

Nasal high-frequency oscillatory ventilation versus nasal continuous positive airway pressure as primary respiratory support strategies for respiratory distress syndrome in preterm infants: a systematic review and meta-analysis

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Abstract

Nasal high-frequency oscillatory ventilation (NHFOV) has been described to be an advanced version of nasal continuous positive airway pressure (NCPAP). However, its beneficial effects among different studies were inconsistent. The aim of the present study was to assess the effects between NHFOV and NCPAP as the primary respiratory supporting strategies on the intubation rate in preterm infants with respiratory distress syndrome(RDS). Medline, the Cochrane library, the Cochrane Controlled Trials Register, EMBASE, Chinese National Knowledge Infrastructure (CNKI), and Wanfang data Information Site were searched from inception to Jan 1, 2021(Prospero2019 CRD42019129316, date of registration:Apr-23,2019). Pooled data from clinically randomized controlled trials(RCTs) comparing NHFOV with NCPAP as the primary respiratory supporting strategies in preterm infants with RDS were performed using the fixed-effects models whenever no heterogeneity was shown. The primary outcome was intubation rate. Four randomized controlled trials involving 570 participants were included. Comparing with NCPAP, NHFOV resulted in less intubation rate(relative risk(RR):0.47; 95% confidence interval(CI):0.31–0.70, $P=0.0002$), and heterogeneity was not found among the trials in the fixed effects model ($P=0.69$, $I^2=0\%$). Similar result also appeared in sensitivity analysis after excluding one study with significant difference(RR:0.49; 95% CI:0.29–0.81, $P=0.006$) ($P=0.52$, $I^2=0\%$).

Conclusion NHFOV is superior to NCPAP in decreasing the risk of intubation as a primary respiratory supporting strategies in preterm infants suffering from RDS.

Introduction

Invasive ventilation(IV) is a key procedure to reduce respiratory mortality and morbidity in preterm infants with respiratory distress syndrome(RDS). However, it inhibits normal respiratory physiological process and is associated with the increased risks of bronchopulmonary dysplasia (BPD),[1] re-hospitalization and brain injury among the survivors.[2–4] How to avoid IV in early life is therefore a critical procedure to reduce respiratory mortality and morbidity.

To date, nasal continuous positive airway pressure(NCPAP) remains one widely used way of the noninvasive ventilation modes to avoid intubation in preterm infants. However, the failure rate is high and ranges from about 20–60%.[5–8] Nasal intermittent positive pressure ventilation (NIPPV) is another respiratory supporting strategy. Systematic review has proven that NIPPV is superior to NCPAP to avoid re-intubation in preterm infants after extubation.[7] However, early use of NIPPV was not shown beneficial effects for decreasing the need for intubation as compared with NCPAP alone in preterm infants with RDS. [5, 6]

Supplying with the combined advantages of NCPAP with higher mean airway pressure and NIPPV without need for synchronization, nasal high-frequency oscillatory ventilation (NHFOV) should be beneficial to reduce the incidences of re-intubation and complications in preterm infants.[9–11] A multicenter study has indicated that NHFOV was related to the reduced numbers of apnea, bradycardia and oxygen desaturation as a remedial measure after failing to other noninvasive modes in preterm infants.[12] And it was consistent with the previous small sample and non-randomized controlled studies.[13–15] Despite no compelling evidences about the safety and efficacy of NHFOV from multicenter randomized controlled trials, NHFOV was widely used and no obvious side effects were observed.[16] In 2017, we reported a small randomized controlled study, and the result showed that, comparing

with NCPAP, NHFOV was associated with lower rate of intubation as primary respiratory support strategy. [17] And it was consistent with the subgroup analysis of Shi et al., [18] of which NHFOV showed a lower rate of treatment failure than NCPAP in the strata of 26^{+0} to 29^{+6} weeks' gestational age (11.9% vs 32.4%, 95%CI, 0.088 to 0.898, $P=0.032$) and $BW < 1500g$ (10.4% vs 29.6%, 95%CI, 0.104 to 0.736, $P=0.010$). However, as far as the primary outcome was concerned, NHFOV was not shown to superior to NCPAP(9.9% vs 17.3%, 95%CI, 0.264 to 1.031, $P=0.066$). And it was consistent with the report of Malakian et al., [19] in which NHFOV did not reduce the need for IV during the first 72 hours after birth as compared with NCPAP. Therefore, there was an urgent need to assess the beneficial effects between NHFOV and NCPAP on intubation rate and the other complications.

