

Place du serum salé hypertonique en réanimation pédiatrique

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Un peu d'histoire



The question now arises: Why did 770 out of 800 men escape beri-beri when all had been subsisting on the same deficient food for months past, when, in fact, all were subjected to the same degree of vitamin insufficiency? And why did 101 out of 105 pigeons escape beri-beri when all were fed alike? Presumably because there was in operation in the 30 men who developed it some factor in addition to the vitamin insufficiency which was absent, or failed to affect in the same degree, the 770 who did not develop it. Similarly with the pigeons. If we look at the matter from the point of view of the heart condition alone we are at once impressed by the fact that some additional factor must have been in operation in beri-beri birds which exercised a specific effect on the heart, for vitamin deficiency alone does not cause cardiac enlargement in pigeons, but, on the contrary, cardiac atrophy. Surmise as to the nature of this factor is permissible, since if it is to be found we must have some line of thought along which to work. It is possible that the subjects of beri-beri may have been carriers of some organism whose products exercised this effect on the heart muscle, just as certain of my pigeons were carriers of an invisible virus which exercised a specific effect on epithelial tissue, and the fact that beri-beri arose only in birds obtained from a certain place is presumptive evidence in favour of such a view; or the gastro-intestinal flora of the sufferers from beri-beri may have been of such a nature as caused the evolution of a poison which exercised this specific effect on the heart; or it may be that certain birds were of such a constitution that the disturbed metabolism resulting from the vitamin insufficiency caused a poison to be evolved in those who suffered from beri-beri which was not evolved, or not to the same extent, in those who escaped. Or was it merely a question of individual idiosyncrasy, and, if so, what directly, in their causation. If there be this variety of beri-beri-like maladies in pigeons, whose staple diet is rice, there is probably a similar variety of beri-beri-like maladies in man—a surmise which proved to be correct in Mesopotamia during the late war. I am not at all convinced from the literature that when we argue as to the causation of "beri-beri" we are always arguing about the same condition. And so much has this been impressed upon me of late that I look for further progress along clinical and pathological lines which will separate these beri-beri-like states into entities recognizable as such by the practising physician. Only then will the causal factors in their production be capable of accurate determination.

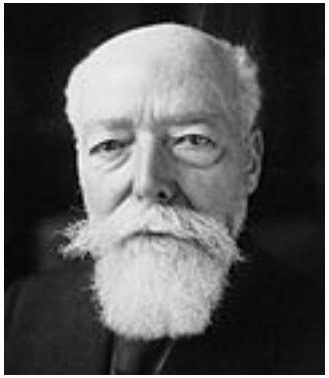
THE USE OF HYPERTONIC SALINE SOLUTIONS IN INCREASED INTRACRANIAL TENSION.*

BY

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IN 1919 Weed and McKibben[1] showed that the intravenous injection of hypertonic saline solutions in cats markedly lowered the cerebro-spinal fluid pressure, as determined by a water manometer connected with the subarachnoid space, whilst hypotonic solutions produced an opposite effect. It was shown later by Foley and Putman[2] that oral or rectal administration of hypertonic saline solutions produced exactly similar experimental results. Since that time a few papers have appeared in which are recorded the application of these experimental results to man. The value and possi-






Un peu d'histoire



J neurosurg 1963

Dehydration and Rehydration of the Brain with Hypertonic Urea and Mannitol*

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The application, by Javid and co-workers[9–11,27] of the osmotic effects of intravenous infusions of urea to problems of intracranial exposure has gained wide acceptance. More recently, hypertonic mannitol has found similar usage.[22,24,31,32] This work was directed to an experimental analysis of the variability, amplitude and durableness of the osmotic relaxations with these two agents. It was carried out by following the cerebrospinal-fluid manometric patterns and the gradients of concentration in brain and plasma in (a), normal dogs and (b), dogs whose intracranial pressures were elevated following subarachnoid injections of blood.

Method

Cerebrospinal-fluid pressures were obtained from the supratentorial subarachnoid space of

designated as experimental animals. Initially, 10 control animals were studied for prolonged periods after these injections, without hypertonic agents.

The dosage of urea was 1.5 gm. per kg. of a 30 per cent solution. This was given slowly (with an infusion pump), in an attempt to parallel the usual or recommended clinical administration.[9] Since the dose was proportionate to weight, it was felt advisable to regulate the loading time to equal the usual clinical one. At a rate of 60 drops per min., a 70 kg. patient will require 117 min. for such an infusion. This delivery time was therefore used for all dogs save 1 who received the injection in 82 min. Infusions of urea were given to 49 animals; these were divided into 4 groups. The first 2 groups were used for prolonged recording of pressures in normal and experimental animals; the other 2 groups were used for determinations of urea in tissue. The intracranial pressures of 11 experimental dogs (Group A) were recorded for periods of 1 hr. after the induction of sustained intracranial hypertension





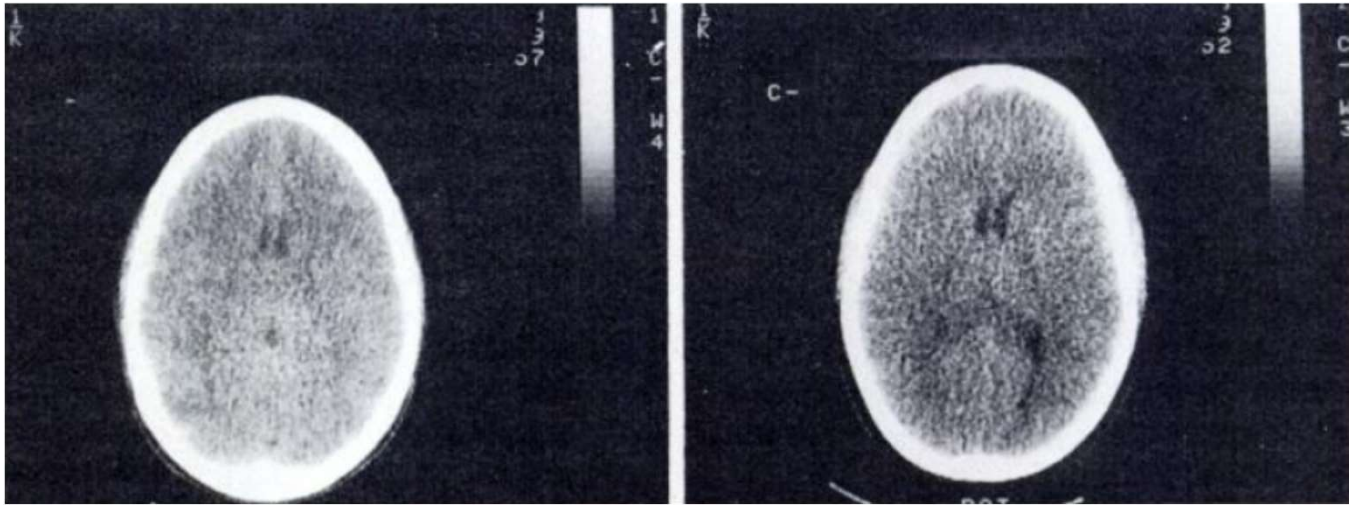


Cerebral Edema and Ophthalmoplegia Reversed by Mannitol in a New Case of Insulin-Dependent Diabetes Mellitus

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OFFICIAL JOURNALS OF THE AANS SINCE 1944

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CASE REPORTS AND TECHNICAL NOTE

Treatment of resistant intracranial hypertension with hypertonic saline
Report of two cases

