Bronchiolite: Quel traitement en pratique en 2017?

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3ème journée de pneumo-allergologie pédiatrique de Midi-Pyrénées

Jeudi 28 septembre 2017

avec Bronchior,
la bronchiolite
je l'a dynamite!

The heterogeneity of viral bronchiolitis: A lack of universal consensus definitions

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Pediatric Pulmonology. 2017;**52**:1234–1240.

TABLE 2 Utility of clinical factors in defining bronchiolitis and its endotypes

Factor	Utility	Comments
Age	Certainly	Simple method for defining the bronchiolitis population, endotypes, and general lack of bronchodilator responsiveness. Clinical overlap between age groups so not a perfect discriminator.
Lack of bronchodilator / steroid responsiveness	Certainly	Pathognomic for bronchiolitis. May not be clinically useful given their lack of benefit and general recommendations against their use in most guidelines.
Likely or proven viral aetiology	Certainly	Pathognomic for bronchiolitis.
Virus sub-type	Possibly	Significant overlap between viruses makes it not useful in a broader definition. Certainly useful for helping to define bronchiolitis endotypes.
Auscultation findings	Possibly	Clinical examination findings of obstructive lower respiratory tract infection certainly useful. Subtle differences in requirements for wheeze and/or crackles not useful given subjectivity.
Exclusion of prematurity	Not useful	May serve as a risk factor for more severe disease, but unlikely to be useful in a broad clinical definition.
Exclusion of other comorbidities	Not useful	May serve as a risk factor for more severe disease, but unlikely to be useful in a broad clinical definition.
First presentation	Not useful	May be useful to distinguish bronchiolitis from recurrent wheezing phenotypes, but restriction to first presentation likely too restrictive.
Biomarkers	Prospective	No biomarkers have been conclusively established to date, partially due to the definition heterogeneity making literature synthesis challenging. Has a massive potential to provide an objective method for bronchiolitis definition that overcomes many of the current limitations.

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TABLE 1 National bronchiolitis guideline definitions

Guideline	Age range (months)	First episode	Definition and diagnostic characteristics
Australia 2008[12]	<18	No	Viral LRTI with acute inflammation, oedema and necrosis of epithelial cells, increased mucus production, and bronchospasm causing obstruction if the bronchioles. Clinical diagnosis of initial URTI, then LRTI with wheeze, inspiratory crepitations, increased WOB, poor feeding.
Canada 2014[5]	<24	No	Viral LRTI with increased mucus production, acute inflammation, oedema and necrosis of epithelial cells causing obstruction of the small airways. Clinical diagnosis with 2-3 DayURTI prodrome, then LRTI, with wheeze, crackles, increased work of breathing (WOB) and possible dehydration. Describes as typically first episode of wheezing age <12 months, however covers up to age 24 months and recurrent.
Finland 2016[11]	<12	Yes	Pathophysiological definition not explicitly included. Clinical diagnosis with crepitations on examination. Commonly seen during RSV season, may present as apnoea in young infants. Differential diagnosis: wheezing bronchitis, defined as wheezing in children aged 12-36 months during viral infection or recurrent wheezing in infants aged 6-12 months.
Italy 2014[4]	<12	Yes	Viral LRTI defined by clinical and aetiological factors. Clinical diagnosis: URTI, then LRTI with crackles, wheezing and respiratory distress, during RSV season. Etiological diagnosis: by viral identification.
Scotland 2006[10]	<12 (or <24 in infants with significant co-morbidities")	No	Pathophysiological definition not explicitly included. Clinical diagnosis of a seasonal viral illness following a typical natural history, with 2-3 days of URTI prodrome, then 3 days of LRTI with dry/wheezy cough, crackles and/or expiratory wheeze. Possible apnoea and poor feeding. Differential diagnosis: consider classifying as viral induced wheeze if wheeze without crackles.
South Africa 2010[6]	<24	No	Viral induced inflammation of the bronchioles leading to clinical manifestations. Clinical diagnosis with mild URTI, low-grade fever, hyperinflation, wheeze, increased WOB and poor feeding. Emphasises signs of hyperinflation.
Spain 2010[14]	<24	Yes	Defined as first episode of lower respiratory tract (bronchi or bronchiole) inflammation, presumably viral-induced. Clinical criteria for diagnosis not explicitly outlined, but findings indicating severity and risk of progression included.
UK 2015[8]	<24	No	Pathophysiological definition not explicitly included. Clinical diagnosis with 1-3 DayURTI prodrome then cough, increased WOB, wheeze and/or crackles. Possible apnoea in young infants, low grade fever and poor feeding. Differential diagnosis: consider diagnosis of viral-induced wheeze or early-onset asthma if older, wheeze without crackles, recurrent episodic wheezing or history (personal/ family) of atopy.
USA 2014[9]	<24	No	Viral LRTI with increased mucus production, acute inflammation, oedema and necrosis of epithelial cells of small airways. Clinical diagnosis on history and examination, with rhinitis and cough, then wheeze, rales and increased WOB.

