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Use Of High Flow Nasal Cannula In Children

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Abstract

The use of high flow nasal cannula (HFNC), also often called Heated Humidified High Flow Nasal Cannula (HHHFNC) is a relatively new non-invasive therapy. HFNC was firstly introduced to treat premature babies as an alternative to CPAP, but recently there has been an increase number of HFNC using in children and adults care. However, the evidence for the safety and effectiveness of HFNC as respiratory support in children is still lacking. Studies of the effects of HFNC was identified to have positive clinical effects on SpO2, PaO2, respiratory rate and blood gas analysis parameters in some children, especially children with bronchiolitis. Most clinical studies in children are observational studies in infants with bronchiolitis. Various positive clinical effects on various respiratory parameters have been found, reducing work of breathing, reducing the need for CPAP and invasive ventilation in infants and children. Until more and more available evidence, HFNC can be used as an additional form of breathing assistance in infants and children, but with a clinical approach based on clinical responses and safety issues that are associated with the introduction of earlier treatment failures especially in children treated with HFNC outside the PICU.[1]

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INTRODUCTION

The use of high flow nasal cannula (HFNC), also often called Heated Humidified High Flow Nasal Cannula (HHHFNC) is a relatively new non-inavsive therapy, seems well tolerated to neonates and adult patients who suffers hypoxemia respiratory failure. Before the introduction of HFNC, the maximum use of nasal cannula oxygen for neonates was 0,5 – 1 L/min and older children or adult was 2 L/min to prevent nasal mucose dryness and discomfort and others nasal mucose complication. High flow is usually defined by flow speed at ≥ 2L L/min, which depends on the types of used cannula, but approximately ranged 4 to 70 L/min. The debate is ongoing whether HFNC can reduce the use of more invasive and less tolerable ventilators such as continuous positive airway pressure (CPAP) and mechanical ventilation.[1]

HFNC was firstly introduced to treat premature babies as an alternative to CPAP, but recently there has been an increase number of HFNC using in children and adults care. In children, its use is highly developed for infants and young children who are treated with bronchiolitis. However, the evidence for the safety and effectiveness of HFNC as respiratory support in children is still lacking as emphasized in 2 Cochrane reviews in 2014. Nevertheless, the implementation of HFNC is increasing in clinical practices therefore it is important for doctors to keep updating of latest knowledge developments. This study aims to find out the most recent evidence of HFNC in the mechanism of action, safety, clinical effects and tolerance for children outside the newborn period.[1]

DEFINITION OF HFNC

Based on 2014 Cochrane review, HHHFNC for children is defined as the administration of oxygen/air using nasal cannula which is mixed, heated, moistened by the flow speed at ≥ 2 L/min, where administered together with high oxygen concentrations and the potential for increaed pressure continuously. (Figure 1)

MECHANISM OF ACTION OF HFNC[3-5]

1. Removing nasopharynx dead space and increasing the oxygen & carbodioxide fraction in alveolus.
2. Reducing inspiration resistance and work of breathing by providing adequate flow
3. Improving airway conduction and lung compliance by reducing the effects of cold air, in an *in vitro* study, it appears that inspiration with low humidity can deteriorate the function of airway epithelial cell in a short time
4. Reducing costs by providing 100% relative humidity air
5. Giving an end-distending pressure to lung

PRESSURE RESULTED BY HFNC

Pressure that reaches the distal airway is difficult to measure. Various indirect methods are used such as pressure in the esophagus, pharynx, nasopharynx, electrical impedance tomography on the chest surface, or electrical activity in the diaphgram.[1] Locke et al. reported that HFNC of 2 L/min in neonates resulted high esophageal pressure up to 9.8 cm H_2O.[6] Measurements in children and adult pharynx and esophagus was 2-4 cm H_20.[7-10] Prospective studies in 25 patients under the age of 18 received greater pleural pressure on HFNC with a flow of 8 L/min compared to 2 L/min.[11]

