Int J Clin Exp Med 2018;11(8):7583-7592
www.ijcem.com /ISSN:1940-5901/IJCEM0072376

Review Article

Nasal synchronized intermittent positive pressure/mandatory ventilation compared with continuous positive airway pressure for successful extubation and reducing the rate of apnea after extubation of preterm infants

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Received September 7, 2017; Accepted August 6, 2018; Epub August 15, 2018; Published August 30, 2018

Abstract: Objective: To compare the efficacy of nasal synchronized intermittent positive pressure/mandatory ventilation (NSIPPV/NSMIV) and conventional nasal continuous positive airway pressure (NCPAP) in increasing the likelihood for successful extubation and reducing the rate of apnea in preterm infants. Method: We searched the Cochrane library, PubMed, China National Knowledge Infrastructure (CNKI) periodical databases. Randomized controlled trials (RCTs) and quasi-RCTs using NSIPPV/NSIMV as an active intervention in preterm infants or low birth weight infants. We performed the meta-analyses using the Cochrane statistical package RevMan 5.0. Results: We included 7 trials met our inclusion criteria. The use of NSIPPV/NSIMV modes resulted in a reduction in the rate of failed extubation (RR 0.26, 95% CI 0.16 to 0.43) and apnea (OR 0.23, 95% CI 0.14 to 0.40). NSIPPV/NSIMV modes also resulted in reductions in the rate of chronic lung disease (CLD) (RR 0.68, 95% CI 0.47 to 0.99), air leaks (RR 0.35, 95% CI 0.13 to 0.93), hypercapnia (RR 0.35, 95% CI 0.16 to 0.78) and retinopathy of prematurity ≥II grade (RR 0.53, 95% CI 0.31 to 0.92). Conclusion: In conclusion, all these reports indicated that preterm infants who were ventilated after extubation using NSIPPV/NSIMV had reduced rate of failed extubation, apnea, CLD, hypercapnia, air leaks and retinopathy of prematurity ≥II grade. However, we graded evidence for these outcomes as moderate, as all trial interventions were unblinded.

Keywords: Nasal synchronized intermittent positive pressure, nasal synchronized intermittent mandatory ventilation, nasal continuous positive airway pressure, preterm infants, lung injury, complications of mechanical ventilation, meta analysis

Introduction

Preterm lungs are particularly susceptible to ventilator induced lung injury (VILI) [1-3]. In an effort to decrease ventilator-induced lung injury, alternative techniques of non-invasive ventilation such as NCPAP, NIPPV, NSIMV and NSIPPV have been employed [4-9].

NSIPPV/NSIMV is a promising non-invasive method to support respiration without endotracheal intubation. A study reported that application of NSIPPV/NSIMV was associated with increased tidal and minute volumes and decreased respiratory effort when compared with NCPAP in the same infant [10]. It is also possible that NSIPPV/NSIMV recruits collapsed alveoli and increases functional residual capacity (FRC). Recently, two studies demonstrated that infants receiving NSIPPV/NSIMV have decreased work of breathing (WOB) [12, 13]. The mechanistic reasons may explain why NSIPPV/NSIMV might be beneficial or more effective than NCPAP.

NSIPPV/NSIMV has been used in preterm neonates with respiratory distress syndrome (RDS) as a primary mode as well as after extubation and for apnea [9, 14-17]. Some clinical trials have reported more successful extubation of

