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ORIGINAL ARTICLE

Prevalence of high flow nasal cannula therapy use for management of infants with bronchiolitis in Australia and New Zealand

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Aim: To determine the prevalence of high flow nasal cannula (HFNC) therapy in infants presenting to hospital in Australia and New Zealand with bronchiolitis over four bronchiolitis seasons. Secondary aims were to determine temporal trends in HFNC use, and associations between HFNC, hospital length of stay (LOS) and intensive care unit (ICU) admission.

Methods: A planned sub-study of a multi-centre international cluster randomised controlled trial investigating knowledge translation strategies for a bi-national bronchiolitis guideline. Demographics, management and outcomes data were collected retrospectively for infants presenting with bronchiolitis to 26 hospitals between 1 May 2014 and 30 November 2017. Prevalence data are presented as absolute frequencies (95% confidence interval (CI)) with differences between groups for continuous and categorical variables analysed using linear and logistic regression, respectively.

Results: 11 715 infants were included with 3392 (29.0%, 95% CI (28.1–29.8%)) receiving oxygen therapy; of whom 1817 (53.6%, 95% CI (51.9–55.3%)) received HFNC. Use of oxygen therapy did not change over the four bronchiolitis seasons ($P = 0.12$), while the proportion receiving HFNC increased (2014, 336/2587 (43.2%); 2017, 609/3720 (57.8%); $P \leq 0.001$). Infants who received HFNC therapy were not substantially different to infants who received oxygen therapy without HFNC. HFNC use was associated with increases in both hospital LOS ($P < 0.001$) and ICU admissions ($P < 0.001$).

Conclusion: Use of HFNC therapy for infants with bronchiolitis increased over 4 years. Of those who received oxygen therapy, the majority received HFNC therapy without improvement in hospital LOS or ICU admissions. Strategies to guide appropriate HFNC use in infants with bronchiolitis are required.

Key words: bronchiolitis; high flow; infant; prevalence.

What is already known on this topic

1 Bronchiolitis is the most common reason for admission to hospital in infants less than 12 months.
2 High Flow Nasal Cannulae (HFNC) therapy use has increased in frequency for infants with bronchiolitis over recent years.
3 Evidence-based guidelines recommend the use of HFNC as a rescue therapy for infants with bronchiolitis when standard low flow oxygen therapy has been trialled and failed.

What this paper adds

1 Quantifies the increase in use of HFNC therapy over a four-year period.
2 Highlights the potential increase in length of stay and intensive care unit (ICU) admissions and health care costs if HFNC is utilised inappropriately.

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In infants less than 12 months of age, bronchiolitis is the most common reason for emergency visits and admission to hospital in the developed world.[1–3] Bronchiolitis management is well defined and is largely supportive focusing on maintaining oxygenation and hydration.[4]

Respiratory support for infants with bronchiolitis has routinely been provided by standard low flow oxygen (LFO) delivered via nasal prongs or masks. Over the last decade, the use of high flow nasal cannula (HFNC) therapy has been increasingly used for respiratory support in infants with bronchiolitis in emergency departments (EDs) and paediatric inpatient settings.[5] This form of non-invasive ventilation delivers humidified heated gas (comprising a blend of oxygen and air) into the nasal passages at flow rates of up to 2–3 l/kg/min compared to standard oxygen delivery via nasal prongs which has a flow rate of 2–3 l/min.[6] Initially, HFNC was used in intensive care unit (ICU) settings with retrospective observational evidence suggesting an association with reduced intubation and invasive ventilation.[7,8] Recent randomised controlled trial (RCT) evidence from EDs and paediatric inpatient wards found no evidence for reduced ICU admissions or hospital length of stay (LOS). Further, current evidence does not support the use of HFNC therapy for work of breathing in the absence of hypoxia or for severe disease in infants with bronchiolitis.[5]

