

# High flow nasal cannula therapy in the pediatric home setting

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## Abstract

**Background:** High-flow nasal cannula (HFNC) therapy may be better tolerated than traditional noninvasive ventilation (NIV) and is rapidly gaining acceptance in pediatric acute care. In Israel, HFNC is approved for domestic use. We aim to describe its indications, efficacy, parental satisfaction, and safety.

**Methods:** Retrospective study of children treated with home HFNC therapy in three pediatric centers. Data included demographic parameters, indication of use, weight and days of hospitalization before and after initiation. Safety, tolerability, and parental satisfaction were assessed via standardized telephone questionnaire.

**Results:** Median (interquartile range [IQR]) age of initiating home HFNC in 75 children was 8.3 (2.2, 29.6) months. Indications were obstructive sleep apnea (33; 44%), airway malacia (19; 25%), chronic lung disease (15; 20%), neuromuscular disease (4; 5%), and postextubation support (4; 5%). Weight standard deviation score rose from  $-2.3$  pre-HFNC to  $-1.7$  at 6.7 months post-HFNC initiation,  $p < 0.001$ . Hospital admission days during the 2 months pre- versus post-HFNC initiation were 22 (5.5, 60) and 5 (0, 14.7) respectively,  $p < 0.008$ . Median (IQR) parental satisfaction score was 5/5 (4, 5). Fifty of 60 (83%) respondents would recommend home HFNC to other families in a similar situation. There were no serious adverse events.

**Conclusion:** In our population, domestic HFNC appeared safe and well tolerated for a variety of indications. Its introduction was associated with improved weight gain, fewer hospitalization days and high parental satisfaction. Further work is required to characterize groups of children most likely to benefit from HFNC, as opposed to traditional modes of NIV.

## KEYWORDS

chronic lung disease, high flow nasal cannula, home therapy, noninvasive ventilation, pediatric

Shay Ehrlich and Inbal G. Tripto contributed equally to the study.

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## 1 | INTRODUCTION

High-flow nasal cannula (HFNC) therapy is a form of noninvasive respiratory support designed to deliver a high flow of heated humidified air, with or without entrained oxygen, via specifically designed nasal prongs. Its physiological benefits include alveolar recruitment, improved compliance and washout of carbon dioxide from the upper airway, as well as to some extent flow-dependent positive airway pressure.<sup>1–3</sup> The reduction of esophageal pressure changes during respiration, compared with standard nonocclusive oxygen facemask, indicates its capacity to ease inspiratory effort.<sup>4</sup>

Initially developed for preterm infants, the application of this technology is rapidly spreading to include pediatric patients with various indications, including hospitalized bronchiolitis,<sup>5</sup> asthma, postextubation support,<sup>6</sup> and even adult hypoxemic respiratory failure.<sup>4</sup> In small children particularly, HFNC therapy may be better tolerated than traditional modes of noninvasive support, such as continuous positive airway pressure (CPAP) and bilevel positive airway pressure (BiPAP) in part owing to its smaller nasal prong interface allowing activities like breastfeeding with greater ease.<sup>7,8</sup> In a recent multicenter, randomized clinical trial addressing acutely ill children aged 0–15 years assessed to require noninvasive respiratory support, HFNC compared with CPAP met the criterion for noninferiority for time to liberation from respiratory support.<sup>9,10</sup>

The rising acceptance of HFNC has led to its increasing use outside the intensive care setting. According to a recent survey addressing 114 hospital sites in the United States, 37 sites (48%) used HFNC in the pediatric ward setting, all for patients with bronchiolitis.<sup>11</sup> Reports of use in the home setting are still scant but are starting to emerge for a number of indications including post adenoviral bronchiectasis,<sup>12</sup> tracheomalacia,<sup>13</sup> obstructive sleep apnea (OSA),<sup>14</sup> and congenital heart disease.<sup>15</sup>

In Israel, heated humidified high-flow nasal cannula therapy is approved for home support of children requiring noninvasive respiratory support on the recommendation of a pediatric pulmonologist or intensivist, provided that CPAP and BiPAP have been trialed and deemed poorly tolerated by the patient. We aim to describe the safety, indications, parameters of utilization, length of treatment, clinical outcomes, and parental satisfaction with HFNC in the pediatric home setting.

