Nasal intermittent positive pressure ventilation (NIPPV) during neonatal endotracheal intubation: A randomized controlled trial

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Abstract

Background: The present study aimed to determine whether the use of nasal intermittent positive pressure ventilation (NIPPV) during neonatal endotracheal intubation increases the rate of successful intubation without physiological instability during all intubation attempts. **Material and Methods:** The present study was designed as a prospective, multicenter, randomized, controlled study conducted with neonates undergoing endotracheal intubation. The infants were assigned randomly to either the NIPPV group or the standard care group. The primary outcome was successful intubation without physiological instability (defined as [?]20% decline in the peripheral oxygen saturation [SpO $_2$] from pre-intubation value or bradycardia with a heart rate of <100 beats per minute) during all intubation attempts. **Results:** A total of 150 infants were enrolled (75 for the NIPPV group and 75 for the standart-care group). The infants had a mean postmenstrual age of 32.5 weeks and a median weight of 1552 g at the time of intubation. The incidence of successful intubation without physiological instability during all intubation attempts was significantly higher in the NIPPV group (64%) compared to the standard-care group (42.7%) (p = 0.009). This difference was particularly significant when inexperienced practitioners were involved. In the NIPPV group, the rate of bradycardia and severe desaturation was significantly lower, while the lowest SpO $_2$ level and the lowest heart rate level were significanlty higher. **Conclusion:** NIPPV during endotracheal intubation increases the incidence of successful intubation without physiological instability during all intubation attempts in neonates, while reducing the rate of hypoxia and bradycardia.

INTRODUCTION

Endotracheal intubation is a high-risk, life-saving procedure implemented during resuscitation and respiratory support.[1] Intubation procedures are associated with certain changes in physiology, including hypoxia or vagal-induced bradycardia, hypertension, and increased intracranial blood pressure, which may cause damage to the immature and developing neonatal brain.[2] Difficult intubations ([?]3) are common in the neonatal intensive care unit (NICU) and are associated with adverse events and severe oxygen desaturation.[3] Moreover, less experience in the intubation procedure is associated with an increased duration of intubation attempts, severe desaturation, intubation-associated adverse events, and lower success rates in intubation.[4] Physiological stability during intubation, therefore, protects the infant from damage, particularly during difficult and prolonged intubation.

Although there are several studies conducted in adults,[5] few studies have been conducted with neonates to explore how to reduce physiological changes during intubation.[6-8] In one of these few studies conducted with preterm infants, Hodgson et al.[6] reported that nasal high-flow (NHF) therapy during the intubation improved the likelihood of successful intubation on the first attempt without causing physiological instability. Foran et al.[7] reported that the rate of decline in oxygen saturation was lower when using NHF during intubation. Another study with a relatively smaller sample size postulated that continuous gas flow via the endotracheal tube during intubation is favorable.[8]

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In neonates, nasal intermittent positive pressure ventilation (NIPPV) increases the mean airway pressure and reopening of the partially collapsed airways, improves minute ventilation and functional residual capacity, and reduces the frequency of bradycardia, apnea, and oxygen desaturation episodes.[9,10] NIPPV prevents treatment failure and decreases the requirement for mechanical ventilation and reintubation rates compared to the use of continuous positive airway pressure and NHF.[10] However, different from previous studies,[6-8] the present study involved the use of NIPPV as it is one of the most used non-invasive ventilation modalities in NICUs and offers several benefits.

The present study aimed to determine whether the use of NIPPV during endotracheal intubation increases the rate of successful intubation without physiological instability during all intubation attempts in neonates.

MATERIALS AND METHODS

The present study was designed as a prospective, multicenter, randomized, controlled trial. The study was conducted at two tertiary NICUs (Mugla Training and Research Hospital, Mugla, Turkey; Akdeniz University School of Medicine, Antalya, Turkey) between May 2023 and May 2024. The study was approved by the Clinical Research Ethics Committee of Mugla Sitki Kocman University (issue: 9/XIV; date: 13/04/2023).

Randomization

Each infant was randomly assigned to either the intervention (NIPPV) group or the standard-care group. Sequential numbers were generated in the NICU's computer with an allocation ratio of 1:1. The numbers were concealed in opaque, sequentially numbered, sealed envelopes. All practitioners followed the instructions provided in the envelopes.

