International Journal of Contemporary Pediatrics
Herakal SU et al. Int J Contemp Pediatr. 2024 Aug;11(8):1097-1103
http://www.ijpediatrics.com
pISSN 2349-3283 | eISSN 2349-3291

DOI: https://dx.doi.org/10.18203/2349-3291.ijcp20242021

Original Research Article

High flow nasal cannula therapy versus standard oxygen therapy in bronchiolitis: a prospective randomized control trial

Santosh U. Herakal*, Shivakumar Indi, Naushad Ali N. Malagi, A. N. Thobbi

Department of Paediatrics, Al-Ameen Medical College, Vijayapura, Karnataka, India

Received: 18 June 2024
Revised: 15 July 2024
Accepted: 20 July 2024

***Correspondence:**
Dr. Santosh U. Herakal,
E-mail: santustill20@gmail.com

ABSTRACT

Background: Bronchiolitis is most common respiratory infection in infants and treatment focuses on management of respiratory distress and hypoxia. The clinical effectiveness of HFNC therapy in bronchiolitis has been reported only in non-experimental observational studies and also there is scarcity of high-grade evidence about HFNC usage in bronchiolitis, hence we intend to study the effectiveness of HFNC in bronchiolitis through prospective randomized control study.
Methods: It is prospective randomized control trial conducted at pediatric ward/ ICU at department of paediatrics, Al Ameen medical college, Bijapur from January 2023 to April 2024 all children diagnosed as bronchiolitis aged between 2 to 24 months were included. All of study participants had thorough histories obtained, including demographic information, vital parameters including SaO_2 in room air. (Clinical severity score) by modified Wood's clinical asthma score (M-WCAS) at admission and 2nd hourly till oxygen support is completely weaned off. Treatment failure is defined as meeting ≥3 out of 4 clinical criteria: persistent tachycardia, tachypnea, hypoxemia and decision of escalation by treating doctor. Primary outcome was treatment failure and need of escalation of therapy.
Results: A total of 65 cases are randomized, among them 33 cases are allocated to standard oxygen therapy and 32 cases to high flow nasal cannula group. HFNC group showed lower proportion of treatment failure than standard oxygen therapy group ($p<0.0005$). Secondary outcomes are also compared with previous studies.
Conclusions: HFNC group showed lower proportions of treatment failure than standard oxygen therapy.

Keywords: Bronchiolitis, Oxygen saturation, Respiratory rate, HFNC

INTRODUCTION

Bronchiolitis is an acute inflammatory condition of the bronchioles that is a result of virus-induced injury. Bronchiolitis is a clinical syndrome of respiratory distress that occurs in children <2 years of age and is characterized by upper respiratory symptoms (e.g., rhinorrhoea) followed by lower respiratory infection with inflammation, which results in wheezing and/or crackles (rales).[1-3] The symptoms are usually mild and may only last for a few days, but in some cases the disease can cause severe illness.[4]

The American academy of paediatrics (AAP) defines bronchiolitis as 'acute inflammation, oedema and necrosis of epithelial cells lining small airways, increased mucus production, and bronchospasm.[5]

Bronchiolitis typically occurs with primary infection or reinfection with a viral pathogen.[1-3] Bronchiolitis typically affects children younger than two years with a peak incidence between two and six months of age.[6]

Bronchiolitis can manifest as full spectrum of severity, from mild tachypnoea and expiratory wheezing to profound, acute, life-threatening respiratory failure as a

result of near-complete lower respiratory tract obstruction and inflammation.[7]

The proven approach for management of children with bronchiolitis is focused on oxygen therapy for hypoxia correction, respiratory support and maintaining hydration. Various treatment options have been proposed, of which only nebulised epinephrine and hypertonic saline have been shown to be useful.[8,9] Respiratory support is common domain of intensive care settings, and this can be provided by oxygen therapy through non-invasive ventilation to invasive ventilation. Invasive ventilation needs highly professional staff and are associated with more incidence of adverse events viz. ventilator induced lung trauma, barotraumas, and neurological problems associated with sedation, so non-invasive ventilations are more preferred now a days. HFNC is one among the non-invasive ventilation tried recently.