## 2 | METHODS

This is an observational retrospective multicenter study, involving three tertiary pediatric hospitals; Schneider Children's Medical Center of Israel (SCMCI), Soroka University Medical Center (SUMC), and Dana-Dwek Children's Hospital (DDCH). Electronic medical records of children aged 0–18 years who were prescribed a HFNC device between January 1, 2014 and December 31, 2019 for use in the home setting were reviewed. No exclusion criteria were applied. Children with severe and life-limiting conditions who were started on HFNC treatment with a palliative intention were also not excluded. Demographic and clinical data were collected.

## 2.1 | Indications for initiation of high-flow nasal cannula treatment

The main medical indication for initiation of HFNC treatment was taken from the referring physician's application form to the medical insurance providing the device. To analyze the various indications, children were allocated the following categories: (1) OSA (clinical diagnosis, formal sleep study not required); (2) Airway malacia (clinical or endoscopic diagnosis, as recorded in the electronic medical records, including laryngo-, pharyngo-, tracheo-, and bronchomalacia as well as any combination thereof); (3) postextubation support; (4) neuromuscular condition, and (5) chronic lung disease. When more than one indication existed, for example, neuromuscular disease and airway malacia, the clinically more relevant indication was chosen, as indicated by the order on the application form, indexed by the prescribing physician.

Due to the relatively frequent use of HFNC and ambiguity about its justification, we additionally considered children who died and those with trisomy 21 as subgroups of interest, and examined them separately.

## 2.2 | Clinical observations

In an effort to gauge possible clinical effect of HFNC treatment, weight as an indicator of general wellbeing and days of hospitalization pre- and post-HFNC initiation were examined. Weight standard deviation score (SDS) was recorded at the time of HFNC initiation and at the date closest to 6 months post initiation available. Median total and respiratory-related hospitalization days were compared between two time periods: 2 months before and 2 months after introduction of HFNC. Each inpatient care episode was classified as respiratory or nonrespiratory according to the electronic medical records diagnosis that led to the admission and hospitalization days were counted for the entire respective episode, including the first and last day of the inpatient stay. We also measured minimum and maximum oxygen saturations during the 48 h preceding and 48 h following HFNC initiation as further indication of treatment efficacy.

## 2.3 | Safety assessment

Safety assessment was performed by reviewing the electronic medical records. Adverse events (AEs) were defined as any untoward medical occurrence, including an exacerbation of a pre-existing condition, in a patient who was treated with HFNC. The clinical judgement of the investigators (SE, PS) was used to determine any causal relationship after considering all relevant factors (such as the temporal relationship between onset of treatment and the AE) and confounding factors (such as concomitant medications and diseases). A serious AE (SAE) was defined as any AE meeting the following criteria: HFNC treatment resulted in death or was immediately

life-threatening; resulted in persistent or significant disability or incapacity; required or prolonged patient hospitalization. Any other important medical event which may have jeopardized the patient, or which may have required medical or surgical intervention to prevent one of the outcomes listed above (based on appropriate medical judgement), was also regarded as an SAE.

## 2.4 | Treatment initiation protocol

Children deemed to require domestic noninvasive ventilation (NIV) support were referred from both the inpatient as well as outpatient settings of the three hospitals. In keeping with the health maintenance organizations' stipulations, the default modes of domestic NIV were CPAP or BiPAP. During inpatient admission, either of these were applied for a period of time stipulated by the treating pediatric pulmonologist or intensivist in charge, according to clinical judgement. When poor tolerance or difficulty achieving satisfactory ventilation were encountered, children were switched to HFNC therapy.