Definitions

An attempt was defined as an airway maneuver, which commenced with the insertion of the laryngoscope blade (conventional) into the mouth of the patient and ended with the removal of the blade.[11]Successful airway management was defined as the placement of an endotracheal tube in the trachea via orally, confirmed based on chest elevation, auscultation, second independent laryngoscopy, carbon dioxide detection, and/or chest radiography.[11] First-attempt success was defined as successful intubation by the first practitioner on the first attempt. Multiple-attempt success was defined as the requirement of over two attempts ([?]3) for successful intubation. The requirement for single, double, or multiple attempts for successful intubation was defined as all intubation attempts. Severe oxygen desaturation during intubation was defined as a decrease of [?]20% in oxygen saturation relative to the highest level of oxygen saturation recorded prior to the first attempt.[11] Bradycardia was defined as a heart rate of <100 beats per minute. Physiological instability was defined as severe desaturation (a decrease of to pre-laryngoscopy) or bradycardia (a heart rate of <100 beats per minute) during the intubation attempts. Hatch et al.[12] defined practitioners as experienced if they had performed more than 40 previous intubations. Based on this knowledge and our NICU conditions, those who performed >35 previous intubations were considered experienced practitioners.

Interventions

All neonates were monitored using a Philips monitor (IntelliVue MX450) that displayed the real-time peripheral oxygen saturation (SpO_2) and heart rate prior to, during, and after the procedure.

The patients were divided into two groups: the NIPPV group and the standard care group. In the NIPPV group, NIPPV was implemented during the entire intubation process (pre-intubation to intubation to the end of successful intubation). Appropriately-sized short binasal prongs (Fisher & Paykel, New Zealand) were placed prior to laryngoscopy as interface for NIPPV implementation. NIPPV was implemented using Leoni Plus (Löwenstein Medical, Bad Ems, Germany) mechanical ventilator. Non-synchronized NIPPV was implemented. NIPPV was initiated prior to intubation, with the peak inspiratory pressure set to 16–20 cmH_2O (selected according to the infant's birth weight and chest wall expansion), positive-end expiratory pressure (PEEP) set to 6 cmH_2O, breathing rate set to 40–50 breaths/min, inspiratory time set to 0.40–0.45 s, and flow rate set to 8–12 L/min. After the first successful intubation attempt, NIPPV was discontinued.

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Prior to laryngoscopy, the fraction of inspired oxygen (FiO_2) was adjusted to maintain SpO_2above 90%. In the standard care group, the intubation attempt proceeded without NIPPV or supplemental oxygen. In the event of failure in the intubation attempt, SpO_2 was increased above 90%, and the heart rate was increased above 120/min by applying positive pressure ventilation using a face mask prior to initiating the next intubation procedure.

If the infant was crying or agitated, midazolam was administered as pre-medication. No medication other than midazolam was used for sedation or premedication. The size of the intubation tube was determined based on the baby's body weight.[13] Stylet was not used during intubation.

Endotracheal intubations were performed either by pediatric research assistants or a neonatologist. A conventional laryngoscope with a straight blade was used for the intubation. Video laryngoscope was not used. Data accuracy was ensured by videotaping the monitor-displayed heart rate and SpO_2 during the intubation procedure. After intubation, an independent assessor who was not part of the intubation team reviewed all recorded videos to document the obtained data on a case report form.

Data collection and management

The demographic data, including age, gender, birth weight, mode of delivery, Apgar scores, underlying patient diagnoses, indications for intubation, respiratory support prior to intubation, operator experience, pre-medication use, post-menstrual age, and weight at intubation, were collected for all patients. A pre-assigned staff member who was not a part of the intubation team noted the vital signs, adverse outcomes, and complications during and after the procedure and also collected blood gas one hour after the intubation for each patient.

Subgroup analysis

The infants were divided into two subgroups according to their gestational ages (<32 and [?]32 weeks). The primary and secondary outcomes were compared between the NIPPV group and standard-care group within the each subgroup.

Sample size

Hodgson et al.[6] reported that the rate of successful intubation on the first attempt without physiological instability was 31% in newborns who did not receive additional respiratory support during intubation. In the present study, it was hypothesized that the success rate of intubation on the first attempt without physiological instability would increase from 31% to 54% upon the implementation of NIPPV during intubation. The sample size was calculated using the "G*Power 3.1.9.4" program with a type I error of 5% level and a power of 80%. Accordingly, it was concluded that 75 intubation episodes were required for each group, and 150 intubation episodes were required in total.

