

ORIGINAL RESEARCH

PEDIATRIC ANESTHESIA

Asynchrony index during noninvasive neurally adjusted ventilatory assist (NIV NAVA) in pediatrics: a systematic review

João Marcos Feliciano de Souza , Celso Moura Rebello  , Carlos Augusto Cardim de Oliveira  , Eduardo Juan Troster 

Author affiliation:

Departamento de Pós-Graduação em Ciências da Saúde da Faculdade Israelita de Ensino e Pesquisa Albert Einstein - São Paulo/SP – Brasil

Correspondence: João Marcos Feliciano de Souza, {ORCID:0000-0003-3900-8264}; E-mail: joaosouzaft@gmail.com; Phone: +55 11 2151 1233; Mobile: +55 11 947721684

Abstract

Background: Noninvasive ventilation (NIV) is considered as the first preferred treatment of pediatric acute respiratory failure (ARF). Conventional NIV (CNIV) modes have a higher asynchrony index (AI) when compared to Noninvasive Neurally Adjusted Ventilatory Assist (NIV NAVA) mode. The present study aimed to compare the AI and clinical outcomes during NIV NAVA vs. CNIV in pediatric patients aged between one month and 18 y.

Methodology: This is a systematic review of clinical trials conducted between April and May 2020 in the electronic databases, Cochrane Library, Embase, Lilacs, Pubmed/Medline, Scopus and Web of Science.

Results: Four out of 184 studies were eligible for qualitative synthesis, presenting 50% “high risk” of bias in the randomization, allocation, and other bias. The sample analyzed 39 participants, aged between 35 days and 15 y, with male predominance (61.5%). The primary outcome analyzed in three out of four studies was the significant decrease ($p < 0.001$) in the AI during NIV NAVA. Clinical outcomes were inconclusive due to methodological limitations.

Conclusion: We conclude that NIV NAVA decreases the AI when compared to CNIV in pediatric patients with ARF. However, the association of the AI reduction and favorable clinical outcomes were inconclusive. Further studies with different methodological formats and larger sample sizes are required to offer definitive conclusions.

Registration: The study protocol was registered in PROSPERO: International Prospective Register of Systematic Reviews (ID: 181785).

Abbreviations: AI – Asynchrony index; ARF – Acute respiratory failure; AT – Automatic trigger; AVB – Acute viral bronchiolitis; DT – Double trigger; EAdi – Electrical activity of the diaphragm; ET – Expiratory time; IE – Ineffective effort; IT – Inspiratory time; LC – Latte cycling; MV – Mechanical ventilation; NCPAP – Nasal continuous positive airway pressure; NIPPV – Nasal intermittent positive pressure ventilation; NIV NAVA – Noninvasive neurally adjusted ventilatory assist; NIV – Noninvasive ventilation; CNIV – Conventional NIV; OI – Oxygenation index; PAC – Pressure assist control; PC – Premature cycling; PS – Pressure support; RoB – Risk of bias; SNIPPV – Synchronized nasal intermittent positive pressure ventilation; TcCO₂ – Transcutaneous carbon dioxide; VILI – Ventilation induced lung injury

Keywords: Noninvasive Ventilation, Child, Support, Interactive Ventilatory, Neurally Adjusted Ventilatory Assist

Citation: de Souza JMF, Rebello CM, Oliveira CACD, Troster EJ. Asynchrony index during noninvasive neurally adjusted ventilatory assist (NIV NAVA) in pediatrics: a systematic review. *Anaesth. pain intensive care* 2021;25(5): 575-582; DOI: 10.35975/apic.v25i5.1622

Received: March 31, 2021, **Reviewed:** May 23, 2021, **Accepted:** May 24, 2021

Introduction

The acute respiratory failure (ARF) is the most prevalent condition in children hospitalized in the Intensive Care Units (ICU) worldwide.¹ According to the classification of severity and impairment of the respiratory system, noninvasive ventilation (NIV) is indicated as the primary choice in the treatment of ARF.²

Conventional NIV (CNIV) has pneumatic components that, when detecting changes in flow or pressure, synchronize the patient's respiratory efforts to the inspiratory flows delivered. Thus, the choice of interfaces with lower leakage rates is directly related to the better synchrony between the patient and the mechanical ventilator.³

Available from Getinge Group© equipment, Noninvasive Neurally Adjusted Ventilatory Assist (NIV NAVA) mode, uses transesophageal electrodes sensitive to changes in electrical activity of diaphragm (EAdi) to exclude the pneumatic component and synchronize inspiratory flow proportional to the respiratory efforts. That is, the greater the diaphragmatic excitation of the patient, the higher the peak of positive inspiratory pressure delivered.⁴