## 2.5 | Devices and settings

Once identified as candidates for HFNC treatment, children were connected to the Precision flow (Vapotherm) for an inpatient trial. This device serves as default for hospital use, but requires a wall oxygen outlet and is thus not suitable for domestic use. Children were monitored clinically and with a pulse oximeter to determine whether they benefitted from the therapy. Measurement of blood gases was not required routinely. Air flow was titrated as tolerated, usually aiming to achieve a flow rate of 2 L/kg/min. Once it was determined that children benefitted from HFNC, a home device was ordered. A humidifier and flow generator device (myAirvo 2; Fisher & Paykel Healthcare) were used to deliver high flow via nasal cannulae that were chosen according to the flow rate, considering the child's weight. Children with a flow rate of up to 25 L/min were connected via the Optiflow Junior 2 Nasal Interface. For flow rates up to 50 L/min, the larger Optiflow Junior 2+ XXL Nasal Interface was used. We aimed to have approximately 50% of the nares patent. A heater and humidifier regulated the temperature and humidity. The nasal cannula maintained a temperature of 34°C and relative humidity of 100% at the nasal outlet as reported by the manufacturer. Children were required to remain inpatients for at least one further night using the home device, to adapt the interface and ensure safety and effective ventilation. Parents were trained in the use of the device and underwent a resuscitation tutorial. They were prescribed a home pulse oximeter and, when required, suction device and oxygen concentrator. A home ventilation team was assembled, consisting of a technician and a physician, tasked with regular home visits, maintenance, and trouble shooting.

## 2.6 | Follow up telephone questionnaire

After retrospective review of the clinical data set, a parental questionnaire (Table 3) was applied in a prospective manner, following parental verbal phone consent obtained by a member of the treating team, as stipulated by the institutional review board. In the absence of a suitable validated tool, the questions were purposely designed by members of the study team (SE, IGT, ML, PS) to evaluate HFNC safety, efficacy, and satisfaction.

## 2.7 | Ethics and statistics

The study was approved by every participating Institutional Review board for Human Studies (SCMCI: 0178-19-RMC, SUMC: SOR-075-20, DDCH: TLV 0900-20). The Shapiro-Wilk test was used for assessing normal distribution. Data are presented as means (SD) or median (interquartile range [IQR]) for continuous variables and frequencies (%) for categorical variables. Primary outcomes were analyzed using paired *t*-tests or Wilcoxon rank-sum test. The analyses were performed by using the IBM SPSS software (Version 26); tests were two-tailed and  $p < 0.05$  were considered to be statistically significant.

## 3 | RESULTS

### 3.1 | Patient characteristics

During the study period, 75 patients from three hospitals were commenced on home HFNC treatment. Their characteristics are shown in Table 1. Median (IQR) age of initiating home HFNC was 8.3 (2.2–29.6) months. The most frequent main indication was OSA ( $n = 33$ , 44%), followed by airway malacia ( $n = 19$ , 25%). The most common comorbidities were failure to thrive ( $n = 44$ , 59%), chronic lung disease (33, 44%), and genetic syndromes (31, 41%).

### 3.2 | Clinical observations

Weight SDS were compared between the time of HFNC initiation and a mean (SD) period of 6.67 ( $\pm 5.2$ ) months post-HFNC initiation. Significant weight gain was noted, from  $-2.3$  SDS pre to  $-1.7$  SDS post,  $p < 0.001$ . This is shown in Table 2 which also displays a subgroup analysis for children with failure to thrive, OSA, and prematurity (not mutually exclusive), showing significant weight gain in all these categories.