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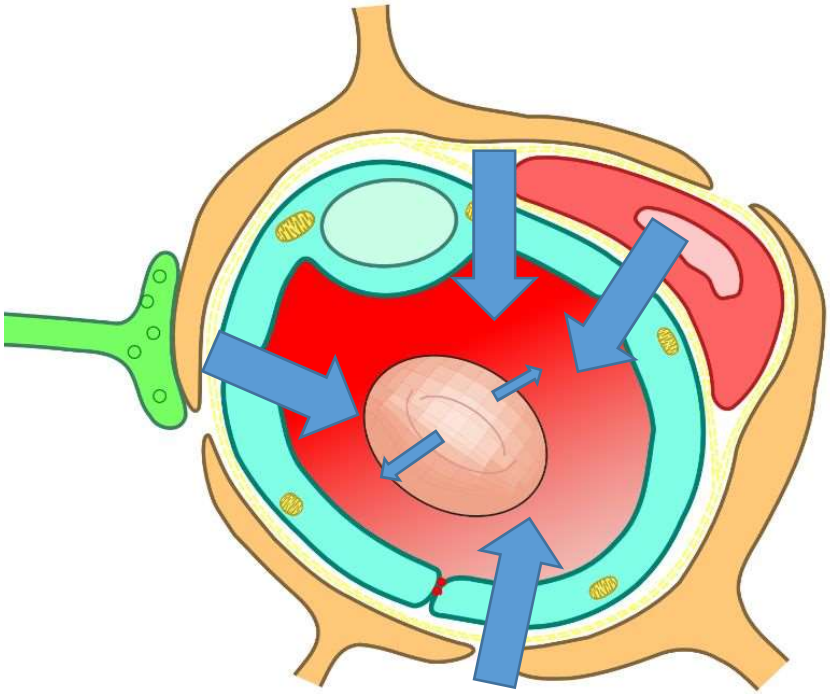
Abstract

✓ The authors describe two patients with traumatic cerebral edema and intracranial hypertension in whom the continued use of mannitol and furosemide resulted in a progressive lessening of the effect of these agents on the intracranial pressure (ICP) and caused prerenal failure. Intravenous administration of hypertonic saline (50 ml and 20 ml of a 5-mmol/ml saline solution over 10 minutes in Cases 1 and 2, respectively) produced a prolonged reduction in the ICP and improved renal function in both cases. It is suggested that if a reduction in ICP without diuresis is required in patients with traumatic cerebral edema, treatment with intravenous hypertonic saline should be considered.

Related Articles

By Keywords: hypertonic saline, intracranial pressure, head injury

Osmothérapie



Perfusion d'un agent osmotique

Création d'un gradient osmotique

Diminution des volumes interstitiel et intracellulaire

« Déshydratation »

Les solutés hyperosmolaires

	Concentration en Sodium (mmol/L)	Osmolalité (mosmol/kg)
Plasma humain	136-145	270-295
Ringer Lactate	130	275
Sérum salé 0,9%	154	302
Sérum salé 1,7%	291	582
Sérum salé 3%	513	1026
Sérum salé 7,5%	1283	2566
Sérum salé 7,2% / 6% HEA (200 / 6%) (Hyper-HES®)	1232	2464
Sérum salé 7,5% / 6% dextran 70 (Rescue-Flow®)	1283	2566
Sérum salé 10%	1712	3424
Sérum salé 20%	3424	6844
Sérum salé 23%	4004	8008
Sérum salé 29%	5000	10000
Mannitol 10%	0	549
Mannitol 20%	0	1098