Conférence de consensus

Prise en charge de la bronchiolite du nourrisson

21 septembre 2000

Conférence de consensus

Prise en charge de la bronchiolite du nourrisson

21 septembre 2000

Salle Louis Armand – Cité des Sciences et de l'Industrie de la Villette – Paris

TEXTE DES RECOMMANDATIONS

Prise en charge de la bronchiolite aiguë du nourrisson de moins de 1 an : actualisation et consensus médical au sein des hôpitaux universitaires du Grand Ouest (HUGO)

Update on the management of acute viral bronchiolitis: Proposed guidelines of Grand Ouest University Hospitals

M. Verstraete[a,*], P. Cros[b], M. Gouin[a], H. Oillic[a], T. Bihouée[a], H. Denoual[b], A. Barzic[b], A.-L. Duigou[b], B. Vrignaud[c], K. Levieux[c], N. Vabres[a], E. Fleurence[d], E. Darviot[e], J. Cardona[f], M.-A. Guitteny[g], Y. Marot[g], G. Picherot[a], C. Gras-Le Guen[a,b,c]

Arch Pediatr. 2014 Jan;21(1):53-62

	Canada 2014	Italie 2014	USA 2014	UK 2015	Finlande 2016
O2	+	+	+	+	
?? O2-HD		-		-	-
CPAP				(+)	
Hydratation	+	+	+	+	
DRP	+	+		+	
Kiné respiratoire	-	-	-	(-)	
?? Nebu SSH	(+)	+	(+)	-	(+)
Nebu béta2	-	(-)	-	-	
Nebu atrovent				-	
Nebu adrénaline	-	-	-	-	-
Nébu CTC		-		-	-
CTC	-	-	-	-	-
ATB	-	-	-	-	
ALT		-		-	

Oxygénothérapie à haut débit (OHD)
et
bronchiolite

Oxygénothérapie à haut débit

Scand J Trauma Resusc Emerg Med. 2016 Jul 12;24:93. doi: 10.1186/s13049-016-0278-4.

High flow nasal cannula in children: a literature review.

Mikalsen IB[1,2], Davis P[3], Øymar K[4,5].

Cochrane Database Syst Rev. 2014 Jan 20;(1):CD009609. doi: 10.1002/14651858.CD009609.pub2.

High-flow nasal cannula therapy for infants with bronchiolitis.

Beggs S[1], Wong ZH, Kaul S, Ogden KJ, Walters JA.

- Amélioration de la FR, alimentation, confort, tolérance
- Peu d'effets secondaires
- Facilité d'utilisation: urgences/service traditionnel/SI

Mais….

faible niveau de preuve => nécessité d'études randomisées

pas de guideline internationale (indications, débit optimal, etc….)

OHD *versus* CPAP

Intensive Care Med (2017) 43:209–216

ORIGINAL

High flow nasal cannula (HFNC) versus nasal continuous positive airway pressure (nCPAP) for the initial respiratory management of acute viral bronchiolitis in young infants: a multicenter randomized controlled trial (TRAMONTANE study)

Christophe Milési[1], Sandrine Essouri[2], Robin Pouyau[3], Jean-Michel Liet[4], Mickael Afanetti[5], Aurélie Portefaix[3,6], Julien Baleine[1], Sabine Durand[1], Clémentine Combes[1], Aymeric Douillard[7], Gilles Cambonie[1*] and Groupe Francophone de Réanimation et d'Urgences Pédiatriques (GFRUP)