Median total and respiratory-related hospitalization days were compared between two time periods: 2 months before and 2 months after introduction of HFNC. There were fewer total and respiratory hospitalization days following HFNC in the total population, as well as in all subgroups (Table 2). Mean ( $\pm$ SD) minimum and maximum recorded oxygen saturations improved from  $91 \pm 9.1$  to  $94.4 \pm 6.4$  ( $p = 0.04$ ) and  $98.1 \pm 6.1$  to  $98.6 \pm 3.3$  ( $p = 0.02$ ) respectively.

**TABLE 1** Patient characteristics (*n* = 75)

|   |                 |
|---|-----------------|
| Age at HFNC initiation (months)—median, IQR         | 8.3, 2.2–29.6   |
| Gestational age (weeks)—median, IQR                 | 38.0, 36–39     |
| Birth weight (g) - median, IQR                      | 2732, 2120–3371 |
| Population group— <i>n</i> (%)                      |                 |
| Jews  | 50 (67)         |
| Arabs   | 21 (28)         |
| Other   | 4 (5)           |
| Gender— <i>n</i> (%)                                |                 |
| Male  | 42 (56)         |
| Period of use (months)—median, IQR                  | 7, 5–16         |
| Main indications— <i>n</i> (%), mutually exclusive  |                 |
| Obstructive sleep apnea                             | 33 (44)         |
| Airway malacia                                      | 19 (25)         |
| Chronic lung disease                                | 15 (20)         |
| Neuromuscular disease                               | 4 (5)           |
| Postextubation support                              | 4 (5)           |
| Comorbidities— <i>n</i> (%), not mutually exclusive |                 |
| Failure to thrive                                   | 44 (59)         |
| Chronic lung disease                                | 33 (44)         |
| Genetic, other than trisomy 21                      | 31 (41)         |
| Structural/vascular airway compression              | 29 (39)         |
| Cardiovascular                                      | 28 (37)         |
| Laryngo-tracheomalacia                              | 27 (36)         |
| Neuromuscular                                       | 22 (29)         |
| Trisomy 21  | 13 (17)         |
| Pierre Robin Syndrome                               | 3 (4)           |
| HFNC treatment details                              |                 |
| Oxygen supplementation, <i>n</i> (%)                | 26 (35)         |
| Referring department, <i>n</i> (%)                  |                 |
| General ward  | 33 (44%)        |
| Pulmonology institute                               | 24 (32%)        |
| Neonatal intensive care unit                        | 12 (16%)        |
| Cardio-thoracic intensive care unit                 | 3 (4%)          |
| Pediatric intensive care unit                       | 3 (4%)          |

Abbreviation: IQR, interquartile range.

### 3.3 | Parental satisfaction

The parental questionnaire is shown in Table 3. Data were obtained for 60/76 (79%) patients. Families of eight children who passed away during the study period in one of the centers were deliberately not contacted due to concerns over aggravating their bereavement.

Parents of five children refused to comply with the request for interview and three were not reachable.

The median satisfaction score was 5 out of 5 (IQR: 4, 5). When infants under the age of 12 months were compared with older children, overall satisfaction scores did not differ. Comparing palliative with nonpalliative patients, overall satisfaction scores did also not differ (median = 5 for each subgroup analysis). Fifty out of 60 (83.3%) parents would recommend the use of the home Airvo device to other families in a similar situation. Forty-six out of 60 (76.7%) parents reported improved quality of sleep while using HFNC.

### 3.4 | Patient subgroups

Fourteen patients died during the study period. All had suffered from severe life-limiting conditions, including complex congenital cardiac disease (4), chromosomal abnormalities with global developmental delay and extreme hypotonia (4), multiple sulfatase deficiency (2), end stage lung disease (2), Menkes syndrome (1), and Tay Sachs disease (1). In all cases, HFNC was used with palliative intention, to reduce distress and work of breathing. None of the children died within the first 3 months of treatment onset and in no case was the HFNC treatment considered a potential cause of death. Of the four families on whom questionnaire data were available, all reported an overall satisfaction score of 5/5, all indicated a positive effect on their child's respiratory distress and all would recommend home HFNC use to other families in a similar situation.

