Transcutaneous electromyography of the diaphragm

Monitoring breathing and the effect of respiratory support in preterm infants

de Waal, C.G.

Publication date
2018

Document Version
Other version

License
Other

Chapter 5

Diaphragmatic activity during weaning from respiratory support in preterm infants

J.V. Kraaijenga
C.G. de Waal
G.J. Hutten
F.H. de Jongh
A.H. van Kaam

Archives of Diseases in Childhood – Fetal and Neonatal Edition
2017 Jul;102(4):F307-F311

Abstract

Objective

To determine if weaning from nasal continuous positive airway pressure (nCPAP) to lesser supportive low flow nasal cannula (LFNC) results in a change in electrical activity of the diaphragm in preterm infants.

Design

Prospective observational study.

Setting

Neonatal intensive care unit.

Patients

Stable preterm infants weaned from nCPAP to LFNC (1 L/min).

Main outcome measures

Change in diaphragmatic activity, expressed as amplitude, peak, and tonic activity, measured by transcutaneous electromyography (dEMG) from 30 minutes before (baseline) until 180 minutes after weaning. Subgroup analysis was performed based on success or failure of the weaning attempt.

Results

Fifty-nine preterm infants (gestational age: 29.0 ± 2.4 weeks, birth weight: 1,210 ± 443 g) accounting for 74 weaning attempts were included. A significant increase in dEMG amplitude (median, IQR: 21.3%, 3.6 – 41.4), peak (22.1%, 8.7 – 40.5) and tonic activity (14.3%, -1.9 – 38.1) was seen directly after weaning. This effect slowly decreased over time. Infants failing the weaning attempt tended to have a higher diaphragmatic activity than those successfully weaned.

Conclusion

Weaning from nCPAP to LFNC leads to an increase in diaphragmatic activity measured by dEMG and is most prominent in preterm infants failing the weaning attempt. dEMG monitoring might be a useful parameter to guide weaning from respiratory support in preterm infants.

Introduction

Respiratory failure is a common complication of preterm birth and is primarily caused by impaired control of breathing (apnea of prematurity) or a compromised lung function.[1] As a result, work of breathing (WOB) is often increased and gas exchange impaired.[1] In an attempt to restore lung function and reduce WOB, preterm infants often receive respiratory support with nasal continuous positive airway pressure (nCPAP) and/or low flow nasal cannula (LFNC) as the most frequently used modes.[2,3]

Despite the frequent use of nCPAP and LFNC, objective criteria to start and guide weaning from non-invasive respiratory support are not well established. Most clinicians use a 'trial and error' strategy during weaning.[3,4] If the infant looks clinically stable, respiratory support is weaned and the response of the infant is monitored. If the clinical condition remains stable during the next few days, the weaning attempt is considered successful. If the condition deteriorates, the weaning attempt failed and the level of support is increased. It is clear that such a 'trial and error' strategy may cause both overtreatment and undertreatment. For this reason more objective weaning parameters are urgently needed.

A possible candidate for guiding weaning of respiratory support in preterm infants is the electrical activity of the diaphragm measured by electromyography (dEMG). dEMG can be measured either invasively using an electrode equipped gastric feeding tube or non-invasively via surface electrodes.[5,6] Previous studies have suggested that changes in WOB are correlated with diaphragmatic electrical activity.[7,8] Recent studies have shown that transcutaneous dEMG measurement is feasible in preterm infants and that it can detect changes in diaphragmatic activity after stimulation with caffeine.[9,10] However, it is unknown if these changes can also be detected during weaning of respiratory support. This information is essential before the role of dEMG in guiding weaning of respiratory support can be further explored.

Therefore, the aim of this study was to determine whether weaning from nCPAP to the lesser supportive LFNC resulted in a change in diaphragmatic activity measured by transcutaneous dEMG in preterm infants. We hypothesized that diaphragmatic activity would increase after weaning from nCPAP to LFNC.

