Transcutaneous electromyography of the diaphragm

Monitoring breathing and the effect of respiratory support in preterm infants

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Chapter 7

Patient-ventilator asynchrony in preterm infants on nasal intermittent positive pressure ventilation

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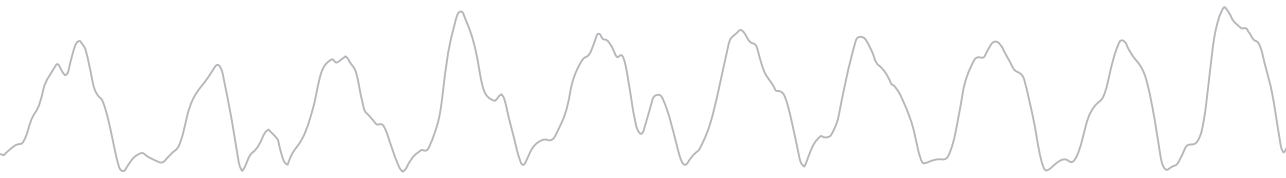

Abstract

Objective

To describe the incidence of patient-ventilator asynchrony and different types of asynchrony in preterm infants treated with non-synchronized nasal intermittent positive pressure ventilation (nIPPV).

Design

An observational study was conducted including preterm infants born with a gestational age (GA) less than 32 weeks treated with non-synchronized nIPPV. During one hour, spontaneous breathing was measured with transcutaneous electromyography of the diaphragm (dEMG) simultaneous with ventilator inflations. An asynchrony index (AI), a percentage of asynchronous breaths, was calculated and the incidence of different types of inspiratory and expiratory asynchrony were reported.

Results

Twenty-one preterm infants with a mean GA of 26.0 ± 1.2 weeks were included in the study. The mean inspiratory AI was 68.3 ± 4.7% and the mean expiratory AI was 67.1 ± 7.3%. Out of 5044 comparisons of spontaneous inspirations and mechanical inflations, 45.3% of the mechanical inflations occurred late, 23.3% of the mechanical inflations were early and 31.4% of the mechanical inflation were synchronous. 40.3% of 5127 expiratory comparisons showed an early termination of ventilator inflations, 26.7% of the mechanical inflations terminated late and 33.0% mechanical inflations terminated in synchrony with a spontaneous expiration. In addition, 1380 spontaneous breaths were unsupported and 611 extra mechanical inflations were delivered.

Conclusion

Non-synchronized nIPPV results in high patient-ventilator asynchrony in preterm infants during both the inspiratory and expiratory phase of the breathing cycle. New synchronization techniques are urgently needed and should address both inspiratory and expiratory asynchrony.

Introduction

Nasal intermittent positive pressure ventilation (nIPPV) is an advanced mode of non-invasive respiratory support to treat preterm infants with apnea of prematurity (AOP) and imminent respiratory failure. Similar to invasive mechanical ventilation, nIPPV provides a positive end-expiratory pressure (PEEP) as well as a peak inflation pressure (PIP). Studies have shown that nIPPV reduces the need for invasive mechanical ventilation in preterm infants, especially if mechanical inflations are synchronized to the infant's spontaneous breathing effort.[1–4]

Synchronization of nIPPV remains a clinical challenge in preterm infants, partly because the few available devices for synchronization are not approved for clinical practice. For this reason non-synchronized nIPPV is mainly used in daily clinical care.[5] Non-synchronized nIPPV can lead to patient-ventilator asynchrony during which spontaneous breathing efforts of the infants are not adequately supported by ventilator inflations. Asynchrony can affect both the start of inspiration and the start of expiration during a spontaneous breathing cycle. The timing of the mechanical inflation may be too early or too late in relation to the onset of spontaneous inspiration or even completely absent. In addition, the duration of mechanical support may be too short or too long based on the spontaneous onset of expiration.[6,7] All of these will result in suboptimal support of the infant's respiration.

Although it is assumed that patient-ventilator asynchrony is present during non-synchronized nIPPV, data on the magnitude of patient-ventilator asynchrony and the incidence of different types of inspiratory and expiratory asynchrony in preterm infants are not available. Therefore, the aim of this study is to describe the incidence of patient-ventilator asynchrony and different types of asynchrony in preterm infants treated with non-synchronized nIPPV.