Statistical analysis

Statistical analysis was performed using Statistical Package for the Social Sciences (SPSS) software (version 25; Armonk, NY: IBM Corp.). The Kolmogorov–Smirnov and Shapiro–Wilk tests were conducted to determine the normal distribution of data. Student's t-test was conducted to compare the continuous parametric variables. The Mann–Whitney U-test was conducted to compare variables with non-normal distribution. Chi-squared or Fisher's exact test was conducted to analyze the categorical variables. Categorical variables were expressed as numbers (%). Normally distributed variables were expressed as mean +- standard deviation values. Non-parametric continuous variables were expressed as median values (interquartile range). The difference with $p < 0.05$ was considered statistically significant.

RESULTS

A total of 150 infants with a gestational age between $22^{0/6}$ and $41^{6/7}$ weeks and birth weight between 400 g and 4020 g were included in the study. The neonates randomly assigned to the NIPPV group (75 infants) or the standard-care group (75 infants). Data on enrolment are outlined in Figure 1. No significant difference was noted between the groups in terms of gestational age, birth weight, and demographic characteristics (Table 1).

The post-menstrual age of these infants at intubation was 31.5 +- 4.6 weeks in the NIPPV group and 33.5 +- 5.5 weeks in the standard care group, and the difference between the two groups was statistically significant ($p = 0.020$) (Table 1). Indications for intubation, respiratory supports before procedure and intubation characteristics are shown in Table 1. The rate of mechanical ventilation and low-flow oxygen was significantly higher in the standart-care group ($p < 0.001$ and $p = 0.028$; respectively), while the rate of non-invasive ventilation was significantly higher in the NIPPV group ($p < 0.001$) prior to intubation procedure. FiO_2 requirement and heart rate was significantly higher in the NIPPV group ($p = 0.023$ and $p = 0.027$; respectively) before intubation. 26.7% of the infants were on mechanical ventilation before intubation in the standart-care group. These patients who underwent reintubation due to reasons such as endotracheal tube obstruction, serious air leakage or unplanned extubation (Table 1).

Primary outcome

The rate of successful intubation without physiological instability during all intubation attempts was significantly higher ($p = 0.009$) in the NIPPV group (64%) compared to the standard care group (42.7%). The primary outcome was also evaluated according to operator experience. It was revealed that the rate of successful intubation without physiological instability during all intubation attempts was higher in the NIPPV group (44.8%) compared to the standard care group (10.7%) when the intubation experience was less than 36 intubations ($p = 0.004$). However, when the intubation experience was above 35 intubations, no significant difference ($p = 0.134$) was observed between the groups in terms of the primary outcome (Table 2).

Secondary outcome

The rate of successful intubation on the first attempt without physiological instability was higher in the NIPPV group, although the difference was not significant ($p = 0.100$). The bradycardia rate and severe desaturation were significantly higher in the standard care group ($p < 0.002$ and $p < 0.020$, respectively). The lowest SpO_2 level and the lowest heart rate during the procedure were significantly higher in the intervention group ($p < 0.001$ and $p < 0.001$, respectively). The rate of SpO_2 dropping below 80% and below 90% was higher in the control group ($p < 0.014$ and $p < 0.002$, respectively). The median duration of severe desaturation was significantly shorter ($p = 0.043$) in the NIPPV group (10 s) compared to the standard care group (20 s) (Table 2).

Subgroup analysis

In infants with a gestational age of [?]32 weeks, the rate of successful intubation without physiological instability during all intubation attempts was significantly higher ($p = 0.014$) in the NIPPV group. This rate was also higher in the practitioners with an intubation experience of <36 intubations ($p = 0.026$) (Table 3). Results for other physiological parameters are shown in Table 3.

No significant difference was noted between the groups in terms of the vital signs measured five minutes after the procedure, the blood gas values obtained one hour after the procedure, and intubation-associated adverse events (Table 4).

DISCUSSION

The present study is, to the best of the author's knowledge, the first randomized controlled trial that compared the use of NIPPV during neonatal intubation with the use of the standard procedure to reduce physiological instability. In the present multicenter study, the rate of successful intubation without physiological instability during all intubation attempts was higher when NIPPV was implemented compared to the implementation of standard care. The results regarding the heart rate and the SpO_2 level during the procedure were more favorable with the use of NIPPV. In addition, NIPPV during intubation was revealed to be more favorable when intubation performed by practitioners with less experience.