The purpose of the systematic review and meta-analysis was to evaluate whether NHFOV would reduce the need for intubation as compared with NCPAP in the treatment of preterm infants with RDS as the primary respiratory supporting mode.

Methods

The protocol of this systematic review and meta-analysis was registered before the studies search in PROSPERO (Prospero2019 CRD42019129316). And it was performed conforming to the Methodological Expectations of Cochrane Intervention Reviews and was shown in accordance with the recommendations of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement. [20]

Types of studies, eligibility criteria and interventions

The criteria for a trial to be included in the meta-analysis were as follows: (1) trial involving human newborn infants in the early stage of RDS, (2) trial comparing NHFOV with NCPAP as the primary respiratory support strategies, (3) it was a clinically randomized controlled trial. Only RCTs were included because they are the best design to obtain unbiased assessment of beneficial effects through restricting the known and underlying confounders affecting the primary and secondary outcomes.

The excluded criteria were: (1) trials involving animal or pre-clinical studies, (2) duplicate reports, (3) studies without the primary outcomes. Furthermore, the studies would be excluded if they were cross-over, quasi-RCTs, or observational studies.

The primary and secondary outcome measures

The primary outcomes was intubation rate, and the secondary outcomes included the incidences of bronchopulmonary dysplasia (BPD), retinopathy of prematurity(ROP), intraventricular hemorrhage(IVH), necrotizing enterocolitis(NEC), air leak and mortality.

Search strategies

A systematic literature search was conducted in Jan 1, 2021, using the methods of the Cochrane Collaboration for Systematic Reviews of Interventions. [20] We searched studies included in Medline, the Cochrane library, the Cochrane Controlled Trials Register, EMBASE, Chinese National Knowledge Infrastructure (CNKI), and Wanfang data Information Site. Furthermore, any ongoing or unpublished trials were also identified. We did not restrict studies according to language, and searched for studies written in any language from inception to Jan 1, 2021.

Following keywords were used: “noninvasive high-frequency oscillatory ventilation” or “nasal high-frequency oscillatory ventilation” or “noninvasive high-frequency oscillation ventilation” or “nasal high-frequency oscillation ventilation” and “preterm” or “infant” were used. Other neonatal experts were asked to search any unpublished or ongoing trials and two studies were identified. We applied the Cochrane sensitivity-maximizing and Cochrane sensitivity and precision-maximizing strategies as our special search strategies. [20]

Collection and assessment of the included and excluded studies

The obtained studies through the search strategies above were imported to an electronic bibliographic management program. We reviewed the titles and abstracts of the remaining articles and excluded those that were not related to our topic and those that did not meet the eligibility criteria. The full text versions were obtained for the relevant articles that could be included in the review.

The research strategies, article-extracting and data analysis were performed independently by three reviewers(Li Jie, Chen Long, Shi Yuan). Data analysis included study design, study interventions, number of subjects in each group, demographic characteristics, inclusion and exclusion criteria, primary and secondary outcomes, and variables used to assess study quality.

Statistical analyses

The Cochrane Risk of Bias tool[20] was applied to assess the methodological quality of the included studies. The statistical analyses were similar to the previous study. [21] Discrepancies among the three reviewers were resolved by discussion. Meta-analysis was performed using version 5.2 of Review Manager. To assess heterogeneity, I^2 distribution and Higgins I^2 statistics were calculated to determine the percentage of total variation across studies resulting from heterogeneity. I^2 statistics approximating 25%, 50%, and 75% were considered low, medium, and high heterogeneity, respectively. The fixed-effects models were present, and the random-effects models were used whenever considerable heterogeneity was shown. For categorical data, the effect is expressed as the relative risk(RR), and for continuous data the effect is expressed as the weighted mean difference(MD) (95% confidence interval(CI)). Otherwise, to further assess effect of the individual study on the primary outcome, sensitivity or subgroup analysis would be performed after excluding the included studies with significant difference.

Results

Description of the included studies

Generally, fourteen randomized controlled studies were identified, of which ten were excluded for the following causes: one was the protocol[22] and one was the preliminary report[23] in Chinese of Zhu et al[17], three were compared after extubation, [24-26] three were randomized crossover studies,[13,27,28] one was compared between NHFOV and DuoPAP[29] and one was compared between NHFOV and BP-CPAP as rescuing treatment of failure of NCPAP.[14] Finally, four eligible studies and 570 participants were included in the subsequent analysis. [17-19,30] Fig.1 Tables 1-3 summarized the characteristics and quality assessments of these studies.