The interaction between the patient and the mechanical ventilator is evaluated by means of the Asynchrony Index (AI), obtained by the sum of asynchronous events: Ineffective Efforts (IE), Automatic Trigger (AT), Double Trigger (DT), Premature Cycling (PC) and Late Cycling (LC), divided by the sum of respiratory cycles and IE multiplied by 100. The calculation: $AI = [(IE + AT + DT + PC + LC) \div (\text{respiratory cycles} + IE)] \times 100$, will result in a percentage of asynchrony.^{5, 6} Rates greater than or equal to 10% are associated with unfavorable clinical outcomes, such as: changes in tidal volume delivery, increased respiratory work, increased need for the use of sedatives, increased time on mechanical ventilation (MV), increased length of stay in the ICU, in addition to higher mortality rates and ventilation induced lung injury (VILI).^{7, 8}

The present study presents two possible hypotheses. The first is that there is correlated evidence between the use of NIV NAVA and lower AI when compared to CNIV in pediatric patients with ARF. The second is that there is correlated evidence between the use of NIV NAVA and favorable clinical outcomes when compared to CNIV in pediatric patients with ARF.

Thus, the aim of this systematic review is to analyze and compare the asynchronous events and clinical outcomes of patients during the use of NIV NAVA vs. CNIV in the treatment of ARF in children aged between 1 month and 18 y.

Methodology

The Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) guidelines were used to delimit the processes of this review. Clinical trials were selected, comparing the use of NIV NAVA vs. CNIV in the treatment of ARF in the pediatric patients, aged between 1 month and 18 y of age incomplete.

Search strategy

The search was performed by two independent reviewers in the electronic databases of the Cochrane Library, Embase, Lilacs, Pubmed/Medline, Scopus and Web of Science between April and May 2020.

Using the thematic blocks: 'Noninvasive Ventilation', 'Children' and 'Neurally Adjusted Ventilatory Assist', the research combined the terms of Medical Subject Headings (MeSH) with Boolean operators "OR" and "AND" as follows: '*Noninvasive Ventilations*' OR '*Ventilation, Noninvasive*' OR '*Ventilations, Noninvasive*' OR '*Non-Invasive Ventilation*' OR '*Non-Invasive Ventilations*' OR '*Ventilation, Non-Invasive*' OR '*Ventilations, Non-Invasive*' OR '*Non-Invasive Ventilation*' OR '*Non-Invasive Ventilations*' OR '*Ventilation, Non-Invasive*' OR '*Ventilations, Non-Invasive*'; AND '*Children*' OR '*Preschool Child*' OR '*Children, Preschool*' OR '*Preschool Children Adolescent*' OR '*Child*'; AND '*Support, Interactive Ventilatory*' OR '*Ventilatory Support, Interactive*' OR '*Neurally Adjusted Ventilatory Assist*'.

Inclusion and exclusion criteria

The primary analysis of the articles was made after reading the title and abstract, applying the following criteria for inclusion: 1. Randomized clinical trials; 2. Age group of research subjects between 1 month and 18 y incomplete; 3. Patients with respiratory failure; 4. In use of the following NIV modes: (a) Nasal intermittent positive pressure ventilation (NIPPV), (b) Synchronized nasal intermittent positive pressure ventilation (SNIPPV) or NIV NAVA.

With no restrictions on the type of language and year of publication, the following exclusion criteria were applied: 1. Retrospective and prospective observational studies; 2. Studies on non-human experimental models; 2. Publications without the full results available for individual analysis of the research subjects; 3. Studies in populations composed exclusively of newborns or adults; 4. Patients using NIV by continuous nasal airway pressure (NCPAP) mode; 7. Patients using invasive MV and 8. Interrupted or ongoing studies.

Risk of bias analysis

Through the Risk of Bias (RoB) tool of the Cochrane Library, it was possible to evaluate the methodological quality and internal validity of the studies. Classifying

Table 1: Sample characteristics

Author/Year	Intervention sequence	Total sample (n = 48)	Eligible sample (n = 39)	Median age (months) of eligible sample (IIQ1–IIQ3)	Male gender (%)
Vignaux <i>et al.</i> 2013	Randomized	6	6	18 (5-27)	66
Baudin <i>et al.</i> 2014	Non-randomized	11	5	1,87 (1,53-2,1)	80
Ducharme <i>et al.</i> 2015	Non-randomized	13	10	53,75 (16,5-125,5)	70
Chidini <i>et al.</i> 2016	Randomized	18	18	13 (8,5-17,75)	50

