Research paper

Real-life study of the role of high-flow nasal cannula for bronchiolitis in children younger than 3 months hospitalised in general pediatric departments

C. Fabre [a,e,1], M. Panciatici [a,e,1], E. Sauvaget [b,e], S. Tardieu [c,e], E. Jouve [c,e], M. Dequin [a,e], K. Retornaz [d,e], J.-M. Bartoli [b,e], N. Stremler-Le Bel [a,e], E. Bosdure [a,e], J.-C. Dubus [a,e,*]

[a] Service de médecine infantile et pneumologie pédiatrique, CHU Timone–enfants, 264, rue Saint-Pierre, 13385 Marseille cedex 5, France
[b] Service de pédiatrie, hôpital Saint-Joseph, 26, boulevard de Louvain, 13008 Marseille, France
[c] Service d'évaluation médicale, pôle de santé publique, hôpital de la Conception, 147, boulevard Baille, 13055 Marseille, France
[d] Service de pédiatrie, hôpital Nord, chemin des Bourrely, 13015 Marseille, France
[e] Aix-Marseille université, IRD, AP–HM, MEPHI, IHU-Méditerranée Infection, 43, boulevard Baille, 13005 Marseille, France

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ABSTRACT

We aimed to describe the real-life role of high-flow nasal cannula (HFNC) for bronchiolitis in infants under 3 months of age admitted to three general pediatric departments during the 2017–2018 epidemic period. We retrospectively assessed the clinical severity (Wang score) for every 24-h period of treatment (H0–H24 and H24–H48) according to the initiated medical care (HFNC, oxygen via nasal cannula, or supportive treatments only), the child's discomfort (EDIN score), and transfer to the pediatric intensive care unit (PICU). A total of 138 infants were included: 47 ± 53 days old, 4661 ± 851.9 g, 70 boys (50.7%), 58 with hypoxemia (42%), Wang score of 6.67 ± 2.58, 110 (79.7%) staying for 48 consecutive hours in the same ward. During the H0–H24 period, only patients treated with HFNC had a statistically significant decrease in the severity score ($n = 21/110$; -2 points, $P = 0.002$) and an improvement in the discomfort score ($n = 15/63$; -3.8 points, $P < 0.0001$). There was no difference between groups during the H24–H48 period. The rate of admission to the PICU was 2.9% for patients treated for at least 24 h with HFNC ($n = 34/138$, 44% with oxygen) versus 16.3% for the others ($P = 0.033$). Early use of HFNC improves both clinical status and discomfort in infants younger than 3 months admitted for moderately severe bronchiolitis, whatever their oxygen status.

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1. Introduction

Acute bronchiolitis is a seasonal epidemic respiratory viral infection in infant with human-to-human transmission, mainly caused by the respiratory syncytial virus (RSV) [1]. The youngest infants, who are at higher risk of hospitalisation, are most severely affected. During the 2017–2018 epidemic period, 56,520 bronchiolitis-related visits to emergency departments for infants under 2 years of age were registered in France, of which 21,000 (38%) led to hospitalisation [2]. Bronchiolitis treatment is only supportive, including isotonic saline nasal instillation, feeding management, and oxygen when necessary [3,4]. High-flow nasal cannula (HFNC) has been increasingly used for the past few years as a respiratory support providing patients a mix of conditioned gas (heated and moistened) through the nasal cannula interface, washing naso-pharyngeal anatomic dead space, reducing metabolic work, creating a low level of positive pressure inside the airways, and eventually improving mucociliary clearance [5]. The literature on the role of HFNC in bronchiolitis has been growing considerably in recent years, with the place of HFNC in bronchiolitis management clearly needing to be better determined [6–11]. Evaluation of HFNC in general pediatric departments is relatively scarce, and of the studies that have included infants under 3 months of age, none enrolled such patients exclusively. Moreover, there are no data on

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the benefit of HFNC for infants' comfort. The aim of our study was to describe the use of HFNC in a real-life study in these very young patients hospitalised for bronchiolitis and to compare the effect of HFNC on the clinical severity and discomfort score development in the recommended management.

