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Title:
Randomised controlled trial of high-flow nasal cannula in preterm infants after extubation

Date:
2021-07-01

Citation:
Manley, B. J., Hodgson, K. A. & Davis, P. G. (2021). Randomised controlled trial of high-flow nasal cannula in preterm infants after extubation. Acta Paediatrica International Journal of Paediatrics, 110 (7), pp.2285-2286. https://doi.org/10.1111/apa.15848.

Persistent Link:
https://hdl.handle.net/11343/298423

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Article type : EBNEO Commentary

Title page

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TITLE OF WRITE-UP

Randomized Controlled Trial of High-Flow Nasal Cannula in Preterm Infants After Extubation

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MANUSCRIPT CITATION

Uchiyama A, Okazaki K, Kondo M, Oka S, Motojima Y, Namba F, Nagano N, Yoshikawa K, Kayama K, Kobayashi A, Soeno Y, Numata O, Suenaga H, Imai K, Maruyama H, Fujinaga H, Furuya H, Ito Y, Non-Invasive Procedure for Premature Neonates (NIPPN) Study Group. Randomized Controlled Trial of High-Flow Nasal Cannula in Preterm Infants After Extubation. Pediatrics 2020; 146(6):e20201101. ADD PMID

COMMENTARY

HFNC therapy is increasingly used as 'non-invasive' respiratory support for preterm infants. A 2016 Cochrane Review found that HFNC had similar efficacy to NCPAP for preterm infants following extubation (1), but that further studies were needed, particularly in extremely preterm infants born <28 weeks' gestation, who are at highest risk of extubation failure.

The trial by Uchiyama *et al*. is the largest randomised trial of HFNC as post-extubation support in preterm infants, and one of only a few to enrol extremely preterm infants (168 infants enrolled; 76 HFNC, 92 NCPAP/NIPPV). This multicentre non-inferiority trial found NCPAP/NIPPV was superior to HFNC (and HFNC did not satisfy non-inferiority criteria) for the primary outcome of treatment failure within 7 days. Reintubation rates were similar; more than 80% of infants who met HFNC treatment failure criteria avoided reintubation due to crossover to NCPAP/NIPPV.

Like previous similar trials (2-4) the intervention was not blinded, although objective treatment failure criteria were used. In the NCPAP/NIPPV group, 149 infants received NCPAP and 47 received NIPPV at extubation. In both groups, the escalation of respiratory support was at clinician discretion. As the control group could receive either NCPAP or NIPPV, the definition of "treatment failure" is blurred: some infants received NIPPV before "treatment failure" and others didn't. It is not reported whether NIPPV inflations were synchronised with the infant's breathing or not, which may be important (5).

A non-inferiority trial design is reasonable given the existing evidence, although the sample size calculation assumed a HFNC treatment failure rate 9% higher than that of NCPAP/NIPPV, and the chosen non-inferiority margin was rather large. There is an imbalance in the allocation of infants to HFNC (47%) and NCPAP/NIPPV (53%). A total of 378 infants were ultimately recruited to the study (38 more than required, even with inflation for anticipated dropouts), however this represents only 33% of eligible infants which has implications for generalisability of the results. The use of respiratory stimulants prior to extubation is not reported. The trial was prospectively registered, however there are inconsistencies between the registration and the published trial in the stated sample size, comparator and primary outcome.

The starting HFNC gas flow was >2 L/min, lower than some previous studies (3, 4), and it is unclear whether infants received the maximal permitted gas flow of 8 L/min prior to treatment failure being determined. As increasing gas flow is associated with increased delivered pressure (6), this may have contributed to decreased efficacy in the HFNC group.

Extubation failure in preterm infants is an important concern for neonatal clinicians, and the optimal mode of post-extubation respiratory support remains uncertain. The results of the trial by Uchiyama *et al*. may tip the balance in favour of NCPAP/NIPPV as initial post-extubation support however, consistent with previous evidence, reintubation rates are similar when HFNC is used with the 'backup' of NCPAP/NIPPV. For the most immature infants at highest risk of extubation failure it seems prudent to avoid using HFNC as initial post-extubation support.

URL LINK: URL TO THE FULL REVIEW ON THE EBNEO WEBSITE

FUNDING

No specific funding was received for this review.

CONFLICT OF INTEREST

The authors have no conflicts of interest to declare.

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