Methods

This prospective observational cohort study was conducted in the level 3 neonatal intensive care unit of the Emma Children's Hospital, Academic Medical Center Amsterdam, the Netherlands. We included clinically stable preterm infants with a gestational age < 36 weeks who were, according to our protocol, successfully weaned to a nCPAP level of 3 cmH_2O and deemed ready by the attending physician to be transitioned to LFNC (1 L/

min). At the time of this study high flow nasal cannula was not yet implemented in daily clinical practice.

Patients with congenital anomalies were excluded from the study. Written informed consent was obtained from both parents and the institutional review board approved the study protocol.

Transcutaneous dEMG was used to continuously measure the electrical activity of the diaphragm from 30 minutes before (baseline) to 180 minutes after weaning the infant from nCPAP to LFNC. During the study period no nursing procedures, except feeding, were conducted.

After weaning from nCPAP to LFNC, patients were followed up for 48 hours. If infants needed to be transferred back to nCPAP within this time period, the attempt was categorized as 'failed' and the reason for failure was recorded. In case infants remained on LFNC for more than 48 hours the attempt was categorized as 'success'.[11] In case of failure, infants could be included at a subsequent weaning attempt. The decision to be transferred back to nCPAP was made by the attending physician and usually based on a significant increase in fraction of inspired oxygen (FiO_2) (> 0.40), and/or more than one (stimulated) cardiopulmonary event per hour, and/or a significant increase in respiratory distress. The medical staff was blinded for the dEMG signals.

We measured transcutaneous dEMG using a portable 16-channel digital physiological amplifier (Dipha-16, Inbiolab BV, Groningen, Netherlands) at the bedside. On the chest we placed three surface electrodes (H59P Cloth Electrodes, Kendall); two electrodes at the costoabdominal margin in the left and right nipple line, and one electrode at the height of the sternum.[9] Without analogue filtering dEMG data were digitized and sent wirelessly to the front end of the Dipha-16 system connected to a personal computer. One raw dEMG waveform combining the left and right diaphragmatic sides was digitally preprocessed and band-pass filtered from 40 Hz to 160 Hz. The gating technique described by O'Brien et al. was used to remove the electrical activity of the heart from the signal.[6] This gating technique involves removal of sections of the dEMG signal centred on the QRS complex, leaving a gated dEMG that was filled with a running average and used for further analysis. More details on sampling rate, filtering algorithm, preprocessing and postprocessing and other technical aspects of the dEMG measurement have been described elsewhere.[6,12] dEMG analysis was performed off-line by the data acquisition and processing software package Polybench (Applied Biosignals, Weener, Germany).

Stable 30-second recordings were selected at fixed time points: just before the wean step on nCPAP (t=-5 min; baseline) and at eight time points on LFNC (t=5, 15, 30, 60, 90, 120, 150 and 180 min). Stable recording was defined as no (movement) artefacts in the dEMG signal. The outcome variables were calculated automatically in Polybench by using the average of all single breaths in the 30-second recording, which contained approximately 30 breathing cycles.[13] In case nursing procedures were needed during the 3-hour measurement or the infant failed on LFNC and was transferred back to nCPAP, only recordings measured before these events were used for data analysis.

From the averaged dEMG signal, we determined the amplitude, expressed in micro voltage (μV), by calculating the difference between the highest ($peak_{dEMG}$) and lowest ($tonic_{dEMG}$) electrical activity within each breathing cycle. The average amplitude of the dEMG signal at each analysis time point after weaning was expressed as the percentage change compared with baseline (% Δ $amplitude_{dEMG}$). Similarly, we calculated the percentage change of the $peak_{dEMG}$ (% Δ $peak_{dEMG}$) and $tonic_{dEMG}$ (% Δ $tonic_{dEMG}$) activity. Next, we derived the following time indices from the averaged dEMG signal: 1) inspiratory time (Ti_{dEMG}), defined as the time from the lowest activity of the diaphragm to the next maximum; and 2) expiratory time (Te_{dEMG}) defined as the time from the maximum to the following lowest diaphragmatic activity.[10,14] The respiratory rate was calculated out of Ti_{dEMG} and Te_{dEMG}. Heart rate was extracted from the ungated dEMG signal.