- Etude prospective randomisée multicentrique
- 152 nourrissons de 1 à 6 mois
- Bronchiolite modérée à sévère

OHD *versus* CPAP

Intensive Care Med (2017) 43:209–216

ORIGINAL

CrossMark

High flow nasal cannula (HFNC) versus nasal continuous positive airway pressure (nCPAP) for the initial respiratory management of acute viral bronchiolitis in young infants: a multicenter randomized controlled trial (TRAMONTANE study)

- Moindre efficacité de OHD sur l'amélioration initiale
- Pas de différence sur taux d'intubation
  durée de VNI
  durée d'hospitalisation en USI
- Meilleure tolérance de OHD

OHD *versus* O2 conventionnel

Lancet 2017; 369: 930–39

High-flow warm humidified oxygen versus standard low-flow nasal cannula oxygen for moderate bronchiolitis (HFWHO RCT): an open, phase 4, randomised controlled trial

Elizabeth Kepreotes, Bruce Whitehead, John Attia, Christopher Oldmeadow, Adam Collison, Andrew Searles, Bernadette Goddard, Jodi Hilton, Mark Lee, Joerg Mattes

- Etude prospective randomisée monocentrique
- 202 nourrissons < 24 mois
- Bronchiolite modérée oxygéno-réquérante

OHD *versus* O2

Lancet 2017; 369: 930–39

High-flow warm humidified low-flow nasal cannula oxyg (HFWHO RCT): an open, pha

Elizabeth Kepreotes, Bruce Whitehead, John Attia, Christopher Oldn Mark Lee, Joerg Mattes

	Standard therapy	HFWHO	p value	Hazard ratio (HR) or difference
Time to oxygen weaning (h; median)				
ITT (n=202)	24·0 (18·0–28·0)	20·0 (17·0–34·0)	0·61	HR 0·9 (0·7–1·2)
Per-protocol (n=186)	24·0 (19·0–30·0)	19·5 (15·0–34·0)	0·69	HR 1·0 (0·7–1·3)
Time to treatment failure (proportion with 24 h event-free survival)				
ITT (n=202)	0·6 (0·5–0·7)	0·9 (0·8–1·0)	<0·0001	HR 0·3 (0·2–0·6)
Per-protocol (n=196)	0·6 (0·5–0·8)	0·9 (0·9–1·0)	<0·0001	HR 0·3 (0·2–0·6)
Length of stay (days; median)				
ITT (n=202)	2·0 (1·0–3·0)*	2·0 (1·0–3·0)*	0·99	..
Treatment failure and care escalation, ITT (n; %)				
Treatment failure (ITT, n=202)	33 (33%)	14 (14%)	0·0016	19% (8–30)
Crossover†	32 (32%)	1 (1%)	<0·0001	31% (17–44)
Rescued†	20 (20%)	..	..	..
ICU transfer†	12 (12%)	14 (14%)‡	0·41	−1% (−7 to 16)
Adverse events				
Any	2	2	..	..
Serious	0	0	..	..
Heart rate (baseline-adjusted beats per min; mean)				
4 h (n=202)	−16·8 (−21·2 to −12·4)	−21·5 (−25·5 to −17·5)	0·40	2·0 (−2·6 to 6·5)
24 h (n=202)	−23·0 (−27·1 to −19·0)	−27·0 (−31·1 to −22·9)	0·59	1·3 (−3·3 to 5·8)
Respiratory rate (baseline-adjusted breaths per min; mean)				
4 h (n=202)	−11·3 (−13·8 to −8·8)	−9·1 (−11·6 to −6·5)	0·0208	−3·0 (−5·5 to −0·5)
24 h (n=202)	−13·5 (−16·0 to −10·9)	−12·9 (−15·7 to −10·0)	0·28	−1·4 (−3·9 to 1·2)
Comfort score (median)				
mITT (n=170)	3 (3–4)*	4 (3–4)*	0·0170	..
Sleep score (median)				
mITT (n=170)	3 (3–4)*	4 (3–4)*	0·08	..
Feeding score (median)				
mITT (n=170)	3 (2–4)*	4 (3–4)*	0·0100	..