Thirteen patients had trisomy 21, eight of whom (62%) were treated with home HFNC for OSA. Out of the remaining five patients, three were primarily treated for airway malacia, but also had OSA as a comorbidity. Median age of treatment initiation in this group was 8.8 months and eight (61%) were classified as failing to thrive, according to trisomy 21 adjusted percentile charts. However, four patients were started on HFNC when they were older than 7.9 years. Eight of nine families of patients with trisomy 21 who had answered the full questionnaire indicated that the device had improved the quality of their child's sleep. Their average satisfaction score was 4.6 out of 5 and all families would recommend it to other families with children in a similar condition.

Four patients were treated for the main indication of neuromuscular disease. In all cases, severe hypotonia was the reason for initiating treatment. The diagnoses were Menkes disease, myasthenia gravis, and two cases of familial hypotonia without specific diagnosis.

### 3.5 | Safety

According to review of the electronic medical records and parental interviews, there were no serious adverse events during home treatment in any of the patients. Seven children were reported to have suffered adverse events, including facial skin irritation (5) and mild epistaxis related to nasal prongs use (2). These were deemed to be related to HFNC therapy, but mild.

**TABLE 2** Clinical observations before and after HFNC initiation (n = 51)

| Population  |                             | Total (n = 51) |                                | FTT (n = 38) |                               | OSA (n = 26) |                                | Preterm <sup>a</sup> (n = 13) |  |
|---|-----------------------------|----------------|--------------------------------|--------------|-------------------------------|--------------|--------------------------------|-------------------------------|--|
|   | Median (IQR)                | p              | Median (IQR)                   | p            | Median (IQR)                  | p            | Median (IQR)                   | p                             |  |
| <b>Weight SDS</b>                                   |                             |                |                                |              |                               |              |                                |                               |  |
| Pre   | -2.3 (-4.4, -1.1)           | <0.001         | -3.5 (-5.2, -2.1)              | <0.001       | -1.6 (-3.5, -0.5)             | <0.001       | -3.4 (-5.2, -1.6)              | 0.002                         |  |
| Post  | -1.7 (-3.5, 0) <sup>b</sup> |                | -2.6 (-3.3, -1.6) <sup>c</sup> |              | -1.1 (-2.6, 0.7) <sup>d</sup> |              | -2.2 (-3.3, -0.9) <sup>e</sup> |                               |  |
| <b>Total days of hospital admission<sup>f</sup></b> |                             |                |                                |              |                               |              |                                |                               |  |
| Pre   | 22 (5.5, 60)                | 0.008          | 4.1 (0.7, 9.9)                 | <0.001       | 0.9 (0.1, 7.8)                | 0.001        | 7.1 (1.2, 10.9)                | 0.001                         |  |
| Post  | 5 (0, 14.7)                 |                | 0.2 (0, 0.7)                   |              | 0.1 (0, 0.3)                  |              | 0.2 (0, 0.6)                   |                               |  |
| <b>Days of respiratory admission<sup>f</sup></b>    |                             |                |                                |              |                               |              |                                |                               |  |
| Pre   | 22 (0.5, 54.2)              | <0.001         | 2.4 (0, 18.5)                  | <0.001       | 0.5 (0, 6.2)                  | 0.003        | 3.7 (0, 8.3)                   | <0.001                        |  |
| Post  | 1 (0, 8)                    |                | 0 (0, 8.5)                     |              | 0 (0, 0.5)                    |              | 0 (0, 0.6)                     |                               |  |

Note: For the purpose of this analysis, out of 75 patients in the cohort, 14 were excluded as they were treated palliatively and another 10 were excluded as they were never discharged home before HFNC initiation, resulting in a sample of 51 children.