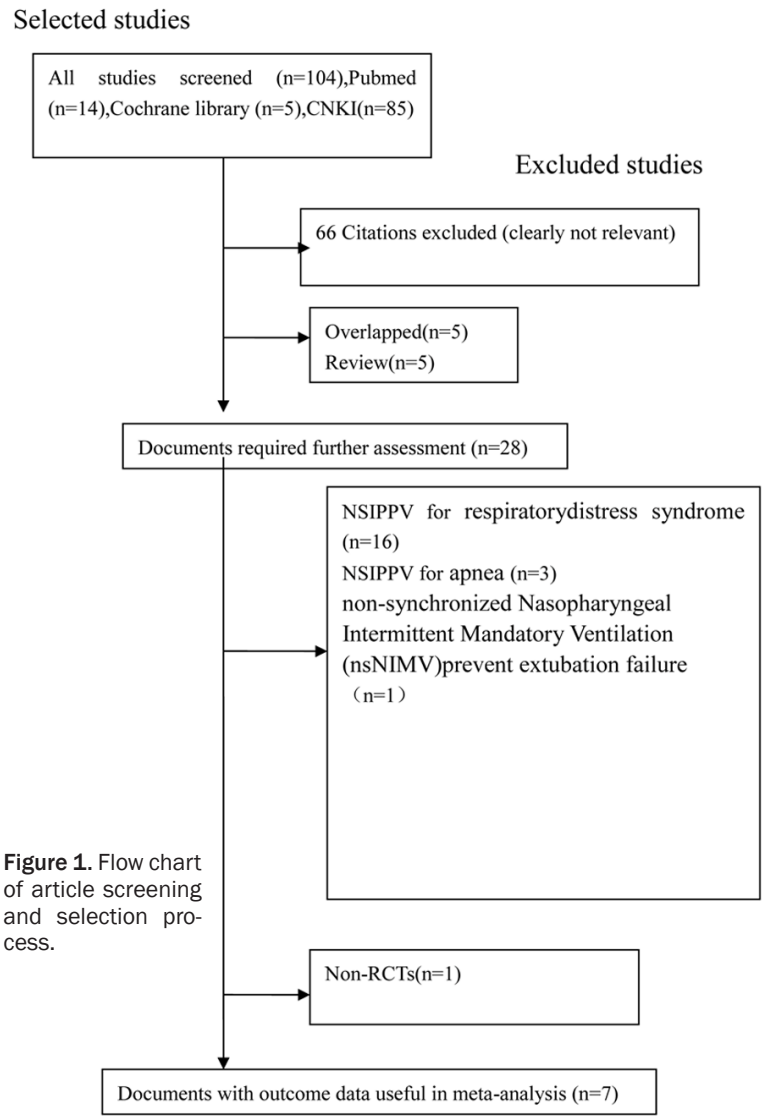

Figure 1. Flow chart of article screening and selection process.

premature neonates on NSIPPV/NSIMV compared to NCPAP [8, 9, 14, 15]. In our review we investigated whether NSIPPV/NSIMV would be more effective than conventional NCPAP in decreasing extubation failures and adverse effects in preterm infants who had been ventilated for RDS.

Methods

Inclusion criteria

We included randomized controlled trials and quasi-RCTs in this review. All infants <37 weeks' gestation and birth weight <2500 g receiving artificial ventilation. The review included studies comparing NSIPPV/NSIMV with CPAP after extubation via the nasal route. The study was approved by the Ethics Committee of the Children's Hospital Affiliated to Soochow University.

Exclusion criteria

RCTs that evaluated NSIPPV/NSIMV and NCPAP as primary mode of treatment for RDS and apnea in preterm infants were excluded. In addition, non-RCTs of NSIPPV/NSIMV and RCTs of NSIPPV/NSIMV in combination with other modes of ventilation for preterm infants were excluded. Finally, all studies published as meeting summaries and review articles were excluded.

Outcome measures

The primary outcomes were the rate of failed extubation and apnea. The secondary outcomes of this review were Oxygen therapy duration, duration of hospitalization, duration of nasal ventilation, the incidence of CLD, air leak, hypercapnia, reintubation, intraventricular haemorrhage (IVH), periventricular leukomalacia (PLV), patent ductus arteriosus (PDA), neonatal sepsis, retinopathy of prematurity (ROP), abdominal distension or feeding intolerance and necrotizing enterocolitis (NEC).

Search methods for identification of studies

We searched the Cochrane library, PubMed, China National Knowledge Infrastructure (CNKI) periodical databases from the establishment of the database to July 5, 2013 by using the following search terms: nasal continuous positive airway pressure OR NCPAP OR nasal intermittent positive pressure ventilation OR NIPPV OR nasal intermittent mandatory ventilation OR NIMV OR nasal distending pressure OR nasal positive pressure OR nasal ventilation OR noninvasive positive pressure ventilation OR synchronized intermittent mandatory ventilation OR SIMV OR nasopharyngeal synchronized intermittent mandatory ventilation OR bilevel CPAPOR BiCPAPOR BiPAPOR SiPAP, plus database-specific limiters for randomised con-

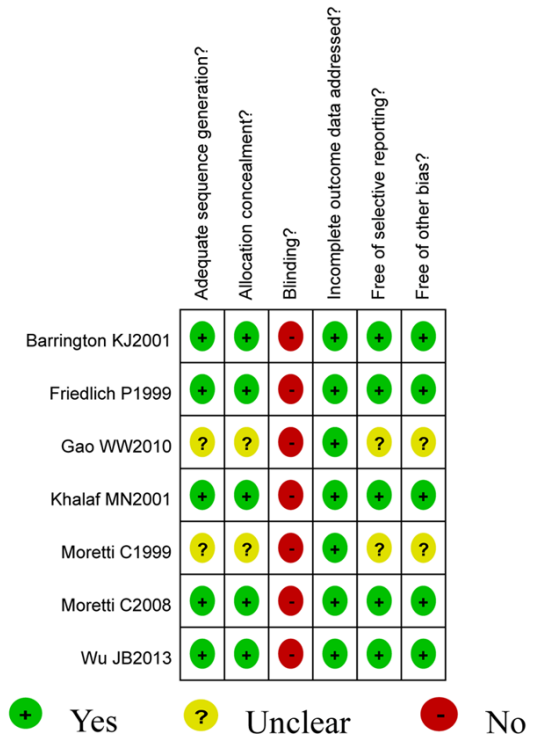

Figure 2. Quality assessment of 7 included studies.

trolled trials and neonates. We applied no language restrictions.

Selection of studies

Two review authors independently assessed the titles and abstracts of all studies identified by the searches. We obtained the full articles when they appeared to meet the inclusion criteria or there were insufficient data in the title and abstract to make a clear decision for their inclusion. We excluded articles that did not meet the inclusion criteria. We noted the reasons for their exclusion. We resolved any disagreements between the two review authors about study inclusion by discussion.