A pilot study involving 61 infants with bronchiolitis using a flow rate of 2l/kg/min showed that HFNC therapy can be safely delivered in a general pediatric ward and admission rate to ICU could be significantly reduced by 2.5 times when compared to standard sub-nasal oxygen therapy group.[10]

Two non-randomized study designs using HFNC therapy have shown a reduction in intubation rate in critically ill infants with the bronchiolitis in intensive care setting.[11,12]

A recent retrospective study showed that HFNC therapy has same effectiveness as that of nasal CPAP in pediatric intensive care unit with 25% escalation to invasive ventilation. Recently reports on usage of HFNC showed good safety profile with rarely requiring sedation when compared to mask delivered non-invasive ventilation.[13]

The clinical effectiveness of HFNC therapy in bronchiolitis has been reported only in non-experimental observational studies and there is deficiency of randomized studies which are appropriate and have clearly defined clinically meaningful outcomes, and also, there is scarcity of high-grade evidence about HFNC usage in bronchiolitis, hence, we wanted to study effectiveness of HFNC in bronchiolitis through prospective randomized control study.[10,14]

METHODS

Source of data

All children diagnosed as bronchiolitis aged between 2 months to 24 months admitted to pediatric ward/ ICU at department of pediatrics, Al Ameen medical college, Bijapur from Jan 2023 to April 2024 after getting approval from institutional ethical committee.

Type of study

It is a prospective randomised control trial.

Inclusion criteria

Children with a clinical diagnosis of bronchiolitis (as defined by the American academy of pediatrics)-symptoms and signs of respiratory distress and oxygen requirement in room air are eligible, aged 2 months to 24 months with an oxygen requirement in room air of SpO_2<94% were included.

Exclusion criteria

Children with urgent need for respiratory support i.e. ventilation by invasive or non-invasive methods and with Low level consciousness, apnoea, cyanotic heart disease, fracture of skull and craniofacial anomalies were excluded from study.

Methods of collection of data

Hypothesis

HFNC therapy will have a lower failure proportion, reduced requirement of intubation, reduced length of stay and reduced length of oxygen therapy in compare to standard sub nasal oxygen.

Randomisation

A computer-generated randomisation will be used to allocate children at 1:1 ratio.

Control arm (Standard oxygen therapy)

Children that are randomized to the control arm will be put on standard sub-nasal cannula with oxygen flows up to maximum of 2 L/min to maintain SpO_2 between 94-98%. Oxygen flows should start from minimal flow rate initially and increased as required (administered maximum of 2 L/min) to maintain SpO_2≥94%. Weaning from oxygen was done at any time to provide the lowest possible oxygen level delivered to maintain an oxygen saturation level of at least 94%.

HFNC therapy arm

Children that are randomized to the HFNC therapy arm with SpO_2 85-93% will be placed on high flow at 2 L/kg/min (up to a maximum of 25 L/min) in room air equating to a fraction of inspired oxygen of 21% (FiO_2). The infant that is randomized to the HFNC therapy arm with SpO_2<85% will commence on high flow with FiO_2 slowly increasing to achieve SpO_2≥94%. If SpO_2 has not altered or improved then the FiO_2 will be slowly increased to maintain SpO_2≥94%. HFNC therapy was stopped after 4 hours of receiving an FiO_2 of 21% while oxygen levels were maintained in expected range.

Treatment failure is defined as fulfilling three out of four specified failure criteria requiring higher treatment

options like intubation. Before escalation to higher treatment 2 to 3 hours of observing children is suggested.

Table 1: Clinical severity score; M-WCAS.

Variables	0	1	2
SpO_2	SpO_2 ≥95%	SpO_2≥90% with FiO_2>21%	SpO_2<90% with FiO_2>21%
Inspiratory breath sounds	Normal	Markedly unequal	Decreased/ absent
Expiratory wheezing	None	Moderate	Marked
Accessory muscles	None	Moderate	Maximal
Cerebral functions	Normal	Depressed/ agitated	Markedly depressed, coma

Interpretation of M-WCAS-Score 0-3: mild distress, score 4-6: moderate distress and score >6: severe distress.