- OHD ne semble pas modifier l'évolution spontanée
- Mais peut éviter un transfert en soins intensifs?

Oxygénothérapie à haut débit

- Indication = Bronchiolite modérée à sévère
  - Oxygéno-réquérance
  - Score de Wood 3-7
  - FR > 60/min
  - pH > 7,30 et pCO2 < 60 mmHg

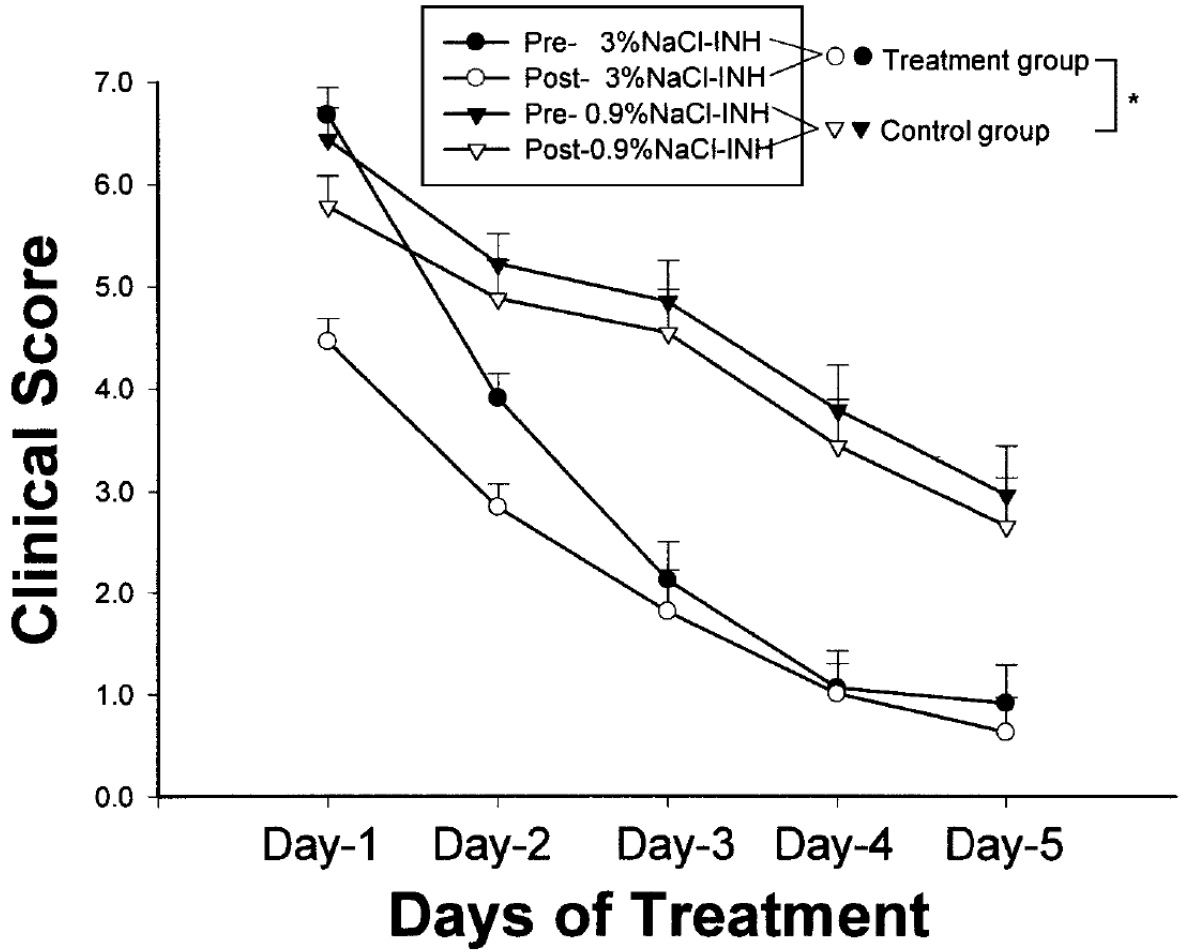
- Mauvaises indications:
  - Bronchiolite sévère (score de Wood > 7)
  - Apnées

- Attention aux NN < 1 mois: à surveiller plutôt en USI?