In addition to the dEMG data, we collected the following patient characteristics: gestational age, birth weight, gender, antenatal steroids, Apgar scores and respiratory history previous to the weaning attempt. At the day of weaning we collected information on postnatal age, weight, mode and settings of respiratory support and the number of cardio-pulmonary events (i.e. bradycardia, desaturation and apnea) 24 hours before and after the weaning attempt.

Statistical analysis

Statistical analysis was performed using SPSS version 22.0 (SPSS, Chicago, Illinois, USA) and Graphpad Prism 5.0 (GraphPad Software, San Diego, California, USA). Data were expressed as mean ± SD or median with IQR. Changes in outcome parameters over time compared with baseline were analyzed with the repeated measurements analysis of variance with post hoc Bonferroni test or repeated measurement Friedman test with post hoc Dunn's test. For comparative analyses between the success and failure groups we used the independent Student's t-test or Mann-Whitney U test. Analyses were done for all recorded weaning attempts and for first attempts only. A p value < 0.05 was considered statistically significant.

Results

Study population

A convenience sample of 61 infants was included in the study of whom two infants were excluded because of a protocol violation (n=1) and technical failure of the equipment (n=1). This left 59 infants accounting for 74 weaning attempts for the final analyses. All infants tolerated the dEMG electrode placement well and no adverse effects were reported. Table 1 shows the characteristics of the study population at the first weaning attempt.

Fifteen (25.4%) infants needed mechanical ventilation after birth with a median duration of 3 (IQR 1 - 4) days. The median nCPAP level before weaning to LFNC was 3 (IQR 3 - 3) cmH_2O with a FiO_2 of 0.21 (IQR 0.21 - 0.21).

Analyses based on the first weaning attempts or all weaning attempts revealed no major differences and for this reason only the latter are presented.

Table 1. Baseline characteristics on first weaning attempts

	n = 59
Gestational age at birth (weeks)	29.0 ± 2.4
Birth weight (gram)	1210 ± 443
Male	37 (62.7%)
Antenatal steroids (number)	49 (83%)
Apgar score at 5 min	8 (7–9)
Postmenstrual age at measurement (weeks)	31.3 ± 1.6
Postnatal age (days)	9 (6–21)
Weight at measurement (gram)	1418 ± 442
Days on nCPAP prior to measurement (number)	9 (6–21)
Cardiopulmonary events in 24 hours prior to measurement (number)	7 (1–18)

Data are expressed as mean ± SD, median (IQR) or number (%). nCPAP, nasal continuous positive airway pressure.

All weaning attempts

Measured dEMG data were available for all 59 infants in the first 30 minutes after transition from nCPAP to LFNC. Due to failure of the weaning attempt (n=8), technical failure (n=1) and necessary nursing procedures (n=10), data collection was stopped early in 19 infants. The data of these infants were included in the analysis up to the time the measurement was stopped.

Following the weaning step from nCPAP to LFNC, there was an immediate (t=5 min) significant increase in electrical activity of the diaphragm, expressed as $amplitude_{dEMG}$ change (median 21.3, IQR 3.6 – 41.4 %). This increase persisted during the first 2 hours after the transition (Figure 1).

The increase in electrical activity was also reflected in a change in the $peak_{dEMG}$ and to a lesser extent in the $tonic_{dEMG}$ activity (Table 2).

No clinically relevant changes in Ti_{dEMG}, Te_{dEMG}, respiratory rate and heart rate were found after weaning from nCPAP to LFNC (Table 2).

Table 2. Parameters at baseline and change over time after transition from nCPAP to LFNC, all attempts