Pulmonary model studies showed an increased positive pulmonary distension pressure by increasing the flow from 0 L/min to 12 L/min. Overall, the the distension pressure of airway depends on the patient's weight/size, flow rate, and diameter of the nasal cannula compared to the nostrils, with higher pressure when the mouth is closed. In conventional nasal CPAP, the pressure on the patient's airway is controlled by the valve of escape route. HFNC has no control valves and drainage routes, leakage is only found in the nostril interface and mouth.[12-13]

FLOW RATE

The maximal of optimized flow rate of HFNC is unknown. Most studies report the use of flow velocities varying from 2 to 8 L/min and adjusted individually to minimize patient respiratory work and SpO_2 values. There are 9 studies of estimated flow rate based on patient weight. Six of the studies used 2 L/kg/min with a maximum of 8-12 L/min in 2 studies.[1] One study reported flow rates from 1 to 3 L/kg/min but a maximum of 8 L/min.[14] Studies in children treated with bronchiolitis in the child care room, giving oxygen with a flow rate of 2 L/kg/min, a maximum of 10 L/min is safe and there are no side effects.[15]

Guidelines for initiation and escalation strategies and weaning of HFNC in general pediatric care are recommended. In local guidelines, the initial flow depends on age, and increased if the point on a particular patient's assessment system is above the trigger level given. Determining the flow rate based on kilograms of weight can be considered but will produce very high flow rate.[16]

Some studies that include infants have used flow rates of more than 10 L/min and no studies have compared flow rates above 10 L/min and pressure, higher flow rates of up to 50 L/min have been used in several studies including adolescents and adults. Flow rates of 1.5-2 L/kg/min have been used in children both in the general child care and PICU. Because of the lack of studies using higher flow rates and some reports of serious cases of air leakage in children treated with HFNC, increasing flow rates higher than 1 L/kg/min or higher than 10 L/minute in infants especially outside PICU should be careful.[1]

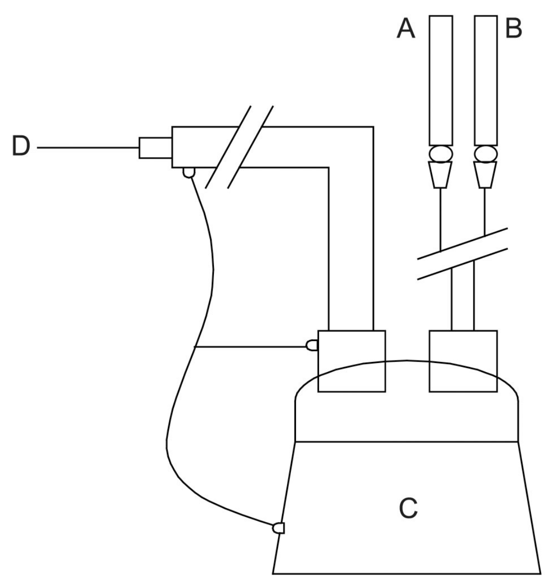


Figure 1. Diagram of the high-flow nasal cannula. A: Compressed air source. B: Oxygen source. C: Heated humidifier. D: Nasal cannula. [20]

CILINICAL EFFECT

Ventilation and oxygenation

In a randomized prospective study of 19 infants treated with bronchiolitis, the median higher SpO2 at 8 and 12 hours and not at 24 hours was found in the HFNC group compared to the oxygen head-box group. Randomized controlled studies of children who underwent cardiac surgery found improvements in partial pressure of oxygen/ fraction of inspired oxygen (PaO2/FiO2) after ectubation in children who received HFNC compared to oxygen given with cannula of a maximum flow rate of 2 L/min. A decreased of respiratory rate and improvement of blood gas parameters were also reported in other studies of bronchiolitis.[1]