Abbreviations: FTT, failure to thrive; HFNC, high-flow nasal cannula; OSA, obstructive sleep apnea; SDS, standard deviation score; weight SDS pre, weight SDS at time of HFNC initiation; weight SDS post, weight SDS at follow up, time closest to 6 months.

<sup>a</sup>= (gestational age < 37 wks).

<sup>b</sup>Follow up weight recorded at mean (SD) 6.7 (±5.2) months postinitiation.

<sup>c</sup>Follow up weight recorded at mean (SD) 6.6 (±4.9) months postinitiation.

<sup>d</sup>Follow up weight recorded at mean (SD) 6.3 (±4.9) months postinitiation.

<sup>e</sup>Follow up weight recorded at mean (SD) 4.9 (±2.4) months postinitiation.

<sup>f</sup>Median total and respiratory-related hospitalization days were compared between two time periods: 2 months before and 2 months after introduction of HFNC.

All 14 patients who died during the study period had severe life-limiting conditions and it was apparent from the review of the electronic medical records that HFNC was used with a palliative intention and it not felt to have hastened the children's demise.

## 4 | DISCUSSION

HFNC therapy is a relatively new mode of noninvasive respiratory support. While its role in acute respiratory disease is well described,<sup>1,6,16</sup> indications, outcomes, and safety in the domestic setting are still being explored.<sup>17–20</sup> To our knowledge, this multicenter study is the largest series to date to address the use of home HFNC therapy for chronic respiratory conditions in children. It contributes to the body of literature characterizing the growing niche between conventional oxygen therapy (COT) and NIV that HFNC is carving out for itself. While COT is ubiquitously available, easily applied, and well tolerated, it can be insufficient in severe hypoxemia and ventilatory abnormalities. The various modes of NIV on the other hand, although highly effective, are often poorly tolerated and expertise is needed to optimize prongs/mask interface, tubing, and ventilatory settings. A further important drawback is the risk of facial bone deformity with long-term use of an NIV mask. By providing high flow of air or oxygen at physiological temperature and humidity conditions, HFNC effectively treats a broad variety of conditions that were previously poorly served by existing modalities.

## 4.1 | Indications

Children in our centers were initiated on HFNC for a variety of indications, with OSA and airway malacia featuring most prominently. This is in keeping with previous reports,<sup>14,21,22</sup> emphasizing its benefit on mechanics of breathing and gas exchange in patients with upper and large airway pathology. As shown by Ameddeo et al. who demonstrated improved compliance as well as correction of OSA in children intolerant of CPAP, HFNC is not only better tolerated but also effective in this group of patients.<sup>22</sup> A similar study evaluated detailed somnography data in a sample of 22 young children with OSA and also found good home tolerability, as well as a significant reduction in obstructive apnea-hypopnea index.<sup>21</sup> We were unable to report on AHI or bicarbonate levels, but the observed clinical improvement and parental satisfaction are corroborated by the findings of the aforementioned OSA studies.

Similarly to previous reports, we treated children with trisomy 21, many of whom have sensory processing difficulties,<sup>23</sup> posing a challenge for adaptation to the often inconvenient conventional NIV. Indeed, their main treatment indication in our trisomy 21 group was OSA and parental satisfaction was very high, following failed attempts at the use of CPAP or BiPAP as stipulated by the treatment protocol.

A small proportion of our patients had neuromuscular disease. This is expected, as hypotonic patients ought preferentially be treated with positive airway pressure that can be dialed precisely to

