Diaphragmatic electromyography monitoring in preterm Infants

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Citation for published version (APA):
CHAPTER 6

Classifying apnea of prematurity by transcutaneous electromyography of the diaphragm

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Submitted.
ABSTRACT

Objective: To compare the accuracy of apnea classification based on transcutaneous electromyography of the diaphragm (dEMG) and chest impedance (CI) tracings in preterm infants.

Methods: 15 central, 5 obstructive and 10 mixed apnea were selected from recordings containing synchronized continuous tracings of respiratory inductive plethysmography (RIP), airway flow, heart rate (HR), oxygen saturation (SpO2) and breathing activity measured by dEMG and CI. RIP was used as the gold standard for apnea classification. Twenty-two assessors (neonatologists, pediatricians-in-training and nurses) classified each apnea twice; once based on dEMG, HR and SpO2 tracings and once based on CI, HR and SpO2. Assessors were blinded for the type of respiratory tracing (dEMG or CI) and for the RIP and flow tracings.

Results: In total 1320 assessments were performed and in 71.1% the apnea was classified correctly. Subgroup analysis based on respiratory tracing showed that 74.8% of the dEMG tracings was classified correctly compared to 67.3% of the CI tracings (p<0.001). This improved apnea classification based on dEMG was present during central apnea (86.7% vs. 80.3%, p<0.02) and obstructive (56.4% vs. 32.7%, p<0.001) apnea. The improved apnea classification based on dEMG tracing was independent of the type of assessor.

Conclusion: Transcutaneous dEMG improves the accuracy of apnea classification compared to CI in preterm infants and this makes this technique a promising candidate for future monitoring systems.

KEY WORDS
Obstructive; Central; Monitoring; Chest Impedance; EMG; Hypoxic Events
INTRODUCTION

Impaired control of breathing resulting in apnea is common in preterm infants with a gestational age (GA) less than 30 weeks. Apnea can be classified into three groups: (1) central apnea, a cease in airflow due to absence of respiratory effort; (2) obstructive apnea, a cease in airflow caused by upper-airway obstruction; and (3) mixed apnea, a cease in airflow caused by a combination of both. Central and mixed apnea account for most of the apneic episodes. The frequency of apnea is inversely proportional to the GA and in almost all infants these apnea are accompanied by hypoxemia and bradycardia.

Hypoxemic episodes, especially if prolonged, are associated with an increased risk of adverse neurodevelopmental outcome in preterm infants. Prompt and adequate treatment of apnea is therefore of the utmost importance. However, the optimal treatment of apnea is highly dependent on the type of apnea and therefore correct classification based on accurate cardiorespiratory monitoring is essential. For instance, central apnea is probably best treated with caffeine while nasal continuous positive airway pressure (nCPAP) might be a better choice for obstructive apnea, as it splints the upper airway.

Chest impedance (CI) is the current standard for bedside cardiorespiratory monitoring of preterm infants. It measures changes in electrical impedance caused by changes in lung aeration and chest wall movement. CI provides continuous monitoring of heart rate (HR), respiratory rate (RR) and breathing pattern and the latter is used for detection of apnea. However, CI has important limitations, such as inaccuracies in monitoring respiration due to cardiac interference and non-breathing related chest wall movement. This may compromise accurate detection and classification of apnea.

Measuring electrical activity of the diaphragm might be a more direct and accurate method to monitor respiration in newborn infants. We recently showed that transcutaneous electromyography of the diaphragm (dEMG) is feasible in preterm infants and provides accurate data on HR and RR, comparable to CI. If dEMG improves apnea detection and classification compared to CI has so far not been studied.

Therefore, the aim of this study was to compare apnea detection and classification by CI and dEMG. We hypothesized that dEMG would allow for more accurate apnea detection and classification compared to CI.
METHODS

For this study we used data collected in a previously published prospective observational cohort study conducted in the Neonatal Intensive Care Unit (NICU) of the Emma Children’s Hospital, Academic Medical Center Amsterdam, the Netherlands. This study assessed the effect of caffeine on the electrical activity of the diaphragm in spontaneously breathing preterm infants with a GA < 34 weeks. Written informed consent was obtained from both parents and the study protocol was approved by the Institutional Review Board.

