

Explore Outcomes of High-Flow Nasal Cannula Versus Classical Oxygen Therapy in Infants with Acute Bronchiolitis: A Comparative Clinical Study

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ABSTRACT

Background: Acute bronchiolitis is a major cause of hospitalization in infancy and supportive oxygen therapy forms an important part of management in hypoxemic patients. High flow nasal cannula (HFNC) therapy has been increasingly used as an alternative to conventional low flow oxygen, particularly in infants with respiratory distress. **Objective:** To compare the clinical outcomes of HFNC therapy with standard oxygen therapy in infants hospitalized with acute bronchiolitis. **Methods:** A comparative clinical study was performed in the general pediatric ward of Karbala Teaching Hospital for Children from January 1 to February 29, 2024 on 100 infants (aged 2–12 months) clinically diagnosed bronchiolitis; standard oxygen therapy (50) and HFNC therapy (50). Standard oxygen was administered through nasal cannula at 1–2 L/min and HFNC at 1–2 L/kg/min with fraction of inspired oxygen adjusted according to oxygen saturation. Clinical severity was assessed by Modified Tal score. The main outcomes were treatment failure, clinical severity after 24 hours and hospital stay length. **Results:** Baseline demographics were similar between the two groups. Initial Modified Tal scores did not differ significantly between standard oxygen and HFNC groups (7.00 ± 1.37 vs. 7.58 ± 2.02 ; $p=0.090$). At 24 hours, clinical severity score was lower in HFNC group than standard oxygen group (5.08 ± 2.28 vs. 6.96 ± 2.09 ; mean difference 1.88; 95% CI 1.03–2.74; $p<0.001$). Mean hospital stay was shorter in HFNC group (3.58 ± 1.26 vs. 4.68 ± 2.76 days; mean difference 1.10 days; 95% CI 0.25–1.95; $p=0.011$). Treatment failure occurred in 19 (38%) infants on standard oxygen but none among infants receiving HFNC. **Conclusion:** In infants hospitalized with acute bronchiolitis HFNC therapy was associated with greater improvement in clinical severity at 24 hours, fewer treatment failures and shorter hospital stay than standard oxygen therapy. Further multicenter studies are needed to confirm these results.

Keywords: Acute Bronchiolitis; High-Flow Nasal Cannula; HFNC; Oxygen Therapy; Infants; Modified Tal Score.

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INTRODUCTION

Acute bronchiolitis is one of the most common lower respiratory tract infections in infancy and an important cause of hospital admission in young children. It is viral disease (respiratory syncytial virus (RSV) accounts for a large proportion of cases), rhinovirus, influenza virus, human metapneumovirus,

adenovirus, parainfluenza virus, coronavirus and human bocavirus may also be involved but clinical course varies considerably from relatively mild respiratory symptoms to severe respiratory distress requiring hospitalization and advanced respiratory support (1–3). Because the bronchiolar diameter is relatively small in infants, clinically significant airway

obstruction occurs more readily than in adults (3) .

Viral infection injures epithelial cells, edema occurs, mucus production increases and cellular debris accumulates in small airways (so airway resistance increases and work of breathing increases; gas exchange may be impaired). Common clinical manifestations are rhinorrhea followed by cough, tachypnea wheezing or crackles chest retractions feeding difficulty hypoxemia (varying degrees) (2). The management of acute bronchiolitis depends mostly on supportive care (4) ; antibiotics, corticosteroids, bronchodilators and epinephrine are not routinely recommended (current guidelines) (5). Instead, maintaining adequate hydration and providing adequate respiratory support remain crucial. In infants with persistent hypoxemia supplemental oxygen is usually given via low-flow nasal cannula; in this specific conventional protocol delivery at 1–2 L/min was titrated to SpO₂ of about 90–94%. Recently heated and humidified high-flow nasal cannula (HFNC) therapy has been adopted more frequently in bronchiolitis treatment (6). HFNC delivers a conditioned air/oxygen mixture at flow rates equal to or greater than the inspiratory demand of the patient. According to proponents of HFNC, oxygenation and work of breathing are improved by washout of dead space nasopharynx, reduced upper-airway resistance, delivery of optimally conditioned gas and modest positive distending airway pressure (7, 8) .

Clinical trial evidence has suggested that HFNC may particularly reduce the need for escalation of respiratory support. For instance, Franklin et al found in a large multicenter randomized trial that escalation of care was less common in infants receiving high flow oxygen compared with those initially managed with standard oxygen (9). Similarly, Kepreotes and his team compared high-flow warm humidified oxygen against standard low-flow oxygen in infants with moderate bronchiolitis (6). More recent systematic reviews have suggested improvement in respiratory parameters and reduction in treatment escalation with HFNC but the magnitude of

benefit across different clinical outcomes is unclear (10, 11) .