Methods

We conducted an observational study in the neonatal intensive care unit of the Academic Medical Center Amsterdam, the Netherlands. We included preterm infants born with a gestational age (GA) less than 32 weeks and treated with non-synchronized nIPPV. Infants with major congenital anomalies were excluded. Written informed consent was obtained from both parents. The study was approved by the institutional medical ethics committee.

Study protocol

The infants received nIPPV through a nasal mask or short nasal prongs (Fisher & Paykel Healthcare Ltd, Auckland, New Zealand) connected to an AVEA® ventilator (Vyaire,

Mettawa, IL, USA). PIP, PEEP, frequency and inspiratory time were set by the attending physician. Spontaneous breathing and ventilator inflations were continuously and simultaneously recorded for one hour. During this period ventilator settings were not changed.

Spontaneous breathing was measured with transcutaneous electromyography of the diaphragm (dEMG). Two skin electrodes (disposable Kendall H59P Electrodes; Covidien, Mansfield, Massachusetts, USA) were placed in the left and right midclavicular line at the costo-abdominal margin and one reference electrode was placed at sternal level. The electrodes were connected to a portable 16-channel physiological amplifier (Dipha-16, Demcon, Enschede, The Netherlands) which wirelessly transmitted the measured data to a bedside personal computer running the software package Polybench (Applied Biosignals, Weener, Germany). The raw electro-physiological signals were digitally transformed into a bipolar EMG signal and the electrical activity of the heart was removed using the gating technique.[8] The averaged dEMG signal was used for all analyses. Additional details on filtering and processing of the dEMG signal are provided elsewhere.[8,9]

Pressure (cmH_2O) and flow (L/min), as delivered by the ventilator, were measured in the patient circuit by a disposable AVEA™ ventilator VarFlex flow transducer connected to a modified Bicore-II (Vyaire, Mettawa, IL, USA). The Bicore-II derived signals were recorded simultaneously and in synchrony with the dEMG signal on the bedside personal computer. The ventilator pressure signal was used for detection of the ventilator inflations.

The following patient characteristics were documented: GA at birth, birth weight (BW), gender, antenatal treatment with glucocorticosteroids, prior intubation and invasive mechanical ventilation, surfactant therapy in the first 72 hours after birth, the age and weight at inclusion and the duration of nIPPV treatment. During the measurement, changes in clinical condition, fraction of inspired oxygen (FiO_2) and apneic events were documented.

Data processing and analysis

All signals were transported to MATLAB (version 2016a, MathWorks, Natick, MA, USA) for data analysis in a custom-made graphical user interface. The one hour measurement of each infant was divided in six blocks of ten minutes. In each block, the last minute of stable (i.e. no movement or measurement artifacts) dEMG and ventilator pressure recordings were selected for analysis. Inspiration and expiration were detected automatically in both signals. In the averaged dEMG signal, the start of the inspiration was defined as the lowest point just before a rise of the signal. The start of the dEMG expiration was defined as 30% decrease in peak activity, based on the work of Sinderby

et al[7]. The start of the inflation in the ventilator pressure signal was defined as the tipping point before the build-up of inspiratory pressure. The termination of an inflation (i.e. start of mechanical expiration) was defined as the turning point after the peak pressure when the pressure starts to fall.

The (a)synchrony of the start and termination of the inflation of the ventilator with the spontaneous dEMG-based inspiration and expiration was determined in four steps. First, the breathing cycles in the dEMG signal were divided in percentages defined windows.[7] To determine inspiratory asynchrony, the time window between the previous start of expiration and the inspiration was marked -100 to 0%, and the time window between start of inspiration and the next expiration was marked 0 to +100%. The same applies for the expiratory asynchrony calculation with the window boundaries being determined by the previous inspiration (-100 to 0%) and the next inspiration (0 to +100%). These time windows are illustrated in Figure 1.