Table 2: Methodological data from selected studies

Author/Year	Total sample (n = 48)	Device	Interface	Washout period (min)	NIV NAVA period (min)	CNIV period (min)
Vignaux <i>et al.</i> 2013	6	Servo i®	Face mask or Nasal prong	> 5	20	25
Baudin <i>et al.</i> 2014	11	Servo i®	Nasal mask	110 - 130	10	10
Ducharme <i>et al.</i> 2015	13	Servo i® + Other*	Nasal Mask + Other**	There is no description	10	20
Chidini <i>et al.</i> 2016	18	Servo i®	Total face mask	20	60	60

* Babylog 8000® – Draeger, VPAP III® – ResMed, BIPAP® e Trilogy 100® – Philips; ** Nasopharyngeal tubes / nasobuccal masks

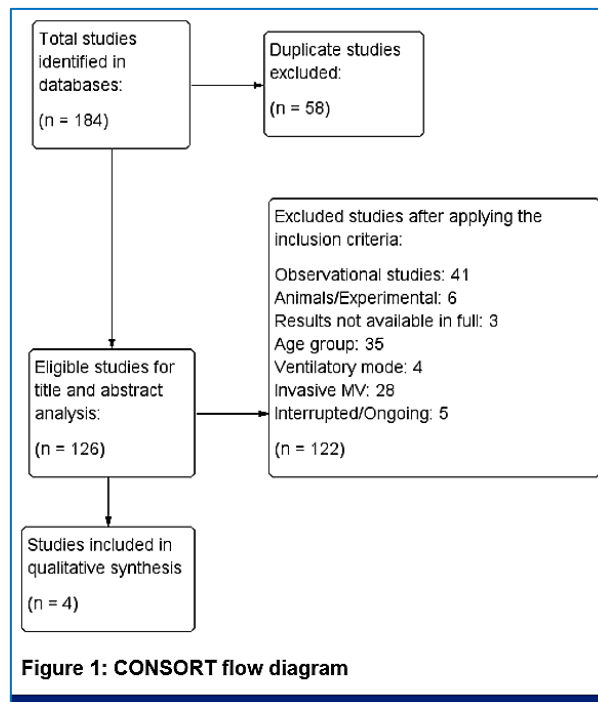
them as high, low or uncertain risk of bias, the following criteria were applied: 1. Generation of the randomization sequence; 2. Confidentiality of allocation; 3. Concealment of allocation; 4. Masking (blinding) of participants and the team of researchers; 5. Masking (blinding) in the evaluation of outcomes; 6. Incomplete data of outcomes; 7. Selective report of outcomes and 8. Other sources of bias identified by the reviewer.⁹

Results

Search results

The bibliographic research conducted between April and May 2020 resulted in the identification of 184 articles. Out of these 69 were obtained from the Cochrane Library's electronic database, 41 from Embase, 22 from Lilacs, 22 from Pubmed/Medline, 5 from Scopus and 25 from Web of Science.

After the removal of 58 duplicate articles, another 122 were excluded because they did not meet the inclusion criteria during the analysis of the title and abstract, as observed in Figure 1. Of these, three studies appeared as discontinued, one study had "unknown" status regarding non-updating of data by the authors for more than two years, while a comparative randomized clinical trial between NIV NAVA and CNIV with an estimated sample of 14 premature participants had "recruiting" status on



the ClinicalTrials.gov platform.

The selection process included four articles for qualitative analysis (Table 1). Two randomized clinical trials^{10, 11} and two non-randomized clinical trials.^{12, 13}

Table 3: Descriptive analysis of selected studies					
	Author	Vignaux et al. 2013 ⁽¹⁰⁾	Baudin et al. 2014 ⁽¹²⁾	Ducharme-Crevier et al. 2015 ⁽¹³⁾	Chidini et al. 2016 ⁽¹¹⁾
	Outcome				
Asynchronies during NIV NAVA	AI	▼	▼	-	▼
	Time spent on asynchrony MV	-	-	■	-
	Feasibility and tolerance	-	-	▲	-
Average Ventilatory Parameters during NIV NAVA	% of Leak	■	-	-	-
	FiO ₂	-	■	-	●
	RR	■	▲	-	-
	Neural RR	-	■	-	▲
	PEEP	-	■	-	-
	Peak EAdi	■	■	-	-
	Peak of inspiratory flow	-	-	-	▼
	Peak of pressure	▲	■	-	▼
	Mean airway pressure	▲	-	-	▼
	ET	-	-	-	■
	IT	-	-	-	■
	Neural IT	■	-	-	-
	Tidal volume	■	-	-	■
	VMin	-	-	-	▲
Clinical Outcomes during NIV NAVA	pH	-	-	-	■
	PaO ₂ /FiO ₂	-	-	-	■
	SpO ₂	-	■	-	-
	OI	-	-	-	▼
	PaCO ₂	-	-	-	■
	TcCO ₂	-	■	-	-
	HR	-	■	-	-
	Respiratory distress	-	■	-	-
	Use of sedatives	-	-	-	■

▼ Significant decrease ($p < 0.05$); ▲ Significant increase ($p < 0.005$); ■ No significant changes ($p \geq 0.05$).