Although HFNC therapy is being increasingly used internationally, healthcare settings remain relatively important because access to pediatric intensive care and invasive respiratory support may be constrained. Insights into the utility of HFNC in a general pediatric ward may provide clinical information on whether it can stabilize respiratory status and prevent escalation of care (12, 13). Thus, the present study aimed to compare the clinical outcomes of HFNC therapy with standard oxygen therapy in infants hospitalized for acute bronchiolitis (treatment failure rates, changes in Modified Tal score and overall length of hospital stay).

METHODS

Study design and setting

A comparative clinical study was carried out in general pediatric ward of Karbala Teaching Hospital for Children (Karbala, Iraq) between January 1 and February 29, 2024. A total of 100 infants diagnosed with acute bronchiolitis were included in the study: 50 infants received standard oxygen therapy and 50 HFNC therapy.

Study population

Infants aged 2–12 months with acute bronchiolitis were included. Bronchiolitis was clinically diagnosed (rhinorrhea, cough, tachypnea, wheezing and work of breathing increased). Infants with chronic lung diseases (bronchopulmonary dysplasia, bronchiolitis obliterans, cystic fibrosis or interstitial lung disease) were excluded. Patients with congenital abnormalities or clinical conditions contraindicating HFNC use were also excluded from the study.

Standard oxygen therapy

Infants in the standard oxygen group were given supplemental oxygen by conventional nasal cannula at 1–2 L/min flow rate adjusted to keep SpO₂ between 90% and 94%. 2.4

High-Flow Nasal Cannula Therapy

Infants in the HFNC group received heated and humidified high flow oxygen at 1–2 L/kg/min flow rate. Fraction of inspired oxygen (FiO₂) was adjusted according to patient saturation and clinical condition. HFNC was delivered using AIRVO 2 system (Fisher & Paykel

Healthcare, New Zealand). Patients were monitored by clinical observation, pulse oximetry and regular assessment of vital signs. Flow and FiO₂ were adjusted according to oxygenation and degree of respiratory distress. HFNC was gradually weaned after clinical improvement and stabilization of oxygen saturation; FiO₂ was reduced toward room air before reduction of flow rate.

Clinical diagnoses

Baseline clinical measurements were respiratory rate, heart rate, oxygen saturation, wheezing and accessory muscle use. Respiratory severity was measured by the Modified Tal score (RR, O₂ sat, wheezing/fine crackles and accessory muscle use). Clinical severity was assessed at admission and reassessed 24 h later to see how respiratory support responded.

Clinical outcomes.

There were three main clinical outcomes in the study: treatment failure, change in Modified Tal score and length of hospital stay. Treatment failure was defined as persistent hypoxemia (SpO₂ <90%), persistent tachypnea or persistent tachycardia requiring escalation of respiratory support. Adverse events of interest were pneumothorax, epistaxis, skin injury and abdominal distension.

Statistical analyses

Statistical analyses were performed using SPSS version 26. Continuous variables were summarized as mean $\pm$ standard deviation, whereas categorical variables were presented as frequencies and percentages. Independent-samples t-tests were used for comparisons of continuous variables between groups. Categorical variables were compared using chi-square or Fisher's exact test, as appropriate. A two-sided p value <0.05 was considered statistically significant.

RESULTS

Patients characteristics

A total of 100 infants with acute bronchiolitis were included. 50 received standard oxygen therapy and 50 HFNC, **Table 1**.

Demographic baseline characteristics were similar between groups (mean age 5.98 ± 4.03 months vs 5.42 ± 3.78 months in the standard oxygen group; $p=0.468$) and body weight (6.74

± 2.39 vs 6.25 ± 2.02 kg; $p=0.264$). Sex, mode of delivery, passive smoking exposure, term status, residence or feeding type did not show significant differences.

Modified Tal score

At admission Mean modified Tal score in standard oxygen group was 7.00 ± 1.37 and in HFNC group 7.58 ± 2.02 , there was no significant difference between the groups ($p=0.090$). After 24 hours of treatment clinical severity was

significantly lower in HFNC group. Mean Modified Tal score with HFNC was 5.08 ± 2.28 vs 6.96 ± 2.09 with standard oxygen; between-group mean difference was 1.88 points (95% CI: 1.03–2.74; $p<0.001$). The categorical severity distribution was the same. At baseline there was no significant treatment group $\times$ severity category interaction ($p=0.101$). After 24 h, 32 (64%) infants in HFNC were mild vs 17 (34%) in standard oxygen and no infant in HFNC was severe. The overall distribution differed significantly between groups (Fisher's exact test, $p=0.006$),

Table 2.

Table 1: Shows the baseline characteristics of infants according to treatment groups.