2. Material and methods

2.1. Patients

This descriptive, multicentre, retrospective study aimed to evaluate professional practices in the medical care of infants younger than 3 months hospitalised in general pediatric departments for their first acute viral bronchiolitis episode during the 2017–2018 epidemic period (from December 1, 2017 to March 31, 2018). Children were hospitalised in one of Marseille's three general pediatric departments (University Timone–Enfants and University Hôpital Nord, Assistance publique–Hôpitaux de Marseille, and Hôpital Saint-Joseph). On admission, all children received supportive treatment (nasal saline instillations, nutritional care, raised mattress), with the first group restricted to this type of management (ST group). The two other groups were treated with either oxygen delivered through nasal cannula (ONC group) in the case of hypoxemia (pulsed oximetry value under 92%) or HFNC (Airvo2 with nasal cannulas adapted to the patient, Fisher & Payckel HealthCare), with a 2-mL/kg/min flow and an inspired fraction of oxygen depending on the pulsed oximetry value (HFNC group). HFNC initiation depended on both the subjective choice of the pediatrician and the availability of the devices (10 devices available for a total of 57 beds).

Infants with an underlying condition, such as congenital heart disease or pulmonary arterial hypertension, chronic pulmonary disease (cystic fibrosis, bronchopulmonary dysplasia, pulmonary malformation), immunodeficiency, long-term use of oxygen at home, craniofacial malformation, and isolated upper airways obstruction, were not included in the study.

3. Methods

Data on weight, sex, previous events (term and birth weight, neonatal respiratory failure, weight evolution), and recent medical history (number of days with rhinitis and respiratory difficulties, feeding difficulties, fever, presence of apnea, treatments) were collected.

For all patients, we noted the following at H0, H24 and H48:

- the type of management (HFNC, ONC, or ST);
- the Wang score (classifying bronchiolitis into mild [score < 4], moderate [4–9], or severe [> 10] and based on the respiratory rate, respiratory accessory muscle utilisation, wheezing/crackles, and infant's general health [12]);
- discomfort assessed with the EDIN score (a "neonatal" score routinely used in our units for children under 3 months of age and based on the facial activity (0–3, from relaxed to edgy), body movements (0–3, from relaxed to permanent agitation), sleep quality (0–3, from easily falling asleep to impossible sleep), social behaviour (0–3, smile answer to contact refusal), and consolability (0–3, from no need to impossible consolability) [13]);
- feeding mode (continuous or discontinuous enteral nutrition, intravenous hydration, baby bottle/breastfeeding).

The duration of oxygen, HFNC, and hospitalisation were also recorded. We noted the number of transfers in the pediatric intensive care unit (PICU), which was common to the three medical units, due to apnea or acute respiratory distress, and the intubation rate.

3.1. Statistical analysis

Average, standard deviation, minimum and maximum were used to define quantitative data. Qualitative data are expressed in percentage. The primary endpoint was the improvement in the clinical severity score (Wang score). Secondary endpoints were discomfort, hospitalisation duration, respiratory support duration, PICU transfer rate, and intubation rate. Since the patients' medical care could be modified throughout the 48-h study duration according to how the symptoms progressed, we compared the improvement in Wang and EDIN scores between the three groups over 24-h periods (H0–H24 and H24–H48). Comparisons were carried out with a mixed model including Wang H0 score and the number of days with bronchiolitis symptoms as covariates. Statistical significance was adjusted using the Tukey–Kramer method. Other parameters (hospitalisation duration, transfer rate, intubation rate, and respiratory support duration) were compared between patients requiring at least 24 h on HFNC and those who underwent standard care using the Chi^2 test or Fisher's exact test.

3.2. Ethics approval

The study was approved by the Ethics Committee of the French Pediatric Society (number CERSFP-2017_067-2) and the National Committee for Informatic and Liberties (CNIL, number 2201809v0). Of note, for retrospective studies such as ours, which rely on data previously collected, parents were informed about the study procedure and had to declare their disagreement to participate if they did not want their child's data to be analysed.