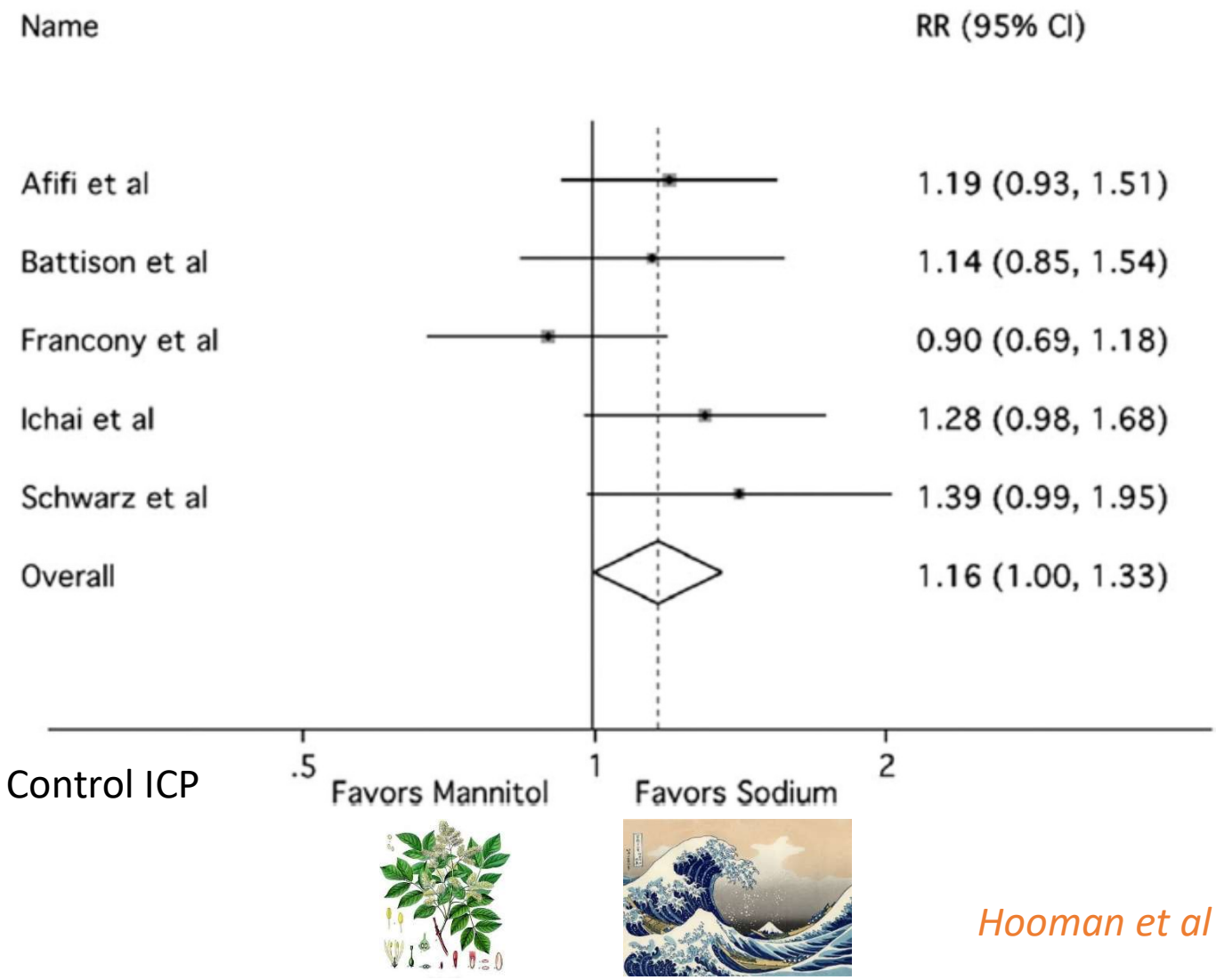
Osmothérapie





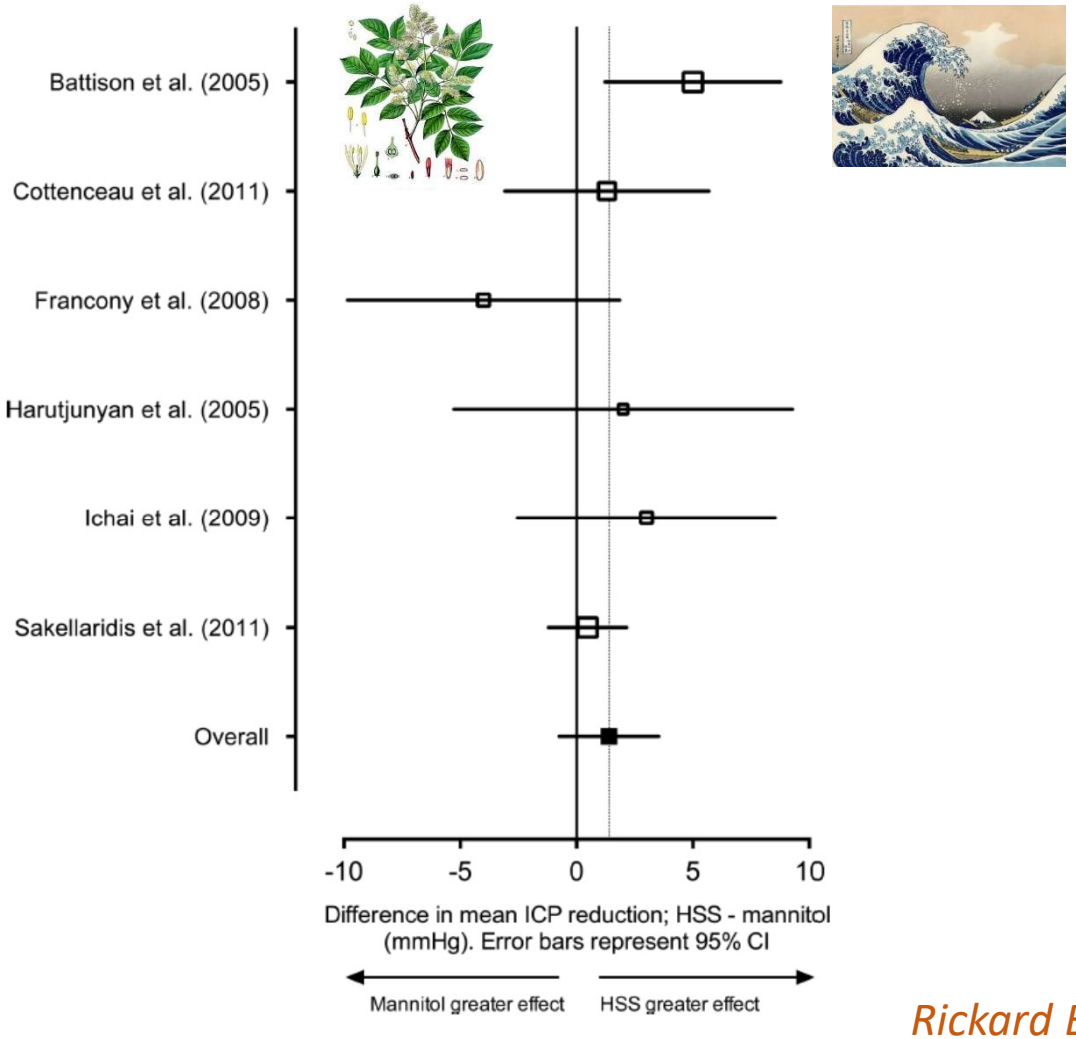
	Mannitol	Sérum salé hypertonique
Composition	Sucre alcoolique	Chlorure de sodium
Posologie	0,25 à 1 g/Kg	**0,1 à 0,3 g/kg**
Augmentation de la volémie (30 min après injection)	111%	3 à 4 fois le volume administré
Effet rhéologique	Oui	Oui
Effet diurétique	+++ Diurèse osmotique d'environ 4 à 5 fois le volume perfusé	+ Diurèse via sécrétion de facteur natriurétique)
Effet hémodynamique	↓ pression artérielle moyenne si bolus rapide Hypovolémie secondaire à compenser	↓ pression artérielle moyenne si bolus rapide ↑ Volémie
Effet cérébral	↓ Pression intracrânienne	↓ Pression intracrânienne
Effet rebond	Possible	Possible en cas d'administration prolongée
Effets secondaires principaux	Hypo/hyperkaliémie Insuffisance rénale aiguë	Surcharge vasculaire Hypokaliémie

Osmothérapie HTIC



Hooman et al CCM 2011

Osmothérapie Trauma cranien



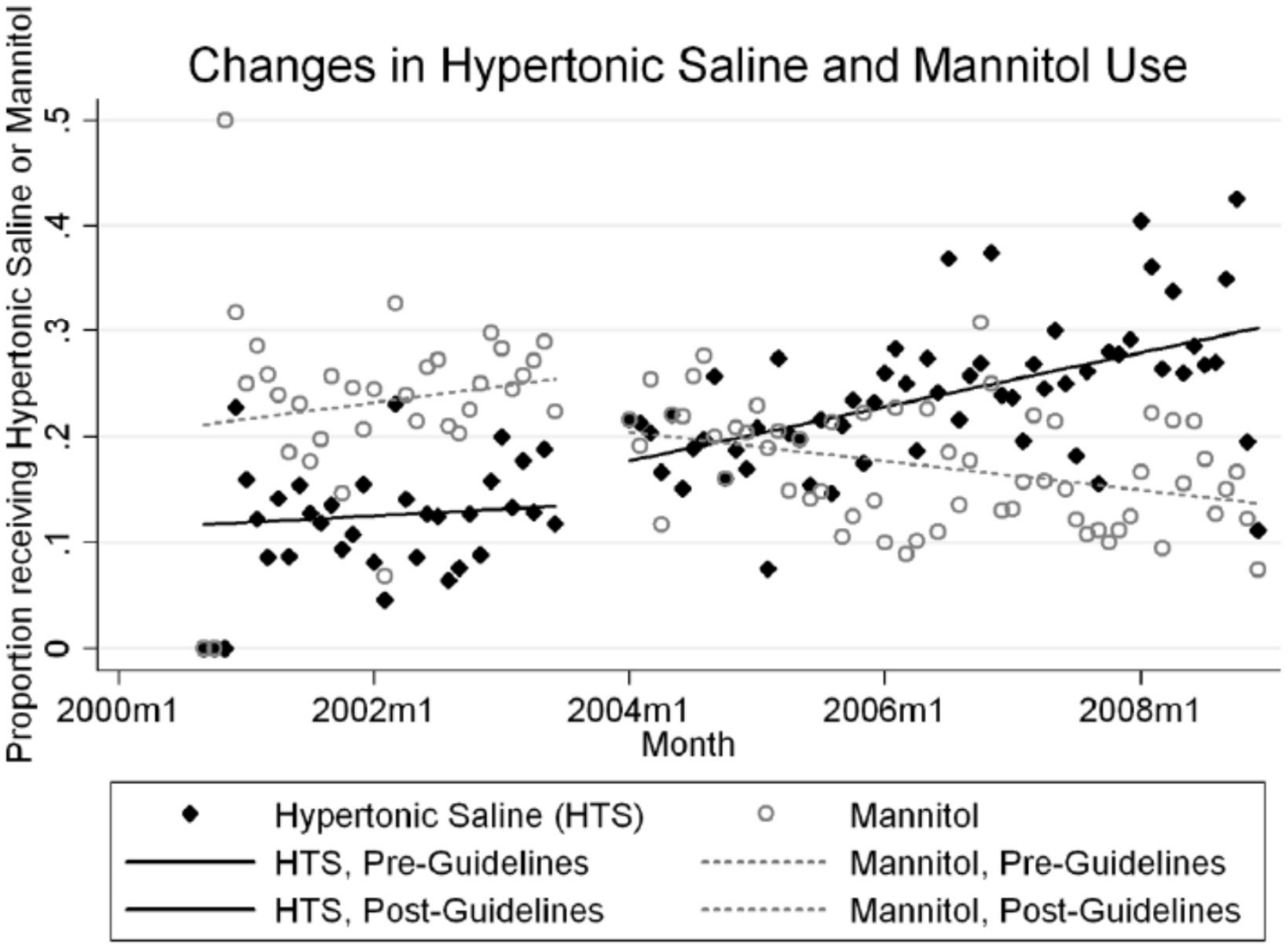
Rickard Emerg med 2014

Recommandations - 2003

Guidelines for the Acute Medical Management of Severe Traumatic Brain Injury in Infants, Children, and Adolescents

Le mannitol est l'agent osmotique de choix mais le serum salé peut être considéré