AI: asynchrony index; EAdi: electrical activity of diaphragm; ET: expiratory time; FiO₂: fraction-inspired oxygen; HR: heart rate; IT: inspiratory time; MV: mechanical ventilation; NIV NAVA: noninvasive neurally adjusted ventilatory assist; OI: oxygenation index; PaCO₂: carbon dioxide blood pressure; PaO₂: oxygen blood pressure; PEEP: positive end-expiratory pressure; pH: hydrogenionic potential; RR: respiratory rate; SpO₂: peripheral capillary oxygen saturation; TcCO₂: transcutaneous carbon dioxide; Vmin: volume minute.

Sample size

The sample size of the four articles ranged from six to 18 participants,^{10, 11} resulting in 48 participants in total.

During the individual analysis of the research subjects, nine (18.75%) were excluded because they did not meet the inclusion criteria of age group (less than 1 month) and ventilatory mode (NCPAP). Thus, the total of 39 (81.25%) subjects were effectively included in the qualitative analysis (Table 1).

Age and gender

The age of the eligible subjects ranged from 35 days of life to 15 y and 10 months, with a male predominance ranging from 66% to 80% (Table 1). The analysis of the study by Vignaux et al. 2013, presented a median age of 18 months of the total sample ($n = 6$), with interquartile interval (IIQ) $1 = 5 - \text{IIQ}3 = 27$. In addition to male predominance in 66%.¹⁰

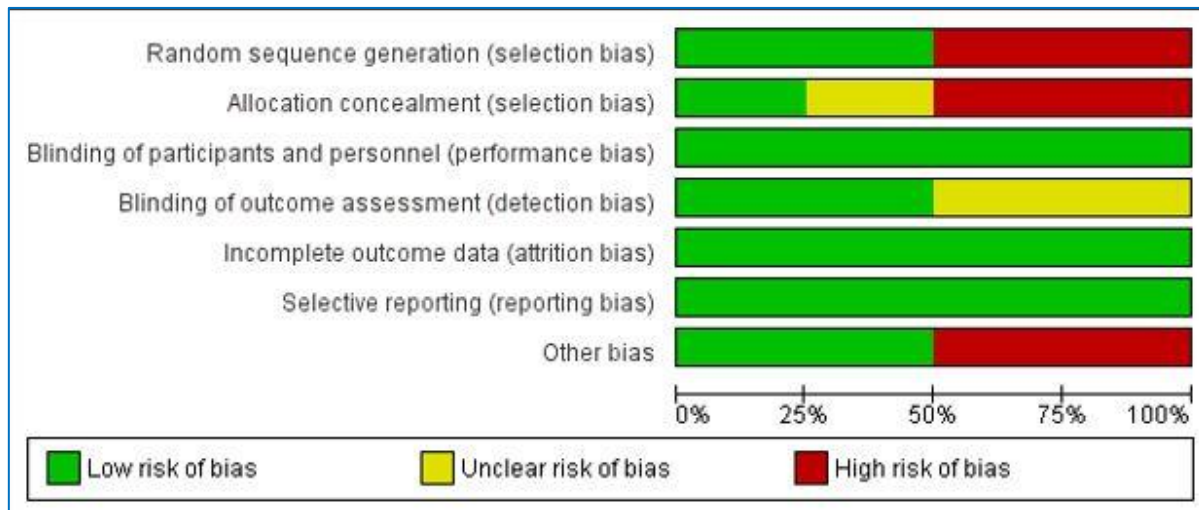


Figure 1: Risk of bias analysis graph: review the authors' judgments about each bias risk item presented as a percentage in all included studies

In the study by Baudin et al., the median age of the total sample ($n = 11$) was 0.9 months (0.53-1.7). However, 6 (54%) subjects were excluded from the analysis because they did not meet the inclusion criteria by age group. Thus, the median age of the eligible sample ($n = 5$) becomes 1.87 months (1.53 - 2.1), with a male predominance of 80%.¹²

In the study by Ducharme et al. 2015, the median age of the total sample ($n = 13$) was 42 months (2 - 76). However, three subjects (23%) were excluded from the analysis because they did not meet the inclusion criteria in a ventilatory mode (NCPAP). Thus, the median age of the eligible sample ($n = 10$) becomes 53.75 months (16.5 - 125.5), with a male predominance of 70%.¹³

In the study by Chidini et al. 2016, the median age of the total sample ($n = 18$) was 13 months (8.5 - 17.75), with no gender predominance.¹¹

Classification

All studies classified the subjects based on the AI during the period of hospitalization in the pediatric ICU.