4. Results

4.1. Patients

Among the 621 infants younger than 3 months who were admitted to one of the three pediatric emergency departments for acute bronchiolitis during the 4 months of the study, 324 were hospitalised in a general pediatric department (hospitalisation rate 52.1%, Fig. 1). Because of missing data, especially an unavailable Wang score or no tracking of the treatment sequence, only 138 (42.6%) infants were included, 110 being hospitalised for 48 h in the same ward.

The characteristics of the patients included in the study are presented in Table 1. The patients were similar in terms of age, sex, and hospital length of stay to the excluded children. Included patients were equally distributed in each hospital. The majority (*n* = 77, 55.8%) were hospitalised on the first day of symptoms. Half of the patients presented with hypoxia at H0, and 75% had RSV infection. Patients not requiring oxygen were hospitalised because of feeding difficulties, parental difficulties to monitor their child, or age younger than 6 weeks. There was no difference in clinical characteristics according to the hospitalisation site. For a majority of patients, the treatment (HFNC, ONC, and ST) changed during the 48 h of hospitalisation. Only 63 patients among the 110 had an unchanged management during the 48 h (Table 2), of whom 16 received HFNC support (14.5%), 25 received OFC support (22.7%), and 22 received only ST (20%). Only one patient treated continuously with HFNC for 48 h also needed oxygen. Of note, 56% (*n* = 19/34) of the infants treated with HFNC for a minimum of 24 h did not require oxygen therapy (use of HFNC in room air). These patients were not different from the whole population, particularly in terms of the Wang score.
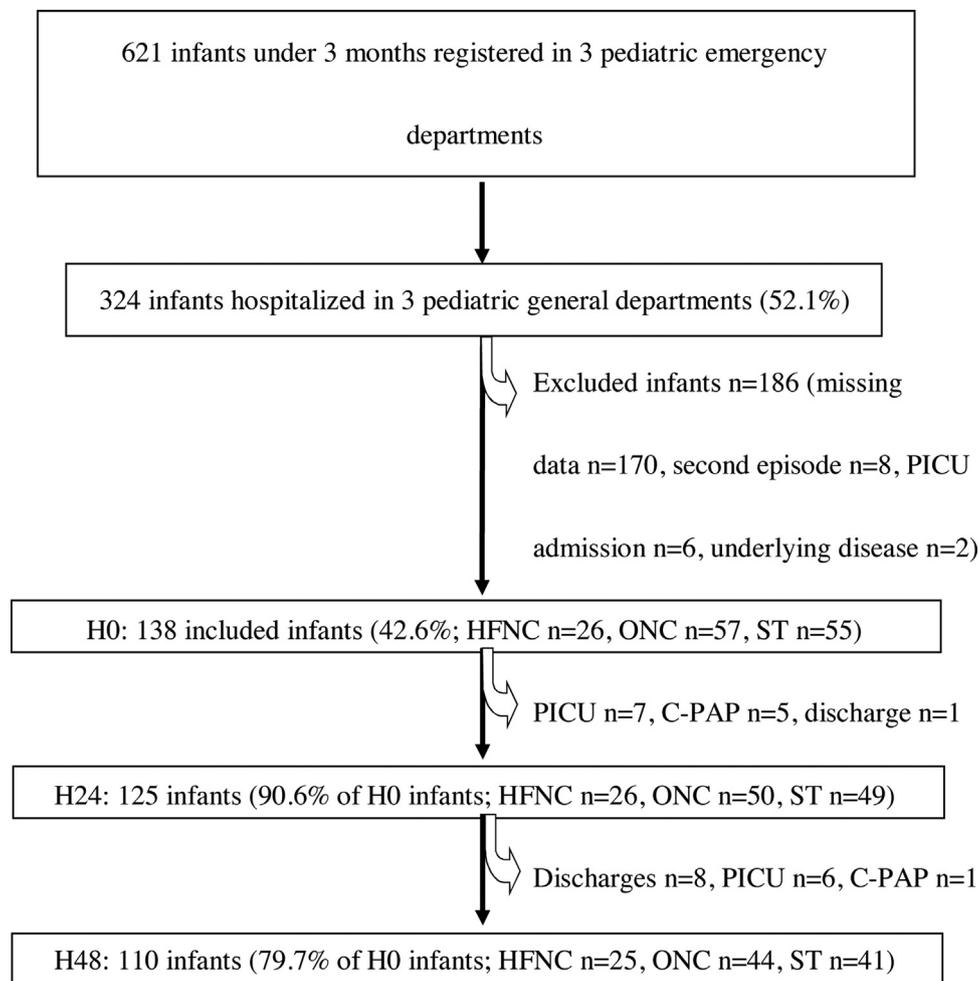
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│     621 infants under 3 months registered in 3 pediatric      │
│                   emergency departments                       │
└─────────────────────────────────────────────────────────────┘
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┌─────────────────────────────────────────────────────────────┐
│  324 infants hospitalized in 3 pediatric general departments  │
│                        (52.1%)                                │
└─────────────────────────────────────────────────────────────┘
                            │        Excluded infants n=186 (missing
                            │        data n=170, second episode n=8, PICU
                            │        admission n=6, underlying disease n=2)
                            ▼
┌─────────────────────────────────────────────────────────────┐
│  H0: 138 included infants (42.6%; HFNC n=26, ONC n=57, ST n=55)│
└─────────────────────────────────────────────────────────────┘
                            │        PICU n=7, C-PAP n=5, discharge n=1
                            ▼
┌─────────────────────────────────────────────────────────────┐
│ H24: 125 infants (90.6% of H0 infants; HFNC n=26, ONC n=50, ST n=49)│
└─────────────────────────────────────────────────────────────┘
                            │        Discharges n=8, PICU n=6, C-PAP n=1
                            ▼
┌─────────────────────────────────────────────────────────────┐
│ H48: 110 infants (79.7% of H0 infants; HFNC n=25, ONC n=44, ST n=41)│
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Fig. 1. Flow chart of a retrospective study of infants under 3 months of age admitted for acute bronchiolitis from December 2017 through March 2018. HFNC: high-flow nasal cannula; ONC: oxygen with nasal cannula; ST: supportive treatment; C-PAP: continuous positive airway pressure; PICU: pediatric intensive care unit.