Adelson PCCM 2003

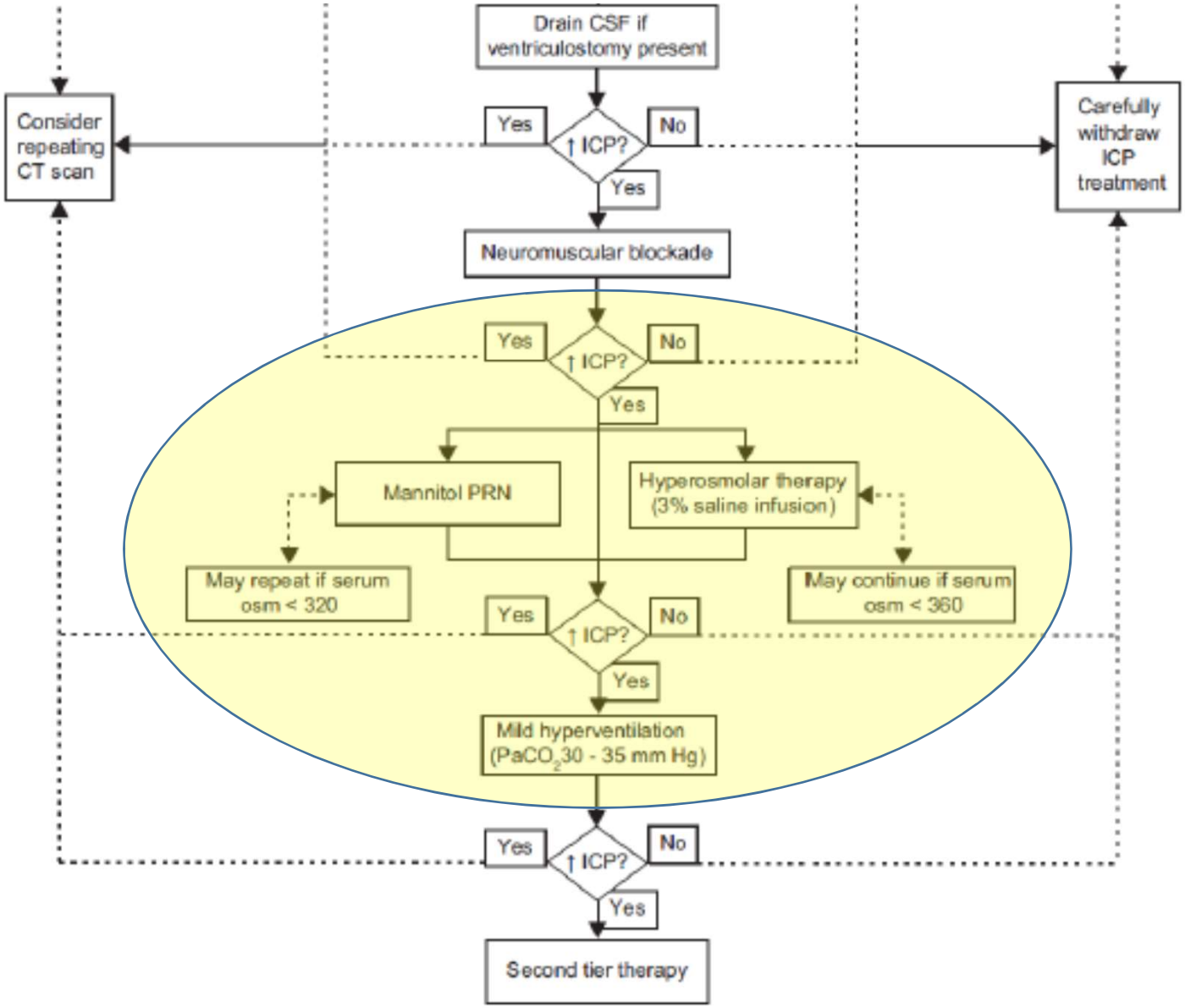

Changes in Hypertonic Saline and Mannitol Use
Proportion receiving Hypertonic Saline or Mannitol
0
.1
.2
.3
.4
.5
2000m1
2002m1
2004m1
2006m1
2008m1
Month
Hypertonic Saline (HTS)
Mannitol
HTS, Pre-Guidelines
Mannitol, Pre-Guidelines
HTS, Post-Guidelines
Mannitol, Post-Guidelines

Recommandations - 2012

- **Guidelines for the Acute Medical Management of Severe Traumatic Brain Injury in Infants, Children, and Adolescents-Second Edition**

  - Pas de recommandation pour le mannitol: absence de travaux pédiatriques
  - **Utilisation de serum salé 3% (niveau de preuve intermédiaire)**
  - Pas de recommandation pour concentration > 3%

Kochanek 2012 PCCM



Bell & Kochanek 2012

SSH 23,4%

0,5 ml/kg (max 30ml)- 30 min

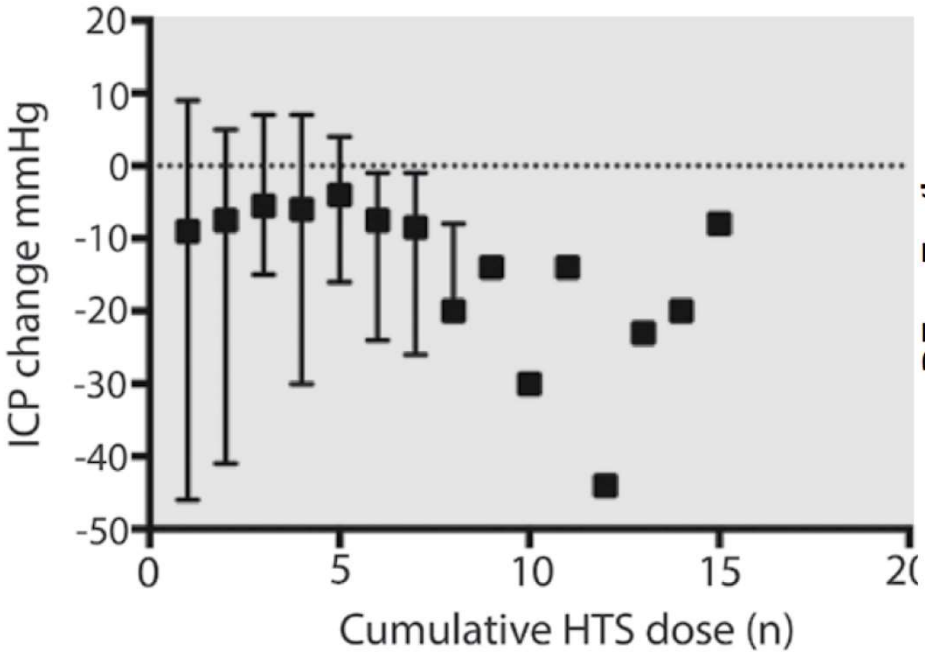


Figure 1: ICP change per dose. Mean change in intracranial pressure (mmHg) per cumulative dose of hypertonic saline. Bar represents range and solid dots represent the mean value. ICP=intracranial pressure, HTS=hypertonic saline solution.

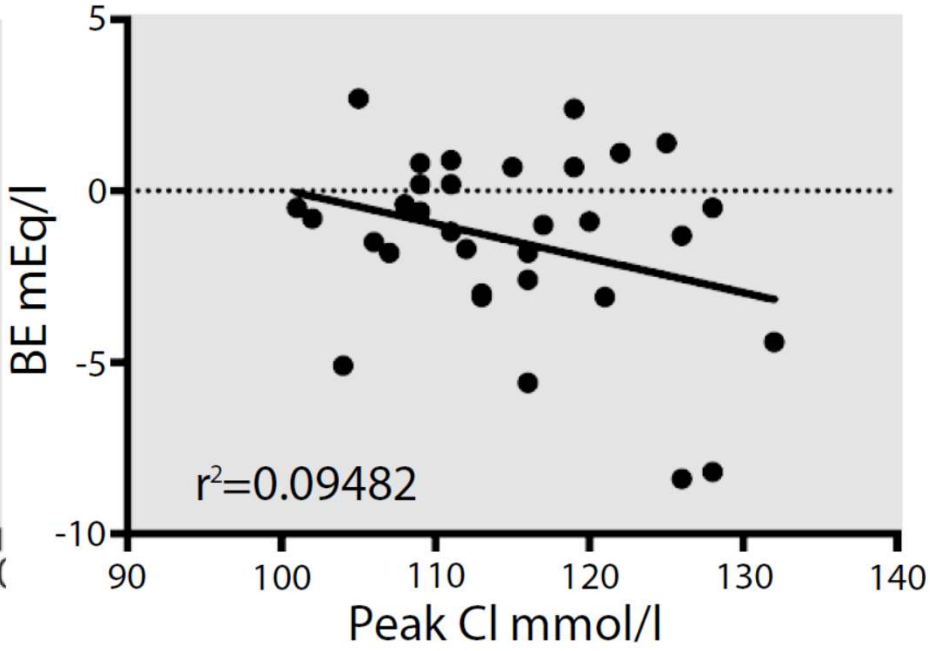


Figure 2: BE at peak serum chloride concentration. BE=base excess, Cl=chloride.