Data extraction and management

Both authors independently extracted data using a pilot-tested data extraction form and entered the data into RevMan 5. When data were missing or unclear, we contacted the trial authors for clarification. For dichotomous outcomes, the number of participants experiencing the event and the number assessed in each group were recorded. For continuous outcomes, the arithmetic means, standard deviations, and number assessed in each group were extracted.

Assessment of risk of bias in included studies

Both authors independently assessed the methodological quality for each trial, according to Cochrane Collaboration's recommendations [18]. Descriptive data were collected on whether participants, care providers, or outcome assessors were blinded; sequence generation was adequate; allocation was concealed; incomplete outcome data was clearly addressed; there was selective reporting; there was other reporting. Assessment results are summarized in the **Figure 2**.

Quality of evidence

The GRADE approach results in an assessment of the quality of a body of evidence according to one of the following four grades [7]. High: We are very confident that the true effect lies close to that of the estimate of effect. Moderate: We are moderately confident in the ef fect estimate: The true effect is likely to be close to the estimate of effect but may be substantially different. Low: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of effect. Very low: We have very little confidence in the effect estimate. Review authors independently assessed the quality of the evidence found for outcomes identified as critical or important for clinical decision making. These important outcomes included: Failed extubation, the rate of apnea after extubation, the rate of CLD, air leaks, hypercarbia, retinopathy of prematurity ≥II grade.

Publication bias

Each outcome index was subjected to intention-to-treat analysis. The potential presence of publication bias was examined for using the funnel plot produced by RevMan 5.2 software.

Statistical analyses

We synthesized dichotomous data using risk ratios (RR), numbers needed to treat (NNT), and 95% CI as the effect measures. We used the mean difference (MD) and 95% CI as the metrics of effect size for continuous outcomes. We assessed heterogeneity in results between

Table 1. Characteristic of 7 RCTs included in the meta analysis

Study	Gestational age (Weeks)	Methodological rigor (randomization/ allocation concealment/blinding/ dropping-out)	Participants	Interventions	Outcomes	
					Failed extubation	Apnea
Moretti C 1999 [10]	28.5±0.5	None/None/Double blinding/No dropping-out	T 11	NSIPPV		
	28.5±0.5		C 11	NCPAP		
Khalaf MN 2001 [14]	27.7±0.4	Random number chart/sealed and opaque envelopes/Double blinding/No dropping-out	T 34	NSIPPV	2/34	1/34
	27.6±0.6		C 30	NCPAP	12/30	12/30
Barrington KJ 2001 [15]	26.1±1.4	Random number chart/sealed and opaque envelopes/Double blinding/No dropping-out	T 27	NSIMV	4/27	3/27
	26.1±1.7		C 27	NCPAP	12/27	10/27
Friedlich P 1999 [19]	28.0±0.6	Random number chart/sealed and opaque envelopes/Double blinding/No dropping-out	T 22	NSIMV	1/22	1/22
	27.6±0.6		C 19	NCPAP	7/19	3/19
Gao WW 2010 [20]	32.3±1.6	None/None/Double blinding/No dropping-out	T 26	NSIMV	5/26	2/26
	32.6±1.4		C 16	NCPAP	10/26	11/26
Moretti C 2008 [21]	27.1±2.6	None/sealed and opaque envelopes/Double blinding/No dropping-out	T 32	NSIPPV	2/32	0/32
	26.9±1.9		C 31	NCPAP	12/31	5/31
Wu JB 2013 [22]	34.1±2.4	Random number chart/sealed and opaque envelopes/Double blinding/No dropping-out	T 31	NSIMV	3/31	6/31
	33.2±2.4		C 30	NCPAP	9/30	14/30

studies using the Cochrane Q test (P<0.1 considered significant) and the I^2 statistic.

Results

Description of studies

The initial search of electronic databases retrieved a total of citations. After reviewing the titles and abstracts, we identified nineteen papers as being potentially relevant, which we reviewed in full text. Seven trials enrolling 346 children met our inclusion criteria [10, 14, 15, 19-22]. The process of trials selection is reported in **Figure 1**.

The gestational age of participants varied from 23 to 36.5 weeks. The birth weight of participants varied from 535 to 2500 g. Study sample sizes range from 11 to 64 infants. Seven studies were randomized trials; six were parallel studies [14, 15, 19-21]. one trials were within-patient crossover studies [10].

A lot of ventilators delivering NSIPPV/NSIMV were used for the experimental groups, including the MOG2000, Siemens Servoi, Infantstar ventilator, Draeger Babylog, Bear Cub, Giulia and San Diego. Ventilation mode was described in the experimental group and control group of studies in **Table 1**. The ventilation settings were not always well described in each trial. Characteristic of 7 trials included in this meta analysis is reported in **Table 1**.

Risk of bias in included studies

Four trials used a block randomization and random number chart to generate the random sequence [14, 15, 19, 22]. The method of generation for random sequence was unclear in 3 trials [10, 20, 21]. Five included studies used sealed and opaque envelopes for allocation concealment [14, 15, 19, 21, 22]. Participants and care providers were not blinded to group assignment in all trials. The number of participants with missing data was small or nil in all trials. Thus, incomplete outcome data may not be a source of bias in this review. There was no evidence of selective reporting of outcomes in 5 included studies [14, 15, 19, 21, 22]. No other potential sources of bias were observed in the 5 trials [14, 15, 19, 21, 22]. Summary assessment of six key domains is presented in **Figure 2**.