**TABLE 3** Parental questionnaire analysis (n = 60)

| Question   | Results  |
|--|--|
| How did your child adjust to HFNC treatment?   | Well (40, 67%)<br>Poorly (20, 33%)<br>Not sure (0)       |
| How was the quality of sleep while on home HFNC treatment, compared to prior?                                | Better (46, 77%)<br>Worse (14, 23%)<br>Unchanged (0)     |
| Please comment on the respiratory distress during home HFNC treatment, compared to prior?                    | More distressed (0, 0%)<br>Less distressed (60, 100%)    |
| How was your child's appetite while on home HFNC treatment, compared to prior?                               | Better (19, 32%)<br>Worse (2, 3%)<br>Unchanged (39, 65%) |
| Please comment on your child's daytime alertness while on home HFNC treatment compared to prior.             | Better (34, 57%)<br>Worse (1, 2%)<br>Unchanged (25, 42%) |
| What is your overall satisfaction of HFNC use on a scale of 1–5 with 5 being most satisfactory (median, IQR) | 5 (4, 5)   |
| How easy was the device was to maintain, on a scale of 1–5 with 5 being the easiest (median, IQR)            | 5 (5, 5)   |
| Would you recommend home HFNC use to other families in a similar situation?                                  | Yes (50, 83%)<br>No (1, 2%)<br>Not sure (9, 15%)         |
| Were there any serious adverse events while using home HFNC treatment?                                       | 0/60   |

Abbreviations: HFNC, high-flow nasal cannula; IQR, interquartile range.

achieve maximal alveolar recruitment and efficient ventilation. This not having been established reliably for HFNC, it would seem that this mode was chosen for the neuro-muscular patients in our sample with the primary intention to keep them comfortable, whilst providing at least some physiological support. Although high-flow devices are not designed to provide significant amounts of airway pressure and the risk of atelectasis and hypercapnia in hypotonic patients must be considered, it has been shown that some positive end-expiratory pressure is achieved with high-flow devices, resulting in alveolar recruitment.<sup>24</sup>

## 4.2 | Clinical observations and parental satisfaction

After HFNC initiation, significant weight gain, fewer hospitalization days, and improved oxygenation were observed in all patient groups. This observation is in keeping with data from the use of NIV in neuromuscular patients, which was associated with improved feeding, weight gain, and growth, suspected to result from a decrease of the work of breathing, consequent caloric burn, and improved

eating and swallowing.<sup>25</sup> In a different cohort of children with neuromuscular diseases, the institution of NIV also resulted in fewer hospitalization rates, as well as health care costs.<sup>26</sup>

With regard to patients who used HFNC in a palliative care setting, not all families were interviewed, due to the reluctance of one of the centers to contact parents following the tragic loss of a child. However, the few responses that we were able to gather indicated high satisfaction, presumably due to the relief of respiratory distress and improved quality of sleep.

## 4.3 | Safety

Although no serious adverse effects were observed in our cohort, one must bear in mind that certain upper airway abnormalities, life-threatening hypoxia, facial bone or skull base trauma, as well as pneumothorax might make HFNC ineffective or potentially dangerous.<sup>27</sup> Concerns have also been raised about the risk of pulmonary aspiration in small children receiving enteral nutrition whilst on HFNC therapy. These have to some extent been allayed by a large prospective observational study that examined infants with bronchiolitis. There was minimal occurrence of aspiration-related respiratory failure and oral nutrition was tolerated across a range of HFNC flow and respiratory rates, encouraging feeding during HFNC treatment.<sup>28</sup> Table 4 summarizes some caveats that we suggest to consider before commencing a child on home HFNC therapy.

## 4.4 | Limitations

Our study has a number of limitations, most of which are rooted in its retrospective design. The designation of children with complex morbidity into distinct diagnostic groups is fraught with difficulty. We tried to minimize observer bias by leaning on the clinical indication as stated by the treating physician. The assessment of clinical treatment effect relied on outcomes like weight and hospitalization days, that are affected by a host of parameters other than HFNC treatment. Children with most pathologies have a tendency to improve and regress to the mean over time, gaining weight and requiring less hospital admissions. Our group is very heterogeneous and no control group was available, making the data difficult to interpret. While no causality can be established, the observed associations between HFNC treatment and the clinical outcomes, all of which improved significantly is encouraging. Although we lack objective outcome markers, such as sleep studies and bicarbonate levels in our largest group, those with OSA, evidence of improvement in these parameters has been provided by others.<sup>14,21</sup>