	Baseline	**5 min**	**15 min**	**30 min**	**60 min**	**90 min**	**120 min**	**150 min**	**180 min**
	n=74	**n=74**	**n=74**	**n=73**	**n=73**	**n=70**	**n=68**	**n=66**	**n=55**
% Δ $Peak_{dEMG}$	0 (0 - 0)	22.1 (8.7 - 40.5)*	12.2 (-4.0 - 34.2*	8.8 (-9.3 - 23.2)	9.6 (-5.8 - 23.1)*	9.2 (-1.8 - 33.8)*	8.5 (-5.3 - 25.7)	5.7 (-8.7 - 28.4)	6.8 (-6.0 - 25.4)
% Δ $Tonic_{dEMG}$	0 (0 - 0)	14.3 (-1.9 - 38.1)*	8.5 (-8.2 - 32.9)*	8.1 (-14.1 - 27.9)	6.7 (-15.6 - 24.3)	4.0 (-12.4 - 29.6)	0.8 (-13.1 - 33.5)	6.9 (-14.8 - 33.8)	2.3 (-13.1 - 30.0)
Ti_{dEMG}	0.4 (0.4 - 0.5)	0.4 (0.4 - 0.5)	0.4 (0.4 - 0.5)	0.4 (0.4 - 0.5)	0.4 (0.4 - 0.5)	0.4 (0.4 - 0.5)	0.4 (0.4 - 0.5)	0.4 (0.4 - 0.5)	0.4 (0.4 - 0.5)
Te_{dEMG}	0.5 (0.4 - 0.6)	0.5 (0.4 - 0.6)	0.5 (0.4 - 0.6)	0.5 (0.4 - 0.6)	0.5 (0.4 - 0.6)	0.5 (0.4 - 0.6)	0.5 (0.4 - 0.6)	0.5 (0.4 - 0.5)	0.5 (0.4 - 0.5)
Respiratory rate (min^{-1})	66 ± 14	64 ± 13	66 ± 13	66 ± 14	65 ± 12	66 ± 12	66 ± 12	67 ± 12	67 ± 13
Heart rate (min^{-1})	150 ± 12	154 ± 12*	153 ± 11	152 ± 12	152 ± 12	150 ± 13	150 ± 13	149 ± 12	151 ± 11

Data are expressed as mean ± SD or median (IQR). *$p < 0.05$ at time point compared with baseline in repeated measurement analysis.
% Δ, percentage change compared with baseline; n, number of infants; $peak_{dEMG,}$ maximal electrical activity of dEMG; $tonic_{dEMG}$, minimal electrical activity of dEMG; Ti_{dEMG}, inspiratory time of dEMG; Te_{dEMG}, expiratory time of dEMG. dEMG, electrical activity of the diaphragm measured by electromyography; LFNC, low flow nasal cannula; nCPAP, nasal continuous positive airway pressure.

5

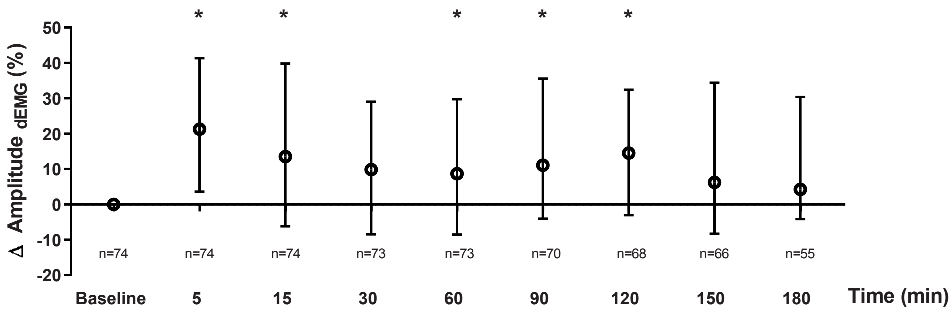

Figure 1. Percentage change of amplitude$_{dEMG}$ in the first 180 min after weaning from nasal continuous positive airway pressure (nCPAP) to low flow nasal cannula (LFNC) compared with baseline. Data are presented as median (IQR). *p < 0.05, repeated measurement Friedman test with post hoc Dunn's test. n, number of weaning attempts included in the analysis. dEMG, electrical activity of the diaphragm measured by electromyography.

Failed versus successful weaning attempts

Of the 74 weaning attempts, 15 failed and the main reasons were: increased oxygen need (n=8), increased rate of apnea of prematurity (n=5) and increased respiratory distress (n=2). Infants failing the first weaning attempt had a lower gestational age at birth compared with infants who were successfully weaned to LFNC (mean ± SD: 27.2 ± 1.6 vs 29.3 ± 2.4 weeks, p < 0.05). No differences in pulmonary condition were seen at baseline between both groups except for a higher number of apnea and bradycardia in the 24 hours before the first weaning attempt in infants failing the attempt (median 22 (IQR 9 - 36) vs 6 (IQR 1 - 16), p < 0.05).