In the largest RCT to date, which compared HFNC therapy versus LFO therapy in 1472 infants with hypoxic bronchiolitis, 23% of the infants in the LFO arm were rescued with HFNC therapy[9] and there were no benefits attributable to HFNC in respect to duration of hospital stay, duration of stay in the ICU, duration of oxygen therapy or rates of intubation. The proportion of infants with bronchiolitis requiring rescue HFNC therapy may be overinflated in the study, as only 16% of the LFO therapy arm participants fulfilled ≥3 out of 4 predetermined physiological failure criteria. The RCT had an eligible population of 2217 possible participants with a further 156 (7% of 2217 + 156) excluded as they were deemed too unwell and admitted directly to ICU. Together these data suggest that rescue HFNC therapy should only be considered in 22% (7% + 16%) to 30% (7% + 23%) of all patients presenting with bronchiolitis (i.e. considered in all those who are directly admitted to ICU or who fail standard LFO therapy).

The Australasian bronchiolitis guideline states that '*HFNC oxygen in bronchiolitis can be considered in the inpatient setting on infants with bronchiolitis with hypoxia (oxygen saturations < 92%). Its use in children without hypoxia should be limited to the RCT setting only*'.[10] In addition, HFNC therapy increases costs in the management of bronchiolitis in comparison to LFO therapy.[11] Therefore, it is necessary to determine the current prevalence of HFNC therapy use in patients presenting with bronchiolitis, and if HFNC therapy is being used excessively. If excessive use is found, intervention programmes should be considered to rationalise HFNC use, benefiting both infants (through avoidance of inappropriate therapy) and health-care systems (through avoidance of unnecessary cost).[5,11]

We hypothesize that HFNC therapy use in infants presenting to hospital with bronchiolitis is increasing over time, and that HFNC therapy is being used outside of international guideline recommendations. The primary aim of this study was to determine the prevalence of HFNC therapy use in infants presenting to hospital with bronchiolitis over four bronchiolitis seasons. The secondary aims were to determine temporal trends in HFNC use over the four bronchiolitis seasons, and the association between HFNC use and hospital LOS and ICU admission.

Methods

Design

This retrospective prevalence study was a planned sub-study of a multi-centre international cluster RCT of targeted, theory-informed knowledge translation interventions compared to passive dissemination of a bi-national bronchiolitis guideline for management of infants presenting to hospital with bronchiolitis[12] conducted by the Paediatric Research in Emergency Departments International Collaborative (PREDICT) network.[13] The cluster RCT found that targeted, theory-informed knowledge translation interventions improved guideline compliance for five key recommendations (no use of chest radiography, salbutamol, glucocorticoids, antibiotics and adrenaline) by 14.1% (95% confidence interval [CI] 6.5–21.7%).[14] In this study, we report respiratory management over the four seasons.

Human Research Ethics Committee approval was granted by the Royal Children's Hospital (EC00238), Australia (HREC/16/RCHM/84), and the Northern A Health and Disability Ethics Committee, New Zealand (16/NTA/146). The RCT was prospectively registered with the Australian New Zealand Clinical Trials Registry (ACTRN 12616001567415).

Setting

This study was undertaken in the EDs and paediatric inpatient wards of 26 hospitals (20 in Australia; 6 in New Zealand; 7 tertiary hospitals (defined as having a dedicated paediatric ICU); 19 secondary hospitals). Hospitals were eligible for participation if they had >135 bronchiolitis ED presentations/year and data could be collected retrospectively from medical records.

Sample/population

Over the four bronchiolitis seasons (1 May 2014 to 30 November 2017), medical records were eligible for inclusion if they were of infants: aged <1 year at hospital presentation and had a diagnosis of bronchiolitis both in ED and as a final discharge diagnosis (regardless of discharge location). There were no exclusion criteria.

All eligible infants were retrospectively identified and a random selection from each hospital was generated using Research Electronic Data Capture (REDCap) version 8.5.1 (Vanderbilt University).

Data were collected on 100 infants per year per hospital from 2014 to 2016, 150 infants per hospital for 2017, or for as many infants as met inclusion criteria if <100 or <150 infants presented.

Data collection

Data collection from the medical records occurred from December 2017 to 2018. Staff who had undergone training in the use of a standardised data collection tool collected data and

entered it into the REDCap study database, housed at Murdoch Children's Research Institute (MCRI), Australia. During site visits, study personnel audited data entry for reliability and accuracy.