The primary and secondary outcomes

The meta-analysis indicated that NHFOV resulted in less intubation rate(RR:0.47; 95% CI:0.31-0.70, P=0.0002) as compared with NCPAP and heterogeneity was not found among the four trials in the fixed effects model (P=0.69, $I^2=0\%$) (Fig. 2). In sensitivity analysis, after excluding the study by Zhu et al. [17], the present study also indicated that NHFOV resulted in less intubation rate(RR:0.49; 95% CI:0.29-0.81, P=0.006) as compared with NCPAP and heterogeneity was not found among the other three trials in the fixed effects model (P=0.52, $I^2=0\%$)

Furthermore, the meta-analysis did not report significant differences in the incidence of BPD(RR:1.14; 95% CI:0.66-1.96, P=0.64), mortality (RR:1.00; 95% CI:0.44-2.25, P=0.99), IVH(RR:0.77; 95% CI:0.39-1.53, P=0.45), NEC(RR:1.19; 95% CI:0.52-2.69, P=0.68), ROP(RR:0.61; 95% CI:0.26-1.44, P=0.26), and air leak(RR:1.71; 95% CI:0.51-5.68, P=0.38) as compared with NCPAP, and heterogeneities were also not found among the four trials in the fixed effects model. (P=0.43, $I^2=0\%$)(P=0.70, $I^2=0\%$)(P=0.29, $I^2=20\%$)(P=0.21, $I^2=37\%$)(P=0.35, $I^2=0\%$)(P=0.54, $I^2=0\%$)(supplementary Fig. 3-8)

Discussion

In the present systematic review and meta-analysis, we aimed to evaluate whether NHFOV would reduce intubation rate as compared with NCPAP as the primary respiratory supporting modes in preterm infants with RDS. As a result, we found that NHFOV was superior to NCPAP in reducing the rate of intubation, and no heterogeneity was found. Similar result also appeared in sensitivity analysis after excluding one study with significant difference. And it was consistent with the subgroup analysis of the multicenter study by Shi et al. [18] The result suggests that NHFOV is a more reasonable selection to reduce the risk of intubation as compared with NCPAP in preterm neonate with RDS.

In the past twenty years, several studies have been enforced to compare the beneficial effects between NHFOV and NCPAP in preterm infants, and the results were encouraging. The study by van der Hoeven M et al. in 1998 demonstrated that, comparing with the NCPAP group, the PCO₂ level was lower in the NHFOV group in preterm and term neonates and the using criteria of NHFOV was deterioration on NCPAP. [31] A multicenter study also indicated the beneficial effects of NHFOV for preterm infants as a remedial measure after failing to other noninvasive modes in the mean number of apneas, bradycardias, or desaturations (3.2±0.4 vs. 1.2±0.3; P< 0.001), FiO₂ (0.48±0.03 vs. 0.40±0.02; P<0.001) and the levels of PCO₂ (74±6 vs. 62 ±4; P= 0.025). [12] Otherwise, a study by Wang et al. in 2017 also indicated that, as a method of rescuing treatment after failure of other noninvasive respiratory supporting strategies, NHFOV significantly reduced the numbers of apnea(1.2±1.1 vs. 6.3±2.1, P<0.01) and SpO₂<0.85(1.1±1.2 vs. 4.3±1.5, P<0.01), the levels of PCO₂(43±8 vs. 56±10, P<0.01) and FiO₂(0.30±0.07 vs. 0.39±0.11, P<0.01). And it was consistent with the meta-analysis by Li et al., [32] in which NHFOV was demonstrated to increase the removal of carbon dioxide and reduce the risk of intubation and IV as compared with NCPAP/BP-CPAP in preterm infants. In contrast, NHFOV did not improve the oxygenation (0.42±0.12 vs. 0.40±0.10, P>0.05) and reduced the levels of PCO₂ (49±8 vs. 48±7, P>0.05) as a prophylactically used mode in neonates after extubation, [33] and which was consistent with another randomized controlled cross-over study by Klotz D et al. [27] and the result did not show difference in levels of PCO₂(54.8±14.6 vs. 52.7±9.3, P=0.44; 49.0±8.1 vs. 47.7±9.5, P=0.55) between the NHFOV-NCPAP and NCPAP-NHFOV periods.