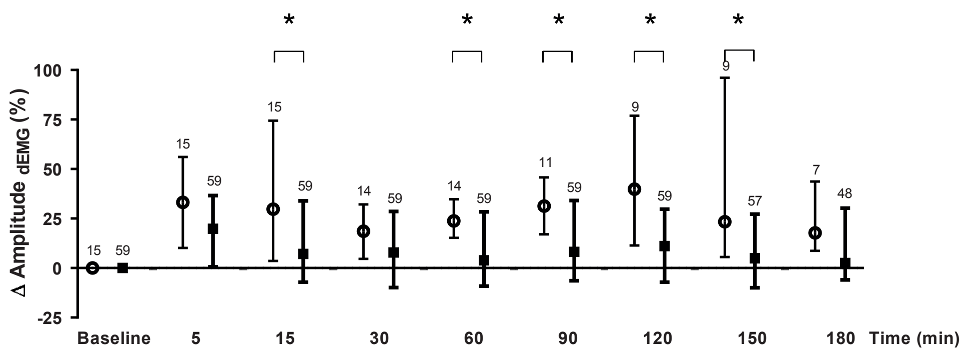

Figure 2. Percentage change of amplitude$_{dEMG}$ in the first 180 min after successful (filled squares) or failed weaning (open circles) from nasal continuous positive airway pressure (nCPAP) to low flow nasal cannula (LFNC) compared with baseline. Data are presented as median (IQR). *p < 0.05, compare group analysis at certain time point (Mann-Whitney U test). Numbers in the figure indicate the number of weaning attempts included in the analysis. dEMG, electrical activity of the diaphragm measured by electromyography.

The electrical activity of the diaphragm, expressed as amplitude$_{dEMG}$, was higher in the infants failing the weaning attempt from nCPAP to LFNC, although this difference did not reach statistical significance at all time points (Figure 2).

Discussion

This study shows for the first time, that diaphragmatic activity measured by transcutaneous dEMG increases when preterm infants are weaned from nCPAP to LFNC.

Although published data are limited, clinicians are often confronted with preterm infants failing weaning of respiratory support in daily clinical practice. In infants weaned from invasive mechanical ventilation to non-invasive support, a failure rate as high as 38% has been reported.[15,16] It illustrates that clinical assessment is a poor predictor of weaning success and that more objective parameters are needed.

There has been an increasing interest in using diaphragmatic activity in delivering respiratory support. Neurally adjusted ventilatory assist ventilation uses diaphragmatic activity, measured via an electrode equipped gastric feeding tube, to synchronize patient ventilator interaction and to deliver a proportional inflation pressure.[5,17] Recent studies have shown that the less invasive transcutaneous dEMG measurement is also feasible in preterm infants and that it provides accurate monitoring of respiratory rate and heart rate and can also detect (induced) changes in diaphragmatic activity.[9,10]

Previous studies have shown that changing the level or mode of non-invasive respiratory support will result in a significant change in WOB, which is correlated to diaphragmatic electrical activity.[7,8,18] We found a 10-20% increase in diaphragmatic activity, expressed as dEMG amplitude, which seems to substantiate that WOB increases after weaning from nCPAP to LFNC. Thereby, the present study shows that transcutaneous dEMG is able to detect changes in the electrical activity of the diaphragm during weaning of respiratory support.

It was interesting to observe that this increase in dEMG activity seemed to attenuate at the end of the measurement period. This may indicate that the respiratory system adapted to the new level of support. However, this attenuation over time may also be caused by the fact that weaning attempts that failed were no longer included in the analysis.