Outcome measures

Infants were defined as receiving oxygen therapy if they received LFO therapy via nasal prongs or mask, HFNC therapy, non-invasive ventilation (continuous positive airway pressure (CPAP), bilevel positive airway pressure (BiPAP)) or invasive ventilation (via endotracheal tube). Infants were defined as receiving HFNC therapy if they received HFNC therapy alone, or with any other respiratory support (LFO via nasal prongs or mask, non-invasive ventilation or invasive ventilation) during their hospital management.

Statistical analysis

Sample size calculations for the cluster RCT trial were based on the hospitals having >135 bronchiolitis presentations per year ($n = 26$ hospitals).[15] A power calculation was not undertaken *a priori* for this current study. Data are presented as absolute and relative frequencies for categorical data and mean (SD) or median (interquartile range (IQR)) for continuous data as appropriate. Prevalence data are presented as absolute and relative frequencies (95% CI). The differences between groups for continuous and categorical variables were analysed using linear and logistic regression and are presented as linear regression beta coefficients and logistic regression odds ratios (ORs) (95% CI). Count data were analysed using Poisson regression and are presented as the incidence rate ratio (IRR) (95% CI).

Results

There were 11 730 infants included in the cluster RCT at 26 hospitals with 11 715 (99.5%) having available data on the provision of oxygen therapy. A total of 7426 (63.4%) were male, 2611 (22.3%) identified as indigenous, 1681 (14.3%) were born preterm and 536 (4.6%) had pre-existing co-morbidities (Table 1).

Oxygen therapy (either LFO and/or HFNC) was administered to 3392 (29.0%, 95% CI (28.1–29.8%)) infants. Infants who were managed with oxygen therapy were more likely to be younger, indigenous, born preterm and have pre-existing co-morbidities (Table 1). Over the 4 study years, the use of oxygen therapy decreased marginally (2014 = 778/2587 (30.1%);

Table 1 Characteristics of infants who presented with bronchiolitis and managed with and without oxygen therapy

	Total	No oxygen therapy received	Oxygen therapy received	Difference between those with and without oxygen therapy		
	$n = 11\,715$	$n = 8323$	$n = 3392$			
	n (%) or *m* (SD)	*n* (%) or *m* (SD)	*n* (%) or *m* (SD)	OR or coefficient†	95% CI	*P* value
Sex (male)	7426 (63.4)	5301 (63.7)	2125 (62.7)	0.96	0.88; 1.04	0.288
Age (months)†	5.92 (SD = 3.14)	6.0 (SD = 3.1)	5.8 (SD = 3.3)	−0.20†	−0.32; −0.07	0.002
Indigenous‡	2611 (22.3)	1573 (18.9)	1038 (30.6)	1.89	1.73; 2.07	<0.001
Premature§	1681 (14.3)	1034 (12.4)	647 (19.1)	1.62	1.46; 1.81	<0.001
Co-morbidities¶	536 (4.6)	293 (3.5)	243 (7.2)	2.10	1.76; 2.50	<0.001

† Linear regression coefficient. ‡ Indigenous includes Aboriginal, Torres Strait Islander and Māori. § Premature includes birth prior to 37 weeks' gestation. ¶ Comorbidities include congenital heart disease, chronic lung disease chronic neurological disorder or failure to thrive. CI, confidence interval; m, mean; OR, odds ratio; SD, standard deviation.

Table 2 Prevalence of oxygen therapy received, both high flow nasal cannula and low flow oxygen therapy, by study year

Year	Infants presenting with bronchiolitis $n = 11\,715$	Oxygen therapy received $n = 3392$ *n* (%) [95% CI]	HFNC (with or without low flow oxygen therapy) received† $n = 1817$ *n* (%) [95% CI]	Low flow oxygen therapy received† $n = 1575$ *n* (%) [95% CI]
2014	2587	778 (30.1) [28.3, 31.9]	336 (43.2) [39.7, 46.8]	442 (56.8) [53.2, 60.3]
2015	2727	796 (29.2) [27.5, 30.9]	423 (53.1) [49.6, 56.7]	373 (46.9) [43.3, 50.4]
2016	2681	764 (28.5) [26.8, 30.2]	449 (58.8) [55.1, 62.3]	315 (41.2) [37.7, 44.8]
2017	3720	1054 (28.3) [26.9, 29.8]	609 (57.8) [54.7, 60.8]	445 (42.2) [39.2, 45.3]