Results of meta analysis

The primary outcomes

Failed extubation: In 6 trials that described the rate of failed extubation in NSIPPV/NSIMV group and NCPAP group (n=335) [14, 15, 19-22]. The pooled RR was 0.26 (95% CI 0.16 to 0.43) (**Figure 3**), with no significant heterogeneity between studies (P=0.57, I^2=0). We graded the quality of evidence for this outcome as moderate (unblinded intervention).

The rate of apnea after extubation: In 6 trials that described the rate of apnea in NSIPPV/

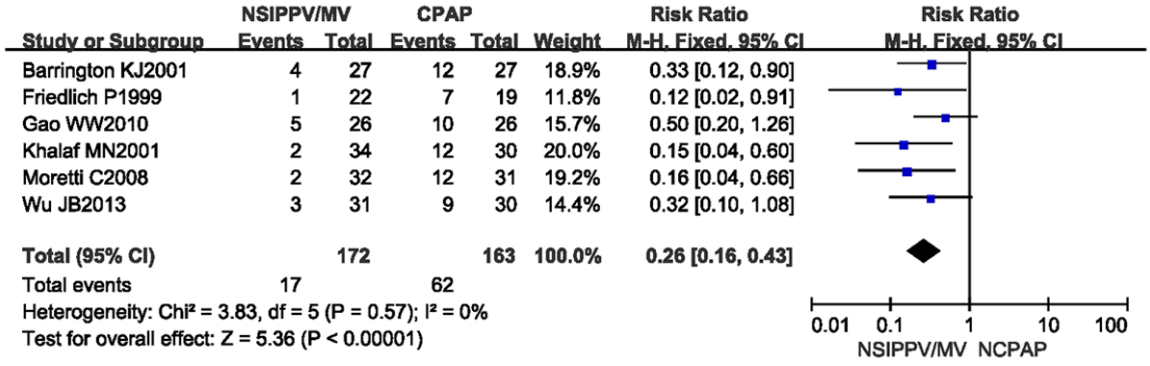

Figure 3. NSIPPV/NSIMV vs NCPAP: the rate of failed extubation.

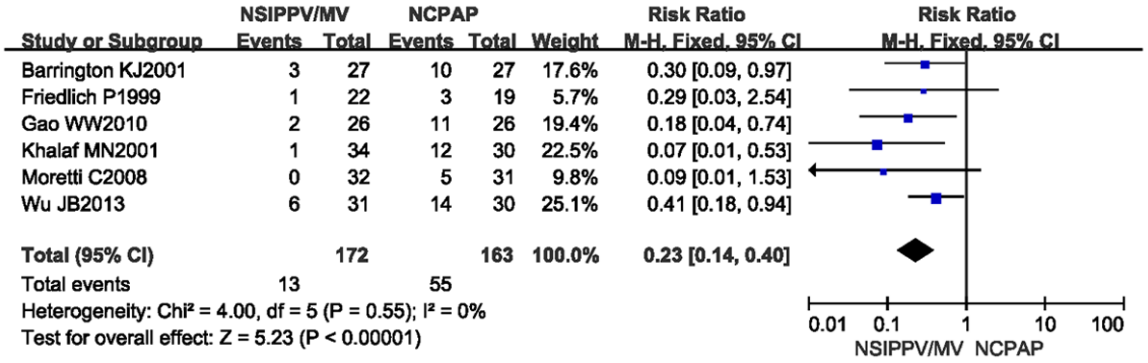

Figure 4. NSIPPV/NSIMV vs NCPAP: the rate of apnea.

NSIMV group and control group [14, 15, 19-22]. The pooled results show that preterm infants treated with NSIPPV/NSIMV had a statistically significant lower rate of apnea after extubation compared to those treated with NCPAP modes, with a pooled RR was 0.23 (95% CI 0.14 to 0.40, **Figure 4**). There was no significant heterogeneity in results between studies (P=0.55, I^2=0). We graded evidence for this outcome as moderate (unblinded intervention).

The secondary outcomes

The rate of CLD: In 4 trials that described the rate of CLD in NSIPPV/NSIMV group and control group [14, 15, 20, 21]. The pooled results show that preterm infants treated with NSIPPV/NSIMV had a statistically significant lower rate of CLD compared to those treated with NCPAP modes, with a pooled RR of 0.68 (95% CI 0.47 to 0.99, P=0.04) (**Table 2**). There was no significant heterogeneity in results between studies (P=0.46, I^2=0). We graded the quality of evidence for this outcome as moderate (unblinded intervention).

Air leaks: In 3 trials that described incidence of air leaks in NSIPPV/NSIMV group and control group (n=168) [14, 19, 21]. The result of Meta analysis show the incidence of air leaks is significant differences in NSIPPV/NSIMV group and control group. The pooled RR was 0.29 (95% CI 0.13 to 0.89, P=0.93), with no significant heterogeneity between studies (P=0.33, I^2=0). We graded the quality of evidence for this outcome as moderate (unblinded intervention).