Any retrospective assessment of safety is prone to unavoidable omission bias. It is possible that some AEs could have occurred, but not collected in the electronic medical records by the clinical team and therefore not reported here. We tried to minimize this by additionally asking the patients' families about AEs. A further weakness is the lack of bronchoscopic airway assessment with

**TABLE 4** Suggested checklist before home use of high flow nasal cannula (HFNC) therapy in children

|   |
|---|
| HFNC ought to be reserved for conditions that require treatment mainly during sleep.  |
| Ensure that the child can tolerate several hours off HFNC therapy or treatment with nasal cannula/environmental oxygen only.  |
| Aim for FiO <sub>2</sub> not above 40%, ideally room air.   |
| Rule out upper airway abnormalities, life-threatening hypoxia, facial bone or skull base trauma, as well as pneumothorax which might render HFNC ineffective or potentially dangerous.            |
| For children with significant neuromuscular disorders, positive airway pressure respiratory support, airway surgery or tracheostomy might be required.  |
| The child should not have an unstable airway or be clinically unstable while on HFNC.   |
| The child should be able to tolerate undetected events of the cannula dislodgement.   |
| Parents ought to be trained in resuscitation and be equipped with an oximeter at home.  |
| A trial of treatment with the device being used in the domestic setting ought to be carried out as inpatient before discharge.  |
| The child and family ought to be supported by a home care team consisting of a technician and a physician familiar with noninvasive respiratory support (pediatric pulmonologist or intensivist). |

Abbreviation: FiO<sub>2</sub>, fraction of inspired oxygen; HFNC, high flow nasal cannula.

formal diagnosis of airway malacia, with was rarely undertaken. We could not find a relevant validated parental questionnaire, and the items were designed by the study members.

Finally, although this is a larger cohort than previously published, it must be considered that it captures data gathered from three hospitals over a period of 6 years, averaging only about four children initiated on HFNC per hospital per year.

## 4.5 | Summary

To conclude, in our population, domestic use of HFNC in children appeared safe and well tolerated for a broad variety of indications. Its introduction was associated with improved weight gain, fewer hospitalization days and high parental satisfaction. As HFNC has made its way out of the neonatal and pediatric intensive care units and onto the wards, it is now starting to be deployed in the home setting. Further work is required to better characterize groups of children most likely to benefit from this treatment, as opposed to traditional modes of NIV.

### AUTHOR CONTRIBUTIONS

**Shay Ehrlich:** Validation; writing – review and editing; data curation; project administration; investigation; conceptualization. **Inbal Golan Tripto:** Conceptualization; writing – review and

editing; formal analysis; data curation. **Moran Lavie:** Conceptualization; writing – review and editing; formal analysis; data curation. **Michal Cahal:** Data curation; validation; formal analysis. **Tommy Shonfeld:** Conceptualization. **Dario Prais:** Writing – review and editing; formal analysis. **Hagit Levine:** Writing – review and editing; investigation. **Meir Mei-Zahav:** Investigation; writing – review and editing. **Ophir Bar-On:** Investigation; writing – review and editing. **Yulia Gendler:** Investigation; writing – review and editing; methodology; conceptualization. **Jonatan Zalcman:** Formal analysis; data curation. **Eahab Sarsur:** Investigation; writing – review and editing. **Micha Aviram:** Investigation; validation. **Aviv Goldbart:** Investigation; validation. **Patrick Staffler:** Conceptualization; investigation; funding acquisition; writing – original draft; methodology; validation; writing – review and editing; formal analysis; project administration; supervision.

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### CONFLICT OF INTEREST

An educational grant was received from Fisher & Paykel. The company did not participate in data collection, statistical analysis, or interpretation of the findings.

### DATA AVAILABILITY STATEMENT

None.

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