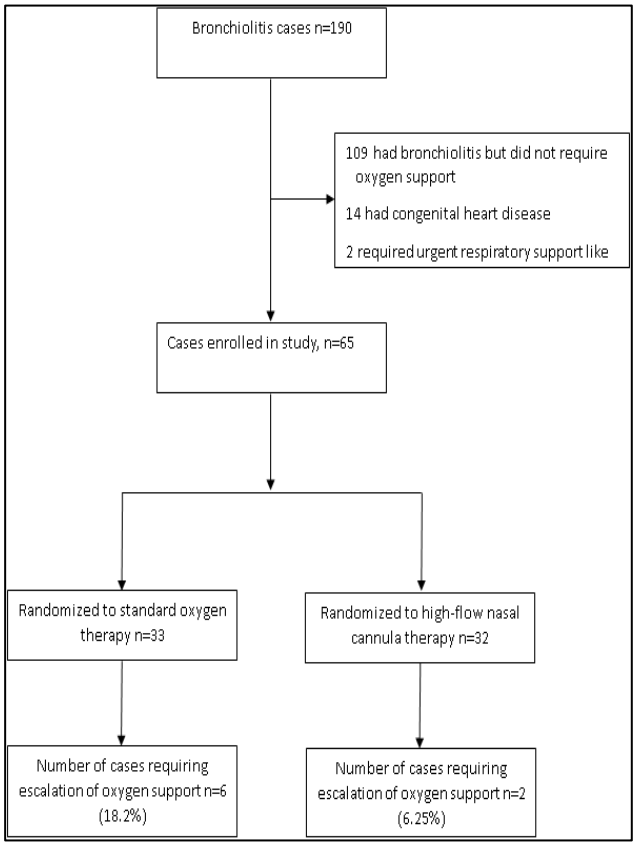

Figure 1: Number of infants who were screened, assigned a trial group and included in primary analysis.

Heart rate remains unaltered or increased compared to admission observations. Respiratory rate remains unchanged or increased compared to admission observations. In HFNC therapy, oxygen therapy requiring FiO_2>40% to maintain SpO_2>94% or in standard sub nasal oxygen therapy arm exceeding >2 l/min to maintain SpO_2>94%. If treating unit/team feels there is need to escalate therapy

Clinical severity is assessed (Clinical severity score) by M-WCAS at admission and 2nd hourly till oxygen support is completely weaned off.

Statistical analysis

Data was entered into Microsoft ® excel and analysed using R statistical software version 3.1 and IBM SPSS Ver. 25 software. Continuous data were summarised as Mean (SD) and categorical data were summarized as frequency (percentage).

Continuous variables were analysed using student t test, categorical data were analysed using chi-square test. Kaplan Meir plot and log rank analysis was used to test the difference in treatment failure (Escalation) between two groups.

Cox regression (or proportional hazards regression) was used to assess the association between intervention and treatment failure (Escalation) rate. P<0.05 was considered statistically significant. Microsoft excel and Microsoft word 2007 was used to obtain various types of graphs.

RESULTS

Out of 65 cases, 33 were randomised into standard oxygen therapy, 32 were randomised into HFNC group. Among randomized cases 43 were males and 22 were females with mean age in males being 8.79 months and 7.36 months in females (Table 2).

In our study cough is the most common symptom, 84.6% cases. Cold was there in 44.6% cases, hurried breathing in 41.5% cases, fever in 36.9 % cases, retraction in 35.4% cases and noisy breathing in 27.7 percentage's cases (Table 3).

Among the all case all had tachypnea, 9 cases (13.8%) were febrile, 10 cases (15.4%) were pale, 8 (12.3%) cases were irritable, 9 (13.8%) cases had pallor, 10 cases (15.4%) were irritable.

Table 2: Demographic characteristics of both groups.

Variables	SOT (n=33) (%)	HFNC (n=32) (%)	Total (n=65) (%)
Age			
<6 months	16 (48.5)	13 (40.6)	29 (44.61)
7-12 months	10 (30.3)	15 (46.9)	25 (38.5)
>12 months	7 (21.2)	4 (12.5)	11 (16.92)
Mean (SD)	7.96 (5.74)	8.59 (6.01)	8.27 (5.84)
Gender			
Male	25 (75.8)	18 (56.3)	43 (66.2)
Female	8 (24.2)	14 (43.8)	22 (33.8)

Table 3: Comparison of symptoms, vital and lab parameters.

