Reply to the Letter to the Editor: “Is High-Flow Nasal Cannula Useful as Primary Respiratory Support in Preterm Infants?”

Srinivas Murki^a Nandkishor S. Kabra^b

^aFernandez Hospital, Hyderabad, India; ^bSurya Hospital, Mumbai, India

Dear Sir,

We thank the readers for their keen interest in and comments on our study published in *Neonatology* [1]. In this study, nearly an equal proportion of infants enrolled in the trial had respiratory distress syndrome (RDS) as the admission diagnosis for respiratory distress. However, among the infants where the cause of respiratory distress was other than RDS, transient tachypnea of newborn or delayed clearance was present in 72 out of

133 (54%) in the high-flow nasal cannula (HFNC) group and 60 out of 139 (43%) in the nasal continuous positive airway pressure (nCPAP) group, respectively. One newborn in the nCPAP group was diagnosed with pneumonia. Among the infants with a cause of respiratory distress other than RDS, the failure rate was significantly higher in the HFNC group (HFNC group 14/72 [19.4%] vs. nCPAP group 3/61 [4.9%], $p = 0.017$). Although

InSurE involves nCPAP as the respiratory support in the majority of cases, any non-invasive support is acceptable for the actual definition. As expected, the need for surfactant therapy (InSurE) was higher in the nCPAP group as the proportion of infants with RDS was higher in this group, although statistically not significant. However, on subgroup analysis, in the infants who received surfactant (HFNC group 58/133 [43.6%] vs. nCPAP group

Table 1. Recent trials comparing HFNC with nCPAP as the primary mode of respiratory support

	Yoder et al. [2] (n = 314)	Lavizzari et al. [3] (n = 316)	Robert et al. [4] (n = 574)	Murki et al. [1] (n = 272)	Shin et al. [5] (n = 85)
<i>Failure criteria</i>					
Maximum FiO ₂	0.60	0.40	0.40	0.60	0.40
Recessions	Marked or severe	–	–	SAS >2 from baseline	–
Apneas	PPV for 30 s	PPV need	PPV need	PPV need	PPV need
Shock or metabolic acidosis	BE >–10 meq/L	–	–	BE >–10 meq/L	–
Respiratory acidosis	PaCO ₂ >65 mm Hg	PaCO ₂ >70 mm Hg	PaCO ₂ >60 mm Hg	PaCO ₂ >60 mm Hg	PaCO ₂ >65 mm Hg
HFNC failure rate	15 (9.8)	17 (10.8)	71 (25.5)	35 (26.3)	19 (38)
CPAP failure rate	9 (5.6)	15 (9.5)	38 (13.3)	11 (7.9)	9 (21)
InSurE criteria	Not clear	Yes (FiO ₂ >0.35)	No Surfactant at intubation	Yes FiO ₂ >0.30 and CXR suggestive of RDS	No
Rescue mode for treatment failure in HFNC	Intubation	Intubation	nCPAP	nCPAP	Intubation or nCPAP

Values in parentheses are percentages. PPV, positive pressure ventilation; SAS, Silverman Anderson score; BE, base excess. CXR, chest X-ray; RDS, respiratory distress syndrome.

68/139 [48.9%]), the failure rate of the support mode was higher in the HFNC group (HFNC group 24/58 [41.4%] vs. nCPAP group 11/68 [16.2%], $p < 0.001$). An updated meta-analysis including all recent trials is needed to improve the evidence base on the use of HFNC as primary respiratory support in preterm infants with respiratory distress. A close look at all the current trials (Table 1) comparing HFNC with nCPAP highlights some of these important findings [2–5].

The criteria for the failure rate are similar across all of the trials. The rescue mode in the HFNC group (either nCPAP or intubation with mechanical ventilation) was different in the separate trials, leading to the differences in the reporting of the trial results.

Infants with significant respiratory distress were not enrolled in most trials and InSurE as a therapy among enrolled infants was not a common adjunct in all. This may explain the different failure rates in the nCPAP groups across the trials.

Assuming all treatment failures in both groups were intubated in our study, the need for intubation or mechanical ventilation would have been significantly higher in the HFNC group (35/133 [26.3%] vs. 11/139 [7.9%], risk difference in treatment failure 18.4% with 95% CI 9.7–27.1%). Considering the results from our study and also from all the other recent trials, we strongly believe that HFNC is inferior to nCPAP in preterm infants with moderate or mild respiratory distress.

References

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