Table 1
Initial characteristics of 138 infants under 3 months of age admitted for acute bronchiolitis in the three participating general pediatric departments during the 2017–2018 epidemic period in Marseille, France, with a special focus on children aged less than 6 weeks.

	Whole population $n = 138$	Infants < 6 weeks $n = 71$
Average age at admission	47.6 ± 53.4 days	23.7 ± 11.2 days
Male sex	$n = 70$ (50.7%)	$n = 32$ (45.1%)
Average weight at admission	4661.5 ± 851.9 g	3927 ± 614 g
Hospitalisation duration	6.04 ± 7.0 days	7.2 ± 9.1 days
Preterm birth	$n = 13$ (9.5%)	$n = 5$ (7%)
Birth weight	3245 ± 521 g	3341 ± 499 g
Bronchiolitis symptoms onset	1.64 ± 0.85 days	1.6 ± 0.8 days
Associated feeding difficulties	$n = 82$ (59.4%)	$n = 38$ (53.5%)
Fever	$n = 32$ (23.2%)	$n = 11$ (15.5%)
Apnea	$n = 10$ (7.2%)	$n = 9$ (12.7%)
Hypoxia	$n = 58$ (42%)	$n = 34$ (47.9%)
Presence of respiratory syncytial virus	$n = 100$ (74.1%)	$n = 57$ (80.3%)
H0 clinical score (Wang)	6.67 ± 2.58	6.4 ± 2.7
H0 discomfort score (EDIN)	3.77 ± 2.88 ($n = 77/138$)	3.3 ± 2.3 ($n = 42/71$)