Variables		Standard, (n=33) (%)	HFNC, (n=32) (%)	Total, (n=65) (%)	P value
Symptoms					
Cough	Absent	4 (12.1)	6 (18.8)	10 (15.4)	0.459
	Present	29 (87.9)	26 (81.3)	55 (84.6)	
Retractions	Absent	19 (57.6)	23 (71.9)	42 (64.6)	0.228
	Present	14 (42.4)	9 (28.1)	23 (35.4)	
Cold	Absent	19 (57.6)	17 (53.1)	36 (55.4)	0.718
	Present	14 (42.4)	15 (46.9)	29 (44.6)	
Fever	Absent	22 (66.7)	19 (59.4)	41 (63.1)	0.543
	Present	11 (33.3)	13 (40.6)	24 (36.9)	
Hurried breathing	Absent	23 (69.7)	15 (46.9)	38 (58.5)	0.062
	Present	10 (30.3)	17 (53.1)	27 (41.5)	
Noisy breathing	Absent	22 (66.7)	25 (78.1)	47 (72.3)	0.302
	Present	11 (33.3)	7 (21.9)	18 (27.7)	
Vital parameters					
RR grade	Normal	0 (0)	0 (0)	0 (0)	NA
	Tachypnoea	33 (100)	32 (100)	65 (100)	
Temperature grade	Normal	27 (81.8)	29 (90.6)	56 (86.2)	0.304
	Febrile	6 (18.2)	3 (9.4)	9 (13.8)	
Peripheries	Warm	33 (100)	32 (100)	65 (100)	NA
	Cold	0 (0)	0 (0)	0 (0)	
Conscious level	Normal	30 (90.9)	27 (84.4)	57 (87.7)	0.423
	Altered	3 (9.1)	5 (15.6)	8 (12.3)	
Pallor	Absent	26 (78.8)	30 (93.8)	56 (86.2)	0.081
	Present	7 (21.2)	2 (6.3)	9 (13.8)	
Icterus	Absent	33 (100)	32 (100)	65 (100)	-
	Present	0 (0)	0 (0)	0 (0)	
Cyanosis	Absent	31 (93.9)	24 (75)	55 (84.6)	0.034*
	Present	2 (6.1)	8 (25)	10 (15.4)	
Edema	Absent	33 (100)	32 (100)	65 (100)	-
	Present	0 (0)	0 (0)	0 (0)	
Lab parameters					
HB grade	Normal (≥11)	7 (21.2)	13 (40.6)	20 (30.8)	0.055
	Mild (10-10.9)	13 (39.4)	4 (12.5)	17 (26.2)	
	Moderate (7-7.9)	13 (39.4)	14 (43.8)	27 (41.5)	
	Severe (<7)	0 (0)	1 (3.1)	1 (1.5)	
TLC grade	Normal	31 (93.9)	32 (100)	63 (96.9)	0.157
	Leucopenia	2 (6.1)	0 (0)	2 (3.1)	
	Leucocytosis	0 (0)	0 (0)	0 (0)	
Platelet grade	Normal	15 (45.5)	16 (50)	31 (47.7)	0.826
	Thrombocytopenia	2 (6.1)	1 (3.1)	3 (4.6)	
	Thrombocytosis	16 (48.5)	15 (46.9)	31 (47.7)	
X ray findings	Normal	0 (0)	0 (0)	0 (0)	NA
	Bronchiolitis	33 (100)	32 (100)	65 (100)	

*Chi-square test, p value not significant.

Table 4: Comparison of clinical severity scores among the groups.

Variables	Standard		HFNC		P value
	Mean (SD)	Median (IQR)	Mean (SD)	Median (IQR)	
CS score at admission	4.94 (0.93)	5 (4-6)	5.22 (1.04)	5 (4.5-6)	0.258
CS score at 2 hrs	4.45 (0.83)	4 (4-5)	4.48 (0.81)	4 (4-5)	0.713
CS score at 4 hrs	3.91 (0.77)	4 (3-4)	4.29 (0.78)	4 (4-5)	0.031*
CS score at 6 hrs	3.42 (0.61)	3 (3-4)	3.9 (0.75)	4 (3-4)	0.004*
CS score at 8 hrs	3.18 (0.64)	3 (3-4)	3.58 (0.85)	3 (3-4)	0.022*
CS score at 10 hrs	2.94 (0.7)	3 (2-3)	3.42 (0.76)	3 (3-4)	0.008*

*Chi-square test, p value significant.