Nébulisation de sérum salé hypertonique
et
bronchiolite

Nebulized 3% Hypertonic Saline Solution Treatment in Ambulatory Children With Viral Bronchiolitis Decreases Symptoms*

Chest. 2002 Dec;122(6):2015-20



Essais randomisés depuis 2014!

A comparative study on use of 3% saline versus 0.9% saline

Hypertonic (3%) Saline Vs 0.9% Saline Nebulization for Acute Viral

A randomized, controlled trial of nebulized 5% hypertonic

Nebulized Hypertonic Saline for Bronchiolitis

7% Hypertonic Saline in Acute Bronchiolitis:

A Randomized Trial of Nebulized 3% Hypertonic Saline

Original Investigation

Nebulized Hypertonic Saline for Bronchiolitis

SABRE: a multicentre randomised control trial of

Nebulised hypertonic saline (3 %) among

The effect of 3% and 6% hypertonic

Balkan Med J. 2016 Mar;33(2):193-7. doi: 10.5152/balkanmedj.2016.16840. Epub 2016 Mar 1.

Comparing the Efficacy of 7%, 3% and 0.9% Saline in Moderate to Severe Bronchiolitis

JAMA Pediatr. 2017 Aug 7;171(8):e171333. doi: 10.1001/jamapediatrics.2017.1333. Epub 2017 Aug 7.

Effect of Nebuliz

Hospitalization R

Respiration. 2017;94(3):251-257. doi: 10.1159/000477495. Epub 2017 Jun 24.

Early Halt of a Randomized Controlled Study with 3% Hypertonic

Carsin A[1], Sauvaget E, Bresson V, Retornaz K, Cabrera M, Jouve E, Truillet R, Bosdure E, Dubus JC.

Sérum salé hypertonique: En résumé…

- Doses multiples
  - ⇒ toutes les 6 à 8h pendant toute la durée d'hospitalisation
- Diminution de la durée d'hospitalisation ??
  - ⇒ Peut-être si hospitalisation prolongée (> 3 jours) *=> donc si sévère?*
- Diminution du taux d'hospitalisation???
  - ⇒ 1 seule étude significative avec nombreux biais, plusieurs études négatives
  - ⇒ Surtout si taux d'hospitalisation élevé *=> donc si sévère… ???*
- Amélioration du score clinique???
  - ⇒ Très difficile à interpréter (score différents, protocoles différents,…)
- Plutôt bonne tolérance

<u>Protocole du CHU de Toulouse</u>:

Uniquement en hospitalisation. A discuter si sécrétions épaisses, selon avis kinés.

Vaccin et immuno-prophylaxie anti-VRS

Type of intervention	Product candidate	Approach	Company/institution	Clinical trial status	Target subject	Clinical trial ID
Vaccines						
Live attenuated	RSV ΔNS2 Δ1313	Recombinant Live-Attenuated RSV	NIAD, Sanofi, LID, NIH	I	Pediatric	NCT01893554
	RSV LID ΔM2-2	Recombinant Live-Attenuated RSV	NIAD, Sanofi, LID, NIH	I	Pediatric	NCT02794870
	RSV D46 cpΔM2-2	Recombinant Live-Attenuated RSV	NIAD, Sanofi, LID, NIH	I	Pediatric	NCT03102034
Particle based	RSV F Vaccine	RSV Recombinant Fusion (F) Nanoparticle	Novavax	I	Pediatric	NCT02296463
	RSV F vaccine with adjuvant	RSV F Nanoparticle with adjuvant	Novavax	II	Maternal	NCT02624947
Subunit	GSK3003891A	RSV prefusion F protein	GlaxoSmithKline	II	Maternal	NCT03191383
Gene-based vectors	GSK3389245A	Viral Proteins Encoded by (ChAd155-RSV)	GlaxoSmithKline	II	Pediatric	NCT02927873
Antibodies						
Monoclonal antibody (mAb)	MEDI8897	RSV F human mAb	Medimmune	II	Pediatric	NCT02878330
	REG222	RSV F human mAb	Regeneron	III	Pediatric	NCT02325791

Hancock D et al., Ped Pulmonol 2017

Merci de votre attention

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