Hypercarbia: In 5 trials that described any episode of hypocarbia in NSIPPV/NSIMV group and control group [14, 15, 19-21]. The pooled results show that preterm infants treated with NSIPPV/NSIMV after extubation had a significant lower episode of hypercarbia compared to those treated with NCPAP modes, with a pooled RR of 0.35 (95% CI 0.16 to 0.78, P=0.01). There was no significant heterogeneity in results between studies (P=0.58, I^2=0). We rated the quality of evidence for this outcome as moderate (unblinded intervention).

Retinopathy of prematurity ≥II grade: In 3 trials that described retinopathy of prematurity

Table 2. Meta-analysis results for secondary outcome between NSIPPV and control group

Outcome	Studies	Participants	Heterogeneity	Statistical Method	Effect Estimate
CLD	14, 15, 20, 21	233	P=0.46, I^2=0	Risk Ratio (M-H, Fixed, 95% CI)	0.68 (0.47, 0.99)
Air leak	14, 19, 21	168	P=0.33, I^2=0	Risk Ratio (M-H, Fixed, 95% CI)	0.35 (0.13, 0.93)
Any episode of hypercarbia	14, 15, 19, 20, 21	274	P=0.58, I^2=0	Risk Ratio (M-H, Fixed, 95% CI)	0.35 (0.16, 0.78)
Retinopathy of prematurity	14, 19, 21	168	P=0.96, I^2=0	Odd Ratio (M-H, Fixed, 95% CI)	0.36 (0.15, 0.87)
Intraventricular haemorrhage	14, 19, 21	168	P=0.41, I^2=0	Risk Ratio (M-H, Fixed, 95% CI)	0.80 (0.43, 1.49)
Nasal complications	19, 21	104	P=0.59, I^2=0	Risk Ratio (M-H, Fixed, 95% CI)	1.16 (0.56, 2.42)
Abdominal distension or feeding intolerance	14, 15, 19, 20, 21	274	P=0.55, I^2=0	Risk Ratio (M-H, Fixed, 95% CI)	0.97 (0.65, 1.45)
Periventricular leukomalacia	14, 19, 21	168	P=0.97, I^2=0	Risk Ratio (M-H, Fixed, 95% CI)	0.19 (0.02, 1.54)
Patent ductus arteriosus	14, 19, 21	168	P=0.67, I^2=0	Risk Ratio (M-H, Fixed, 95% CI)	0.88 (0.60, 1.28)
Necrotizing enterocolitis	14, 15, 19, 20, 21	274	P=0.51, I^2=0	Risk Ratio (M-H, Fixed, 95% CI)	0.82 (0.29, 2.32)
Sepsis	14, 20, 21	169	P=0.84, I^2=0	Risk Ratio (M-H, Fixed, 95% CI)	0.69 (0.44, 1.08)
Reintubation	14, 19, 21	168	P=0.19, I^2=40%	Odd Ratio (M-H, Fixed, 95% CI)	0.76 (0.37, 1.56)
Duration of hospitalization	14, 20, 21	179	P=0.006, I^2=81%	Mean Difference (IV, Random, 95% CI)	0.75 (-5.09, 6.59)
Nasal ventilation	14, 19, 20, 21, 22	281	I^2=96%	Mean Difference (IV, Random, 95% CI)	-3.74 (-8.03, 0.55)

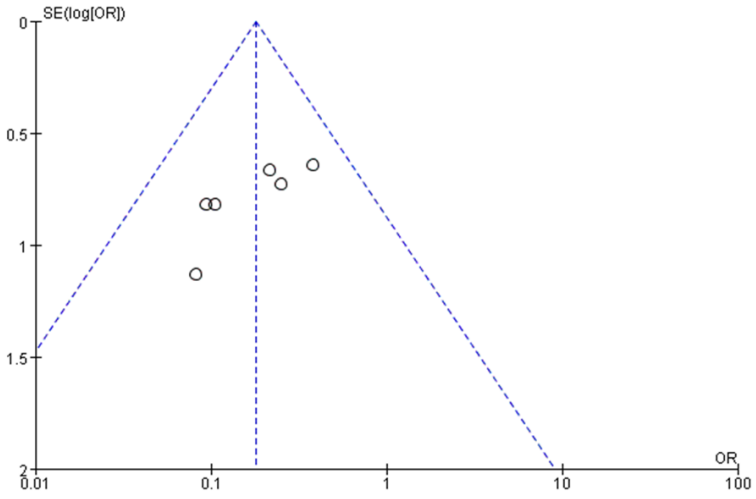

Figure 5. The publication bias of the enrolled studies.

≥II grade in NSIPPV/NSIMV group and control group [14, 19, 21]. The pooled RR of 0.53 (95% CI 0.31 to 0.92, P=0.02) with no significant heterogeneity between studies (P=0.64, I^2=0). We graded the quality of evidence for this outcome as moderate (unblinded intervention).