Piper & Harrigan Anaesth Intens. Care 2015

SSH 7,5% Echec du mannitol

1-5 ml/kg – 1H

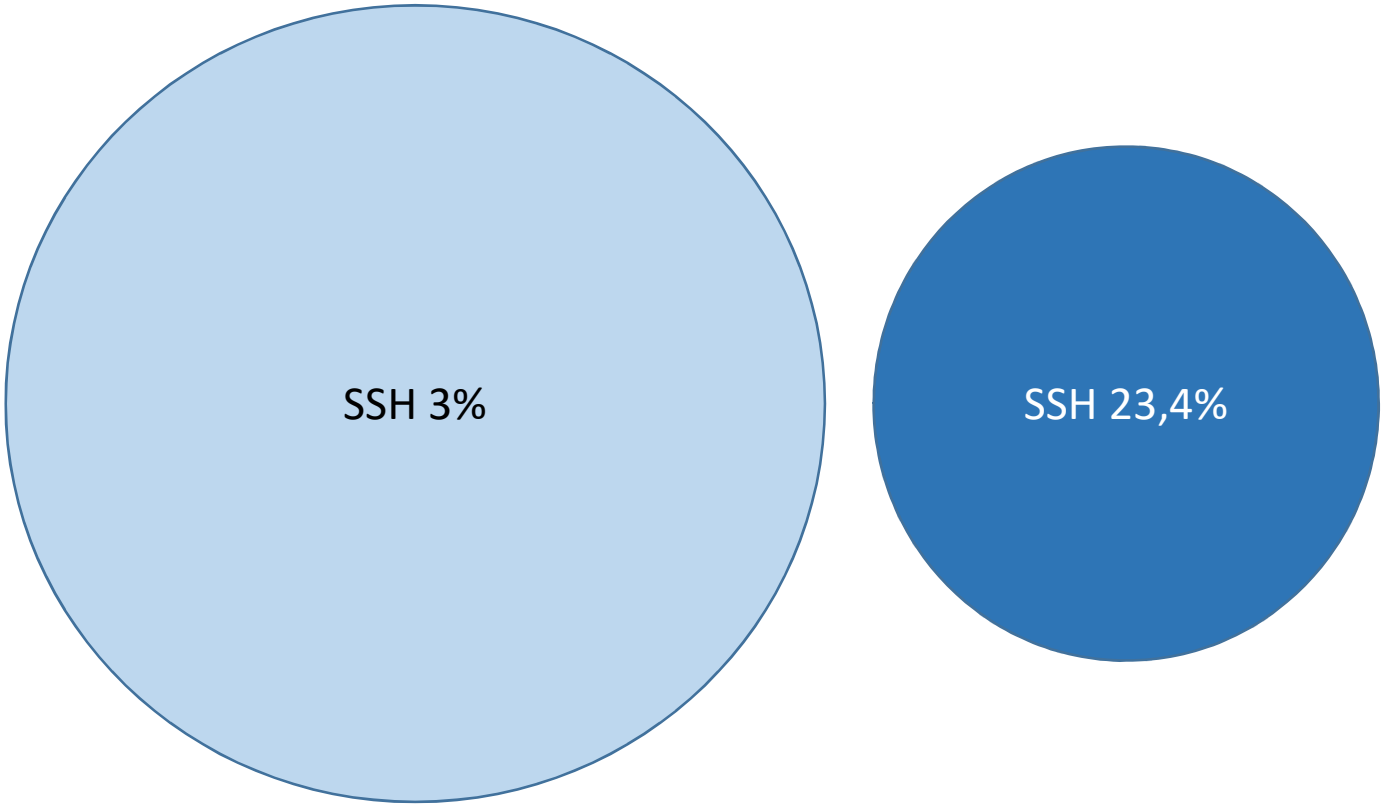
Table 3
Hypertonic saline 7.5% effect on ICP, CPP, and serum sodium (episodes = 136)

Variables	Open pressure	Before	After					
			30 minutes	*P*	60 min	*P*	120 min	*P*
ICP, mm Hg	23 (14.5-30)	29 (26-35)	18 (13-21)	<.001	17 (12-22)	<.001	18 (13-23)	<.001
ICP <20 mm Hg			100 (74)		97 (71)		87 (64)	
ICP difference, mm Hg			−12 (−18 to −6)		−13 (−21 to −6)		−11 (−20 to −6)	
CPP, mm Hg	44 (33-55)	50 (41-55)	57 (51-68)	<.001	58 (51-69)	<.001	58 (49-67)	<.001
CPP >40 mm Hg			128 (94)		124 (91)		126 (93)	
CPP difference, mm Hg			6.5 (0-18)		7.5 (0-20)		8 (0-18)	
Sodium, mmol/L		142 (141-152)					149 (143-158)	<.001
Sodium difference, mmol/L							5.5 (1-9)	

Continuous variables expressed as mean ± SD or median (IQR). Categorical variables expressed as n (%). *P* values of Wilcoxon signed rank test.

Rallis Journal of Critical Care 2017

Volume? Concentration?



Mannitol vs SSH en pédiatrie

TABLE I–*Causes of Cerebral Edema in various Groups*

Etiology	Group I (n = 22)	Group II(n = 25)	Group III(n = 20)
Meningoencephalitis	9 (40%)	10 (40%)	9 (45%)
Hypoxic ischemic encephalopathy	4 (18%)	6 (24%)	4 (20%)
Intracranial hemorrhage	4 (18%)	5 (20%)	3 (15%)
Meningitis	2 (9%)	2 (8%)	2 (10%)
Metabolic encephalopathy	3 (15%)	2 (8%)	2 (10%)

TABLE II–*Highest Serum Na Concentration, Osmolarity, Duration of Comatose State and Mortality Rate Between Groups*

Parameters	Group I (n = 22)	Group II (n=25)	Group III (n =20)		p
			A*	B*	
Osmolarity (mOsm/L)	321.5 ± 10.8 (305-40)	343.8 ± 20.4 (313-74)	325.0 ± 11.5 (305-37)	337.6 ± 19.8) (309-37)	0. 5
Serum-Na(mEq/L)		157.5 ± 8.8 (144-176)	137.5 ± 10.4 (130-150)	157.3 ± 9.3 (148-175)	0. 8
Duration of comatose state	123.0 ± 48.2 (18-196)	88.6 ± 42.5 (28-138)	87.5 ± 26.1 (24-144)	87.5 ± 26.1 (24-144)	0. 004
Mortality (%)	50	25	20	20	0. 003

Subgroup A shows patients who received hypertonic saline and mannitol together.
Subgroup B shows patients who received hypertonic saline after stopping mannitol.

Yildizdas, Indian Pediatr 2006

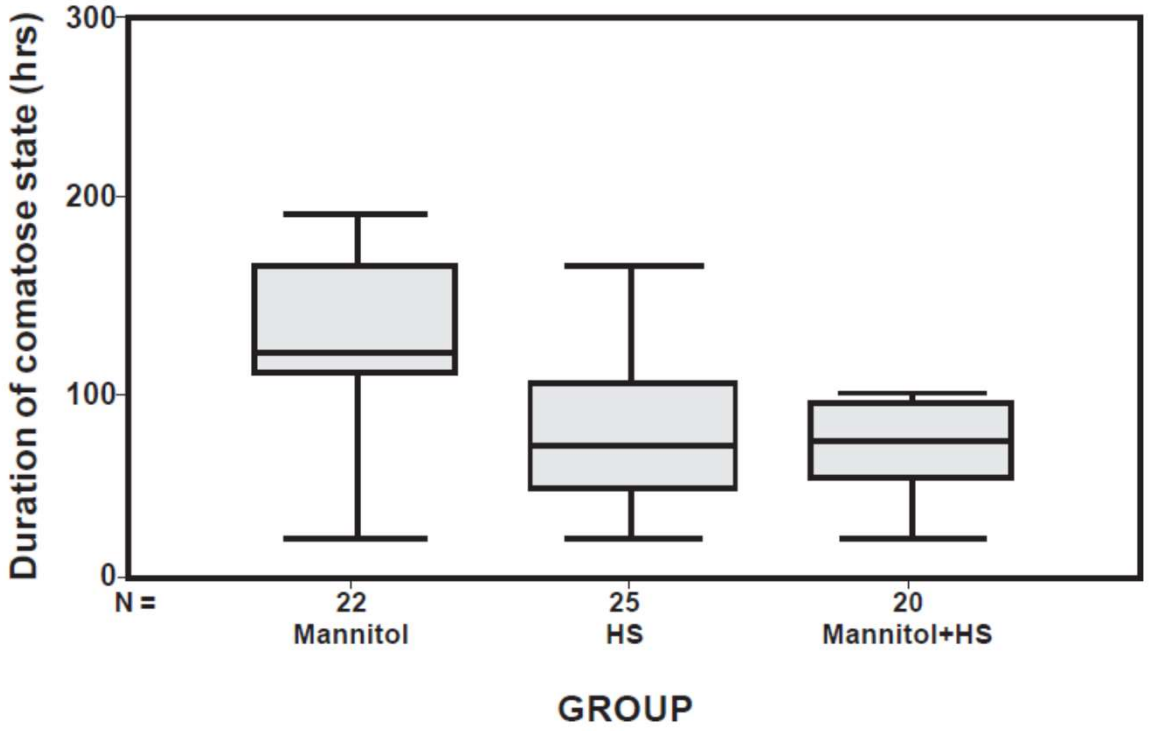


Fig.1. Duration of comatose state of groups.