More detailed analysis showed that the higher electrical activity of the diaphragm was caused by an increase in peak diaphragmatic activity and (to a lesser extent) tonic activity. The latter may be indicative of a compromised end-expiratory lung volume after transitioning from nCPAP to LFNC. Indeed, studies have shown that nCPAP improves end-expiratory lung volume, even at low distending pressure.[19,20] Our study seems to support this finding, as transitioning infants from a relatively low nCPAP pressure (3 cmH_2O) to LFNC already results in an increase in diaphragmatic activity. The increase in tonic activity is consistent with previous reports suggesting that diaphragmatic contraction at the end of expiration is one of the endogenous mechanisms to maintain end-expiratory lung volume.[21,22]

Consistent with clinical practice a substantial number (20%) of the weaning attempts failed. Although not the primary focus of our study, explorative analysis revealed that infants failing weaning were significantly younger in terms of gestational age, which is consistent with previous studies.[11,15] More interestingly, the dEMG amplitude was significantly higher at most time points in the failure group compared with the success group. This might be considered a first and important indication that diaphragmatic activity measured by transcutaneous dEMG could play a role in guiding the weaning process. However, considering the fact that the group of weaning failure was relatively small, these findings need to be interpreted with caution. Future studies with sufficient sample size need to refute or confirm this finding.

In the final analysis we also included repeated weaning attempts in the same infant, because this reflects daily clinical practice. From a statistical perspective these repeated attempt are not truly independent observations. This is especially true when comparing patient characteristics and for this reason these data were analyzed based on first weaning attempts only. In addition, we also analyzed the effects of weaning on diaphragmatic activity using only the first weaning attempts, which did not change the major findings of our study.

This study has several limitations that need to be addressed. First, the number of infants that dropped out during the measurement period was relatively high which limited our power in the last hour of recording. Second, our study only assessed relatively stable infants on non-invasive support. The results may differ in infants with different pathology or modes of respiratory support.

In conclusion, this study shows that weaning from nCPAP to LFNC leads to an increase in diaphragmatic activity measured by transcutaneous dEMG. Furthermore, this increase is most prominent in infants failing the weaning attempt. These results indicate that measuring the electrical activity of the diaphragm is a potential candidate to optimize weaning of respiratory support in preterm infants and warrants future studies. These studies should monitor diaphragmatic activity in a large group of patients being weaned from different modes of respiratory support and assess its predictive value for weaning success and failure.

Acknowledgements

The authors thank Leo A. van Eykern for the technical assistance in this study.

What is already known on this topic

- There is a lack of objective parameters to guide weaning of respiratory support in preterm infants.
- Clinicians often use a 'trial and error' approach based on changes in clinical condition.
- Electrical activity of the diaphragm measured by transcutaneous electromyography is feasible in preterm infants and might be a candidate for guiding weaning.

What this study adds

- Weaning from nasal continuous positive airway pressure to low flow nasal cannula in preterm infants leads to an immediate increase in diaphragmatic activity.
- The higher diaphragmatic activity is caused by an increase in peak and, to a lesser extent, tonic activity.
- The increase in diaphragmatic activity seems to be most prominent in infants failing the weaning attempt.