Other outcomes: **Table 2** specifically shows the comparison of other outcomes between preterm infants with NSIPPV/NSIMV and NCPAP. The incidence of NEC, abdominal distension or feeding intolerance, nasal complications, sepsis, PDA, reintubation, IVH and PVL were not significantly different between NSIPPV/NSIMV and NCPAP. There were no differences in duration of hospital stay and nasal ventilation between NSIPPV/NSIMV and NCPAP.

Publication bias

Publication bias was assessed using funnel plot produced by RevMan 5.2 software. The produced funnel plot was symmetrical, which indicated that no significant publication bias existed among the enrolled studies (**Figure 5**).

Discussion

Although conventional mechanical ventilation via an endotracheal tube has undoubtedly led to improvement in neonatal survival in the last 30 years, the prolonged use of an endotracheal tube and mechanical ventilation may cause lower airway damage and predispose the infant to the development of CLD [23, 24]. Avoiding mechanical ventilation is thought to be a critical goal, but early weaning seems now a more feasible aim of neonatal intensive care units. Nevertheless, early extubation often presents difficulties because of upper-airway instability, poor respiratory drive, alveolar atelectasis, hypercarbia and residual lung damage [17, 25, 26]. Recently published data regarding the use of NCPAP in the postextubation period have reported a need for reintubation of 25% to 40% in low birth weight infants [27-29]. The need for re-intubation after mechanical ventilation is associated with increased mortality and prolonged mechanical ventilation, and are more likely to have longer hospital stays and incur higher hospital costs. In an effort to further reduce the need for reintubation in this high-risk population, new methods for noninvasive ventilation were investigated.

In our review, we assessed the primary and secondary outcomes of NSIPPV/NSIMV versus NCPAP in the postextubation period following endotracheal mechanical ventilation. Seven randomized trials compared the efficacy of NSIPPV/NSIMV and NCPAP during the postextubation period in preterm infants. Six trials focused on failed extubation of NSIPPV/NSIMV and NCPAP. The pooled results of these 6 trials showed a 82% reduction in the rate of failed extubation among participants treated with NSIPPV/NSIMV compared to those treated with NCPAP. The benefit of NSIPPV/NSIMV in reducing the incidence of apnea after extubation was assessed by 6 trials. The pooled results of these trials showed a 85% reduction in the incidence of apnea among preterm infants treated with NSIPPV/NSIMV compared to those treated with NCPAP. Five trials demonstrated preterm infants treated with NSIPPV/NSIMV after extubation had a significant lower episode of hypercarbia compared to those treated with NCPAP modes. Moretti C et al reported transcutaneous PCO_2 was significantly lower during NSIPPV than NCPAP [10]. However, there was no evidence that NSIPPV/NSIMV reduced the rate of reintubation in our review. Some failed extubation patients in NCPAP group were rescued with NSIPPV and remained extubated successfully in two trials [14, 21]. The reasons may be

explained why SNIPPV did not reduced the rate of reintubation.

In this review, we found that NSIPPV/NSIMV modes resulted in reductions in the rate of CLD. As MV in the first days of a preterm infant is a major factor for BPD [30, 31], avoiding endotracheal tube ventilation remains of paramount importance in preventing ventilator-induced lung injury. NSIPPV/NSIMV has been shown to be associated with a decrease in CLD when introduced into a NICU setting [32]. Two recent prospective trials reported that NSIPPV as a form of ventilatory support in the early phase of RDS was associated with a significant decrease in the incidence of bronchopulmonary dys-plasia (BPD) [8, 33]. NSIPPV/NSIMV modes also resulted in reductions in the rate of air leaks and ROP ≥II grade.

Meta-analysis of the 7 trials does not identify any significant differences in duration of hospital stay, duration of nasal ventilation, NEC, abdominal distension or feeding intolerance, nasal complications, sepsis, PDA, IVH and PVL. Further large randomized controlled trials, preferably multi-centered, are still required to evaluate the effectiveness of NSIPPV/NSIMV during the postextubation period in preterm infants.

Detailed review of methodological characteristics of each study included in our analysis allowed for a rigorous selection of those studies that contained the essential features of randomized controlled trials. The availability of original data from these studies facilitated the use of optimal statistical methods, providing the opportunity to gain more accurate insights into clinically-based evidence. The number of participants who withdrew after randomization was small in each of the seven trials; thus, the lack of application of an intention-to-treat principle was unlikely to cause significant bias in our meta-analysis. It is important to note, however, that the sample size of this review study was still relatively small and the statistical power might not be sufficient for some outcome measurements. The small number of studies included in this review also precluded our ability to pursue an analytic approach to investigate heterogeneity across studies. The included trials were of high methodological quality, with low risk of bias. Thus, the overall methodological quality and strength of evidence in all four studies were deemed as low to moderate.

We are aware of some limitations of our analysis. First, none of the studies included in this review attempted to mask the caregivers to the group assignment. In the majority of studies, the allocated treatment method of each patient was known to those assessing the trial outcomes. Second, an important limitation of our meta-analysis is a lack of consistency in ventilation mode and ventilators, birth weight, gestational ages and methodology of literatures. Third, we do our best to collect literatures, but publication bias may exist. Additionally, the studies included in this systematic review are diverse in parameters settings of ventilators and times at which studies were conducted. These differences may be potential source of bias.