Clinical severity

Clinical severity score at admission was assessed. There were 2 cases categorized to mild distress, 58 cases to moderate and 5 cases to severe respiratory distress. Clinical severity of patients described in the Table 4.

Primary outcome and secondary outcomes

Kaplan-Meier survival analysis was conducted to compare the two different interventions for their effectiveness in preventing treatment failure. The percentage of censored cases present in the standard therapy (81.8%), and HFNC (93.8%) groups was not similar. Participants that underwent the HFNC therapy had a median escalation free time of 168 hrs days. This was longer than the groups receiving Standard therapy which had median escalation free time of 26 Hrs. A log rank test was conducted to determine if there were differences in the survival distributions for the different types of intervention. The survival distributions for the two interventions were statistically significantly different, $\chi^2(2)=12.7$, $p<0.0005$.

There was requirement of escalation as low flow, dry oxygen has no effect on distention of alveoli, whereas HFNC delivers fixed concentration of oxygen, generation of positive end-expiratory pressure, reduction of the work of breathing and clearance of the nasopharyngeal dead space, while providing optimal gas conditioning.[15]

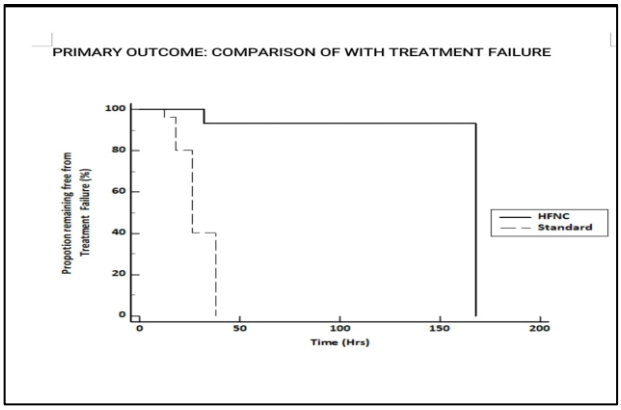

Figure 2: Kaplan-Meier plot of the proportion of infants with bronchiolitis remaining free from treatment failure.

After adjusting for age, gender and CS (Clinical severity) score at admission, children with standard intervention experienced a significantly higher risk of escalation during follow-up than children with HFNC (RR=46.72, 95% CI 2.86 to 761.94, p=0.007).

Table 5: Number of treatment failures in each group.

Intervention	Total	No. of events (Treatment failures)	Censored	
			N	Percent (%)
Standard	33	6	27	81.80
HFNC	32	2	30	93.80

Table 6: Comparison of mean and median escalation free time.

Intervention	Mean escalation free time				Median escalation free time				Log rank
	Estimate	SE	95% CI		Estimate	SE	95% CI		
			Lower	Upper			Lower	Upper	
Standard	29.04	4.01	21.17	36.90	26	5.73	14.78	37.22	$\chi^2=12.7$, $p<0.005$
HFNC	158.93	12.39	134.65	183.21	168	NA	NA	NA	

Table 7: Comparison of secondary outcomes.

		SOT	HFNC
Total length of stay (In days)	Mean (SD)	3.79 (1.54)	4.75 (2.27)
	Median (IQR)	4 (3-5)	5 (3-6)
Duration of oxygen therapy (in hours)	Mean (SD)	16.73 (6.87)	25.75 (15.73)
	Median (IQR)	18 (12-18)	21 (14-36)
Intubation rate	Not intubated	33	30
	Intubated	0	2
	Intubation rate	0	6.25
Adverse events		0	0

DISCUSSION

Bronchiolitis is a common respiratory tract infection below the age of 12 months.[5] The diagnosis of bronchiolitis is mainly clinical. The mainstay of current management is supportive care, which mostly consists of hydration and humidified oxygen. There is currently

nonspecific treatment for bronchiolitis that has sufficient or persuasive data supporting its efficacy.

Humidified oxygen can be delivered through high-flow nasal cannula. According to the research that are now available, HFNC is a method for administering oxygen to children that is generally safe, well-tolerated, and practicable. Compared to a face mask, it is more tolerable. According to a retrospective study conducted by Schibler found that the usage of HFNC therapy in children with acute bronchiolitis increased, leading to a marked decline in the intubation rate from 37% to 7%.[12] The clinical effectiveness of HFNC therapy in bronchiolitis has been reported only in non-experimental observational studies. In our open labelled, single centre, prospective randomized control trial involving infants with bronchiolitis, we observed that significantly fewer children require escalation of oxygen support in HFNC arm than in standard oxygen therapy arm.