The first reasonable cause to explain the differences among the studies might be the diagnosis, and NHFOV might be more suitable in newborn infants with more severe respiratory distress. Previous studies were mainly enforced in the pre-neonatal acute respiratory distress syndrome(ARDS) era. In 2017, the first consensus definition for neonatal acute respiratory distress syndrome(ARDS) was provided, [34] and RDS and ARDS should be therefore diagnosed and compared independently. Our previous randomized controlled study also compared the beneficial effects between NHFOV with NCPAP on the need for IV in preterm infants with RDS and ARDS after extubation, and the results indicated that NHFOV did reduce significantly the need for endotracheal ventilation and levels of the PCO₂ as compared with NCPAP, especially in the subgroup of infants diagnosed with ARDS. [24] Among the trials included in the present study, the diagnosis of "the included criteria" were no completely consistent and ARDS was not included. The diagnosis of "the included criteria" was "RDS" in the studies by Shi et al. [18], Malakian et al. [19] and ranpour et al. [30]. But it was "moderate-severe RDS" in the study by Zhu et al. [17] And it was consistent with the previous reports by Mukerji et al. [12] and Wang et al., [33] in which NHFOV was successfully used in reduced PCO₂ and/or intubation rate as rescuing treatment after failure of other noninvasive ventilation. In contrast, there was similar intubation rate between NHFOV and NCPAP when the infants was stable on NCPAP after extubation. [27]

The second cause to explain the inconsistency might be the observation time of "need for mechanical ventilation". Among the trials included, the observation time of "need for mechanical ventilation" were different. The time of observation of "failure of NIPPV or NCPAP" was "7 days after birth" in the study by Shi et al. [18] and "within the first 72hr of life" in the studies by Malakian et al. [19] and Zhu et al. [17] and Iranpour et al. [30] did not limit the observation time of "failed nasal support".

The third cause might be the initial setting and subsequent adjustment of respiratory parameters of NHFOV. Among the four trials included, the parameters were different.(table 2) To further verify the results, a summary of all clinical studies referring to NHFOV in newborn infants was made and it was shown in table 4. [35-38] According to the summary, four reasons were accessible. Firstly, according to the report of Mukerji et al., [39] visible chest oscillation was not necessary because of elimination of CO₂ during NHFOV also occurring in the upper respiratory airway deadspace; Secondly, the mean tidal volume was higher with I:E at 50% than at 33% (2.4 ml vs. 1.4 ml; P < 0.001); [10] Thirdly, the setting of respiratory parameters should also be adjusted according to diagnosis and purpose, and an example was that Luca et al. suggested different parameters boundaries for NHFOV use in BPD-risk and postextubation newborn infants. [40] Last, the classifications of respiratory failure should be considered. Insufficient removal of carbon dioxide was usually one of the most important causes to induce higher incidence of intubation. Therefore, besides amplitude firstly up-regulated, frequency should be adjusted within the reported ranges to avoid hypercarbia. [11,39]

Besides efficacy, safety is another important focus when NHFOV was used. Similar to other noninvasive ventilation, NHFOV could also result in side effects. In the four included studies, Malakian et al. [19] reported that there were no differences in traumatization of nasal skin and mucosa, air leaks, IVH, feed intolerance and time to full feeds between the two groups. And there were no relevant reports in the studies by ranpour et al. [30] and Zhu et al. [17]. Shi et al. [18] indicated that the rate of thick secretions causing an airway obstruction was higher in the NHFOV group than in the NCPAP group(13.8% vs 5.3%; 95% CI of risk difference, 1.218 to 6.645; P = 0.018).

and it was consistent with the study by Fischer HS et al.. [16] Other than, air-trapping and NEC were shown in the study of Czernik Cet al. [41]

The major limitations of the present study: 1) The included studies were mainly performed in the pre-ARDS era, and no ARDS was included. 2) The initial respiratory parameters of NHFOV were different among the four trials. 3) The assessment for secondary outcomes were not enough in the small sample size. They might induce potential bias, including restricted application scope. These problems could be overcome in additional studies according to the present data. Recently, we have organized a multi-centers, randomized controlled trials regarding comparing NHFOV and NCPAP as the respiratory support modes after extubation in preterm infants (NCT03099694), and the results could give us more reasonable explanations.

In summary, among preterm infants with RDS, NHFOV was superior to NCPAP with respect to reducing the risk of intubation as the primary respiratory support strategies in the early life. Larger trials are needed to verify the beneficial effects.

Abbreviations

acute respiratory distress syndrome: ARDS; bronchopulmonary dysplasia: BPD; conventional mechanical ventilation: CMV; invasive ventilation: IV; intraventricular hemorrhage: IVH; necrotizing enterocolitis: NEC; nasal continuous positive airway pressure: NCPAP; nasal intermittent positive pressure

ventilation: NIPPV; nasal high frequency oscillatory ventilation: NHFOV; periventricular leukomalacia: PVL; retinopathy of prematurity: ROP; respiratory distress syndrome: RDS;

Declarations

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Code availability: Not applicable

Author Contributions:

Li Jie: Dr Li accomplished the article-extracting and data analysis, drafted the initial manuscript and reviewed the manuscript.