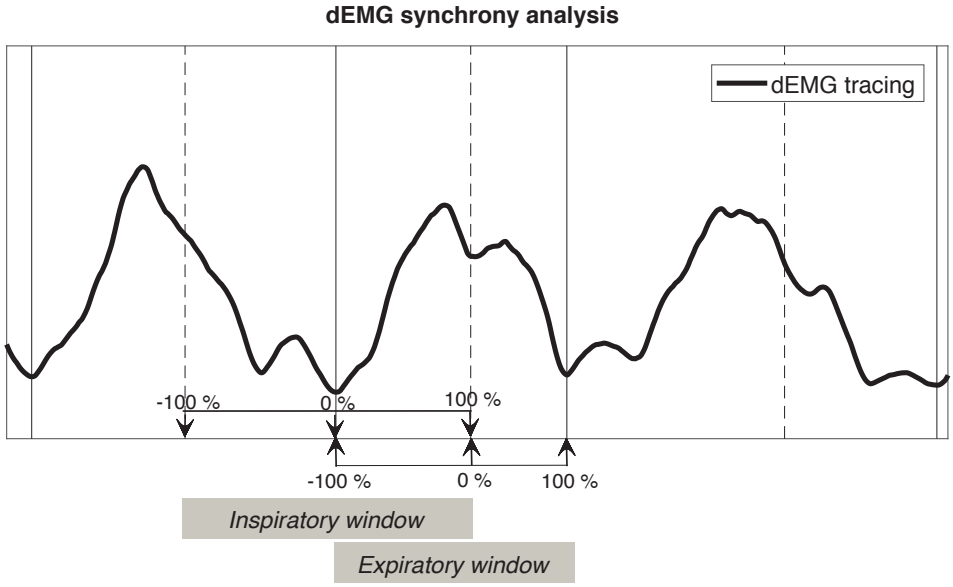

Figure 1. Three dEMG breathing cycles are displayed. Solid vertical lines indicate the start of each inspiration and interrupted vertical lines indicate the start of each expiration (30% after peak activity). Both the inspiratory and expiratory window are shown ranging from -100 to +100%. dEMG, transcutaneous electromyography of the diaphragm.

Second, a comparison was made between the timing of each ventilator inflation relative to the inspiration in the dEMG signal, provided with a percentage deviation ranging from -100% up to +100%. An inflation outside the time window of -33 to +33% of the onset of a spontaneous dEMG inspiration was considered asynchronous while

the inflations within this window were classified as synchronous.[7] In case more than one mechanical inflation was present in a single dEMG inspiratory window, a comparison was made for each mechanical inflation within that window. The same analysis was done for each termination of a ventilator inflation compared to the start of expiration in the dEMG signal.

Third, the scored asynchrony percentages were subdivided in different types, as illustrated in Figure 2: (1) early mechanical inflation: the timing of the mechanical inflation is >33% before the spontaneous inspiration; (2) late mechanical inflation: the timing of the mechanical inflation is >33% after the spontaneous inspiration; (3) early termination of the mechanical inflation: the timing of the mechanical inflation's termination is >33% before the spontaneous expiration and (4) late termination of the mechanical inflation: the timing of the mechanical inflation's termination is >33% after the spontaneous expiration.[6] The sum of (1) and (2) were considered asynchronous inspirations and the sum of (3) and (4) were asynchronous expirations.