In conclusion, preterm infants who were ventilated after extubation using NSIPPV/NSIMV had reduced the rate of failed extubation, apnea after extubation, CLD, hypercapnia, air leaks and retinopathy of prematurity ≥II grade. Meta-analysis of the 7 trials does not identify any significant differences in duration of hospital stay, duration of nasal ventilation, NEC, abdominal distension or feeding intolerance, nasal complications, sepsis, PDA, IVH and PVL.

Future trials should enrol sufficient infants to detect differences in important outcomes such as death or chronic lung disease and should compare different categories of devices. These trials should establish the impact of synchronisation of NIPPV on safety and efficacy of the technique as well as the best combination of settings for NIPPV (rate, peak pressure and positive end expiratory pressure).

Disclosure of conflict of interest

None.

Abbreviations

NSIPPV, nasal synchronized intermittent positive pressure; NSMIV, nasal synchronized mandatory ventilation; NCPAP, nasal continuous positive airway pressure; CNKI, China National Knowledge Infrastructure; RCTs, randomized controlled trials; RR, relative risk; CI, confidence interval; OR, odds risk; CLD, chronic lung disease; FRC, functional residual capacity; WOB,

work of breathing; RDS, respiratory distress syndrome; IVH, intraventricular haemorrhage; PLV, periventricular leukomalacia; PDA, patent ductus arteriosus; ROP, retinopathy of prematurity; NEC, necrotizing enterocolitis; NNT, numbers needed to treat; BPD, bronchopulmonary dys-plasia.

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References

[1] Dreyfuss D and Saumon G. Ventilator-induced lung injury: lessons from experimental studies. Am J Respir Crit Care Med 1998; 157: 294-323.

[2] Loring SH, Pecchiari M, Della Valle P, Monaco A, Gentile G and D'Angelo E. Maintaining end-expiratory transpulmonary pressure prevents worsening of ventilator-induced lung injury caused by chest wall constriction in surfactant-depleted rats. Crit Care Med 2010; 8: 2358-2364.

[3] Slutsky AS. Lung injury caused by mechanical ventilation. Chest 1999; 116 Suppl: 9S-15S.

[4] Davis PG and Henderson-Smart DJ. Nasal continuous positive airways pressure immediately after extubation for preventing morbidity in preterm infants. Cochrane Database Syst Rev 2003; 2: CD000143.

[5] Subramaniam P, Henderson-Smart DJ and Davis PG. Prophylactic nasal continuous positive airways pressure for preventing morbidity and mortality in very preterm infants. Cochrane Database Syst Rev 2005; 20: CD001243.

[6] Dunn MS, Kaempf J, de Klerk A, de Klerk R, Reilly M, Howard D, Ferrelli K, O'Conor J and Soll RF. Randomized trial comparing 3 approaches to the initial respiratory management of preterm neonates. Pediatrics 2011; 128: 1069-1076.

[7] Tang S, Zhao J, Shen J, Hu Z and Shi Y. Nasal intermittent positive pressure ventilation versus nasal continuous positive airway pressure in neonates: a systematic review and meta-analysis. Indian Pediatr 2013; 50: 371-376.

[8] Bhandari V, Finer NN, Ehrenkranz RA, Saha S, Das A, Walsh MC, Engle WA and VanMeurs KP; Eunice Kennedy Shriver National Institute of Child Health and Human Development Neonatal Research Network. Synchronized nasal intermittent positive pressure ventilation and neonatal outcomes: a retrospective study. Pediatrics 2009; 124: 517-526.

[9] Gizzi C, Papoff P, Giordano I, Massenzi L, Barbàra CS, Campelli M, Panetta V, Agostino R and Moretti C. Flow-Synchronized nasal intermittent positive pressure ventilation for infants <32 weeks' gestation with respiratory distress syndrome. Crit Care Res Pract 2012; 14: 18-20.

[10] Moretti C, Gizzi C, Papoff P, Lampariello S, Campoferri M, Calcagnini G and Bucci G. Comparing the effects of nasal synchronized intermittent positive pressure ventilation (nSIPPV) and nasal continuous positive airway pressure (nCPAP) after extubation in very low birth weight infants. Early Hum Dev 1999; 56: 167-177.

[11] Owen LS, Morley CJ, Dawson JA and Davis PG. Effects of non-synchronised nasal intermittent positive pressure ventilation on spontaneous breathing in preterm infants. Arch Dis Child Fetal Neonatal Ed 2011; 96: F422-F428.

[12] Chang HY, Claure N, D'ugard C, Torres J, Nwajei P and Bancalari E. Effects of synchronization during nasal ventilation in clinically stable preterm infants. Pediatr Res 2011; 69: 84-89.

[13] Aghai ZH, Saslow JG, Nakhla T, Milcarek B, Hart J, Lawrysh-Plunkett R, Stahl G, Habib RH and Pyon KH. Synchronized nasal intermittent positive pressure ventilation (SNIPPV) decreases work of breathing (WOB) in premature infants with respiratory distress syndrome (RDS) compared to nasal continuous positive airway pressure (NCPAP). Pediatr Pulmonol 2006; 41: 875-881.