Chen Long: Dr Chen conceptualized and designed the study, revised the initial manuscript.

Shi Yuan: Dr Shi conceptualized and designed the study, accomplished the article-extracting and data analysis, critically reviewed the manuscript for important intellectual content.

All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

Ethics approval: Not applicable

Consent to participate: Not applicable

Consent for publication: Not applicable

What's Known:

Nasal high-frequency oscillatory ventilation (NHFOV) has been described to be another advanced version of nasal continuous positive airway pressure (NCPAP). However, its beneficial effects among different studies as the primary modes in early life of preterm infants with respiratory distress syndrome(RDS) were inconsistent.

What is new:

Comparing with NCPAP, NHFOV decreases the risk of intubation as a primary respiratory supporting strategies in early life for preterm infants suffering from RDS.

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Tables

Table 1 The characteristics of included studies

		Iranpour et al. 2019	Malakian et al. 2019	Shi et al. 2019	Zhu et al 2017
No. of centers		2	1	18	1
No. of patients	NHFOV	34	63	152	37
	NCPAP	34	61	150	39
Gestational age(weeks)	NHFOV	33.1±2.5	31.1±2.9	30.6±1.7	31.7±1.7
	NCPAP	32.8±2.4	31.1±2.8	30.9±1.8	32.0±1.9
Birth weight(kg)	NHFOV	2.16±0.76	1.49±0.47	1.56±0.37	1.67±0.35
	NCPAP	1.96±0.61	1.51±0.49	1.58±0.34	1.74±0.33
Male	NHFOV	19	28	91	22
	NCPAP	21	25	79	21
prenatal steroids(yes)	NHFOV	8	36	105	13
	NCPAP	10	31	101	15
Apgar 5 min	NHFOV	8.6±1.7	7.5±0.7	9(8-10)	6.9±2.4
	NCPAP	8.4±1.3	7.6±0.7	9(8-10)	6.7±2.2
Cesarean section(yes)	NHFOV	31	44	89	11
	NCPAP	31	40	81	17

NHFOV: nasal high frequency oscillation ventilation; NCPAP: nasal continuous positive airway pressure

Table 2: Details of included papers

		Iranpour et al. 2019	Malakian et al. 2019	Shi et al. 2019	Zhu et al 2017
ventilators	NHFOV	Fabian	medin	medin, or SLE5000	medin
	NCPAP	Fabian	medin	medin, or SLE5000 or carefusion	Stephan
Type of surfactant		Curosurf	Survanta	Curosurf	Curosurf
surfactant administration		INSURE	INSURE	INSURE	INSURE
surfactant use(yes)	NHFOV	18	21	119	37
	NCPAP	18	23	104	39
Initial pressure(cmH ₂ O)	NHFOV	8	4	6	6
	NCPAP	6-7	4	6	6
Initial frequency (Hz)/ amplitude	NHFOV	10/vibration of the upper chest wall and neck	5/7cmH ₂ O	8/7 in Medin or 20 in SLE	10/slight chest oscillation
	NCPAP	-	-	-	-
Aim of O ₂ saturation		89-95%	≥90%	89-94%	90-94%
criteria of surfactant use		35%	PEEP≥5 or FiO ₂ ≥40%	30% of <30w 40% of ≥30w	FiO ₂ >40%
The first/second dose of surfactant		200/100 mg/kg	4ml/kg/-	200/100 mg/kg	200/100 mg/kg
caffeine		-	-	-	yes
Weaning criteria	NHFOV	Transfer to HHFNC when FiO ₂ <30%	PEEP=4, FiO ₂ = 30%, frequency of 5Hz and amplitude of 3	Minimal or no signs of respiratory distress, PEEP<6, and FiO ₂ = 30%	-
	NCPAP				
Fail criteria for NHFOV or NCPAP		apnea or PH < 7.2 and PCO ₂ > 60	pH ≤7.20 or PaCO ₂ ≥ 60 mm Hg, PaO ₂ ≤ 50 mm Hg with FiO ₂ ≥ 0.6 or apnea ≥3/h or a episode requiring bag-and-mask ventilation	severe respiratory acidosis(PCO ₂ >65 mmHg with pH< 7.20); apnea 3/h, or a episode requiring bag /mask ventilation; hypoxia for at least 2h; pulmonary hemorrhage, and cardiopulmonary arrest	severe respiratory acidosis(PCO ₂ >60 with pH<7.20); apnea ≥3/h, or a episode requiring bag and mask ventilation, hypoxia (FiO ₂ >0.5 with PaO ₂ <50), and pulmonary hemorrhage
Time scope of fail criteria		-	72 h	7 days after birth	-