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NIPPV augments continuous positive airway pressure (CPAP) by providing inflations to a set peak pressure by a nasal mask or nasal prongs. NIPPV provides stabilization of the upper airways and the compliant preterm chest wall and prevention of end-expiratory alveolar collapse, thus, maintains functional residual capacity and reduces ventilation- perfusion mismatch, which improves oxygenation and work of breathing.[14] NHF therapy was not designed originally to deliver PEEP, but to washout the anatomical and physiological dead space.[15] NHF prongs are designed to avoid occlusion of the nares; leak around the prongs serves to avoid excessive pressure generation,[16] therefore, the generated-pressure was not measurable and could not be regulated.[17] Some studies reported NIPPV was more effective in decreasing the requirement of mechanical ventilation and treatment failure than NHF.[18,19] NIPPV also reduces re-intubation, treatment failure and air leaks compared to CPAP.[10] In light of this information and because NIPPV is one of the most commonly used non-invasive ventilation modes, we preferred to use NIPPV during intubation in this study. We concluded that the improvement in oxygenation and work of breathing due to the multiple physiological mechanisms of NIPPV mentioned above improved the primary outcome.

Severe desaturation, bradycardia, and tracheal intubation-associated events may occur during neonatal intubation.[6,7,11,12]Tracheal intubation-associated events, including bradycardia and severe oxygen desaturation, increase substantially with the number of intubation attempts.[20-22] In the case of multiple attempts ([?]3), the risk of severe oxygen desaturation increases 6-fold compared to that on the first attempt.[20] Multiple intubation attempts are more common in newborns than in children and adults, and also when the practitioners are pediatric residents rather than experienced ones.[3,20] Among newborns, multiple intubation attempts are reportedly more common in neonates <32 weeks corrected gestation and <1500 g at the time of intubation.[3] The rate of successful intubation on the first attempt for newborns is 64% when the practitioner is experienced, while the lowest success rates are reported for cases handled by pediatric residents (20%–26%).[23] Severe oxygen desaturation is more common in resident airway practitioners compared to the fellows and attendings.[4] Physiologic instability, including oxygen desaturation, is the most common reason for unsuccessful intubation.[24] In a recent study conducted on a small number of newborn infants, Foran et al.[7]noted that physiological instability appeared to increase with the increase in the number of intubation attempts, particularly when inexperienced practitioners were involved. In the present study, it was demonstrated that the rate of successful intubation without physiological instability during all intubation attempts was significantly higher in the NIPPV group (64%) compared to the standard care group (47%). Moreover, this difference was statistically significant only when inexperienced clinicians were involved. Hodgson et al.[6] compared NHF during intubation with standard care in preterm infants and reported that successful intubation on the first attempt without physiological instability was achieved in 50.0% of the cases of intubations in the NHF group and 31.5% of the cases of intubations in the control group, with the difference between the two groups being significant. While this finding was similar to that observed in the present study, the aforementioned study did not involve evaluating NHF beyond the first intubation attempt. The rate of successful intubation on the first attempt without physiological instability was also evaluated in the present study, and while this rate was higher in the NIPPV group (50%) compared to the control group (37%), significance was not reached. These percentiles were, however, similar to those reported by Hodgson et al.,[6] who suggested a greater benefit of using NHF when the intubations were performed by inexperienced operators (<20 previous intubations). Similarly, in the present study, the rate of successful intubation without physiological instability during all intubation attempts was noted to be lower when NIPPV was implemented by inexperienced practitioners (<36 previous intubations).

Severe oxygen desaturation is reported to occur in 29% to 69% of intubations, while bradycardia is reported in 24% of intubations during procedure in NICU.[11,12] Hodgson et al.[6] reported that the rate of severe desaturation during neonatal intubation was significantly lower in the NHF group (28.2%) compared to the control group (39.4%). These authors also stated that the median oxygen saturation was higher, and the time to desaturation was longer in the intervention group during the first attempt. However, the bradycardia rate was similar (<100 bpm) in both groups (8.9% in the NHF group and 12.6% in the control group) in their study. However, the authors did not report any significant difference in the duration of severe desaturation and time to bradycardia between the groups. In the present study, consistent with the findings reported

