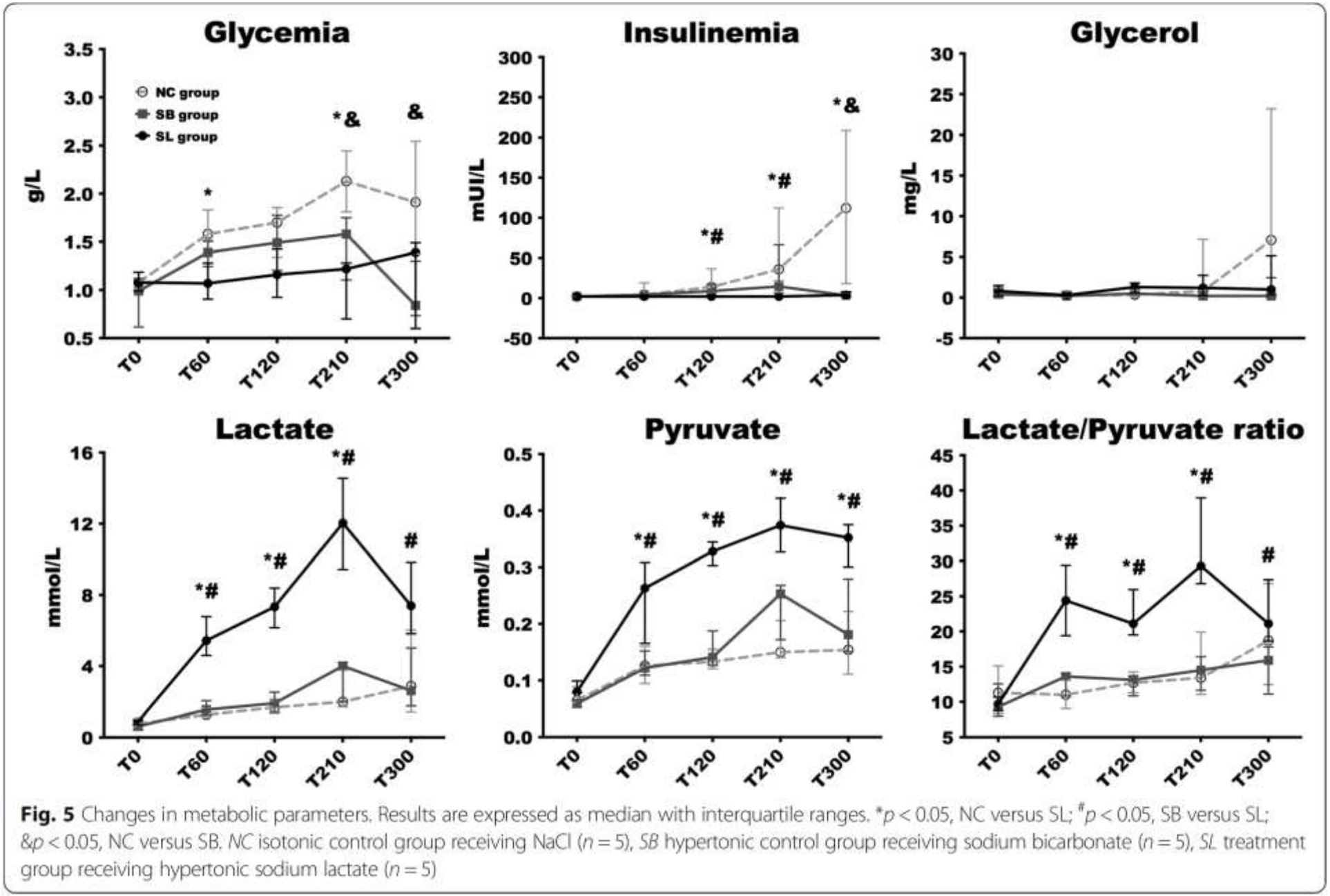


Fig. 5 Changes in metabolic parameters. Results are expressed as median with interquartile ranges. *$p < 0.05$, NC versus SL; #$p < 0.05$, SB versus SL; &$p < 0.05$, NC versus SB. *NC* isotonic control group receiving NaCl ($n = 5$), *SB* hypertonic control group receiving sodium bicarbonate ($n = 5$), *SL* treatment group receiving hypertonic sodium lactate ($n = 5$)

On produit bien a priori du pyruvate !