Yildizdas, Indian Pediatr 2006

Table 2

Etiological distribution of trial group

Etiology	Group A	Group B	Group C
Meningoencephalitis	73 (74.48)	75 (75)	2 (100)
Neurocysticercosis (Anoxic Encephalopathy)	12 (12.24)	8 (8)	
Head trauma	6 (6.12)	8 (8)	
Space occupying lesion	5 (5.10)	5 (5)	
Global Infarction	2 (2.04)	4 (4)	
Total (n)%	98	100 (100)	2

Thus etiological distribution in group A&B were found to be comparable, Figures in the parentheses are in percentage

Journal of Pediatric Neurosciences

Upadhyay et al 2010

Table 3

Comparison of various parameters between group A & B

Parameter (X±SD)	Group A	Group B	Group C	't' value	'*P*' value	Inference
S. Osm (mosm/kg)	310±4.3 (285-319)	308±5.6 (288-322)	330±8.4 (324-336)	1.41	>0.05	Not Significant
S.Na (meq/l)	128±2.4 (123-130)	136±6.2 (122-153)	138±8.4 (132-144)	6.20	<0.001	Highly Significant
Duration of coma (hrs)	98.6±21.25 (28-138)	77.50±13.05 (24-144)	123±18.3 (110-136)	8.40	<0.001	Highly Significant
S.Chloride (mmol/l)	96.0±1.3 (85-99)	102±1.6 97-106)	100±2 (98-104)	3.00	<0.05	Significant
Mortality	5	4	0	Z=0.34 Fisher Z	>0.05	Not Significant

Journal of Pediatric Neurosciences

Upadhyay et al 2010

Variations de la pression artérielle moyenne

Relationship between group A and group B female subjects

Hrs	Group A) (X±SD)	Group B (X±SD)	't' value	'*P*' value	Significance of B
0	7±1.88	8.2±1.74	4.80	<0.001	Highly Significant
6	5.8±1.16	4.4±2.02	3.15	<0.001	Highly Significant
12	5.0±1.47	6.1±1.80	2.9	<0.01	Moderate Significant
18	2.7±1.18	3.3±1.99	1.66	>0.05	Not Significant
24	3.4±1.91	4.0±2.06	1.36	>0.05	Not Significant
30	4.6±1.17	3.38±1.06	3.20	<0.01	Moderate Significant
36	4.2±1.20	4.35±1.27	0.55	>0.05	Not Significant
42	2.6±1.73	3.0±1.60	1.35	>0.05	Not Significant
48	1.6±1.33	1.30±0.56	1.36	>0.05	Not Significant

X=mean of differnce between pre and post drug mean map at definite time intervals

Relationship between group A and group B male subjects

Hrs	Group A (X±SD)	Group B (X±SD)	't' value	'*P*' value	Significance of B
0	7±3.25	11.5±4.48	6.33	<0.001	Highly Significant
6	7±2.58	8.2±3.52	2.14	<0.05	Significant
12	5.7±1.62	5.4±1.97	0.97	>0.05	Not Significant
18	6.6±2.89	6.1±2.6	1.0	>0.05	Not Significant
24	6.2±2.56	5±2.51	2.60	<0.05	Significant
30	4.7±2.14	4±2.59	1.62	>0.05	Not Significant
36	3.3±2.58	3.6±2.25	0.68	>0.05	Not Significant
42	2±2.19	2.8±2.45	2.00	<0.05	Significant
48	2±1.8	1.9±1.14	0.37	>0.05	Not Significant

X=mean of differnce between pre and post drug mean map at definite time intervals

Journal of Pediatric Neurosciences

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SSH et Etats de Chocs

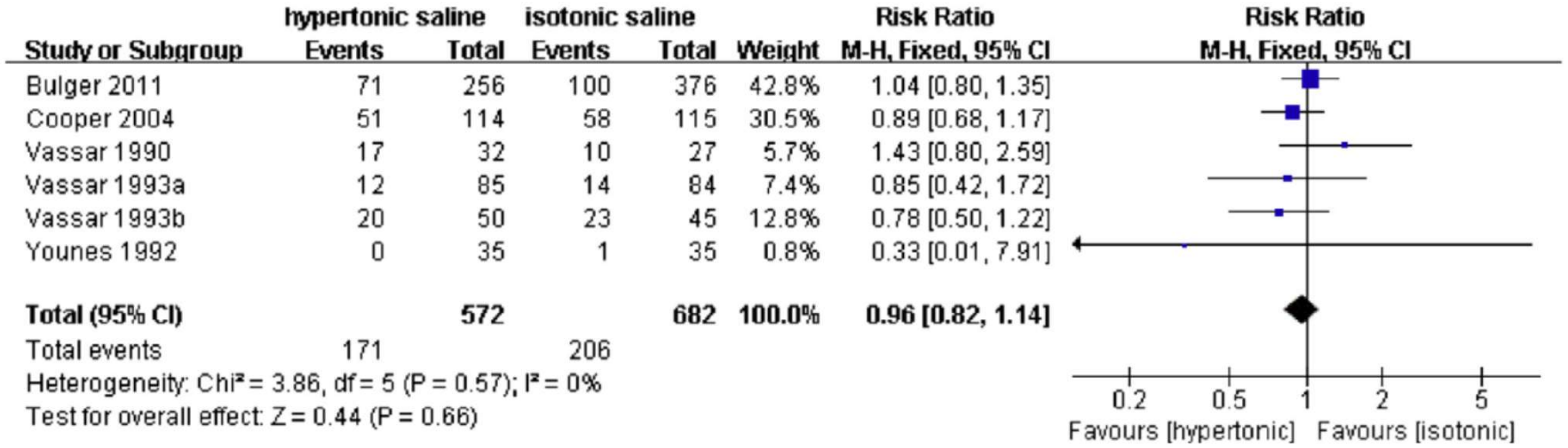
Mécanismes d'action du SSH

- Expansion volémique par effet osmotique rapide
- Amélioration de la contractilité myocardique (Diminution de l'œdème et restauration des potentiels transmembranaires)
- Diminution de l'œdème endothéliale des vaisseaux et des capillaires diminuant les résistance et améliorant la perfusion tissulaire
- Vasodilatation périphérique par libération de prostaglandine
- Immunomodulation

Oliveira Crit care 2002

SSH 3% vs NaCl 0,9%

- SSH et hypovolémie méta-analyse adulte
- Mortalité



Study or Subgroup	hypertonic saline Events	Total	isotonic saline Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Bulger 2011	71	256	100	376	42.8%	1.04 [0.80, 1.35]
Cooper 2004	51	114	58	115	30.5%	0.89 [0.68, 1.17]
Vassar 1990	17	32	10	27	5.7%	1.43 [0.80, 2.59]
Vassar 1993a	12	85	14	84	7.4%	0.85 [0.42, 1.72]
Vassar 1993b	20	50	23	45	12.8%	0.78 [0.50, 1.22]
Younes 1992	0	35	1	35	0.8%	0.33 [0.01, 7.91]
Total (95% CI)		**572**		**682**	**100.0%**	**0.96 [0.82, 1.14]**
Total events	171		206			

Heterogeneity: Chi² = 3.86, df = 5 (P = 0.57); I² = 0%
Test for overall effect: Z = 0.44 (P = 0.66)

Fig. 2 – Forest plot comparing the mortality at hospital discharge between the groups treated with either HS or isotonic saline. M-H = Mantel–Haenszel. (Color version of figure is available online.)

