Respiratory illness and/or distress is the commonest reason for non-elective paediatric intensive care unit (PICU) admission. Respiratory conditions represent 26.3% of dedicated PICU admissions and 50.5% of general ICU paediatric admissions. Treatment of respiratory distress has changed over the years from predominantly intubation and mechanical ventilation to widespread use of non-invasive ventilation, particularly continuous positive airway pressure (CPAP). This has markedly reduced complications from ventilator use but is often poorly tolerated.

High-flow humidified oxygen delivery with a nasal cannula is a newer technology rapidly increasing in use. A blend of oxygen and air is delivered at a high flow rate (2–60 L/min) through a heated and humidified circuit and is often better tolerated than CPAP or standard nasal oxygen. First used in preterm infants as an alternative to CPAP, its use is now widespread in adults and children although its underlying mechanism of action is poorly understood. Three commonly proposed mechanisms include the generation of CPAP which has shown varied, unpredictable and confounding results. There is stronger evidence for pharyngeal distending pressure causing meaningful expiratory pressure generation with flows of 2 L/kg/min and improved CO2 clearance due to deadspace washout.

In recent years, a limited number of studies have assessed the use of high-flow nasal cannula (HFNC) therapy in the PICU, with most reviewing its use specifically in bronchiolitis and excluding other causes of respiratory distress. We conducted a review of our use of HFNC therapy in the PICU since its introduction in 2011.

Methods

After obtaining ethics committee approval, we performed a retrospective analysis of patients weighing under 20 kg and treated with HFNC therapy for any diagnosis (excluding those on HFNC therapy after extubation) in our PICU between January 2011 and September 2013. A child was considered to be receiving HFNC treatment when the flow reached ≥ 1 L/kg/min. Our primary outcome was failure of HFNC therapy, which was defined as the patient needing escalation of treatment to CPAP or intubation. Secondary data were collected on underlying risk factors, cardiorespiratory parameters, time to failure of HFNC therapy and length of stay (LOS) in hospital and the PICU. The PICU was a 13-bed tertiary, mixed surgical–medical unit (no cardiothoracic surgery). Admissions were sourced from the emergency department, general wards and high-dependency unit. The wards and high-dependency unit could supply limited HFNC therapy (not included in our study), and PICU admission generally occurred when flows ≥ 1.5 L/kg/min and/or FiO2 ≥ 0.5 were needed, or sooner, at the discretion of the PICU doctor. Several devices were used to supply the high-flow oxygen–air blend over the survey period, pre-
dominantly humidified nasal cannulae (Fisher and Paykel Healthcare), and Optiflow and Optiflow Junior (Fisher and Paykel Healthcare) devices were also used. We used a Fisher and Paykel respiratory humidifier for humidification and a Bird air–O\textsubscript{2} blender (BD) to achieve required Fi\textsubscript{O}\textsubscript{2}. Higher flows were achieved using two 30 L flow meters with a dual-flow adaptor.

The database was accessed and data from eligible patients were collected, including age, sex, weight, retrieval status (patient presenting following retrieval from another health care service), previous ICU admissions, primary diagnosis, viral testing results and comorbidities (eg, prematurity, chronic lung disease, airway disease, congenital heart disease and neuromuscular disease). Data on hospital and ICU LOS and discharge outcome, and HFNC, CPAP and intubation parameters were collected. Cardiorespiratory parameters included respiratory rates, heart rates, oximeter saturations and Fi\textsubscript{O}\textsubscript{2}. These were recorded before the start of HFNC therapy; then 1, 4 and 8 hours after initiation of HFNC therapy. If a blood gas measurement was available it was recorded but was not a routine practice.

HFNC therapy success was defined as discharge from the PICU without escalation of treatment to CPAP or intubation. HFNC therapy was defined as having failed if escalation of treatment to CPAP or intubation became necessary, and was further categorised as “requiring CPAP only”, “CPAP then intubation” or “direct intubation”. Intubation was at a doctor’s discretion but generally occurred if Fi\textsubscript{O}\textsubscript{2} > 0.6 or there was a worsening clinical state, and a similar guideline was followed in the PICU. All statistical analyses were performed using SPSS, version 19 (SPSS). Statistical significance was set at $P \leq 0.05$.

Results

Sixty-eight patients were identified from the database search and 14 were excluded (of these, four never received HFNC therapy due to transcribing errors; one was on long-term HFNC therapy, electively admitted with no change in respiratory requirements; and nine were on HFNC therapy after extubation) (Figure 1). The median age of included patients was 3.5 months (interquartile range [IQR], 1–10 months) and 59% were female. One patient died from underlying oncological disease. The median hospital LOS was 8 days (IQR, 5–27 days) and the median PICU length of stay was 65.2 hours (IQR, 42.4–114.2 hours). Fourteen patients (26%) were retrieved from another hospital before admission and 25 patients (46%) had previously been admitted to an ICU (paediatric or neonatal).