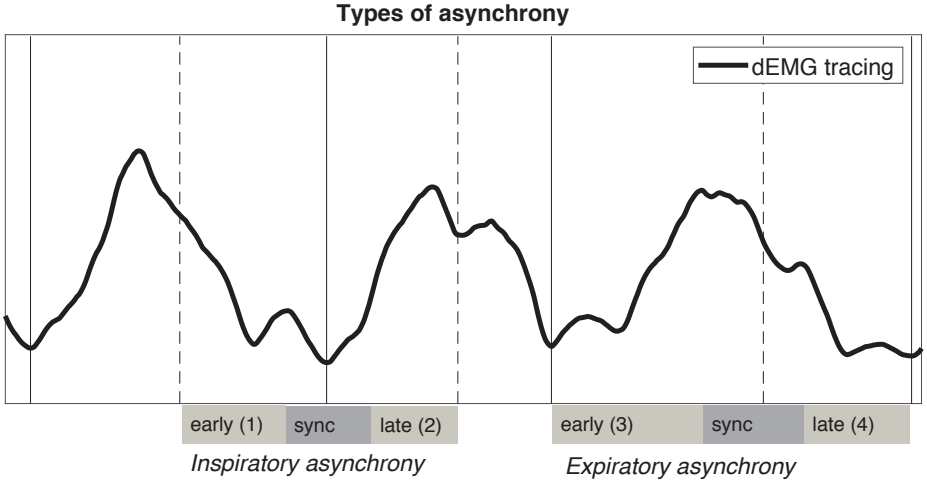

Figure 2. A schematic view of time-windows determining the different types of both inspiratory and expiratory asynchrony. dEMG, transcutaneous electromyography of the diaphragm.

Finally, based on the scoring of each mechanical inflation an inspiratory asynchrony index (AI) and expiratory AI was calculated as *(asynchronous inspirations/total inspirations)*100%* and *(asynchronous expirations/total expirations)*100%,* respectively, per selected 60 seconds recording. The total number of comparisons between dEMG inspirations or expirations and ventilator inflations was used as the denominator.

In addition, two situations can occur in which either spontaneous breathing or mechanical inflations are not detected in the dEMG or ventilator pressure signal respectively, and thus no comparison could be made. First, spontaneous breaths

based on the dEMG signal can occur with no mechanical inflation present; these were classified as unsupported breaths. Second, ventilator inflations can be present without spontaneous breathing efforts in the dEMG signal; these inflations were classified as extra mechanical inflations. The incidence of both unsupported breaths and extra mechanical inflations were reported separately.

Statistical analysis

SPSS Statistics version 24 (IBM, Armonk, NY, USA) was used for statistical analysis. Depending on their distribution, data were expressed as mean ± standard deviation (SD) or median (interquartile range (IQR)). Quantitative data were expressed as number (n) and percentage (%) of total.

For each patient, two AI's were calculated, one for the inspiration and one for the expiration based on the six selections of 60 seconds recordings for each patient. Frequencies of each type of asynchrony, unsupported breaths and extra mechanical inflations were calculated.

Results

Study population

Twenty-one preterm infants with a mean GA of 26.0 ± 1.2 weeks and mean BW of 905 ± 193 gram were included and completed the one hour measurement. The characteristics of the study population are described in Table 1. The median postnatal age at data collection was 15 (IQR 10 – 23) days and the indication for nIPPV treatment was frequent apnea due to AOP (n=16) or (suspected) infection (n=5). All infants were treated with caffeine. The ventilator settings are displayed in Table 2.

Table 1. Baseline characteristics of the study population

	n = 21
Gestational age at birth (weeks)	26.0 ± 1.2
Birth weight (gram)	905 ± 193
Male, n (%)	12 (57%)
Complete course of antenatal steroids, n(%)	12 (57%)
Surfactant treatment, n (%)	16 (76%)
Invasive mechanical ventilation, n (%)	12 (57%)
Duration of invasive mechanical ventilation (days)	3 (1 - 7)
Duration of nIPPV treatment (days)	12 (4 - 19)
Postmenstrual age at measurement (weeks)	28.3 ± 1.2
Weight at measurement (gram)	959 ± 192

Mean ± SD or median (IQR). nIPPV, nasal intermittent positive pressure ventilation