In all patients the breathing pattern measured by dEMG was recorded at the bedside using a portable 16-channel digital physiological amplifier (Dipha-16, Macawi, Enschede, Netherlands). Two transcutaneous electrodes were placed at the costo-abdominal margin in the left and right nipple line, and one ground electrode at height of the sternum. dEMG data were digitized without analogue filtering and sent wirelessly to the front-end of the Dipha-16 system connected to a personal computer. More details on pre- and post-processing, sampling rate, filtering algorithm and other technical aspects of the dEMG measurement have previously been described.

Respiration was also recorded with respiratory inductance plethysmography (RIP) which measures rib cage (RC) and abdominal (AB) excursions via two elastic bands containing a teflon coated wire connected to a Bicore-II device (Vyaire, Yorba Linda, USA). An electrical oscillating signal is sent simultaneously through both wires and the frequency modulation due to expansion and contraction of the RC and AB bands is converted to voltage changes. The sum signal of the RC and AB bands was also calculated (summed RIP).

CI and transcutaneous oxygen saturation (SpO₂) recorded by Intellivue MP-90 monitor (Philips Healthcare, Eindhoven, The Netherlands) were captured by a personal computer at a sample rate of 500 Hz using custom made software.

Finally, a flow sensor (Vyaire, Yorba Linda, USA) was placed at the expiratory limb of the nCPAP system, allowing for measurement of inspiratory and expiratory flow variation during breathing in all patients.

All tracings were recorded in sync (Figure 1) and analysis was performed off-line using a custom-made software package (Polybench version 1.25.2, Applied Biosignals, Weener, Germany).
Figure 1. Example of respiratory tracings of dEMG, CI and RIP combined with SpO₂, HR and flow for an apnea classified as central. From top to bottom: Chest Impedance (CI), diaphragmatic EMG (dEMG), saturation (SpO₂), heart rate (HR), flow (Flow), summed ribcage and abdominal signal of RIP (RIP sum), ribcage (RC) and abdominal (AB) signal of RIP.

Using only stable tracings of flow, SpO₂ and HR we identified all recorded apnea, defined as a cessation of breathing in the flow signal for more than 20 seconds or of shorter duration if accompanied by a hypoxemia (SpO₂ < 80%) or bradycardia (HR < 100 beats per minute).

Using only the RIP recording (gold standard), apnea were classified by three reviewers independently using the following criteria: 1) central apnea: both the RC and AB tracings were flat lines; 2) obstructive apnea: RC and AB tracings moved in opposite (paradoxical) direction while the summed RIP signal approached zero; 3) mixed apnea: both central and obstructive components were visible in the RIP tracings. In case of disagreement, the reviewers tried to reach consensus on apnea classification.

Based on the flow and RIP tracings, 49 apnea were identified of which 34 were classified as central, 5 as obstructive and 10 as mixed. From the 34 central apnea we randomly selected 15 apnea for the final analysis.

Next, for each apnea (n=30) the HR and SpO₂ tracing recorded by the Intellivue MP90 monitor and RR tracing recorded by either CI (Intellivue MP90 monitor) or dEMG was captured in one image. As a result each apnea was captured twice, once using the respiratory tracing based on the CI data and once based on the dEMG recording. The source of the respiratory tracing was only known to the investigators and was not visible in the image of the apnea (Figure 2). The 60 apnea images were then mixed and emailed as a PowerPoint presentation to 22 assessors, consisting of neonatologists (n=9), paediatricians in training (n=8) and neonatal nurses (n=5). They were asked to classify each apnea as either central, obstructive or mixed.
Figure 2. Example of apnea image (classified as central) as scored by the assessors. Respiratory tracing (blinded for source), saturation (SpO₂) and heart rate (HR).

Statistical analysis
Statistical analysis was performed using SPSS version 23 (SPSS, Chicago, Illinois, USA). Data were expressed as mean ± standard deviation (SD). The number of correctly scored apnea in total and for the dEMG and CI tracings separately were expressed as proportion of the total number of scored apnea images (%). Subgroup analyses were performed for the type of apnea and the different assessors. For between groups analysis the McNemar t-test was used. A p-value less than 0.05 was considered statistically significant.