References

1. Harris T, Wood B. Physiologic Principles. In: Goldsmith J, Karotkin E, editors. Assisted Ventilation of the Neonate. Third. Philadelphia, Pennsylvania: W.B. Saunders Company; 1996. p. 21–68.
2. Heiring C, Steensberg J, Bjerager M, Greisen G. A Randomized Trial of Low-Flow Oxygen versus Nasal Continuous Positive Airway Pressure in Preterm Infants. Neonatology. 2015;108(4):259–65.
3. Jardine L, Inglis G, Davies M. Strategies for the withdrawal of nasal continuous positive airway pressure (NCPAP) in preterm infants (Review). Cochrane Database Syst Rev. 2011;(2): CD006979.
4. Jardine L, Davies MW. Withdrawal of neonatal continuous positive airway pressure: Current practice in Australia. Pediatr Int. 2008;50(4):572–5.
5. Stein H, Firestone K, Rimensberger PC. Synchronized Mechanical Ventilation Using Electrical Activity of the Diaphragm in Neonates. Clin Perinatol. 2012;39(3):525–42.
6. O'Brien M, van Eykern L, Prechtl H. Monitoring respiratory activity in infants - a non-intrusive diaphragm EMG technique. Non-invasive physiological measurements. Londen: Academic Press Inc. 1983. p. 131–77.
7. Guslits BG, Gaston SE, Bryan MH, England SJ, Bryan AC. Diaphragmatic work of breathing in premature human infants. J Appl Physiol. 1987;62(4):1410–5.
8. Pham TMT, O'Malley L, Mayfield S, Martin S, Schibler A. The effect of high flow nasal cannula therapy on the work of breathing in infants with bronchiolitis. Pediatr Pulmonol. 2015;50(7):713–20.
9. Kraaijenga JV, Hutten GJ, de Jongh FH, van Kaam AH. Transcutaneous electromyography of the diaphragm: A cardio-respiratory monitor for preterm infants. PediatrPulmonol. 2014;50(9):889–95.
10. Kraaijenga JV, Hutten GJ, de Jongh FH, van Kaam AH. The Effect of Caffeine on Diaphragmatic Activity and Tidal Volume in Preterm Infants. J Pediatr. 2015;167(1):70–5.
11. Dimitriou G, Greenough A, Endo A, Cherian S, Rafferty GF. Prediction of extubation failure in preterm infants. Arch Dis Child Fetal Neonatal Ed. 2002 Jan;86(1):F32-5.
12. Maarsingh EJ, van Eykern LA, Sprikkelman AB, Hoekstra MO, van Aalderen WM. Respiratory muscle activity measured with a noninvasive EMG technique: technical aspects and reproducibility. J Appl Physiol. 2000;88(6):1955–61.
13. Bates JH, Schmalisch G, Filbrun D, Stocks J. Tidal breath analysis for infant pulmonary function testing. ERS/ATS Task Force on Standards for Infant Respiratory Function Testing. European Respiratory Society/American Thoracic Society. Eur Respir J. 2000 Dec;16(6):1180–92.
14. Hutten GJ, van Eykern LA, Latzin P, Kyburz M, van Aalderen WM, Frey U. Relative impact of respiratory muscle activity on tidal flow and end expiratory volume in healthy neonates. Pediatr Pulmonol. 2008;43(9):882–91.
15. Kavvadia V, Greenough A, Dimitriou G. Prediction of extubation failure in preterm neonates. Eur J Pediatr. 2000 Apr;159(4):227–31.
16. Stefanescu BM, Murphy WP, Hansell BJ, Fuloria M, Morgan TM, Aschner JL. A randomized, controlled trial comparing two different continuous positive airway pressure systems for the successful extubation of extremely low birth weight infants. Pediatrics. 2003 Nov;112(5):1031–8.

17. Stein H, Beck J, Dunn M. Non-invasive ventilation with neurally adjusted ventilatory assist in newborns. Semin Fetal Neonatal Med. 2016;21(3):154–61.
18. Liptsen E, Aghai ZH, Pyon KH, Saslow JG, Nakhla T, Long J, et al. Work of breathing during nasal continuous positive airway pressure in preterm infants: a comparison of bubble vs variable-flow devices. J Perinatol. 2005;25(7):453–8.
19. Elgellab A, Riou Y, Abbazine A, Truffert P, Matran R, Lequien P, et al. Effects of nasal continuous positive airway pressure (NCPAP) on breathing pattern in spontaneously breathing premature newborn infants. Intensive Care Med. 2001;27(11):1782–7.
20. Miedema M, van der Burg PS, Beuger S, de Jongh FH, Frerichs I, van Kaam AH. Effect of nasal continuous and biphasic positive airway pressure on lung volume in preterm infants. J Pediatr. 2013;162(4):691–7.
21. Emeriaud G, Beck J, Tucci M, Lacroix J, Sinderby C. Diaphragm electrical activity during expiration in mechanically ventilated infants. Pediatr Res. 2006 May;59(5):705–10.
22. Lopes J, Muller NL, Bryan MH, Bryan AC. Importance of inspiratory muscle tone in maintenance of FRC in the newborn. J Appl Physiol Respir Env Physiol. 1981;51(4):830–4.