4.2. Wang score

For the 110 patients hospitalised for 48 h in the same ward and with a Wang score measured at H0, H24, and H48, the H0 Wang score was similar between those treated with HFNC ($n = 21$, 8.2 ± 1.8) and those treated with ONC ($n = 44$, 7.2 ± 2.8). Patients treated with only ST had an understandably substantially lower score than those receiving respiratory support ($n = 45$, 5.5 ± 2.1 with, respectively, $P = 0.026$ and $P = 0.044$ compared with HFNC and ONC treatments). A decrease in the Wang score was noted during the H0–H24 period in all three groups, but it was only significant in infants treated with HFNC (−2 points vs. −0.6 and −0.4 points, respectively, in infants treated with ONC and only ST, $P = 0.002$) (Fig. 2).

The H24 Wang score was not significantly different in infants under HFNC and ONC (6.2 ± 1.9 vs. 6.6 ± 2.7, respectively; $P = 0.99$). A decrease in the Wang score was observed for all groups during the H24–H48 period, but this decrease was more pronounced in ST infants ($P = 0.024$). At H48, the Wang score was higher in the ONC group than in the ST group (HFNC 5.0 ± 2.2; ONC 6.2 ± 2.6; symptomatic treatment 3.7 ± 2.3).

4.3. Other parameters

Among the 110 patients, the EDIN score was collected for the H0–H24 period and the H24–H48 period for 63 (57.3%) and 61 (51.45%) of the patients, respectively. The H0 EDIN score was significantly lower in patients under ST than in those under HFNC (HFNC: $n = 15$, 5.8 ± 3.1; ONC $n = 19$, 4.4 ± 3.3; ST $n = 29$, 2.7 ± 1.9, $P = 0.005$). Discomfort decreased for all groups during the H0–H24 period, but statistically more in infants treated with HFNC (−3.8 points vs. −1.3 and −0.4 points, respectively, in the ONC and ST

Table 2

Comparison of the main clinical characteristics of 63 infants admitted for acute bronchiolitis and managed with the same respiratory support during the first 48 h in the three participating general pediatric departments during the 2017–2018 epidemic period in Marseille, France.

	Whole population $n=63$			Infants $<$ 6 weeks $n=29$		
	HFNC $n=16$	ONC $n=25$	ST $n=22$	HFNC $n=7$	ONC $n=14$	ST $n=8$
Average age at admission	48.4 ± 29.5 days	56.2 ± 81.3 days	49.4 ± 21.2 days	18.6 ± 9.5 days	26.6 ± 10.7 days	27.3 ± 7.9 days
Hospitalisation duration	6.06 ± 2.3 days	6.9 ± 3.9 days	2.7 ± 1.1 days	5.7 ± 1.8 days	6.2 ± 2 days	2.1 ± 0.4 days
Bronchiolitis symptoms onset	1.9 ± 1.1 days	1.8 ± 0.8 days	1.6 ± 0.8 days	1.7 ± 1.1	1.9 ± 0.7	1.3 ± 0.7
Oxygen therapy	$n=1$ (6.2%)	$n=25$ (100%)	$n=0$	$n=0$	$n=14$ (100%)	$n=0$
Enteral alimentation	$n=8$ (50%)	$n=12$ (48%)	$n=6$ (27.3%)	$n=4$ (57.1%)	$n=7$ (50%)	$n=1$ (12.5%)
Intravenous hydration	$n=0$	$n=5$ (20%)	$n=1$ (4.5%)	$n=0$	$n=1$ (7.1%)	$n=1$ (12.5%)
Apnea	$n=0$	$n=1$ (4%)	$n=1$ (4.5%)	$n=0$	$n=1$ (7.1%)	$n=0$
H0 clinical score (Wang)	8.4 ± 1.8	8.5 ± 2.2	5 ± 2.1	7.3 ± 1.3	8.2 ± 2	3.6 ± 1.6
H0 discomfort score (EDIN)	6.4 ± 2.9	5.4 ± 3.9	2.9 ± 2.1	6.3 ± 2.5	3.8 ± 2.6	2.8 ± 2.4