Age

A total of 65 cases were randomized in this trial, the mean age of presentation is 8.27 (±5.84) months. Most common age group affected is <6 months (44.6%), followed by 7 months to 12 months (38.5%) and then >12 months (16.9%). Similar finding is noted in a study where >70% cases belonged to infant age group.[16] Mean age in children belonging to sot group was 7.96(±5.74) months and 8.59(±6.01) in HFNC group. In a study conducted by Franklin et al mean age in sot group was 6.1 months and 5.76 in HFNC group.[7] Majority of cases are noted in the infancy, this is probably secondary to decreased immunity towards viral infection in that age group.[17]

Gender

In our study, male children are affected predominantly with male to female ratio of 1.95:1. These results are comparable to other studies.[19-21] there was increased incidence of bronchiolitis in a male probably due to the increased sensitivity of males to aeroallegerns.[18]

Clinical features

In our study most common presenting complaint was cough (84.6%) and other symptoms in the order of frequency are cold (44.6%), hurried breathing (41.5%), fever (36.9%), retraction (35.4%), noisy breathing (27.7%). The findings are comparable with other study.[17] But none of these findings were statistically significant.

Primary outcome: groups with treatment failure

In our study, we found that significantly fewer infants in the high-flow group than in the standard therapy group received escalated ($p<0.0005$). In SOT group, there was treatment failure in 6 cases (18.2%) compared only two cases (6.3%) in HFNC group.

Kaplan-Meier survival analysis was conducted to compare the two different interventions for their effectiveness in preventing treatment failure. The percentage of censored cases present in the standard therapy (81.8%), and HFNC (93.8%) groups was not similar. Participants that underwent the HFNC therapy had a median escalation free time of 168 hrs which was longer than the groups receiving standard therapy which had median escalation free time of 26 Hrs. A log rank test was conducted to determine if there were differences in the survival distributions for the different types of intervention. The survival distributions for the two interventions were statistically significantly different, $\chi^2(2)=12.7$, $p<0.0005$. Our results are supported by a RCT with similar results, which demonstrated a lower failure rate in HFNC group than in the SOT group (14% vs 33%).[16]

Secondary outcomes

The mean total length of stay in hospital in SOT group is 3.79(±1.54) days, compared to 4.75(±2.27) days in HFNC group. This finding was not statistically significant ($p>0.05$). This finding is supported by RCTs.[7,16] It is observed that intubation rate in HFNC arm is compared to standard oxygen therapy. As per protocol treatment failure in a case due to respiratory support should be scaled up, hence HFNC arm received invasive mechanical ventilation. Likewise in study by Schiebler et al the rate of intubation reduced from 37% to 7%.[12] Duration of oxygen therapy is observed more in HFNC group and it is statistically significant ($p<0.05$) compared to standard oxygen therapy. Likewise in a study by Milani et al duration of oxygen therapy is less in HFNC group 2 days less than SOT.[22] No adverse events (pneumothorax, gastric distension, pneumonia).

Strengths

Prospective randomized control trial.

Limitations

Oxygen delivery method could not be concealed. Follow up cases could not be done.