Le groupe bicar est un contrôle *effectif* d'apport calorique

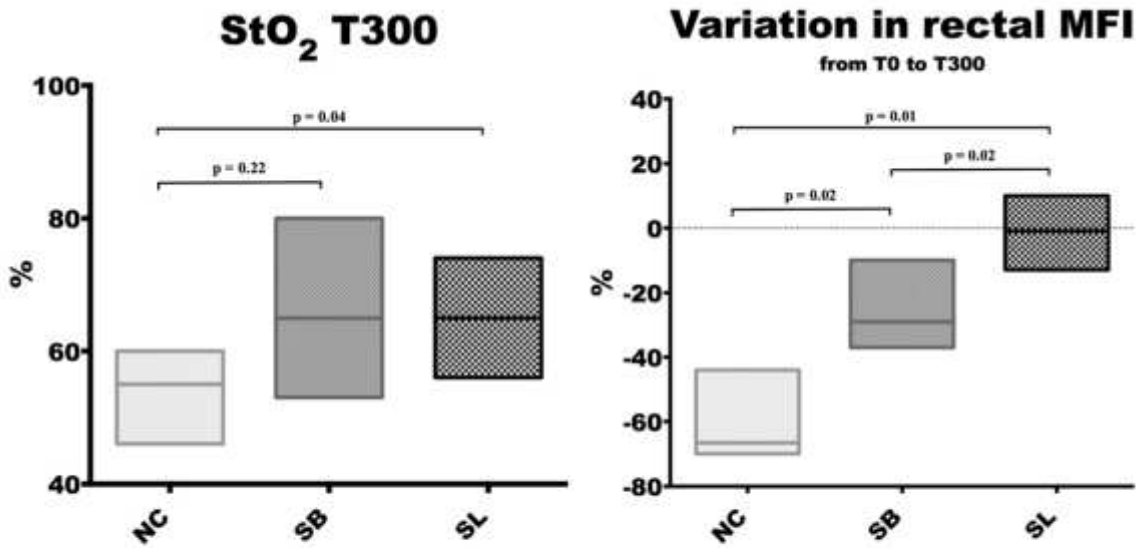


Fig. 3 Changes in basal tissue oxygen saturation (StO_2) and variation in rectal microvascular flow index (*MFI*) score between 0 min (*T0*) and 300 min (*T300*). Results are expressed as median with interquartile ranges. *NC* isotonic control group receiving NaCl ($n = 5$), *SB* hypertonic control group receiving sodium bicarbonate ($n = 5$), *SL* treatment group receiving hypertonic sodium lactate ($n = 5$)

Amélioration microcirculation rectale

PERSPECTIVES

ULIS-1: Utility of Lactate Infusion in Sepsis – 1: 90 patients (Dr Thibault Duburcq)

- Groupe posologie forte : perfusion IV de 5 mL/kg sur 60 min puis perfusion continue à la posologie de 0,5 mL/kg/h de H1 à H24.
- Groupe posologie faible : perfusion IV de 3 mL/kg sur 60 min puis perfusion continue à la posologie de 0,3 mL/kg/h de H1 à H24.
- Groupe cristalloide
- CJP: balance hydrique à J7
- Surveillance Na/pH

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Phase Focus	Salvage	Optimization	Stabilization	De-escalation
	Obtain a minimal acceptable blood pressure	Provide adequate oxygen availability	Provide organ support	Wean from vasoactive agents
	Perform lifesaving measures	Optimize cardiac output, SvO_2, lactate	Minimize complications	Achieve a negative fluid balance

The NEW ENGLAND JOURNAL of MEDICINE

REVIEW ARTICLE

CRITICAL CARE MEDICINE

Simon R. Finfer, M.D., and Jean-Louis Vincent, M.D., Ph.D., *Editors*

Circulatory Shock

Jean-Louis Vincent, M.D., Ph.D., and Daniel De Backer, M.D., Ph.D.

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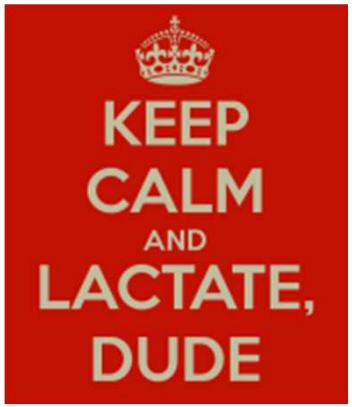

Le lactate de Na

- Balance hydrique moins positive
- Effet métabolique en situation de crise énergétique
- Effet microcirculatoire
- Effet anti-inflammatoire
- Étude clinique à venir..
- Etude au labo (rat LPS)
  - Fabienne Tamion
  - Déborah Boyer
  - Emmanuel Besnier
  - Olivier Lesur..