HFNC: high-flow nasal cannula; ONC: oxygen delivered through nasal cannula; ST: supportive treatment.
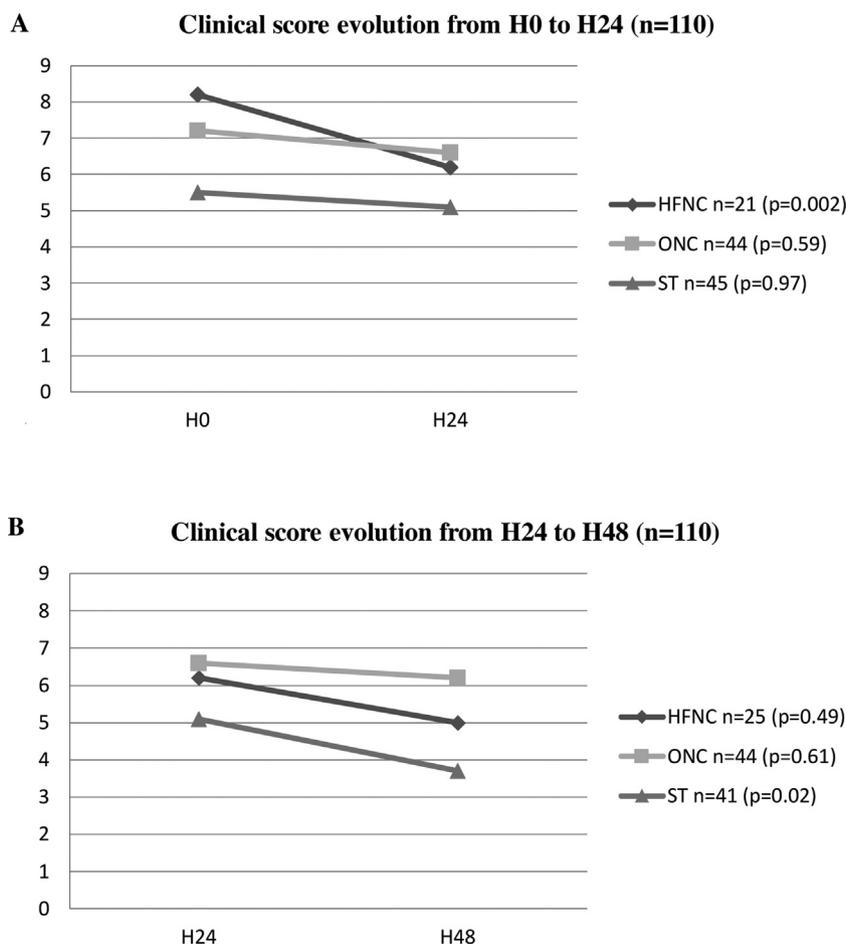

Fig. 2. Evolution of clinical severity score (WANG score) in 110 infants under 3 months of age hospitalised for acute bronchiolitis (A, between H0 and H24; B, between H24 and H48), according to medical care started on the previous day and adjusted to H0 Wang score and the date of symptom onset. HFNC: high-flow nasal cannula; ONC: oxygen with nasal cannula; ST: supportive treatment.

groups, $P = 0.0001$) (Fig. 3). The H24 EDIN score was not significantly different between the three groups (HFNC $n = 18$, 2 ± 2; ONC $n = 16$, 3.1 ± 2.6; ST $n = 27$, 2.3 ± 1.9). Discomfort decreased during the H24–H48 period in every group, statistically more in the ONC group ($P = 0.023$). No significant difference in the H48 EDIN score was found between the three groups (HFNC $n = 18$, 1.4 ± 2; ONC $n = 16$, 1.4 ± 1.5, ST $n = 27$, 1 ± 1.2).