A ratio $\text{PaO}_2/\text{FiO}_2$ less than 300, respiratory rate (RR) above the predicted value for age, use of accessory respiratory muscles and difficulty in feeding were the classification criteria used by Chidini et al.¹¹

The continuous use of NIV for a period longer than 6 h was one of the classification criteria in the study by Ducharme et al.¹³ Therapeutic failure in the use of NCPAP, recurrent apnea events in an interval of less than 1 hour, signs of respiratory distress with gasometric changes such as: $\text{pH} < 7.30$ and $\text{PaCO}_2 > 60$ mmHg were the classification criteria adopted by Baudin et al.

2014.¹² While Vignaux et al. 2013 applied NIV after extubation of intubated patients for surgical procedures.¹⁰

Intervention

According to the cross-over method adopted by the authors, all subjects participated simultaneously in the NIV NAVA and CNIV groups (Table 2).

The period of analysis of the outcomes in each group ranged from 10 to 60 min. Since the time interval between interventions, called "washout period", ranged from five to 70 min in three studies.¹⁰⁻¹² The washout period was not described in the studies by Ducharme et al.¹³

During NIV NAVA and CNIV, only one device (Servo I® - Maquet) was used by three researchers.¹⁰⁻¹² During Ducharme et al. studies, NIV NAVA was used by Servo i® - Maquet, but during CNIV five different devices (Babylog® 8000 plus - Draeger; Servo i® - Maquet; VPAP III® - ResMed; BIPAP® and Trilogy 100® - Philips) was described.¹³ Five different types of NIV interfaces have also been described. Face mask and nasal prong were used by Vignaux et al.¹⁰, nasal mask was used by Baudin et al.¹², nasopharyngeal tubes, nasal masks and nasobuccal (face mask) were used by Ducharme et al.¹³, and only total face mask was used by Chidini et al.¹¹

Vignaux et al. applied randomly, a total of 25 min of CNIV pressure support (PS) followed by 20 min of NAVA NIV. The same device (Servo i® - Maquet) was used with a minimum washout period of 5 min. While the choice of interf

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Baudin 2014	●	●	+	+	+	+	+
Chidini 2016	+	+	+	+	+	+	+
Ducharme 2015	●	●	+	?	+	+	●
Vignaux 2013	+	?	+	?	+	+	●

Figure 2: Summary of the risk of bias: analyze the authors' judgments about each risk item of bias for each study included

aces (facial mask and nasal prong) could vary according to the tolerance and agitation of the participant.¹⁰

Baudin et al. applied a non-randomized sequence with 2 h in CNIV (Pressure Assist Control - PAC) followed by a washout period between 110 and 130 min, and finally another 2 hours in NIV NAVA. The authors used only the last 10 min of each intervention for comparative analyses. The same device (Servo I[®] - Maquet) and interface (nasal mask) were used in both interventions.¹²

Ducharme et al. applied a non-randomized sequence, without a specific washout period, composed of three interventions periods. Initially 30 min in CNIV (NCPAP, PAC or PS), followed by 60 min in NIV NAVA, and finally another 30 min in CNIV. The authors used only the last 10 min of each intervention period for comparative analyses. Five different types of devices (Babylog 8000[®] - Draeger; Servo i[®] - Maquet; VPAP III[®] - ResMed; BIPAP[®] and Trilogy 100[®] - Philips) and interfaces (nasopharyngeal tubes, nasal masks and face) masks were used in this study.¹³

Chidini et al. applied randomly 60 min of CNIV (PS) and 60 min of NIV NAVA, with a washout period of 20 min. The same device (Servo i[®] - Maquet) and the same

interface (total face mask) were used in both interventions.¹¹

Outcomes

The primary outcome observed in three of the four articles was the AI (Table 3). It was possible to observe a significant decrease in AI during NIV NAVA when compared to CNIV ($p < 0.001$).¹⁰⁻¹²

In the study by Ducharme et al. synchrony-related outcomes were quantified according to the percentage of the time spent on asynchronies, and not by AI. It was possible to observe a decrease in the percentage of time spent on asynchronies during NIV NAVA when compared to CNIV ($p = 0.05$). The authors defined as primary outcome the feasibility and tolerance of NIV NAVA. Concluding that its use was feasible, according to its ability to obtain a correct signal from the EAdi, to decrease the percentage of time spent on asynchronies and by not interrupting the ventilatory support, besides being tolerable because it did not present differences in the clinical conditions of ICU patients.¹³

Other outcomes such as mean ventilatory parameters, clinical characteristics, gas exchange and sedative use were also evaluated (Table 3). Presenting significant increase in the values of: inspiratory peak pressure ($p = 0.03$) and mean airway pressure ($p = 0.016$) during NAVA NIV. There were no significant changes in the values of RR ($p = 0.37$), tidal volume ($p = 0.562$), peak of EAdi ($p = 0.077$), neural Inspiratory Time (IT) ($p = 0.95$) and percentage of leaks ($p = 0.817$) between interventions in the studies by Vignaux et al.¹⁰