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by Hodgson et al.,[6] the rate of severe desaturation was noted to be significantly lower, while the lowest SpO_2 level was significantly higher in the NIPPV group. However, in contrast to the findings of Hodgson et al.,[6] the bradycardia rate was noted to be higher, and the duration of severe desaturation was longer in the control group in the present study. All of the findings reported by Hodgson et al.[6] were noted for the first intubation attempt, while the findings of the present study are for all intubation attempts. This difference in the number of intubation attempts included could be the reason for the different findings between the two studies. In a recent meta-analysis that included eight randomized controlled trials, Fuchs et al.[25] evaluated the efficacy and effectiveness of apnoeic oxygenation (low-flow oxygen or high-flow nasal oxygen) during laryngoscopy conducted for tracheal intubation in newborns and children. The meta-analysis confirmed that apnoeic oxygenation during intubation significantly increases the success rate of first-pass intubation and reduces the incidence of hypoxia (SpO_2 <90%). The meta-analysis also revealed that the lowest SpO_2 level was higher when apnoeic oxygenation was applied. Therefore, it was inferred that apnoeic oxygenation facilitates stable physiological conditions by maintaining oxygen saturation within the normal range.[25] However, in the same study, no reduction was noted in the incidence of bradycardia when apnoeic oxygenation was applied.[25]Consistent with the findings of the afore-stated meta-analysis, lower incidences of hypoxia and the lowest SpO_2 level were recorded for the intervention group during the procedure in the present study.

The incidence of intubation-associated adverse events ranged from 22% to 39%.[4,12] Two studies showed that nasal high-flow oxygen or continuous gas flow via the endotracheal tube during intubation did not increase the risk of unexpected adverse events in neonates compared to the control group.[6,8] In line with these previous studies,[6,8,12] no difference was noted between the groups in the present study in terms of the incidence of non-severe and severe adverse events.

The present study also has certain limitations. The first limitation is that a nasal cannula was not used for the control group during the procedure, which could have led to bias in the outcomes. However, to reduce this bias, an independent reviewer performed a video review. So our study was not blinded. Another limitation arose because the accuracy of the pulse oximeter decreases at extremely low saturation levels (<70%). In addition, video-laryngoscopy was not performed due to its unavailability at the NICU of our hospital. This could be a limitation as video-laryngoscope reportedly improves intubation success and reduces adverse events.[11,22] Finally, since the study was conducted only in the NICU, the generalization of the findings to the delivery room and operating room may be limited.

In conclusion, NIPPV implementation during oral endotracheal intubation increases the rate of successful intubation without physiological instability during all intubation attempts in newborn infants. This difference is particularly significant in inexperienced practitioners. In addition, the procedure is associated with lower incidences of hypoxemia and bradycardia.

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None.

Disclosure statement

The authors declare no conflict of interest.

AUTHOR CONTRIBUTION

Ozkan llhan: collected data, carried out the initial analysis, drafted the initial manuscript, wrote and revised the manuscript.**Kiymet Celik:** carried out the initial statistical analysis and reviewed and revised the manuscript, final approval of the version.**Nurten Zarif Ozkan:** responsible for data collection.**Ipek Kocaoglu:** conceptualised and designed the study, responsible for data collection. **Sema Arayıcı:** coordinated and supervised data collection. **Nilay Hakan:** contributed to data analysis and interpretation of results.

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Table 1. Clinical and demographic characteristics of the patients, indications for intubation, respiratory supports before procedure

	NIPPV Group (n = 75)	**Standart-Care Group (**
Gestational age (w)*	31.0 ± 4.4	31.8 ± 5.2
Birth weight (g)#	1470 (989-2468)	1640 (910-2670)
Delivery by cesarean section, n (%)	65 (86.7)	68 (90.7)
Male gender, n (%)	47 (62.7)	50 (66.7)
Apgar score at 5 min#	8 (7-9)	8 (6-9)
Postmenstrual age at intubation (w)*	31.5 ± 4.6	33.5 ± 5.5
Weight at intubation (g)#	1470 (956-2518)	1850 (1020-2910)
Age at intubation (h)#	30 (4-120)	53 (8-360)
Respiratory support before intubation		
MV, n (%)	2 (2.7)	20 (26.7)
NIV, n (%)	73 (97.3)	40 (53.3)
Low-flow oxygen, n (%)	0	6 (8)
None, n (%)	0	9 (12)
Oxygenation and heart rate before intubation		
FiO_2 (%)#	50 (40-60)	45 (40-50)
SpO_2 (%)#	93 (90-97)	92 (90-95)
Heart rate (bpm)#	148 (142-162)	142 (135-162)
Primary indication for intubation		
Ventilation failure, n (%)	31 (41.3)	23 (30.7)