† As a proportion of all infants receiving oxygen therapy. CI, confidence interval; HFNC, high flow nasal cannula. Linear regression coefficient for temporal trend for oxygen therapy received (vs. no oxygen therapy received) = 0.97, 95% CI [0.94, 1.01]; $P = 0.12$. Linear regression coefficient for temporal trend for proportion receiving HFNC (vs. low flow oxygen therapy alone) = 1.21, 95% CI [1.14, 1.28]; $P < 0.001$.

Table 3 Characteristics of infants who received high flow nasal cannula therapy versus low flow oxygen therapy

	HFNC (with or without low flow oxygen therapy) received $n = 1817$ n (%) or m (SD)	Low flow oxygen therapy received $n = 1575$ n (%) or m (SD)	Difference between those receiving HFNC therapy and low flow oxygen therapy		
			OR or coefficient†	95% CI	*P* value
Sex (male)	1178 (64.8)	947 (60.1)	1.22	1.06; 1.41	0.005
Age (months)†	5.8 (SD = 3.3)	5.7 (SD = 3.3)	0.12†	−0.10; 0.35	0.274
Indigenous‡	582 (32.0)	456 (28.9)	1.16	1.00; 1.34	0.052
Preterm§	342 (18.8)	305 (19.4)	0.97	0.82; 1.15	0.744
Co-morbidities¶	135 (7.4)	108 (6.9)	1.09	0.84; 1.42	0.527

† Linear regression coefficient. ‡ Indigenous includes Aboriginal, Torres Strait Islander and Māori. § Preterm includes birth prior to 37 weeks' gestation. ¶ Comorbidities include congenital heart disease, chronic lung disease chronic neurological disorder or failure to thrive. CI, confidence interval; HFNC, high flow nasal cannula; m = mean; OR, odds ratio; SD, standard deviation.

Table 4 Outcomes of infants who received high flow nasal cannula therapy versus low flow oxygen therapy

	HFNC (with or without LFO therapy) received $n = 1817$ n (%) or median (IQR)	LFO therapy received $n = 1575$ n (%) or median (IQR)	Difference between those who received HFNC therapy and LFO therapy		
			OR or IRR†	95% CI	*P* value
Admitted to ward	1816 (99.9)	1532 (97.3)	50.97	7.01; 370.57	<0.001
Length of stay (days)†	2.83 (1.83–4.38)	2.04 (1.38–3.13)	1.29†	1.24; 1.34	<0.001
Admitted to ICU	262 (14.4)	36 (2.3)	7.24	5.07; 10.32	<0.001
Non-invasive (CPAP/BIPAP) or invasive ventilation	172 (9.5)	44 (2.8)‡	3.64	2.60; 5.11	<0.001
Non-invasive ventilation only (CPAP/BIPAP)	138 (7.6)	30 (1.9)‡	4.23	2.83; 6.32	<0.001
Invasive ventilation	34 (1.9)	13 (0.8)‡	2.29	1.21; 4.36	0.011
Death	0 (0)	0 (0)			

† Incidence rate ratio. ‡ Missing data point – It is unknown if one LFO therapy patient received invasive ventilation or not. They received non-invasive ventilation and so are therefore included in the non-invasive or invasive total ($n = 44$), but do not contribute to the non-invasive only ($n = 30$), or invasive ventilation ($n = 13$) numbers. BIPAP, bilevel positive airway pressure; CI, confidence interval; CPAP, continuous positive airway pressure; HFNC, high flow nasal cannula; ICU, intensive care unit; IQR, interquartile range; IRR, incidence rate ratio; LFO, low flow oxygen; OR, odds ratio.

2017 = 1054/3720 (28.3%); linear regression coefficient = 0.97, 95% CI (0.94, 1.01); $P = 0.12$) (Table 2).