Wang et al. J Surg res. 2014

SSH 3% vs NaCl 0,9%

- SSH et hypovolémie méta-analyse adulte
- Pression artérielle

	hypertonic saline			isotonic saline				Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
Bulger 2011	52.1	46.1	256	44.7	40.9	376	54.4%	7.40 [0.40, 14.40]
Cooper 2004	40	42	114	45	58	115	15.5%	-5.00 [-18.11, 8.11]
Vassar 1990	24	44	32	18	46	27	5.0%	6.00 [-17.10, 29.10]
Vassar 1993a	55	40	85	48	41	84	17.9%	7.00 [-5.21, 19.21]
Vassar 1993b	34	46	50	11	49	45	7.2%	23.00 [3.83, 42.17]
Total (95% CI)			**537**			**647**	**100.0%**	**6.47 [1.31, 11.63]**

Heterogeneity: Chi² = 5.87, df = 4 (P = 0.21); I² = 32%
Test for overall effect: Z = 2.46 (P = 0.01)

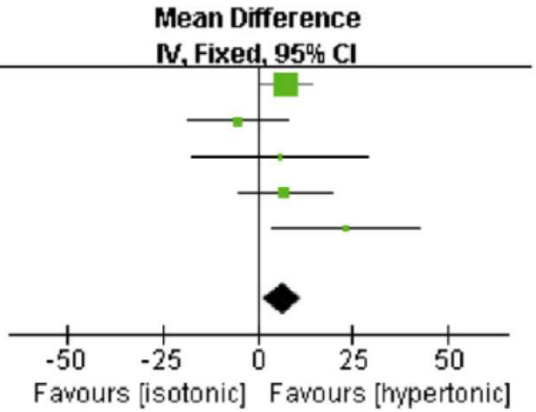
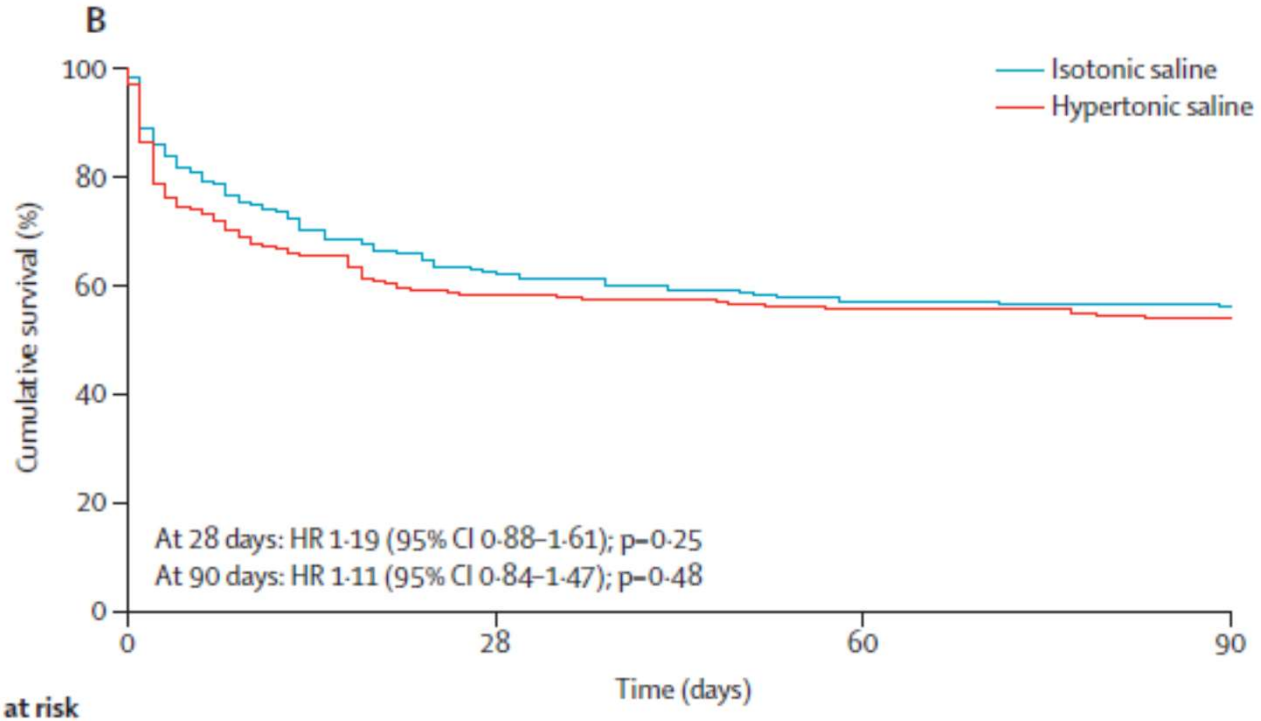


Fig. 3 – Forest plot comparing the change in systolic blood pressure after the infusion of study fluid from baseline between the groups treated with either HS or isotonic saline. IV = inverse variance. (Color version of figure is available online.)

Wang et al. J Surg res. 2014

Hyperoxia and hypertonic saline in patients with septic shock (HYPERS2S): a two-by-two factorial, multicentre, randomised, clinical trial

Pierre Asfar, Frédérique Schortgen, Julie Boisramé-Helms, Julien Charpentier, Emmanuel Guérot, Bruno Megarbane, David Grimaldi, Fabien Grelon, Nadia Anguel, Sigismond Lasocki, Matthieu Henry-Lagarrigue, Frédéric Gonzalez, François Legay, Christophe Guitton, Maleka Schenck, Jean Marc Doise, Jérôme Devaquet, Thierry Van Der Linden, Delphine Chatellier, Jean Philippe Rigaud, Jean Dellamonica, Fabienne Tamion, Ferhat Meziani, Alain Mercat, Didier Dreyfuss, Valérie Seegers, Peter Radermacher, for the HYPER2S Investigators and REVA research network*