Modified Tal severity	Standard oxygen (n=50)	HFNC (n=50)	p value
At admission			
Mild	7 (14%)	12 (24%)	0.101
Moderate	43 (86%)	36 (72%)	
Severe	0	2 (4%)	
After 24 hours			
Mild	17 (34%)	32 (64%)	0.006
Moderate	31 (62%)	18 (36%)	
Severe	2 (4%)	0	

Table 2: Shows clinical severity at admission and after 24 hours .

Characteristic	Standard oxygen (n=50)	HFNC (n=50)	p value
Age, months	5.98 ± 4.03	5.42 ± 3.78	0.468
Weight, kg	6.74 ± 2.39	6.25 ± 2.02	0.264
Male	33 (66%)	26 (52%)	0.15
Female	17 (34%)	24 (48%)	
Vaginal delivery	23 (46%)	24 (48%)	0.84
Cesarean delivery	27 (54%)	26 (52%)	
Passive smoking	13 (26%)	20 (40%)	0.13
Term birth	48 (96%)	49 (98%)	0.55
Preterm birth	2 (4%)	1 (2%)	
Urban residence	29 (58%)	23 (46%)	0.23
Rural residence	21 (42%)	27 (54%)	
Breastfeeding	23 (46%)	22 (44%)	0.27
Bottle feeding	27 (54%)	28 (56%)	
Data are presented as mean ± SD or n (%).			
Values are mean ± SD or n (%). HFNC, high-flow nasal cannula			

Treatment failure and length of hospital stay

Treatment failure occurred in 19 of 50 infants (38%) on standard oxygen compared to 0 of 50 infants (0%) HFNC; the findings state this difference was statistically significant (p=0.0001). Hospitalization duration was also shorter in infants receiving HFNC. Mean

hospital stay was 3.58 ± 1.26 days for the HFNC group compared with 4.68 ± 2.76 days in standard oxygen group (mean difference = 1.10 days; 95% CI: 0.25–1.95; p=0.011), as shown in Table 3.

Table 3: Major clinical outcomes based to treatment groups.

Outcome	Standard oxygen (n=50)	HFNC (n=50)	p value
Modified Tal score at admission	7.00 ± 1.37	7.58 ± 2.02	0.090
Modified Tal score at 24 h	6.96 ± 2.09	5.08 ± 2.28	<0.001
Hospital stays, days	4.68 ± 2.76	3.58 ± 1.26	0.011
Treatment failure	19 (38%)	0 (0%)	<0.001

DISCUSSION

The present study compared HFNC therapy to standard low-flow oxygen therapy in 100 infants hospitalized with acute bronchiolitis. Three main conclusions were drawn: First, although clinical severity was similar at admission HFNC infants had significantly lower Modified Tal scores after 24 hours; second, treatment failure occurred in 38% of infants on standard oxygen but not in those on HFNC; third, HFNC therapy was associated with a shorter hospital stay. Taken together these results indicate that HFNC was associated with better short term clinical outcome in this population of infants. At baseline the two groups were generally similar in age, weight, sex, gestational status, mode of delivery, residence and feeding pattern. The initial Modified Tal scores were also not different between groups (7.00 ± 1.37 with standard oxygen vs 7.58 ± 2.02 with HFNC; $p=0.090$). This similarity at baseline is important when interpreting subsequent differences in clinical severity but residual confounding cannot be excluded since allocation method was not specified (14–16).

One important finding was that the severity of disease in infants treated with HFNC improved more than standard oxygen. At 24 hours mean Modified Tal score for HFNC was 5.08 ± 2.28 vs 6.96 ± 2.09 (standard oxygen group) which was a mean difference of 1.88

points (95% CI: 1.03–2.74; $p<0.001$) (11). Categorical assessment at 24 hours showed that 64% of infants receiving HFNC were mild disease compared to 34% receiving standard oxygen while no infant in HFNC remained severe. These results are biologically plausible because HFNC has been proposed to have physiological effects. Heated and humidified high-flow gas may reduce nasopharyngeal dead space, decrease inspiratory resistance, improve gas conditioning and generate some positive airway pressure (17, 18). Several important mechanisms may potentially explain the work for breathing reductions and oxygenation improvements, which are broadly consistent with published data (19).