Table 2. Asynchrony indexes per infant

Patient number	Gestational age (weeks)	Birth weight (gram)	Respiratory rate (breaths/min)	nIPPV settings				Inspiratory AI (%)	Expiratory AI (%)
				PIP (cmH_2O)	PEEP (cmH_2O)	Frequency (/min)	Inspiratory time (s)		
1	27,1	1100	44	16	7	40	0,50	67,8	56,2
2	25,3	870	52	15	6	50	0,35	69,4	69,7
3	26,1	865	66	19	7	40	0,35	67,2	71,5
4	27,6	1165	57	15	5	50	0,50	73,8	70,2
5	28,9	1150	37	14	5	50	0,35	72,0	71,5
6	26,3	1195	58	15	6	50	0,35	69,8	57,9
7	25,4	885	58	15	6	40	0,50	62,8	70,1
8	25,3	870	46	15	6	60	0,35	57,9	65,0
9	25,7	935	75	18	6	40	0,35	69,7	57,1
10	25,1	970	77	19	7	60	0,50	64,7	60,6
11	26,6	670	81	16	7	60	0,35	69,4	85,9
12	27,0	1140	41	15	6	60	0,35	65,4	65,0
13	25,9	925	50	15	6	60	0,35	66,1	65,3
14	25,0	840	63	15	6	60	0,35	76,1	65,6
15	24,7	630	62	17	7	60	0,35	79,2	73,2
16	24,7	510	41	17	7	50	0,35	62,3	72,8
17	25,1	760	47	15	6	40	0,50	65,6	75,1
18	24,9	935	47	19	7	60	0,35	68,6	57,4
19	27,7	1100	48	16	7	40	0,35	66,9	61,0
20	24,7	625	56	15	7	60	0,50	69,7	72,8
21	26,9	875	54	15	7	50	0,35	71,0	65,3
Total[a]	26.0 ± 1.2	905 ± 193	55 ± 12.1	15 (15 - 17)	6 (6 - 7)	50 (40 - 60)	0.35 (0.35 - 0.50)	68.3 ± 4.7	67.1 ± 7.3

[a]Total expressed as mean ± SD or median (IQR). nIPPV, nasal intermittent positive pressure ventilation; PIP, peak inflation pressure; PEEP, positive end-expiratory pressure; AI, asynchrony index

Patient-ventilator asynchrony

The mean inspiratory AI was 68.3 ± 4.7% and the mean expiratory AI was 67.1 ± 7.3% for all infants (Table 2).

To calculate the inspiratory asynchrony, 4840 spontaneous inspirations were analyzed leading to 5044 comparisons due to 204 multiple mechanical inflations within a dEMG-based inspiratory window. Of the analyzed inspiratory comparisons, 1174 (23.3%) mechanical inflations were early, 2288 (45.3%) mechanical inflations were late and 1582 (31.4%) mechanical inflations were synchronous compared to spontaneous inspirations.

The expiratory asynchrony was based on 4893 analyzed spontaneous expirations accounting for 5127 comparisons due to 234 multiple mechanical inflations analyzed within a dEMG expiratory time window. 2062 (40.3%) comparisons were classified as an early termination of the mechanical inflation and 1371 (26.7%) mechanical inflations terminated late compared to the dEMG expiration. In total, 1694 (33.0%) mechanical inflations terminated in synchrony with a spontaneous expiration.

Besides the asynchronous and synchronous inflations, 1380 spontaneous breaths were unsupported and 611 extra mechanical inflations were delivered.

Discussion

In this observational study the incidence of patient-ventilator asynchrony in preterm infants treated with non-synchronized nIPPV was high during both inspiration and expiration.

To our knowledge, this is the first study that systematically describes the incidence and classification of patient-ventilator asynchrony in preterm infants treated with non-synchronized nIPPV. The high AI found shows that patient-ventilator asynchrony is common as can be expected because the ventilator inflations are delivered with a fixed frequency and inspiratory time, independent of the infant's own breathing efforts.

Two previous studies, primarily designed to assess the effect of synchronization during nIPPV on work of breathing and gas exchange, also reported on the rate of synchrony defined as the delivery of a ventilator inflation within the first half of a spontaneous inspiration measured with the Graseby capsule. The inspiratory synchrony in these studies varied between 23 to 26%, which is slightly lower than in the present study. The definition of synchrony and the method used for measuring spontaneous breathing effort may explain this difference. Both studies did not provide more details on inspiratory asynchrony nor did they report on expiratory asynchrony.[10,11]

Besides asynchronous breaths, unsupported breaths and extra mechanical inflations were quite common as well. Unsupported breaths can be explained by the irregular breathing of preterm infants with fluctuating respiratory rates in relation to the set

frequency of the ventilator.[12,13] The rate used in this study during nIPPV is relatively high. Using a lower ventilator rate will probably result in a higher rate of unsupported breaths. The extra mechanical inflations delivered during apneic episodes may have clinical relevance. Some studies have shown that non-synchronized nIPPV is superior to nasal continuous positive airway pressure (nCPAP) in preventing hypoxic events and reducing the need for invasive mechanical ventilation.[3,14,15] Although speculative, the extra mechanical inflations during apneic events may, in part, contribute to this reported benefit. It is clear that these extra mechanical inflations will only result in effective tidal ventilation if the glottis is open, a condition that may not always be present in apneic preterm infants.[16] Another explanation for the beneficial effect of non-synchronized nIPPV on reducing the need for mechanical ventilation might be the higher mean airway pressure provided during this mode of respiratory support compared to nCPAP.