Number at risk

Isotonic saline	220	140	126	124
Hypertonic saline	214	125	119	116

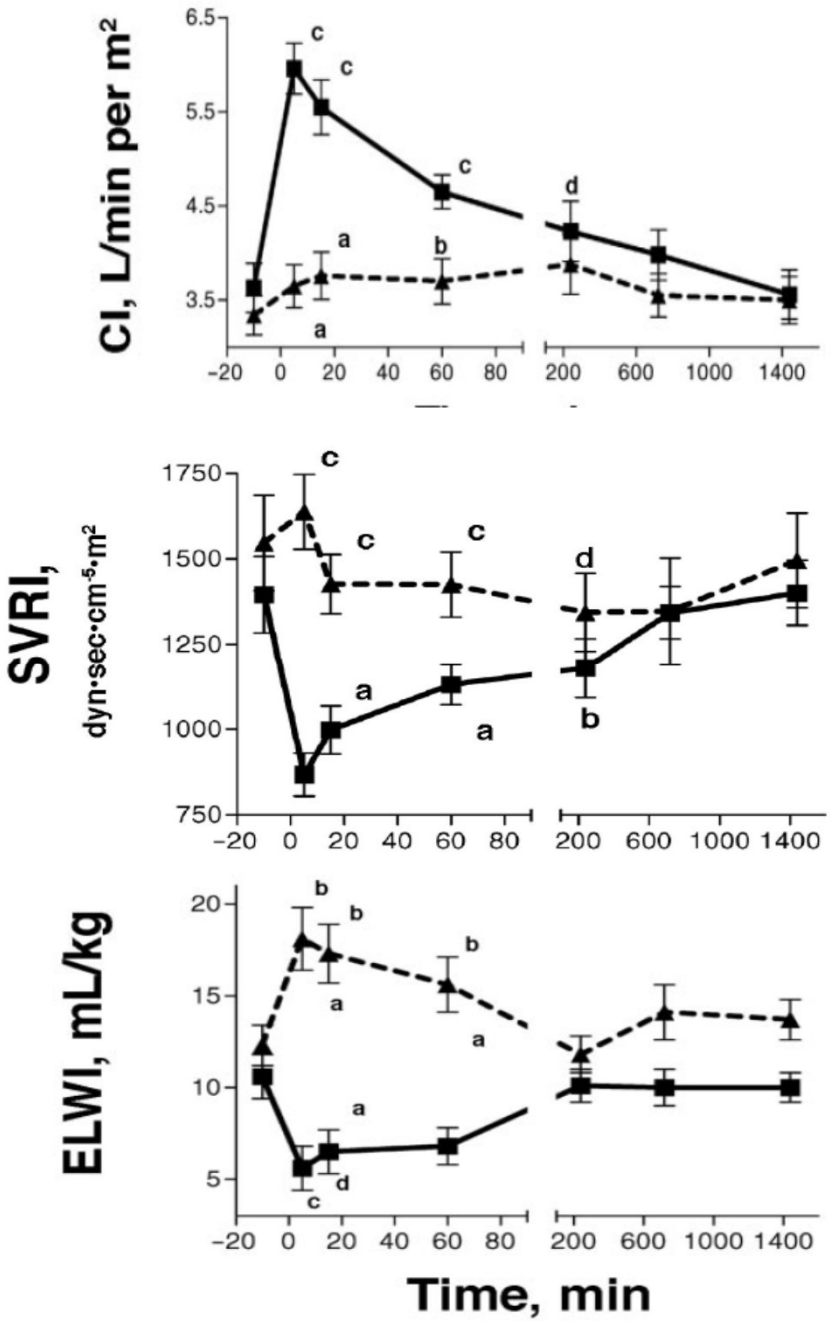
Asfar *et al.* Lancet respir med 2017

Hyperoxia and hypertonic saline in patients with septic shock (HYPERS2S): a two-by-two factorial, multicentre, randomised, clinical trial

Pierre Asfar, Frédérique Schortgen, Julie Boisramé-Helms, Julien Charpentier, Emmanuel Guérot, Bruno Megarbane, David Grimaldi, Fabien Grelon, Nadia Anguel, Sigismond Lasocki, Matthieu Henry-Lagarrigue, Frédéric Gonzalez, François Legay, Christophe Guitton, Maleka Schenck, Jean Marc Doise, Jérôme Devaquet, Thierry Van Der Linden, Delphine Chatellier, Jean Philippe Rigaud, Jean Dellamonica, Fabienne Tamion, Ferhat Meziani, Alain Mercat, Didier Dreyfuss, Valérie Seegers, Peter Radermacher, for the HYPER2S Investigators and REVA research network*

- Groupe Serum salé plus grave
  - Lactates plus élevés
  - Plus de cirrhose

- Enfants
- Chirurgie cardiaque
- SSH 7,5% vs 0,9%



Schroth Pediatrics 2006

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

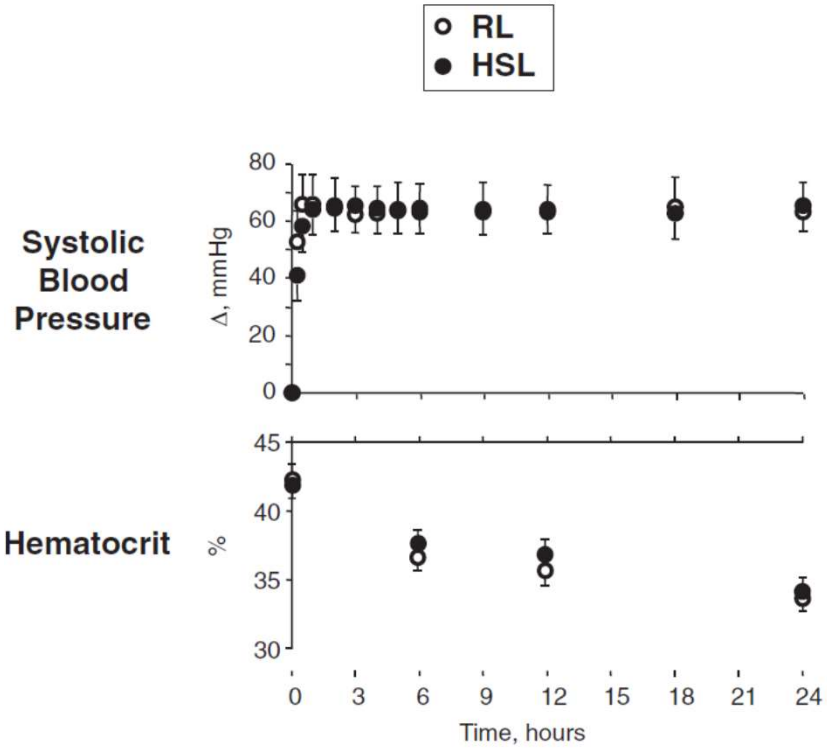
CRITICAL CARE

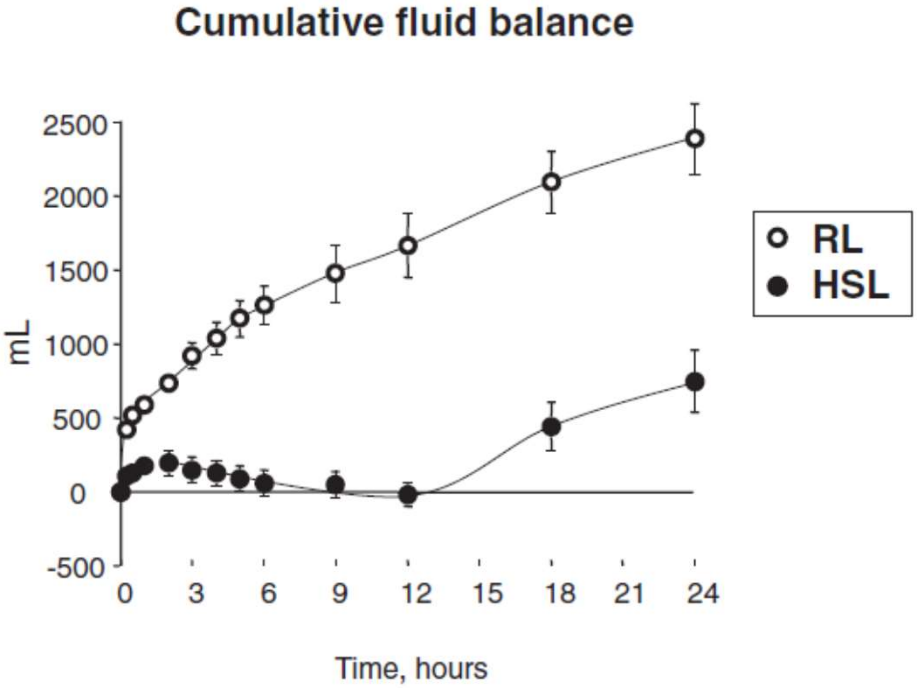
RESEARCH Open Access

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^]

50 enfants randomisés : RL vs Lactate de sodium hyper osmolaire


RL
HSL
Systolic Blood Pressure
Δ, mmHg
80
60
40
20
0
Hematocrit
%
45
40
35
30
0
3
6
9
12
15
18
21
24
Time, hours


Cumulative fluid balance
mL
2500
2000
1500
1000
500
0
-500
0
3
6
9
12
15
18
21
24
Time, hours
RL
HSL

Effets secondaires du SSH

- Chute de la pression artérielle si injection rapide
- Hypernatrémie – Myelinolyse
- Acidose hyperchlorémique
- Insuffisance rénale
- Augmentation du risque de thrombose cérébrale

Webster *et al* JCC 2015

Il est probablement souhaitable de maintenir

Na < 160 mmol/l

Conclusion

- Les effets du SSH sont nombreux
- L'intérêt dans la prise en charge de l'HTIC est indéniable – reste à en préciser les modalités précises
- Les solutés hypertoniques ont des effets cardiovasculaires intéressants et pourraient permettre de réduire les apports hydriques en réanimation
- Niveaux de preuve insuffisants
- Na+… oui mais combien?





- **Olivier Paut**
- Isabelle Suprano
- Valérie Chauvet
- Marco Caruselli
- Frédéric Blanc
- Maria Minero
- Amélie Mansuy
- Fabrice Ughetto
- Christian Raphael
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- Anne-Pascale Wasier
- Michael Tsapis
- Marion Fiorini
- Céline Grimaldi

Anesthésie et réanimation de l'enfant
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