RESULTS

The 30 selected apnea originated from the recordings of twelve preterm infants with a mean GA of 29.0 ± 0.8 weeks and mean birth weight of 1279 ± 222 gram. There was no disagreement between the reviewers classifying the selected apnea based on the flow and RIP tracing. All RIP and flow based apnea were also detected by either CI or dEMG. Based on the 60 apnea images and the 22 assessors a total of 1320 apnea scores were collected and analyzed.

In total, 71.1% of all apnea images were scored correctly as central, obstructive or mixed (Table 1). 74.8% of the apnea based on the respiratory tracings of dEMG were classified correctly compared to 67.3% of the apnea based on the respiratory tracings of CI. This difference was statistically significant (p<0.001).

Table 1. Correctly scored apnea in the dEMG and CI group for classification of apnea

<table>
<thead>
<tr>
<th></th>
<th>Total (%)</th>
<th>dEMG (%)</th>
<th>CI (%)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>All apnea (n=1320)</td>
<td>71.1 ± 10.0</td>
<td>74.8 ± 12.1</td>
<td>67.3 ± 9.9</td>
<td>p&lt;0.001</td>
</tr>
<tr>
<td>Central % (n=660)</td>
<td>83.5</td>
<td>86.7</td>
<td>80.3</td>
<td>p&lt;0.02</td>
</tr>
<tr>
<td>Obstructive % (n=220)</td>
<td>44.5</td>
<td>56.4</td>
<td>32.7</td>
<td>p&lt;0.001</td>
</tr>
<tr>
<td>Mixed % (n=440)</td>
<td>65.7</td>
<td>66.4</td>
<td>65.0</td>
<td>p=0.8 ns</td>
</tr>
</tbody>
</table>

Percentage correctly scored apnea are presented as mean ± SD. The p-value represents the difference between the dEMG and CI group, analysis performed with McNemar t-test. Total: all apnea scored based on both dEMG and CI. dEMG: all apnea scored based on the dEMG tracing. CI: all apnea scored based on the CI tracing. n= the number of included images.
Subgroup analyses based on the type of apnea showed that this improvement in apnea classification in favor of dEMG was most prominent in the obstructive apnea subgroup and, to a lesser extent, in the central apnea subgroup (Table 1). Furthermore, the highest correct rate was reached in the central apnea group (83.5%) and the lowest correct rate in the obstructive apnea group (44.5%).

Subgroup analysis also showed that the improved apnea classification in the dEMG subgroup compared to the CI subgroup was a consistent finding across the three different groups of assessors (Table 2). The differences in correct classification of all apnea were small between the groups of assessors.

Table 2. Correctly scored apnea in total and for the dEMG and CI group by different assessors

<table>
<thead>
<tr>
<th></th>
<th>Total (%) (n=1320)</th>
<th>dEMG (%) (n=660)</th>
<th>CI (%) (n=660)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>All assessors (n=22)</td>
<td>71.1 ± 10.0</td>
<td>74.8 ± 12.1</td>
<td>67.3 ± 9.9</td>
<td>p&lt;0.001</td>
</tr>
<tr>
<td>Neonatologists (n=9)</td>
<td>68.0 ± 11.2</td>
<td>70.7 ± 12.4</td>
<td>65.2 ± 11.3</td>
<td>p=0.1 ns</td>
</tr>
<tr>
<td>Paediatricians in training (n=8)</td>
<td>72.7 ± 10.7</td>
<td>77.1 ± 13.4</td>
<td>68.3 ± 10.7</td>
<td>p&lt;0.02</td>
</tr>
<tr>
<td>Nurses (n=5)</td>
<td>74.0 ± 6.0</td>
<td>78.7 ± 9.0</td>
<td>69.3 ± 6.4</td>
<td>p=0.055 ns</td>
</tr>
</tbody>
</table>

Percentage correctly scored apnea are presented as mean ± SD. P-value represents the difference between the dEMG and CI group, analysis performed with McNemar t-test. Total: all apnea scored based on both dEMG and CI. dEMG: all apnea scored based on the dEMG tracing. CI: all apnea scored based on the CI tracing. n= the number of included images (column heads) and assessors (row heads) in the analysis.