Clinical implications

In preterm infants, the consequences of patient-ventilator asynchrony during nIPPV are not investigated, however asynchrony may have adverse effects and may lead to less effective support of breathing when compared with synchronized non-invasive ventilation.[4,17]

The high rate of asynchrony found in this study and its potential adverse effects underline the need for synchronization of nIPPV with spontaneous breathing. However, synchronization in premature infants is a challenge because of high respiratory rates and irregular breathing. Different techniques have been investigated to achieve synchronization.[18] First, the Graseby capsule, a pneumatic sensor placed on the abdominal wall, has been used to synchronize non-invasive ventilation in preterm infants.[10,16,19] The accuracy of the Graseby capsule is questioned and triggering of the ventilator based on this technique is relatively slow.[19,20] Furthermore, the Graseby capsule can only be used to synchronize inspiration and does not improve expiratory synchrony. Second, flow triggering for non-invasive ventilation has been described.[21,22] The major limitations of this technique are the instability of the signal and disturbances due to leak of airflow.[18] Third, triggering of nIPPV based on the neural breathing effort of preterm infants can be achieved with non-invasive neurally adjusted ventilatory assist (NIV-NAVA).[23,24] This technique is based on transesophageally measured electrical activity of the diaphragm, which enables synchronization of nIPPV during both inspiration and expiration. However, this technique is relatively invasive, expensive and only available on systems of one specific ventilator distributor. Transcutaneous dEMG might be an alternative candidate to trigger both inspiration and expiration during nIPPV. Breath detection with this technique is appropriate and it detects spontaneous breathing effort early during the breathing cycle.[20] Further research is needed to investigate the clinical application of this technique and other possible new synchronization methods.

While awaiting developments on synchronized nIPPV, non-synchronized nIPPV remains a widely used mode of respiratory support in daily clinical practice. Clinicians need to be aware of the high rate of asynchrony. Theoretically, some of this patient-ventilator asynchrony during non-synchronized nIPPV might be reduced by adjusting the ventilator settings to the spontaneous breathing effort of the individual infant. For instance, matching the ventilator rate to the spontaneous respiratory rate or adjusting the inspiration time, may result in less inspiratory and expiratory asynchrony. However, these theoretical advantages need to be tested in future studies.

Limitations

Several assumptions have been made during data analysis that have to be taken into account when interpreting the results of this study. The cut-off values for asynchrony used in this study, based on work of Sinderby et al[7], are arbitrary and altering them will change the AI. Furthermore, the definition of the start of expiration was based on unpublished observations in an adult population and is not validated in preterm infants.[7] Therefore, further research is needed to find the most accurate cut-off points for the start of inspiration and expiration in the dEMG signal of preterm infants.

Conclusion

In conclusion, non-synchronized nIPPV results in high patient-ventilator asynchrony in preterm infants during both the inspiratory and expiratory phase of the breathing cycle. Further research is needed to investigate possible adverse effects of patient-ventilator asynchrony during nIPPV and to develop new synchronization techniques for nIPPV.

What is already known about this topic

- Nasal intermittent positive pressure ventilation (nIPPV) is an advanced mode of non-invasive respiratory support to treat preterm infants.
- nIPPV reduces the need for invasive mechanical ventilation especially when mechanical inflations are synchronized to the infant's spontaneous breathing effort.
- Synchronization of nIPPV remains a clinical challenge in preterm infants and therefore non-synchronized nIPPV is mainly used in daily clinical care.

What this study adds

- The incidence of patient-ventilator asynchrony is high in preterm infants treated with non-synchronized nIPPV.
- Patient-ventilator asynchrony occurs frequently during both the inspiratory and the expiratory phase of the breathing cycle.
- New synchronization methods need to be developed that address both inspiratory and expiratory asynchrony.

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