The studies of Baudin et al. showed a significant increase in MV RR ($p = 0.03$) during NIV NAVA. There were no significant changes in the values of inspiratory peak pressure ($p = 0.09$), FiO₂ ($p = 0.22$), PEEP ($p = 0.95$), neural RR ($p = 0.16$), peak EAdi ($p = 0.80$), SpO₂ ($p = 0.07$), heart rate (HR) ($p = 0.18$), transcutaneous carbon dioxide (TcCO₂) ($p = 0.3$) and respiratory distress ($p = 0.87$) between interventions.¹²

The studies of Chidini et al., presented significant changes in the decrease in oxygenation index (OI) ($p = 0.043$), peak inspiratory flow ($p = 0.001$), inspiratory peak pressure ($p = 0.006$) and mean airway pressure ($p = 0.038$), in addition to increased minute volume (Vmin) ($p = 0.038$) and neural RR ($p = 0.013$) during NIV NAVA. There were no significant changes in pH, PaCO₂, PaO₂/FiO₂, use of sedatives ($p = 0.752$), FiO₂ ($p = 0.871$), tidal volume ($p = 0.631$), Neural IT ($p = 0.051$), neural Expiratory Time (ET) ($p = 0.657$) and peak EAdi ($p = 0.013$) between interventions.¹¹

Risk of bias analysis

The methodological quality analysis of the studies, observed in Figure 2 and Figure 3, was obtained using the evaluation criteria of the RoB tool.⁹ With except the

study published by Chidini et al., all classified at least one item as being "high risk" or "uncertain risk" of methodological bias.

The non-randomization of the interventions applied by Baudin et al. and Ducharme et al., present a "high risk" of methodological bias.^{12, 13} The non-blinding in the allocation of subjects in the studies published by Baudin et al. and Ducharme et al. present a "high risk" of bias.^{12, 13} While the non-description of this item in the study published by Vignaux et al., classifies it as an "uncertain risk" of bias.¹⁰

In none of the four articles analyzed, the subjects or the research team were blinded. According to the judgment of the authors of this review, it did not present interferences in the analysis of the results. Thus, the studies are classified as "low risk" of bias.¹⁰⁻¹³

Blinding during the evaluation of outcomes was described in the studies by Baudin et al. and Chidini et al., and was classified as "low risk" of bias.^{11, 12} The non-description of this item in the studies by Vignaux et al. and Ducharme et al. was classified as "uncertain risk" of bias.^{10, 13}

All studies appear to be free of friction and communication bias, related respectively to incomplete data and selective reporting of outcomes.¹⁰⁻¹³

Other risks such as the use of two types of interfaces, the heterogeneity of the subjects and the restricted analysis of breaths triggered by the EAdi, appear a "high risk" of bias in the analysis of the results published by Vignaux et al.¹⁰ As well as the non-description of washout period, the use of several types of interfaces and MV devices during the application of the interventions, classified the study by Ducharme et al. as "high risk" of bias.¹³

Discussion

Four studies analyzed the synchrony and clinical outcomes associated with the application of NIV NAVA compared to CNIV during the treatment of children of 39 children (eligible) with ARF.¹⁰⁻¹³

Three studies showed a significant decrease ($p < 0.001$) in AI during NIV NAVA,¹⁰⁻¹² while one study showed a decrease in the percentage of time spent on asynchronies during NIV NAVA ($p = 0.05$).¹³ According to the authors, the choice of this type of variable was due to the particular importance of inspiratory asynchronies and cycling on the pediatric population. One of the related disadvantages is the impossibility of comparing similar effects obtained from different variables. Being that AI expresses the percentage of asynchronous events per minute and not by the cumulative time spent on each form of asynchrony.^{6, 13-15}

The relationship between the use of NIV NAVA and clinical outcomes were inconclusive between studies.

While Vignaux et al. reported an increase in peak inspiratory pressure and mean airway pressure¹⁰, Chidini et al. reported divergent results on the same variables.¹¹ Baudin et al. and Chidini et al., showed similar results in the increase in RR^{11, 12} and Vmin¹¹, while Vignaux et al. did not observe significant changes in the same variables.¹⁰ The clinical outcomes reported by the authors were inconclusive, diverging from the findings described in the previous literature,^{4, 7, 8, 16} thus preventing confirmation of the hypothesis of correlation between favorable clinical outcomes and the use of NIV NAVA.