PICU Care and length of stay

A case control study of HFNC effect in PICU suggested that children with fourfold smaller HFNC was found compared to children who receive standard therapy.[15] There was no length of stay differences. However, small observational prospective studies in children with bronchiolitis received a shorter 3-day length of stay who received HFNC than low-flow oxygen.[17] Other prospective bronchiolitis studies suggested a median length of stay of 4 days versus 3 days before and after HFNC was given a general care. There was no difference in length of stay in studies comparing children with bronchiolitis treated with HFNC and hypertonic saline, or in bronchiolitis studies comparing children with CPAP and HFNC for two sessions. Likewise there was no difference in length of stay in a randomized controlled study comparing children with cardiac surgery who received conventional oxygen therapy and HFNC.[18] Or in a retrospective case-control study in children aged 0-18 years treated in PICU with acute respiratory insufficiency due to various respiratory diseases.[19] Median LOS in PICU decreased from 6 to 4 hours in children with bronchiolitis treated with HFNC compared to children treated at time before the introduction of HFNC but this study may have limitation of clinical importance, because LOS is very briefly reported.[1]

In conclusion, studies of the effects of HFNC was identified to have positive clinical effects on SpO2, PaO2, respiratory rate and blood gas analysis parameters in some children, especially children with bronchiolitis. In children with bronchiolitis, some effects of HFNC have also been found in the length of stay and treatment in PICU but not in children with other respiratory diseases.[1]

Patient comfort

Only one small study of children outside the neonatal period investigated the patient tolerance and adherence. This study consisted of 46 children with various causes of respiratory disorders aged range of 0-12 years old and found that patient comfort as measured by the COMFORT scale improved when the oxygen administration was changed to nasal cannula or simple mask to HFNC.[9] Small studies in 20 adults suggested that high flow rate found more comfortable and associated with reduced tightness and mouth dryness compared to oxygen administration through simple mask.[20] (Figure 2) Studies of newborns in Norway have no difference results in patients with HFNC and CPAP, but parents choose HFNC instead of CPAP, reportedly their children are more satisfied and they find it easier to interact with their children when using HFNC. But studies in premature infants have reported no differences of noise levels between CPAP and HFNC.[21] The results of these studies in neonates may also apply to infants treated with bronchiolitis.[1]

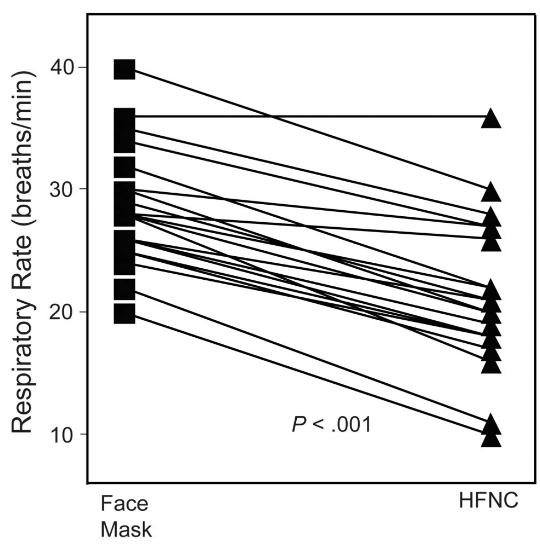


Figure 2. Change in respiratory rate with change from face mask to High-flow nasal cannula (HFNC).[20]

Surveys from Australia and New Zealand aimed at senior medical staff and nurses have gotten results despite a lack of guidelines, that HFNC is considered easier to use and convenient for infants.[22] The results of this assessment show that patient tolerance is better in using HFNC than other forms of respiratory support, but it can also explain the popularity in the clinical staff and as one of the reasons of increased use in recent years although lack of clinical effectiveness evidence.