Of the 3392 infants who received oxygen therapy, 1817 (53.6%, 95% CI (51.9–55.3%)) received HFNC therapy (with or without LFO therapy). Infants who received HFNC therapy were more likely to be male (HFNC 1178/1817 (64.8%) vs. LFO 947/1575 (60.1%); $P = 0.005$); with no other differences in the risk characteristics of infants who received HFNC therapy compared to infants who received LFO therapy (Table 3). Over the 4 study years, the use of HFNC therapy increased from 43.2% in 2014 (336/258), to 57.8% in 2017 (609/3720) (linear regression coefficient = 1.21, 95% CI (1.14–1.28); $P < 0.001$) (Table 2).

Most infants who received oxygen therapy were admitted to hospital (99.9%). Hospital LOS for infants who received HFNC was longer than those who received LFO therapy (median HFNC 2.83 days vs. LFO 2.04 days; $P < 0.001$). Admission to ICU for infants who received HFNC was higher than for infants who received LFO therapy (HFNC 262/1817 (14.4%) vs. LFO 36/1575 (2.3%); $P < 0.001$). The use of non-invasive and invasive ventilation for infants who received HFNC therapy was higher than for infants who received LFO therapy (non-invasive ventilation HFNC 138/1817 (7.6%) vs. LFO 30/1575 (1.9%), $P < 0.001$; invasive ventilation HFNC 34/1817 (1.9%) vs. LFO 13/1575 (0.8%), $P = 0.011$) (Table 4).

Discussion

Our study demonstrated an increased use of HFNC therapy from 43 to 57% over four bronchiolitis seasons (2014–2017) for infants with bronchiolitis who were admitted and managed with oxygen therapy in 26 Australian and New Zealand hospitals. This increased use of HFNC therapy occurred despite no change in the proportion of all bronchiolitis infants being managed with oxygen therapy. This indicates that the increased use of HFNC therapy cannot be explained solely by increased severity of disease but rather reflecting increased use of HFNC therapy at the expense of LFO therapy for patients of similar severity. This is supported by our data showing no difference in risk factors for severe disease (age, indigenous infants, ex-preterm birth and presence of co-morbidities) in infants with oxygen therapy managed with and without HFNC.

Management of bronchiolitis is well defined[4] and supported by high-quality international guidelines.[3,10,16,17] Despite this, therapies of no known benefit continue to be used for infants with bronchiolitis.[15] Evidence for use of HFNC therapy for infants with bronchiolitis has evolved over recent years with HFNC therapy specifically recommended for infants who require escalation of care due to deterioration in their condition on LFO therapy.[5] Data from the largest RCT of HFNC therapy in bronchiolitis demonstrated that between 23 and 30% of patients requiring respiratory support for bronchiolitis would receive HFNC if managed according to the guidelines.[9] In our study over 50% of infants receiving oxygen therapy for bronchiolitis received HFNC therapy. It appears that the use of HFNC therapy in the 26 hospitals included in this study is in excess of this estimated appropriate use. As with other therapies known to be used inappropriately in bronchiolitis management,[12] our findings suggest there is a requirement to undertake de-implementation of HFNC therapy use.

When HFNC therapy was initially used in the management of infants with bronchiolitis, use was confined to the ICU environment. Several studies have shown an increase in ICU admission for infants with bronchiolitis over time, contemporary with the introduction and restriction of HFNC therapy to the ICU environment. Mahant *et al.*[18] found a relative increase of 130% in ICU admissions despite stable hospitalisation rates over a 14-year period in Canada from 2004 to 2018. Pelletier *et al.*[19] found a stable invasive mechanical ventilation rate (3.3–2.8%) but a 7-fold substantial increase in the use of non-invasive ventilation (including HFNC therapy) rate (1.2–9.5%) over a 10-year period in the United States (US) from 2010 to 2019. Similarly, in Australia and New Zealand, ICU bronchiolitis admission rates increased from 62.5 per 100 000 in 2002 to 208.9 per 100 000 in 2014 in infants <24 months of age. The use of HFNC for the management of bronchiolitis in Australian and New Zealand ICUs was not routinely used prior to 2010, by 2014, 72.6% of infants managed in Australian and New Zealand ICUs received HFNC therapy, coinciding with the increase seen in ICU admission rates.[20]