DISCUSSION

This study shows that detection of apnea using transcutaneous dEMG is feasible in preterm infants. It also suggests that dEMG might improve apnea classification compared to the current monitoring standard, i.e. chest impedance.

There is a growing interest in using the neural activity of the diaphragm for respiratory management of preterm infants. Most studies have reported on the use of diaphragmatic activity measured by a special transesophageal nasogastric catheter to synchronize invasive and non-invasive respiratory support in preterm infants. Some have suggested that transesophageal dEMG can also be used for assessing breathing pattern and apnea, but this has so far not been systematically studied. Our study is the first to compare apnea detection and classification using dEMG to CI. Furthermore, it is the first study to use the non-invasive and cheaper transcutaneous interface.

We used RIP as the gold standard for apnea classification. Previous studies have shown that this technique is able to detect apnea, has no interference of cardiac artefacts and is especially suitable for distinguishing between central and obstructive apnea. Consistent
with our hypothesis, dEMG monitoring resulted in more accurate classification of central and obstructive, but not mixed, apnea compared to CI monitoring. It has been suggested that CI has a limited ability to distinguish obstructive apnea from normal respiration. Although air entry will be limited or absent, air can still move back and forth within the chest wall cavity during airway obstruction, resulting in a normal or slightly reduced breathing pattern. While in fact respiratory muscle activity will be significantly increased during obstructive apnea and the concomitant increase in electrical diaphragmatic activity will be picked up by dEMG monitoring. This may explain the improved classification of obstructive apnea with dEMG.

During central apnea, there is a cessation of inspiratory effort and flow, which results in absent electrical activity of the diaphragm and no change in lung aeration. Both dEMG and CI tracings should therefore show no activity (flat line). However, previous reports have shown that cardiac activity may interfere with the CI tracing and (falsely) suggest breathing activity. Such cardiac interference is not present in the dEMG tracing due to a special filtering technique and this may explain the superior classification of central apnea.

We can only speculate why classification of mixed apnea did not differ between dEMG and CI. The fact that both central and obstructive components are present in the CI and dEMG tracings might make classification of mixed apnea less dependent on the source (CI or dEMG) of breathing activity.

This was the first time that neonatologists, pediatricians-in-training and neonatal nurses assessed respiratory tracings based on dEMG. It seems that the assessors did not have any difficulty interpreting the dEMG tracings since the results of our study show that the rate of correctly scored apnea based on the dEMG tracings was comparable or better than based on CI tracings. We speculate that classification of apnea will improve even further once the assessors are more familiar with interpreting the dEMG tracings.

This study has some limitations that need to be addressed. First, we only assessed a limited number of apnea to keep the workload for each individual assessor within reasonable limits. However, the total number of assessments was 1320 and we think this is a sufficient number to explore a possible role of dEMG in apnea detection and classification. Second, we only selected apnea from stable RIP, flow, SpO₂ and HR tracings. However, apnea can also occur when tracings are unstable due to, for instance, patient movement. It is unclear how dEMG will compare to CI under such circumstances. Finally, we did not measure (absolute) flow directly at the airway opening but at the expiratory limb of the nCPAP system. Although unconventional, the variation in flow did allow us to assess cessation of flow in the respiratory system.

In conclusion, this study shows that electrical activity of the diaphragm measured by transcutaneous dEMG can be used for apnea detection and classification in preterm infants. dEMG improves classification of central and obstructive, but not mixed, apnea compared
with the current standard CI and this finding is consistent across different assessors. These findings suggest that transcutaneous dEMG is a promising candidate for improved analysis of breathing patterns in future monitoring systems.

ACKNOWLEDGEMENTS

We thank all assessors of our department for scoring the apnea and we thank Leo van Eykern and Tom Leenhoven for the technical assistance in this study.
REFERENCES