Non Responder Identification

A study in children treated for bronchiolitis aimed to identify responders and non responders to HFNC in 60 minutes of therapy. In the responders group the heart rate and respiratory rate were lower where there was no change in the non-responders group.[2] Likewise the initial non-responders identification was found in children with HFNC who were treated in PICU due to various causes of respiratory disorders. There was an increase in median respiratory rate at 1 hour of HFNC use in the failing group.[23] Another study, also in younger children with bronchiolitis, suggested results of no improvement in respiratory rate from non-responders group after HFNC initiation, more hypercapnia and also lower respiratory rates before HFNC started, allegedly they were exhausted.[24] Studies in children under 2 years of age, who came to the emergency department with respiratory distress, non-responders group had respiratory rate above 90th precentile age, initial $PaCO_2$ above 50 mmHg (6.7 kPa) and initial venous pH less than 7,30.[25] Blood gas measurements and identification of hypercapnia, respiration and tachypneu acidosis, can be used as early identification in infants and children at high risk of not responding to HFNC, so that additional respiration assistance therapy may be needed.[1]

HFNC VS CPAP

There is only one randomized controlled study comparing CPAP to HFNC in children after newborns. The study of children with severe pneumonia in Bangladesh found that when CPAP was compared with low flow oxygen, there was found improved outcomes (intubation, death, clinical failure) but no differences between children treated with HFNC or CPAP.[26] A small retrospective study compared HFNC to CPAP for 2 seasons, suggested that no differences were

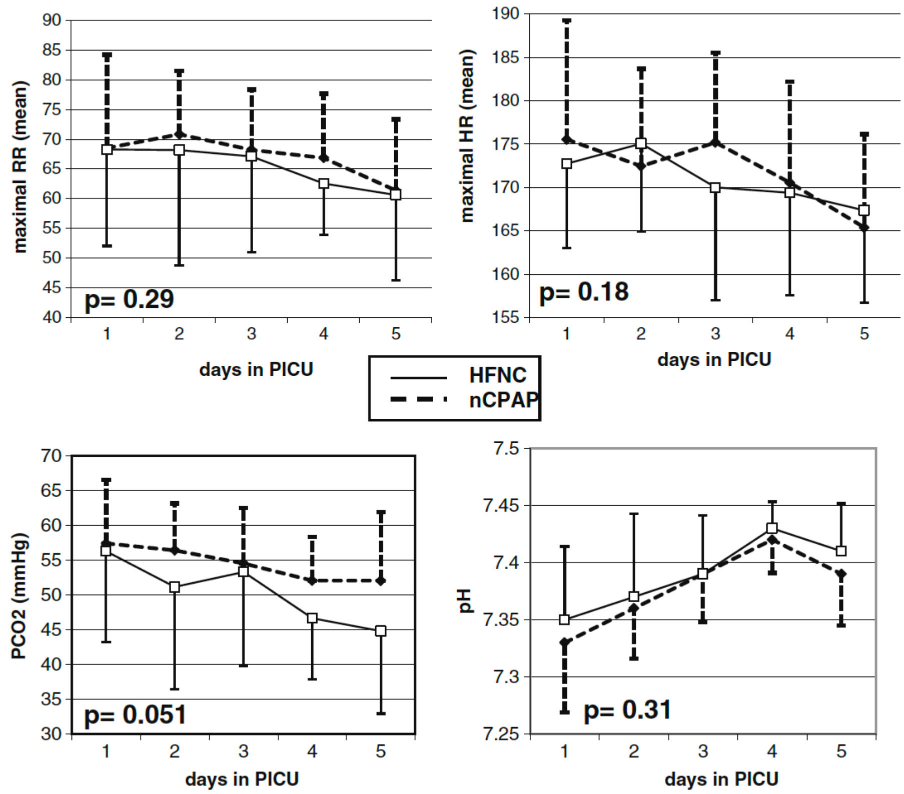


Figure 3. Maximal value of heart rate, respiratory rate, PCO2, and pH during the first 5 days in PICU. pediatric intensive care unit, HR heart rate, nCPAP nasal continuous positive airway pressure, HFNC high-flow nasal cannula.

found between groups in length of stay, respiratory rate, PaCO2, F1O2 or duration of oxygen administration.[14] (Figure 3) Other prospective studies did not get a significant difference between children with HFNC and CPAP in breathing rate, heart rate, oxygen saturation or distress breathing, In this study 26% of the children with HFNC needed relief escalation of respiration compared to 18% in the CPAP group (p = 0.27).[1]