Over the last decade, HFNC has been increasingly used outside of the ICU environment. Yet definitive studies confirming safety of HFNC use on inpatient wards were not published until 2017[18] and 2018.[9] This maturing of data confirming the safety of HFNC use outside the ICU environment occurred in the final months of our study, and may partially explain the association between HFNC use and increased rates of ICU admissions; having started HFNC therapy on inpatient wards, clinicians may have been more cautious (resulting in earlier ICU admission) if infants appeared to be distressed by the therapy. Our study did not collect reasons for escalation of therapy. Regardless, in the largest bronchiolitis dataset available in Australia and New Zealand, rather than suggesting that HFNC decreased LOS and ICU admission, we found an association between HFNC use and increased LOS and ICU admissions.

While this study is unable to report the rationale for increasing usage of HFNC, we postulate that increased availability of HFNC equipment and its benign safety profile may be contributing factors. In addition, qualitative evidence suggests that clinicians have a strong desire to provide interventions when managing infants with bronchiolitis, even in the face of evidence showing a lack of clinical benefit for the interventions provided.[19] The degree to which these factors, and others, play in the potentially excessive use of HFNC therapy in bronchiolitis remains unknown and requires further investigation.

Our study has several strengths. It was conducted at 7 tertiary and 19 secondary hospitals in Australia and New Zealand, encompassing a range of metropolitan and regional hospitals, as well as dedicated paediatric and mixed (adult and paediatric) EDs making our results generalisable for the Australia and New Zealand population, and likely applicable to other developed countries where drivers of HFNC therapy appear similar. Data were rigorously collected using standard data collection forms, within an international multi-centre RCT. Although the data were collected retrospectively, the use of LFO and HFNC was well recorded in the medical records.

A limitation of our study is the inability to differentiate the infants who only received HFNC without LFO versus those who received both HFNC and LFO therapies during their admission. We did not report which treatment modality of LFO or HFNC was started first, or length of the therapy. Further, our study methodology did not allow identification of infants who received HFNC as an escalation in care, compared to those managed with HFNC therapy alone. However, with over half of patients requiring oxygen therapy receiving HFNC therapy, and HFNC therapy use increasing over time, the availability of these data are unlikely to change the key finding that HFNC therapy appears to be overused in bronchiolitis. For eligibility to the study as a site, hospitals were required to have a minimum of 135 ED presentations of infants with bronchiolitis per year. This requirement excluded smaller and potentially more remote hospitals, where bronchiolitis management may be escalated due to lack of medical and equipment resources, time and ability to transfer to tertiary care. The extrapolation of our data to these smaller hospitals must therefore be made with caution.

Additionally, eight of our study hospitals had participated in an RCT[9] investigating the use of HFNC therapy in infants with bronchiolitis, which may have contributed to the familiarity, availability and increased use of this therapy. However, the RCT stopped recruitment in August 2016, and so recruitment into the RCT does not explain the increased use of HFNC therapy in the second half of the 2016 bronchiolitis season or in 2017.

The Australasian Bronchiolitis Guideline was released and freely available in 2017.[10] The data analysed in this study were from infants managed prior to and after the release of the guideline. It is noted that these data are now 5 years old and it is unknown whether the high use of HFNC therapy has continued in Australian and New Zealand hospitals. However, similar trends of over-utilisation of HFNC therapy have been noted in other countries[20] despite evidence that early HFNC use has no impact on key clinical outcomes.[9,18]

Conclusion

Our study demonstrated that use of HFNC therapy for infants with bronchiolitis increased over time, with the majority of infants requiring respiratory support receiving HFNC therapy. It would appear that use of HFNC therapy for bronchiolitis is excessive. Further, we found no evidence that HFNC therapy improved LOS or ICU admission rates, indeed LOS and ICU admission rates increased. Next steps will be to investigate and understand the drivers of HFNC therapy in infants with

bronchiolitis to guide development of interventions to promote the evidence-based use of HFNC.

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