The use of the cross-over method adopted by the authors¹⁰⁻¹³, makes it impossible to correlate an intervention to specific clinical outcomes; for example, length of ICU stay, total time of mechanical ventilation, risk of VILI and risk of mortality. Just as the non-standardized washout period may interfere in the analysis of the results due to the remaining therapeutic effect unknown among the interventions.

The authors of this review hypothesize that such limitations presented in the studies may be associated with the high relative cost of the neural interaction device, since NAVA technology is private and patented by Getinge Group®, and is available only on Servo i®, Servo n® and Servo u® equipment. Studies comparing the relationship between cost and effectiveness of technology are scarce and limited to adult participants under invasive MV.¹⁷

Part of the heterogeneity of the research subjects has a direct relationship between the age group of the population and the cause of the ARF. Younger children, such as those observed in the study by Baudin et al.¹², are more susceptible to developing ARF for viral infections, such as Acute Viral Bronchiolitis (AVB).¹⁸ As children with a median age older, such as those observed in the study by Ducharme et al.¹³, are more susceptible to developing ARF after surgical procedures or bacterial infections as pneumonia and SEPSIS, for example.^{19, 20} Thus, it may present very heterogeneous outcomes during the treatment of ARF.

Limitations related to the small size of samples with high heterogeneity among the research subjects may be associated with confounding factors in the analysis of the results, thus reducing the internal and external validity of the studies.

Conclusion

After a systematic review of the four eligible articles, we conclude that NIV NAVA has a lower AI when compared to the conventional NIV in pediatric patients with ARF. However, due to methodological limitations, clinical outcomes related to the effectiveness of gas exchange, mean ventilatory parameters, respiratory

distress and use of sedatives were inconclusive. It is understood that new randomized clinical trials, with homogeneous samples allocated in different groups (control and intervention), using the same equipment and interfaces, as well as a longer follow-up time of participants, will be necessary to establish a more precise relationship between better synchrony and favorable clinical outcomes.

Conflict of interest

The authors declare that there is no funding source for the project, and that they are exempt from any kind of conflict of interest related to the brands or companies mentioned.

Authors' contribution

JMFS: Research and writing.

CMR: Conducting, reviewing, and correcting the study.

CACO: Research and methodological support.

EJT: Orientation, conducting, reviewing, and correcting the study.