NHFOV: nasal high frequency oscillation ventilation; NCPAP: nasal continuous positive airway pressure; "-": no data available;

Table 3: Bias assessment of included papers

	Iranpour et al. 2019	Malakian et al. 2019	Shi et al. 2019	Zhu et al 2017
Sequence generation	Low risk	Low risk	Low risk	Low risk
Allocation concealment	Low risk	Low risk	Low risk	Low risk
Blinding (participants)	Low risk	Low risk	Low risk	Low risk
Blinding (outcome assessors)	High risk	High risk	Low risk	Low risk
Incomplete data address	High risk	High risk	Low risk	Low risk
Selective reporting	Unclear risk	Unclear risk	Low risk	Low risk
Other sources	Unclear risk	Unclear risk	Low risk	Low risk
Overall	High risk	High risk	Low risk	Low risk

table 4 the characteristics, initial settings for respiratory parameters and key results of the published clinical studies referring to NHFOV.

	Study types	Sample size	Weight(g)	diagnosis	Gestational age(weeks)	modes	interface	Initial respirator (cmH2O, Hz)
Van der Hoeven et al.1998 ³¹	Case series	21	1010 (750-2170)	RDS,TTN, sepsis hypoventilation airleak, NEC	29 (27-32)	failing to NCPAP	nasopharyngeal tube	MAP:≥NCPAP; I keep SpO ₂ of 86 Frequency: 10; A oscillations; I:E:
Hoehn et al. 2000 ¹⁵	Case report	1	560	apnea	24	after extubation	nasopharyngeal tube	MAP:7; FiO ₂ :0.2 Amplitude: 100%
Colaizy et al. 2008 ³⁵	Non-RCT	14	995 (438-1374)	RDS	27(25-30)	stable status on NCPAP/compared with CPAP	nasopharyngeal tube	MAP: equal to N adjusted to keep desired range; F Amplitude: ches 1:4.5
Czemik et al. 2012 ⁴¹	Case series	20	635 (382-1020)	Severe respiratory failure	25.3 (23.7-27.6)	after extubation	nasopharyngeal tube	MAP:8; FiO ₂ : ad saturation in the Frequency: 10; A I:E:1:2
Mukerji et al. 2014 ¹²	Case series	79	740 (500-2860)	-	25 (23-35)	failure of other noninvasive mode or prophylactic mode	nasal prong or mask	MAP: equal to N FiO ₂ : titrated to SpO ₂ goal; Freq Amplitude: ches
Aktas et al. 2016 ³⁶	Case series	3	900,830,890	RDS	28,29,27	after extubation/ failure of NIPPV	nasal prong	MAP: 9-13; FiO ₂ Frequency: -; Ar
Mukerji et al. 2017 ¹⁴	RCT	16	831.9±150.1	-	26.1±1.3	failure of NCPAP/ compared with BP-CPAP	nasal prong or mask	MAP: 8; FiO ₂ : <6 14; Amplitude: c
Klotz et al. 2018 ²⁷	RCT- crossover	13	1083.5±359.1	RDS	27±2	after extubation or NIV with surfactant /compared with CPAP	nasal prong or mask	MAP: Equal to N Frequency: 10; A oscillation; I:E:-
Lou et al. 2017 ²⁵	RCT	65	1790±350	RDS	32.5±1.3	after extubation/ compared with CPAP	-	MAP: NCPAP pl 30%-40%; Freq Amplitude: ches
Wang et al. 2017 ³³	Case series	36	980±318	BPD, apnea, pneumonia	27.5±2.5	Rescuing after failure of other NIV or Prophylaxis	nasal prong	MAP: 5-15; FiO ₂ 89%-93%; Freq Amplitude: ches
Rüegger et al. 2018 ²⁸	RCT- crossover	40	881±181	-	26.5±1.5	stable on NCPAP after extubation/ compared with CPAP	-	MAP: Equal to N FiO ₂ :adjusted to 91%-95%; Freq Amplitude:20; I:
Lou et al. 2018 ²⁹	RCT	65	1790±330	RDS	33.5±1.5	Primary mode/ compared with DuoPAP	-	MAP: 8; FiO ₂ : 30 Frequency:6-12; oscillation; I:E:-
Thatrimontrichai et al.2019 ³⁷	Retrospective case series	78	1298 (975-2076)	-	30 (28, 33)	after extubation/ compared with CPAP	face mask	MAP:4-8; FiO ₂ : ε saturation in the Frequency:10;Ar
Łoniewska et al.2019 ³⁸	Retrospective case series	32	620-3230	RDS,TTN, pneumonia	24-38	Primary mode after birht/after extubation	nasal prong	MAP: NCPAP;4; keep SpO ₂ in de Frequency:10;Ar
Bottino et al. 2018 ¹³	RCT- crossover	60	921 ±177	RDS	26.4 ±1.8	stable respiratory status on NCPAP/ compared with CPAP	nasal prong	MAP: 4-8; FiO ₂ : SpO ₂ of 91%-95 Amplitude:10; I:
Chen et al. 2019 ²⁴	RCT	206	1859.1±569.1	RDS and ARDS	32.5±2.5	After extubation/ compared with CPAP	Nasal prong	MAP:10; FiO ₂ : 2 Frequency:10; A I:E:1:1