[14] Khalaf MN, Brodsky N, Hurley J and Bhandari V. A prospective randomized, controlled trial comparing synchronized nasal intermittent positive pressure ventilation versus nasal continuous positive airway pressure as modes of extubation. Pediatrics 2001; 108: 13-17.

[15] Barrington KJ, Bull D and Finer NN. Randomized trial of nasal synchronized intermittent mandatory ventilation compared with continuous positive airway pressure after extubation of very low birth weight infants. Pediatrics 2001; 107: 638-641.

[16] Santin R, Brodsky N and Bhandari V. A prospective observational pilot study of synchronized nasal intermittent positive pressure ventilation (SNIPPV) as a primary mode of ventilation in infants > or =28 weeks with respiratory distress syndrome (RDS). J Perinatol 2004; 24: 487-493.

[17] DePaoli AG, Davis PG and Lemyre B. Nasal continuous positive airway pressure versus nasal intermittent positive pressure ventilation for preterm neonates: a systematic review and meta-analysis. Acta Paediatr 2003; 92: 70-75.

[18] Higgins JPT and Green S. Cochrane handbook for systematic reviews of interventions version 5.1.0 [updated March 2011]. The Cochrane Collaboration 2011.

[19] Friedlich P, Lecart C, Posen R, Ramicone Ea, Chan L and Ramanathan R. A randomized trial of nasopharyngeal-synchronized intermittent mandatory ventilation versus nasopharyngeal continuous positive airway pressure in very low birth weight infants after extubation. J Perinatol 1999; 19: 413-418.
[20] Gao WW, Tan SZ, Chen YB, Wang Y, Huang DP, Jiang JB and Wang YL. Clinical efficacy of two kinds of nasal assisted ventilation mode in very low birth weight infants after extubation. Chin Pediatr Emerg Med 2010; 17: 535-537.
[21] Moretti C, Giannini L, Fassi C, Gizzi C, Papoff P and Colarizi P. Nasal flow-synchronized intermittent positive pressure ventilation to facilitate weaning in very low-birthweight infants: unmasked randomized controlled trial. Pediatr Int 2008; 50: 85-91.
[22] Wu JB, Jang HX, Tian ZS, Xu H and Liu HL. Clinical effect analysis of nasal synchronized intermittent mandatory ventilation in hyaline membrane disease weaning. Chinese General Practice 2013; 16: 1047-1049.
[23] Taghizadeh A and Reynolds ED. Pathogenesis of bronchopulmonary dysplasia following hyaline membrane disease. Am J Pathol 1976; 82: 241-264.
[24] Palta M, Gabbert D, Weinstein MR and Peters ME. Multivariate assessment of traditional risk factors for chronic lung disease in very low birth weight neonates. J Pediatr 1991; 119: 285-292.
[25] Fox WW, Schwartz JG and Shaffer TH. Successful extubation of neonates: clinical and physiological factors. Crit Care Med 1981; 9: 823-826.
[26] Bhat R and Zikos-Labrapolou E. Resuscitation and respiratory management of infants weighing less than 1000 grams. Clin Perinatol 1986; 13: 285-297.
[27] Higgins RD, Richter SE and Davis JM. Nasal continuous positive airway pressure facilitates extubation of very low birth weight neonates. Pediatrics 1991; 88: 999-1003.
[28] Annibale DJ, Hulsey TC, Engstrom PC, Wallin LA and Ohning BL. Randomized, controlled trial of nasopharyngeal continuous positive airway pressure in the extubation of very low birth weight infants. J Pediatr 1994; 124: 455-460.
[29] Tapia JL, Bancalari A, Gonzalez A and Mercado M. Does continuous positive airway pressure (CPAP) during weaning from intermittent mandatory ventilation in very low birthweight infants have risks or benefits? A controlled trial. Pediatr Pulmonol 1995; 19: 269-274.
[30] Avery ME, Tooley WH, Keller JB, Hurd SS, Bryan MH, Cotton RB, Epstein MF, Fitzhardinge PM, Hansen CB and Hansen TN. Is chronic lung disease in low birth weight infants preventable? A survey of eight centers. Pediatrics 1987; 79: 26-30.
[31] Van Marter LJ, Allred EN, Pagano M, Sanocka U, Parad R, Moore M, Susser M, Paneth N and Leviton A. Do clinical markers of barotrauma and oxygen toxicity explain interhospital variation in rates of chronic lung disease? Pediatrics 2000; 105: 1194-1201.
[32] Kulkarni A, Ehrenkranz RA and Bhandari V. Effect of introduction of synchronized nasal intermittent positive-pressure ventilation in a neonatal intensive care unit on bronchopulmonary dysplasia and growth in preterm infants. Am J Perinatol 2006; 23: 233-240.
[33] Bhandari V, Gavino RG, Nedrelow JH, Pallela P, Salvador A, Ehrenkranz Ra and Brodsky NL. A randomized controlled trial of synchronized nasal intermittent positive pressure ventilation in RDS. J Perinatol 2007; 27: 697-703.