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	NIPPV Group (n = 75)	Standart-Care Group (
Oxygenation failure, n (%)	14 (18.7)	14 (18.7)
Frequent apnoea events, n (%)	10 (13.3)	11 (14.7)
Surfactant administration, n (%)	17 (22.7)	8 (10.7)
Unplanned extubation, n (%)	2 (2.7)	12 (16)
Others, n (%)	1 (1.3)	7 (9.3)
Number of intubation attempts#	1 (1-5)	1 (1-4)
Multipl attempts ([?]3 attempts), n (%)	11 (7.3)	10 (7)
Premedication use, n (%)	12 (16)	19 (25.3)
Operator experience level for previous intubation, n (%)		
[?]35	29 (38.7)	28 (37.3)
>35	46 (61.3)	47 (62.7)

Data are presented as *mean ± standard deviation,#median (interquartile range) or number (%)

FiO_2; fraction of inspired oxygen; MV, mechanical ventilation; NIV, non-invasive ventilation; SpO_2, peripheral oxygen saturation.

Table 2. Comparison of primary and secondary outcomes between the groups

Successful intubation on the first attempt without physiological instability, n (%)
Successful intubation on the first attempt without physiological instability according to operator experience
[?]35 previous intubations, n / total n (%)
>35 previous intubations, n / total n (%)
Successful intubation without physiological instability throughout all intubation attempts, n (%)
Successful intubation without physiological instability throughout all intubation attempts according to oper
[?]35 previous intubations, n / total n (%)
>35 previous intubations, n / total n (%)
Successful intubation on the first attempt, n (%)
Lowest SpO_2 during procedure (%)
Lowest heart rate during procedure (bpm)
SpO_2 <90%, n (%)
SpO_2 <80%, n (%)
Bradicardia (<100/bpm), n (%)
Severe desaturation, n (%)
Time to SpO_2 <90% (s)
Time to severe desaturation (s)
Duration of severe desaturation (s)
Time to bradicardia (s)
Duration of bradicardia (s)
Duration of first intubation attempt (s)
Time to successful intubation (s)

Data are presented as median (interquartile range) or number (%)

SpO_2, peripheral oxygen saturation.

Tablo 3. Comparison of primary and secondary outcomes in the subgroups

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Gestational age (w)
[?]35 previous intubation, n (%)
Successful intubation on the first attempt without physiological instability, n (%)
Successful intubation on the first attempt without physiological instability according to operator experience
[?]35 previous intubations, n / total n (%)
>35 previous intubations, n / total n (%)
Successful intubation without physiological instability throughout all intubation attempts, n (%)
Successful intubation without physiological instability throughout all intubation attempts according to oper
[?]35 previous intubations, n / total n (%)
>35 previous intubations, n / total n (%)
Successful intubation on the first attempt, n (%)
Lowest SpO_2 during procedure (%)
Lowest heart rate during procedure (bpm)
SpO_2 <90%, n (%)
SpO_2 <80%, n (%)
Bradicardia (<100/bpm), n (%)
Severe desaturation, n (%)
Time to SpO_2 <90% (s)
Time to severe desaturation (s)
Duration of severe desaturation (s)
Time to bradicardia (s)
Duration of bradicardia (s)
Duration of first intubation attempt (s)
Time to successful intubation (s)

Data are presented as median (interquartile range) or number (%)

SpO_2, peripheral oxygen saturation.

Table 4. Comparison of vital signs, blood gas values and complications after the procedure between the groups.

	NIPPV Group	**Standart-Care Group**	**p**
Vital signs (5 minutes after the procedure)	**(n = 66)**	**(n = 70)**	
SpO_2 (%)*	96.0 ± 2.7	95.5 ± 2.7	0.243
Heart rate (bpm)*	148.7 ± 14.5	144.8 ± 12.3	0.076
Systolic blood pressure (mmHg)*	68.9 ± 9.9	70.5 ± 11.2	0.387
Mean blood pressure (mmHg)*	50.8 ± 10.5	51.7 ± 10.5	0.633
Blood gas values (1 hour after the procedure)	**(n = 47)**	**(n = 47)**	
pH$^{\#}$	7.34 (7.28 – 7.39)	7.36 (7.22 – 7.41)	0.985
$PaCO_2$ (mmHg)$^{\#}$	46 (36.9 – 52.4)	43.9 (37.7 – 53)	0.783
HCO_3 (mmol/L)$^{\#}$	21.7 (18.4 – 27.5)	20 (18 – 25.9)	0.405
Base excess (mmol/L)$^{\#}$	-3 (-6.3 – 2.1)	-3 (-6.8 – 4.1)	0.818
Lactate (mmol/L)$^{\#}$	2.1 (1.5 – 2.9)	2.3 (1.7 – 3.1)	0.122
Any TIAE	30 (40)	36 (48)	0.324
Non-severe TIAE	28 (37.3)	32 (42.7)	0.505
Esophageal intubation, n (%)	25 (33.3)	24 (32)	0.862
Vomiting without aspiration, n (%)	2 (2.7)	5 (6.7)	0.442
Gum or oral trauma, n (%)	12 (16)	14 (18.7)	0.666