Fischer et al. 2019 ²⁷	RCT	6	420-786	-	23+4-26+3	After extubation	Nasal prong	MAP:8; FiO ₂ : ad SpO ₂ of 90%-94 Amplitude:20; I:I
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RDS, respiratory distress syndrome; TTN, transient tachypnea of newborn; NCPAP, nasal continuous positive airway pressure; RCT, randomized controlled trial; MAP: mean airway pressure;

NEC, necrotizing enterocolitis; NIV, noninvasive ventilation;

Figures

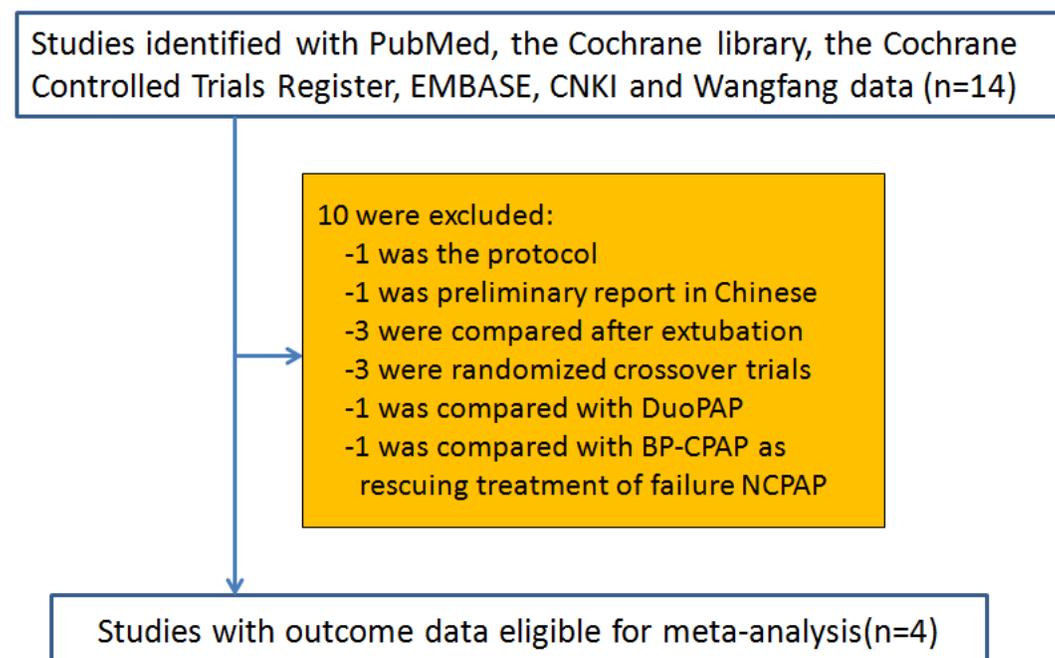


Figure 1

These lection course of the included papers

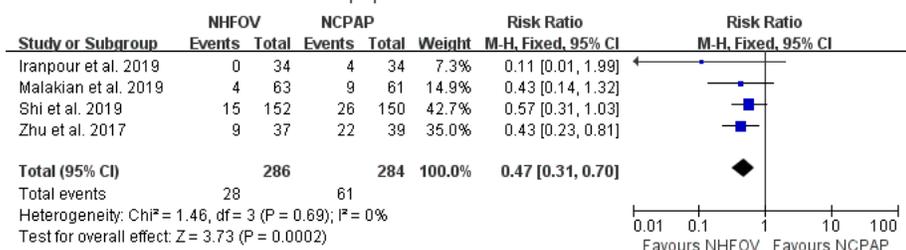


Figure 2