References

- Friedman ML, Nitu ME. Acute respiratory failure in children. *Pediatr Ann.* 2018;47(7):e268-e73. [PubMed] DOI: [10.3928/19382359-20180625-01](https://doi.org/10.3928/19382359-20180625-01)
- Wolfler A, Raimondi G, Pagan de Paganis C, Zoia E. The infant with severe bronchiolitis: from high flow nasal cannula to continuous positive airway pressure and mechanical ventilation. *Minerva Pediatr.* 2018;70(6):612-22. [PubMed] DOI: [10.23736/S0026-4946.18.05358-6](https://doi.org/10.23736/S0026-4946.18.05358-6)
- Al Otair HA, BaHamam AS. Ventilator- and interface-related factors influencing patient-ventilator asynchrony during noninvasive ventilation. *Ann Thorac Med.* 2020;15(1):1-8. [PubMed] DOI: [10.4103/atm.ATM_24_19](https://doi.org/10.4103/atm.ATM_24_19)
- Suarez-Sipmann F. New modes of assisted mechanical ventilation. *Medicina Intensiva (English Edition).* 2014;38(4):249-60. [PubMed] DOI: [10.1016/j.medin.2013.10.008](https://doi.org/10.1016/j.medin.2013.10.008)
- Colombo D, Cammarota G, Alemani M, Carenzo L, Barra FL, Vaschetto R, et al. Efficacy of ventilator waveforms observation in detecting patient-ventilator asynchrony. *Crit Care Med.* 2011;39(11):2452-7. [PubMed] DOI: [10.1097/CCM.0b013e318225753c](https://doi.org/10.1097/CCM.0b013e318225753c)
- Sousa MLA, Magrans R, Hayashi FK, Blanch L, Kacmarek RM, Ferreira JC. Predictors of asynchronies during assisted ventilation and its impact on clinical outcomes: The EPISYNC cohort study. *J Crit Care.* 2020;57:30-5. [PubMed] DOI: [10.1016/j.jcrc.2020.01.023](https://doi.org/10.1016/j.jcrc.2020.01.023)
- Subira C, de Haro C, Magrans R, Fernandez R, Blanch L. Minimizing asynchronies in mechanical ventilation: current and future trends. *Respir Care.* 2018;63(4):464-78. [PubMed] DOI: [10.4187/respcare.05949](https://doi.org/10.4187/respcare.05949)
- Lee J, Kim HS, Jung YH, Choi CW, Jun YH. Neurally adjusted ventilatory assist for infants under prolonged ventilation. *Pediatr Int.* 2017;59(5):540-4. [PubMed] DOI: [10.1111/ped.13233](https://doi.org/10.1111/ped.13233)
- Higgins JPT, Thomas J, Chandler J, Cumpston M, Li T, Page MJ, et al. *Cochrane Handbook for Systematic Reviews of Interventions* version 6.2. Cochrane; 2021. Available from: www.training.cochrane.org/handbook
- Vignaux L, Grazioli S, Piquilloud L, Bochaton N, Karam O, Levy-Jamet Y, et al. Patient-ventilator asynchrony during noninvasive pressure support ventilation and neurally adjusted ventilatory assist in infants and children. *Pediatr Crit Care Med.* 2013;14(8):e357-64. [PubMed] DOI: [10.1097/PCC.0b013e3182917922](https://doi.org/10.1097/PCC.0b013e3182917922)
- Chidini G, De Luca D, Conti G, Pelosi P, Nava S, Calderini E. Early noninvasive neurally adjusted ventilatory assist versus noninvasive flow-triggered pressure support ventilation in pediatric acute respiratory failure: a physiologic randomized controlled trial. *Pediatr Crit Care Med.* 2016;17(11):e487-e95. [PubMed] DOI: [10.1097/PCC.0000000000000947](https://doi.org/10.1097/PCC.0000000000000947)
- Baudin F, Pouyau R, Cour-Andlauer F, Berthiller J, Robert D, Javouhey E. Neurally adjusted ventilator assist (NAVA) reduces asynchrony during non-invasive ventilation for severe bronchiolitis. *Pediatr Pulmonol.* 2015;50(12):1320-7. [PubMed] DOI: [10.1002/ppul.23139](https://doi.org/10.1002/ppul.23139)
- Ducharme-Crevier L, Beck J, Essouri S, Juvet P, Emeriaud G. Neurally adjusted ventilatory assist (NAVA) allows patient-ventilator synchrony during pediatric noninvasive ventilation: A crossover physiological study. *Crit Care.* 2015;19(1). [PubMed] DOI: [10.1186/s13054-015-0770-7](https://doi.org/10.1186/s13054-015-0770-7)
- Thille AW, Rodriguez P, Cabello B, Lellouche F, Brochard L. Patient-ventilator asynchrony during assisted mechanical ventilation. *Intensive Care Med.* 2006;32(10):1515-22. [PubMed] DOI: [10.1007/s00134-006-0301-8](https://doi.org/10.1007/s00134-006-0301-8)
- Chao DC, Scheinhorn DJ, Stearn-Hassenpflug M. Patient-ventilator trigger asynchrony in prolonged mechanical ventilation. *Chest.* 1997;112(6):1592-9. [PubMed] DOI: [10.1378/chest.112.6.1592](https://doi.org/10.1378/chest.112.6.1592)
- Chen C, Wen T, Liao W. Neurally adjusted ventilatory assist versus pressure support ventilation in patient-ventilator interaction and clinical outcomes: a meta-analysis of clinical trials. *Ann Transl Med.* 2019;7(16):382. [PubMed] DOI: [10.21037/atm.2019.07.60](https://doi.org/10.21037/atm.2019.07.60)
- Hjelmgren J, Bruce Wirta S, Huetson P, Myrén KJ, Göthberg S. Health economic modeling of the potential cost saving effects of Neurally Adjusted Ventilator Assist. *Ther Adv Respir Dis.* 2016;10(1):3-17. [PubMed] DOI: [10.1177/1753465815603659](https://doi.org/10.1177/1753465815603659)
- Nair H, Nokes DJ, Gessner BD, Dherani M, Madhi SA, Singleton RJ, et al. Global burden of acute lower respiratory infections due to respiratory syncytial virus in young children: a systematic review and meta-analysis. *Lancet.* 2010;375(9725):1545-55. [PubMed] DOI: [10.1016/S0140-6736\(10\)60206-1](https://doi.org/10.1016/S0140-6736(10)60206-1)
- Balcells Ramírez J, López-Herce Cid J, Modesto Alapont V. Prevalence of mechanical ventilation in pediatric intensive care units in Spain. *An Pediatr (Barc).* 2004;61(6):533-41. [PubMed] DOI: [10.1016/s1695-4033\(04\)78440-4](https://doi.org/10.1016/s1695-4033(04)78440-4)
- Farias JA, Fernández A, Monteverde E, Flores JC, Baltodano A, Menchaca A, et al. Mechanical ventilation in pediatric intensive care units during the season for acute lower respiratory infection: a multicenter study. *Pediatr Crit Care Med.* 2012;13(2):158-64. [PubMed] DOI: [10.1097/PCC.0b013e3182257b82](https://doi.org/10.1097/PCC.0b013e3182257b82)