HFNC therapy failed for 12 patients (22%), necessitating escalation of treatment, with five patients (9%) needing intubation. Seven patients (58%) needed CPAP alone, two needed CPAP then intubation (17%) and three needed direct intubation (25%). The median time to failure of HFNC therapy was 5.5 hours (IQR, 3.6–9 hours), with 75% of failures occurring within 8.25 hours (Figure 2). Bronchiolitis was the commonest primary diagnosis (61%), then chronic lung disease (13%), pneumonia (9%), congenital
heart disease (7%), asthma (5%) and apnoea (4%) (Table 1). The patients admitted with a primary diagnosis of asthma and apnoea had no associated HFNC therapy failures. HFNC therapy failure rates, by primary diagnosis, were chronic lung disease 14%, bronchiolitis 21%, pneumonia 40% and congenital heart disease 50%.

There were no statistically significant differences between the demographic data of patients for whom HFNC therapy succeeded and patients for whom HFNC therapy failed, although there was a non-significant correlation between younger age and failure ($P = 0.06$) (Table 2). There was a significant difference identified in the PICU LOS ($P = 0.04$), but the hospital LOS difference did not reach significance ($P = 0.06$). All other baseline characteristics were similar between groups.

High flow rates were described in L/kg/min, and the mean maximum flow rate in both groups was 2 L/kg/min. Flow rates were prescribed and varied at the discretion of the doctor. Between the HFNC therapy failure and success groups, respiratory rates were significantly different at 1 hour ($P = 0.037$) (Figure 3). All other cardiorespiratory parameters were similar at all times they were measured.

**Discussion**

HFNC devices are being increasingly used in pediatrics for a variety of conditions, despite a paucity of research. Since their introduction, the indications for use and recommendations for flow rates have varied dramatically, making comparisons between studies difficult. They were initially used primarily for bronchiolitis but their use is now more widespread. Flow rates were initially limited by the available technology to 2–8 L/min, but can now vary between 2 L/min and 60 L/min, varied by patient weight, with maximum flows generally set at 2 L/kg/min.$^{8,9,11}$ Our unit introduced HFNC therapy in 2011 and, on review, we showed similar outcomes to previous studies with most patients successfully avoiding treatment escalation (78%) and a 9% intubation rate, which is consistent with previously reported rates of 8%–18%.$^{3,9,13-15}$ Failure of HFNC therapy was associated with an 80% increase in the median ICU length of stay, but a non-significant increase in hospital LOS. This result may have been skewed by including data from the entire hospital admissions of long-term, patients with complex medical problems. The demographic data were similar in the HFNC therapy success and failure groups with the exception that younger age was non-significantly associated with HFNC failure ($P = 0.06$). This difference is not reflected in other current pediatric research, which has found no consistent demographic data associated with failure of HFNC therapy. This is in contrast to findings that younger age and prematurity have been associated with failure of CPAP therapy.$^{3,5,13-15}$

HFNC therapy in the PICU has been reviewed in a limited number of studies. Abboud and colleagues showed, in a retrospective study of 113 patients with bronchiolitis using flow rates of 2–8 L/min, a higher overall intubation rate of 18%.$^3$ They also identified predictors of HFNC therapy failure, including lower mean weight and higher $P_{CO_2}$ at admission and after initiation of therapy. McKiernan and colleagues retrospectively studied 115 patients with bronchiolitis using flow rates of 2–8 L/min, and showed a 14% reduction in intubation rates compared with the previous comparable period (before HFNC therapy was implemented),