The comparison of the incidence of in tubation

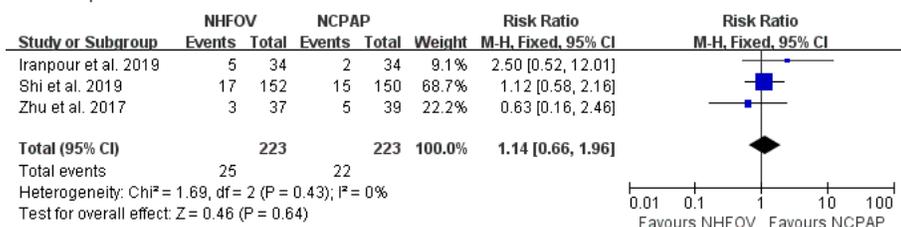


Figure 3

The comparison of the incidence of BPD

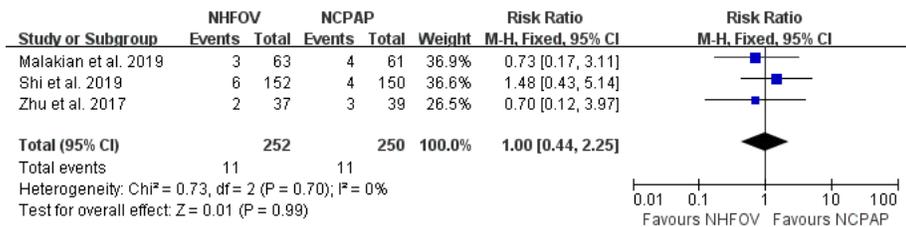


Figure 4

The comparison of the mortality rate

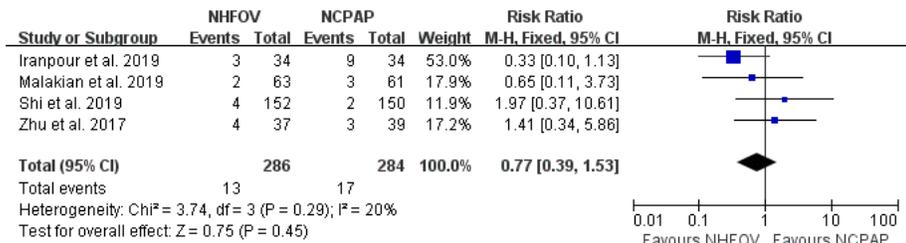


Figure 5

The comparison of the incidence of IVH

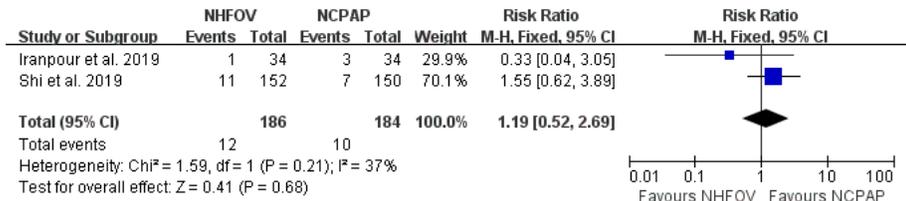


Figure 6

The comparison of the incidence of NEC

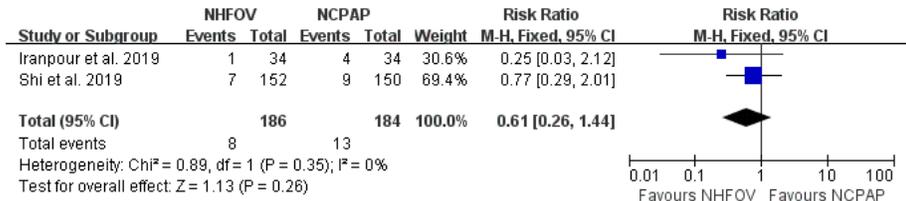


Figure 7

The comparison of the incidence of ROP

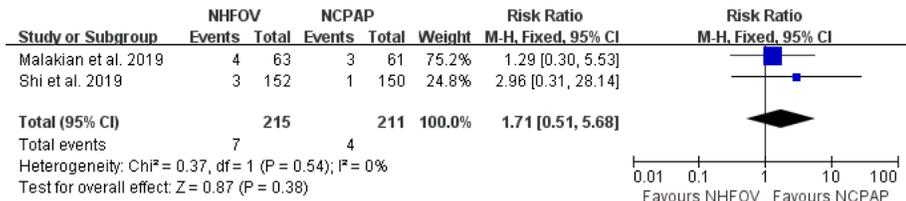


Figure 8

The comparison of the incidence of air leak