	NIPPV Group	Standart-Care Group	p
Pain or agitation delaying intubation, n (%)	10 (13.3)	12 (16)	0.644
Hypertension, n (%)	1 (1.3)	2 (2.7)	>0.99
Dysrhythmia (<60/bpm), n (%)	0	2 (2.7)	0.497
Severe TIAE	3 (4)	7 (9.3)	0.190
CPR requires adrenalin (within 1 h), n (%)	0	1 (1.3)	>0.99
Pneumothorax (within 72 h), n (%)	2 (2.7)	1 (1.3)	>0.99
Mortality (within 72 h), n (%)	1 (1.3)	6 (8)	0.116
Vomiting with aspiration, n (%)	0	1 (1.3)	>0.99

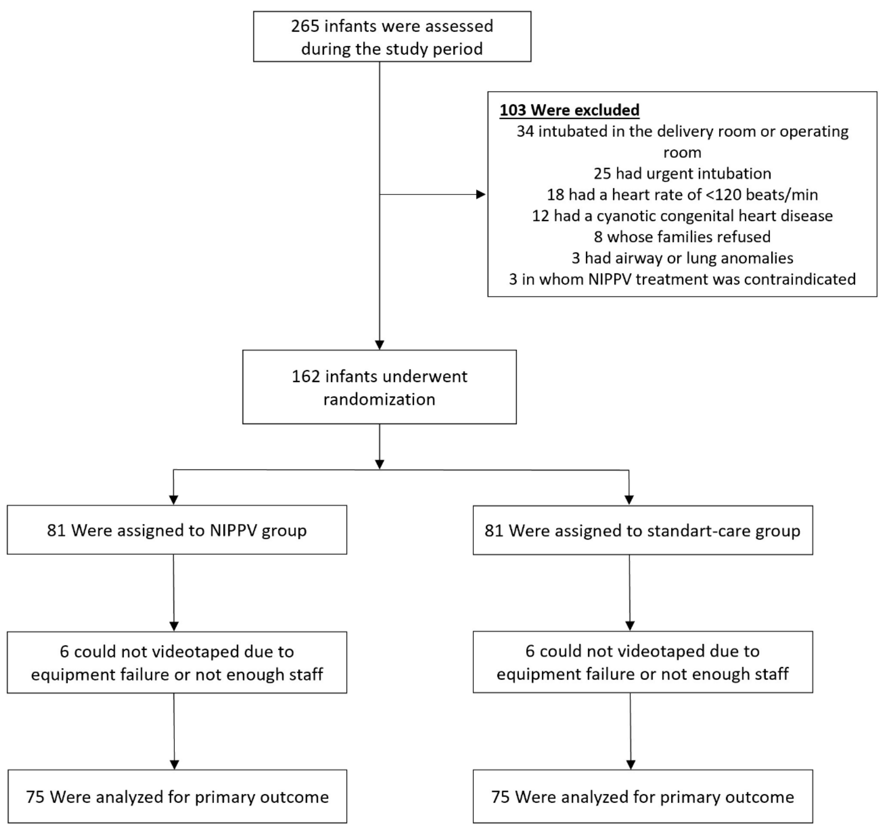
Data are presented as *mean ± standard deviation,#median (interquartile range) or number (%)

BE, base excess, CPR, cardiopulmonary resuscitation; HCO_3, bicarbonate, $PaCO_2$, partial pressure of carbon dioxide; SpO_2, peripheral oxygen saturation, TIAE, tracheal intubation associated event.

FIGURE LEGENDS

Figure 1. Flow diagram of recruitment

NIPPV, nasal intermittent positive pressure ventilation.



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