**Table 2. Baseline patient characteristics**

<table>
<thead>
<tr>
<th>Baseline variables</th>
<th>Success (N = 42)</th>
<th>Failure (N = 12)</th>
<th>$P^*$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, months$^†$</td>
<td>4.5 (2.0–10.0)</td>
<td>1.0 (0.5–5.5)</td>
<td>NS</td>
</tr>
<tr>
<td>Weight, kg$^†$</td>
<td>6.0 (3.6–9.0)</td>
<td>4.0 (3.3–6.8)</td>
<td>NS</td>
</tr>
<tr>
<td>Hospital LOS, days$^†$</td>
<td>7.5 (4.0–24.0)</td>
<td>9.5 (5.5–33.5)</td>
<td>NS</td>
</tr>
<tr>
<td>ICU LOS, hours$^†$</td>
<td>59.6 (37.3–95.8)</td>
<td>107.1 (75.0–147.0)</td>
<td>0.04</td>
</tr>
<tr>
<td>Male$^‡$</td>
<td>18 (42.8%)</td>
<td>4 (33.3%)</td>
<td>NS</td>
</tr>
<tr>
<td>Retrieved from other hospital$‡$</td>
<td>11 (26.1%)</td>
<td>3 (25.0%)</td>
<td>NS</td>
</tr>
<tr>
<td>Previous ICU adm.$‡$</td>
<td>21 (50.0%)</td>
<td>4 (33.3%)</td>
<td>NS</td>
</tr>
<tr>
<td>Any risk factor$‡$</td>
<td>25 (59.5%)</td>
<td>7 (58.3%)</td>
<td>NS</td>
</tr>
<tr>
<td>&gt; 1 risk factor$‡$</td>
<td>16 (38.1%)</td>
<td>3 (25.0%)</td>
<td>NS</td>
</tr>
<tr>
<td>RSV-positive$‡$</td>
<td>17 (40.5%)</td>
<td>7 (58.3%)</td>
<td>NS</td>
</tr>
<tr>
<td>Other virus-positive$‡$</td>
<td>21 (50.0%)</td>
<td>3 (25.0%)</td>
<td>NS</td>
</tr>
</tbody>
</table>

IQR = interquartile range. LOS = length of stay. Adm. = admission. RSV = respiratory syncytial virus. NS = non-significant. * NS if $P > 0.05$; significant if $P < 0.05$. † Median (IQR). ‡ n (%).
with an intubation rate of 9%, and a decreased mean PICU LOS.14 In a retrospective study of 298 patients with any diagnosis using flows of 2–8 L/min, Schibler and colleagues showed a 30% reduction in intubation rates from the previous comparable period, with an intubation rate of 7%.15 All three studies showed a significant association between HFNC therapy success and an improvement in respiratory rate within 1–2 hours. An absence of this improvement was associated with escalation in management. Schibler and colleagues also showed a similar association with heart rate at 1 hour. All studies identified 1–2 hours as the critical period for identifying patients at risk of HFNC therapy failure. Our study showed an association between respiratory rate at 1 hour and HFNC therapy failure (P=0.037) but showed a median increase in respiratory rate in the HFNC therapy failure group rather than a decrease in the success group. This may reflect the fact that our hospital can supply HFNC therapy outside the PICU, at rates similar to those used in the comparable studies, and therefore at the time of PICU transfer, patients may have been less stable and more likely to deteriorate than respond to HFNC therapy. Most had already started HFNC therapy before transfer, so the improvements in respiratory rates may have already occurred at the flow rates used on the ward.

Despite identifying 1–2 hours as the critical period, the above studies generally did not report the timing of escalation of treatment, with the exception of one which showed a mean intubation time of 14 (±11) hours.3 Our study showed that for most patients (75%), HFNC therapy failed within 8 hours (within 5 hours for half the patients), and we found no reliable predictor of HFNC therapy failure. Given that all the described studies were retrospective and involved varied diagnoses and flow rates, it is impossible to make firm conclusions on predictors and timing of HFNC therapy failure that can be applied to daily use of high flow, but they suggest that clinicians should be wary of patients with unchanged or poorly responsive respiratory rates.

Our study also looked at the diagnosis specific risk of failure rates and showed that asthma, apnoea and chronic lung disease had low HFNC therapy failure rates (<15%), with increasingly poor responses in bronchiolitis (21%), pneumonia (40%) and heart disease (50%). Schibler and colleagues showed similar HFNC therapy failure rates, particularly in patients with bronchiolitis (19%) and cardiac disease (50%).15 Although no large, prospective study has been performed, this similarity suggests that starting patients on HFNC therapy primarily for heart-related disease should be done with caution.

Our study was weakened by the inherent limitations of being a single-centre, small, retrospective study. It was also assessed during a period when HFNC therapy was being introduced and therefore use, adjustments and patient identification may have varied. Commencement on HFNC therapy could not be controlled and clinical appearances, including respiratory effort, were not reported. It is possible that patients were included who would not have fulfilled the respiratory criteria for HFNC therapy in a prospective study, although this effect may have been slightly mitigated by the fact that, to qualify for PICU admission, our centre required patients to have deteriorated beyond the capability of the general ward and high-dependency unit to provide HFNC therapy. Despite this, it is clear that HFNC therapy is successful for most patients, and further studies may identify reliable cardiorespiratory and diagnostic predictors of therapy failure. Ideally, a large, prospective, multicentre study should be performed to better define this.

Conclusion

HFNC therapy was successful in most patients, and success was associated with a shorter PICU LOS. Most therapy failures occurred within 8 hours. Heart disease was associated with a higher failure rate, and HFNC therapy should be used with some caution in these patients. Several cardiorespiratory parameters are likely to be good predictors of failure but further prospective research is needed to confirm this.

Competing interests

None declared.

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ORIGINAL ARTICLES

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200