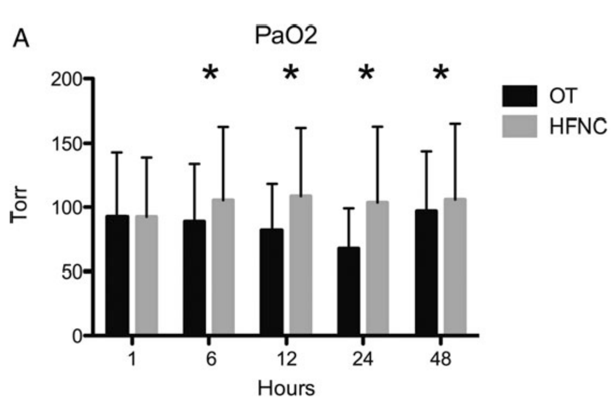
Observational studies measuring the pressure of delivery systems *in vitro* and *in vivo* in newborns have almost the same esophageal end-aspiration pressure between neonates treated with HFNC and CPAP. Controlled randomized studies in neonates and adults found no differences in the effects of CPAP and HFNC on intubation. In premature infants, there are 3 non-inferior randomized controlled studies that have a similar effect between HFNC and CPAP after intubation.[1]

INTUBATION

There are 5 retrospective observational studies that assess the use of HFNC and the risk of intubation in children. Three of the studies concluded that the use of HFNC was associated with a decreasing intubation rate, but had a low level of evidence. Two of the studies in children with bronchiolitis aged under 24 months, began with a flow rate of 8 L/min. A study conducted by Wing et al in children aged 0-18 years with conditions other than bronchiolitis with flow varying from 8 to 50 L/min depending on the age of the child. The fourth study with intubation as outcome used a flow rate of 2 L/kg/min but was not included in the control group. They reported that 12% of infants and children treated in PICU with various respiratory disorders supported by HFNC, further therapy in the form of CPAP or intubation was needed. Another study reported no difference in the level of intubation before and after HFNC initiation in the general pediatric care. While subsequent observational studies of approximately one third of children with HFNC in the emergency room require escalation of higher respiratory assistance (CPAP or intubation). It should be noted that even though RCTs in new adults were published, there was a decrease in overall mortality in HFNC with a flow rate of 50 L/min compared to noninvasive ventilation, there was no overall decrease in the level of intubation when compared to standard or non-invasive ventilation.[1]

ROLE OF HIGH FLOW IN ADDITION TO BRONCHIOLITIS

The 2014 Cochrane analysis that assessed the effect of HFNC on children with conditions other than bronchiolitis, obtained a results of no randomized controlled studies and concluded that there was no available evidence to determine the safety and effectiveness of HFNC as a form of respiration assistance in children.[2] One small study reported less effects in children with respiratory distress due to congenital heart disease compared to bronchiolitis.[27] The relationship between heart disease and a higher failure rate of HFNC was also found.[23] But new RCT publications examined HFNC versus conventional oxygen therapy during the first 48 hours after ectubation for heart surgery, HFNC improves PaO2 but not PaCO2.[18] (Figure 4) Clinical improvement with HFNC in children with obstructive sleep apnea is reported in 2 small studies. Some case reports also reported the effects of HFNC in children with acute pulmonary edema and burnt pediatric patients with stridor post ectubation.[1]