Other criteria were analysed for the whole population ($n = 138$). A total of 13 patients were transferred to the PICU (9.4%). Among the 34 patients requiring at least 24 h of HFNC support, only one was transferred to the PICU (2.9% vs. 16.3% in the non-24-h HFNC

group, $P = 0.033$). Only one child of the non-24-h HFNC group required intubation ($P = 0.75$). We did not find a shorter hospitalisation duration (5.76 ± 8 days vs. 6.13 ± 2.4 days, $P = 0.67$) or a longer respiratory support duration (92 ± 53 h vs. 75 ± 89 h, $P = 0.19$) in the 24-h HFNC group compared with the non-24-h HFNC group.

5. Discussion

The results of this real-life study confirm that HFNC are now a part of the treatment of infants with acute bronchiolitis outside of
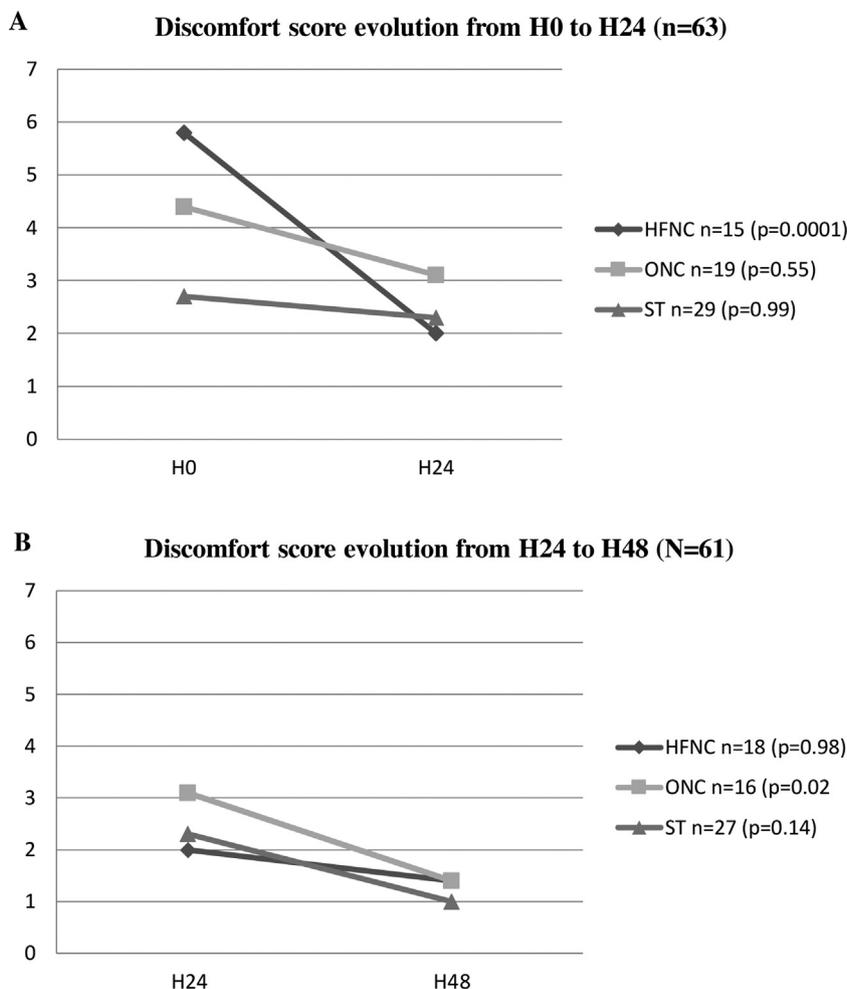
A

Discomfort score evolution from H0 to H24 (n=63)

Legend:
- HFNC n=15 (p=0.0001)
- ONC n=19 (p=0.55)
- ST n=29 (p=0.99)

B

Discomfort score evolution from H24 to H48 (N=61)

Legend:
- HFNC n=18 (p=0.98)
- ONC n=16 (p=0.02
- ST n=27 (p=0.14)

Fig. 3. Evolution of discomfort score (EDIN score) (A, between H0 and H24 in 63 infants under 3 months of age hospitalised for acute bronchiolitis; B, between H24 and H48 in 61 infants under 3 months of age), according to medical care started on the previous day and adjusted to H0 Wang score and the date of symptom onset. HFNC: high-flow nasal cannula; ONC: oxygen with nasal cannula; ST: supportive treatment.

the PICU [6,7,10,14–18], as suggested in other studies where 53% of hospitals in France and up to 85% in Finland report using HFNC outside of the PICU [19,20]. We found that HFNC improves both the clinical severity score and the discomfort score in very young patients, significantly more compared with supportive treatments and oxygen, when used early in the course of the disease. The PICU transfer rate is fivefold lower for patients younger than 3 months benefiting from at least 24 h of HFNC support. Similar results were found for children requiring oxygen or not requiring any.