In the 2024 Cochrane review of 16 studies involving 2813 infants HFNC was associated with greater reductions in respiratory and heart rates than low flow oxygen. At 24 hours pooled evidence showed that HFNC reduced respiratory rate more but there was considerable heterogeneity between studies (20, 21). So, the present study adds data on clinical severity score rather than a single physiological parameter (22, 23). Treatment failure was the largest difference between the two study groups. Nineteen of 50 infants (38%) on standard oxygen failed treatment; none of the 50 infants on HFNC did so. This direction of effect is consistent with previous trials and pooled evidence that HFNC reduces the need for escalation of respiratory support: pooled risk ratio for escalation of treatment with HFNC compared with low-flow oxygen in eight studies involving 2,215 infants was 0.55 (95% CI 0.39–0.79) (updated

Cochrane review) (24, 25). However, the complete absence of treatment failure in the HFNC group in the present study should be taken cautiously. Only 50 infants were in each treatment group, and the study does not show random sequence generation or allocation concealment; definitions of treatment failure and thresholds for escalation differ across studies too (hence different observed failure rates). Thus, the present results support an association between HFNC use and reduced treatment failure but they should not be interpreted as showing HFNC eliminates risk of treatment failure. Another clinically relevant finding was the reduction in hospital stay. Infants on HFNC were hospitalized for 3.58 ± 1.26 days versus 4.68 ± 2.76 days for those on standard oxygen; absolute difference of about 1.1 days ($p=0.011$). This finding was consistent in direction with the updated Cochrane evidence but somewhat stronger magnitude in the present study (26, 27).

Seven studies with 1,951 infants were included and HFNC was associated with a mean reduction of hospital stay of 0.65 days (95% CI: 0.06–1.23 days shorter) compared with low-flow oxygen; however, certainty of evidence for this outcome was considered low and heterogeneity substantial (28). Therefore, differences in patient characteristics, disease severity, institutional discharge criteria, HFNC protocols and healthcare resources may affect magnitude of reduction in length of stay. The potential reduction in hospitalization duration might be particularly important in healthcare systems where pediatric beds and higher-level respiratory support are scarce. A shorter hospital stay would reduce bed occupancy and caregiver burden (29). These results should be interpreted with caution because the study was performed at one center and only 100 infants were included (which might limit generalizability). Viral etiology was not evaluated so it could not be determined if response to HFNC differed by respiratory virus causing infection. Adverse

events were not systematically recorded so conclusions about comparative safety cannot be made; details of outcomes after treatment failure (i.e., escalation to intensive care or invasive respiratory support) were not available for analysis.

Although these limitations exist the study provides clinically relevant data on HFNC use for acute bronchiolitis in a general pediatric ward. The improvement of clinical severity, lower treatment-failure rate and shorter hospital stay after HFNC suggest that further evaluation of HFNC in larger prospective multicenter studies with standardized treatment and escalation criteria is warranted.

STRENGTHS AND LIMITATIONS

The study provides clinical data on HFNC use in infants with bronchiolitis in an Iraqi pediatric hospital and several clinically relevant outcomes (treatment failure, change of disease severity, hospital stay) were evaluated. The Modified Tal score also provided a structured assessment of respiratory severity at admission and follow-up. Several caveats should be noted here though. First, this was a single center study with small sample size so generalizability is limited. Second, although the groups were broadly comparable at baseline the current study does not report how treatment allocation was done so cannot rule out selection bias and residual confounding. Third, viral testing was not performed so we could not determine if respiratory virus etiology influenced treatment response; fourth adverse events were not systematically recorded so conclusions about safety cannot be drawn; fifth escalation after failure of treatment, duration of oxygen therapy, admission to intensive care and need for invasive or noninvasive ventilation were not reported as patient level outcomes. Finally, clinical severity was assessed at admission and 24 hours later but repeated longitudinal measurements were not reported (Methods); although the Methods state that clinical

observations were obtained during treatment. Future studies with repeated measurements could describe trajectory and timing of clinical response better.

CONCLUSION

In infants hospitalized with acute bronchiolitis HFNC therapy was associated with greater improvement in Modified Tal clinical severity scores at 24 hours, lower treatment failure rate and shorter hospital stay than standard low-flow oxygen therapy. These results are consistent with evidence that HFNC may be beneficial to the infant requiring respiratory support but single-center design, small sample size, unknown allocation of treatments and absence of systematic adverse event recording make interpretation cautious. Larger prospective multicenter studies with standardized treatment-failure criteria and safety assessment are needed to confirm these findings.

DECLARATION

Ethical approve

The study was ethically approved by the ethical committee from general pediatric ward of Karbala teaching hospital at Karbala province with approval# KTH-SUMS00334. The study followed the ethical principles of the Helsinki Declaration. Written informed consent obtained from parents or legal guardians prior to enrollment.

Authors contributions

L.F. data collection, analyzing, writing original manuscript. A.M. analyzing the data, design, conceptualization. M.A.M. clinical examination, managing, conceptualization. M.Z.A. clinical examination, experimental design, data collection. M.H.A. recording the data, clinical examination. S.J. manuscript revision, statistical analyses and supervision. All authors reviewed and approved the final revision of the manuscript before final submission.

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Conflict of interests

The authors declare that they have no competing of interests.

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