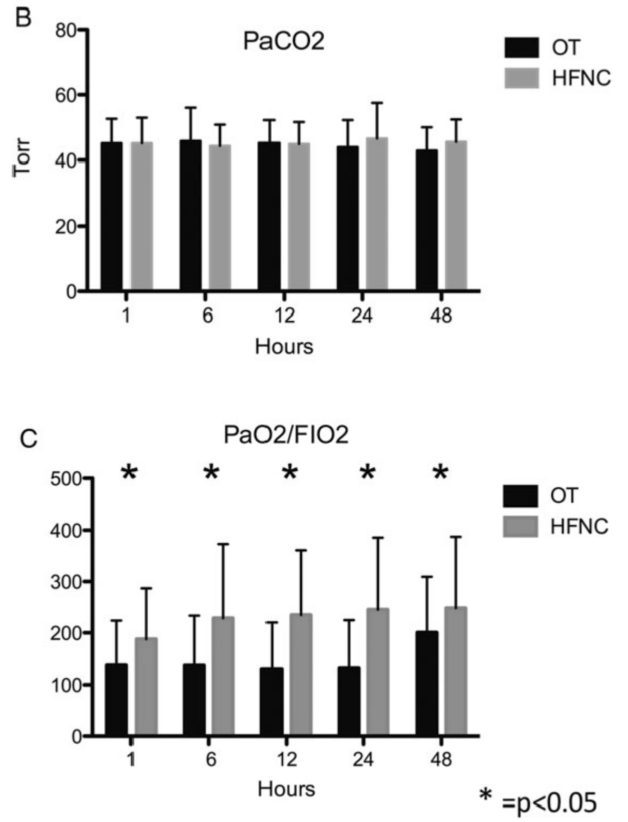


Figure 4. Oxygen therapy (OT) is represented by black bars and high-flow nasal cannulas (HFNCs) is represented by gray bars. 'Hours' are depicted after extubation. $*P < 0.05$. (A) Arterial PaO2 values; (B) Arterial PaCO2 values; (C) the PaO2/fractional inspired oxygen (FiO2) ratio.[18]

ADVERSE EFFECT AND SAFETY

Most studies reported no side effects in children with HFNC and concluded that the use of HFNC was safe in the general child care, emergency unit, and PICU.[1] But there were 2 reports that revealed 4 serious pneumothorax cases in children with HFNC: (1) 2-month-old child treated with RSV bronchiolitis (flow rate 6-8 L/min); (2) 16-year-old child with cerebral palsy (flow rate 15-20 L/min); (3) 22-month-old child with subdural hematoma (flow rate 6 L/min); and (4) 4-year-old child with asthma treated with HFNC (40 L/min). Unlike CPAP, which can carry through a system with an integrated pressure release valve, it is impossible to regulate or establish the pressure applied to the airway at HFNC Research *in vitro* and *in vivo* underlines the risk of high pressure HFNC devices with higher flow pressures, especially if there is minimal leakage.[1]

Three studies reported the incidence of abdominal distension in children with HFNC, therefore it should be taken carefully in children with intra-abdominal abnormalities. Mucosal injury with nasal bleeding and ulceration has been reported in children with HFNC but in RCTs preterm infants under 32 weeks of nasal trauma are less frequent in the HFNC group than in the CPAP group. In the event of an outbreak *Ralstonia mannitolilutica*, a pathogenic bacterial that spreads through water, has been reported in pediatric patients who received HFNC in America in 2005. These extraordinary incidence are related to intrinsic contamination of HFNC devices but since they have been replaced, there are no reports of events.[28]

CONCLUSIONS

Most of the research on the use of HFNC outside the newborn period is a small observation study with a limited level of evidence for infants and children. The results of the study found that HHFC was relatively safe, well tolerated and a feasible method of administering oxygen for infants and children in the general child care. Differences in mechanisms such as negating nasopharyngeal dead space, increasing pulmonary compliance are postulated but there may be a number of widening airways due to pressure as the main cause.[1]

Most clinical studies in children are observational studies in infants with bronchiolitis. Various positive clinical effects on various respiratory parameters have been found, reducing work of breathing, reducing the need for CPAP and invasive ventilation in infants and children. RCTs conducted in premature and adult infants get the results of HFNC having the same effectiveness as CPAP after ectubation. Children undergoing cardiac surgery have improved oxygenation in the post-extubation period when compared with low flow oxygen.[1]

There are no international guidelines of flow rate, and the varying flow rates used in various studies can explain the differences in the effects of HFNC. HFNC RCTs involving children outside the newborn period are ongoing. Until more and more available evidence, HFNC can be used as an additional form of breathing assistance in infants and children, but with a clinical approach based on clinical responses and safety issues that are associated with the introduction of earlier treatment failures especially in children treated with HFNC outside the PICU.[1]

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