CONCLUSION

In our study we observed that, a considerably lower rate of treatment failure is observed in HFNC group compared to standard oxygen therapy. Hence, we conclude that HFNC is a better option than standard oxygen therapy.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Bordley WC, Viswanathan M, King VJ, Sutton SF, Jackman AM, Sterling L, et al. Diagnosis and testing in bronchiolitis: a systematic review. Arch Pediatr Adolesc Med. 2004;158(2):119-26.
2. Fitzgerald DA, Kilham HA. Bronchiolitis: assessment and evidence-based management. Med J Aust. 2004;180(8):399-404.
3. Ralston SL, Lieberthal AS, Meissner HC, Alverson BK, Baley JE, Gadomski AM, et al. Clinical practice guideline: the diagnosis, management, and prevention of bronchiolitis. Pediatrics. 2014;134(5):e1474-502.
4. Ricci V, Nunes VD, Murphy MS, Cunningham S. Bronchiolitis in children: summary of NICE guidance. Bmj. 2015;350:h2305.
5. American Academy of Pediatrics. Subcommittee on Diagnosis and Management of Bronchiolitis. Diagnosis and management of bronchiolitis. Pediatrics. 2006;118:1774-93.
6. Verma N, Lodha R, Kabra SK. Recent advances in management of bronchiolitis. Indian pediatrics, 2013;50(10):939-49.
7. Franklin D, Babl FE, Schlapbach LJ, Oakley E, Craig S, Neutze J, et al. A Randomized Trial of High-Flow Oxygen Therapy in Infants with Bronchiolitis. N Engl J Med. 2018;378(12):1121-31
8. Hartling L, Bialy LM, Vandermeer B, Tjosvold L, Johnson DW, Plint AC, et al. Epinephrine for bronchiolitis. Cochrane Database Syst Rev. 2011(6):CD003123.
9. Zhang L, Mendoza-Sassi RA, Wainwright C, Klassen TP. Nebulised hypertonic saline solution for acute bronchiolitis in infants. Cochrane Database Syst Rev 2017;(12):CD006458.
10. Mayfield S, Bogossian F, O'Malley L, Schibler A. High-flow nasal cannula oxygen therapy for infants with bronchiolitis: Pilot study. J Paediatr Child Health. 2014;50(5):373-8.
11. Keenan SP, Sinuff T, Cook DJ, Hill NS. Does noninvasive positive pressure ventilation improve outcome in acute hypoxemic respiratory failure? A systematic review. Crit Care Med. 2004;32(12):2516-23.
12. Schibler A, Pham TM, Dunster KR, Foster K, Barlow A, Gibbons K, et al. Reduced intubation rates for infants after introduction of high-flow nasal prong oxygen delivery. Intensive Care Med. 2011;37(5):847-52.
13. Ten Brink F, Duke T, Evans J. High-flow nasal prong oxygen therapy or nasopharyngeal continuous positive airway pressure for children with moderate-to severe respiratory distress? Pediatr Critical Care Med. 2013;14(7):e326-31.
14. Lazner MR, Basu AP, Klonin H. Non-invasive ventilation for severe bronchiolitis: analysis and evidence. Pediatr Pulmonol. 2012;47(9):909-16.
15. Nolasco S, Manti S, Leonardi S, Vancheri C, Spicuzza L. High-Flow Nasal Cannula Oxygen Therapy: Physiological Mechanisms and Clinical Applications in Children. Frontiers Med. 2022;9:920549.
16. Kepreotes E, Whitehead B, Attia J, Oldmeadow C, Collison A, Searles A, et al. High-flow warm humidified oxygen versus standard low-flow nasal cannula oxygen for moderate bronchiolitis (HFWHO RCT): an open, phase 4, randomised controlled trial. The Lancet. 2017;389(10072):930-9.
17. Guilbert TW, Morgan WJ, Zeiger RS, Bacharier LB, Boehmer SJ, Krawiec M, et al. Atopic characteristics of children with recurrent wheezing at high risk for the development of childhood asthma. J Allergy Clin Immunol. 2004;114(6):1282-7.
18. Kulhalli P, Dakshayini JN, Ratageri VH, Shivanand I, Wari PK. Risk factors for bronchiolitis. Indian Academy Pediatr. 2020;7(2):79.
19. Nagayama Y, Tsubaki T, Nakayama S, Sawada K, Taguchi K, Tateno N, et al. Gender analysis in acute bronchiolitis due to respiratory syncytial virus. Pediatric Allergy Immunol. 2006;17(1):29-36.
20. Boezen HM, Jansen DF, Postma DS. Sex and gender differences in lung development and their clinical significance. Clin Chest Med. 2004;25(2):237-45
21. Simoes EA. Environmental and demographic risk factors for respiratory syncytial virus lower respiratory tract disease. J Pediatr. 2003;143(5):118-26
22. Milani GP, Plebani AM, Arturi E, Brusa D, Esposito S, Dell'Era L, et al. Using a high-flow nasal cannula provided superior results to low-flow oxygen delivery in moderate to severe bronchiolitis. Acta Paediatr. 2016;105(8):e368-72.

Cite this article as: Herakal SU, Indi S, Malagi NAN, Thobbi AN. High flow nasal cannula therapy versus standard oxygen therapy in bronchiolitis: a prospective randomized control trial. Int J Contemp Pediatr 2024;11:1097-103.