Our study has some limitations. In this retrospective study, only 43% of the hospitalised patients were included because of numerous missing data. The Wang and the discomfort scores were clearly underused by practitioners/nurses working in the three general pediatric departments we studied. Tracking the switch in respiratory support was also insufficient. Our population is nonetheless unique, since it is a group of infants affected by bronchiolitis of moderate severity, with little need for oxygen therapy at the time of admission to a general pediatric department. To our knowledge, there is no study to date that focuses on infants younger than 3 months. Moreover, to our knowledge, no study has followed the development of practices taking into account the availability of different respiratory support.

In our study, the hospitalisation rate of children younger than 3 months with bronchiolitis was 52% after admission to the pediatric emergency department. In fact, this population is known to be at risk for rapid worsening and complications [21]. Classically,

bronchiolitis severity substantially decreases after 2 days, no matter the type of medical care offered. Nevertheless, HFNC is the only medical management allowing for a significant decrease in the clinical score within the first 24 h. These findings are in accordance with the literature where early HFNC treatment has been shown to improve respiratory rate, cardiac frequency, and clinical score [6,7,14,15,22,23]. This was confirmed in a randomised study concluding that the first day of disease represents the key period for optimum medical care [16].

The Wang score was higher at the time of inclusion in the HFNC group, probably because infants treated with HFNC were intuitively considered at higher medical risk by physicians. Two prospective randomised surveys, conducted with 202 and 1472 infants requiring oxygen therapy, have demonstrated that therapeutic failures were less frequent in patients receiving HFNC support than in those receiving standard support [17,18]. In these studies, more than half of the patients encountering a failure in standard care with low-flow oxygen therapy, were successfully treated after subsequent HFNC. Our study, which is one of the few to include patients using HFNC in room air [7,15], suggests that these findings equally apply to our population.

Discomfort is not a usual HFNC initiation criterion in the different clinical studies, but it seems to be important for practitioners [19]. In our study, the discomfort score improved faster during the H0–H24 period in patients treated with HFNC than those treated with ONC or ST. However, the EDIN score was

not significantly different in those patients at H24. Comfort appears to be a genuine motivation for the instauration of HFNC by pediatricians, even if the less comfortable patients are probably also the most severe cases.

We show an important decrease in the PICU transfer rate according to the prescription of HFNC. These findings can be easily compared with those of a study conducted in Madrid in 2011, in which the presence of HFNC in general pediatric departments led to a decrease in the PICU transfer rate from 12.8% to 4.8% [7]. Similar findings have been shown in other studies [6,24], as well as a decrease in the intubation rate [9,25]. We were unable to confirm the results of studies showing a shortened hospitalisation duration of 2 or 3 days after HFNC initiation [8,10], which lowered the global cost of hospitalisation [11,26]. This could be explained by a prompt, but not continuous, improvement in the clinical score seen in the infants of our study. Of note, prospective studies on HFNC did not confirm these findings either [17,18]. Whether respiratory support or oxygen therapy duration is modified by HFNC use, is more controversial [6,10,23], especially as there is no standardised protocol regarding their use [14,20].

6. Conclusion

In a real-life setting, use of HFNC seems to improve bronchiolitis symptoms and comfort in infants younger than 3 months, even in those with no associated hypoxia. HFNC helps to minimise the PICU transfer rate. However, larger studies are required to specify its initiation and management modes.

Disclosure of interest

The authors declare that they have no competing interest.

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