IDENTIFYING OBSTRUCTIVE FROM CENTRAL APNEOAS IN INFANCY USING PULSE TRANSIT TIME

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ABSTRACT

The prevalence of obstructive sleep apnea syndrome (OSAS) can be common for infants. Current gold standard for its diagnosis is nocturnal polysomnography (PSG) but this procedure can be complex to perform. Pulse transit time (PTT) shows potential to indicate abrupt blood pressure (BP) changes during upper airway obstruction. Objective of this study was to assess the capability of PTT to differentiate central from obstructive sleeping respiratory events. This study involved 4 infants with mean age of 7.8 ± 1.9 months. 58 valid respiratory events free from motion artefacts were pre-scored by 2 blinded observers. PTT results were then evaluated against the corresponding PSG scorings. Tidal breathing varied with standard deviation (SD) of 5.13 ms and maximal decrease of 3.57% from baseline. Obstructive events showed a mean change of 4.95% (p < 0.05), with SD of 13.10 ms and maximal decrease of 14.92% (p < 0.05) from tidal breathing. Central events showed a mean change of 1.72% (p > 0.05) change, with SD of 2.47 ms and maximal decrease of 2.90% (p > 0.05). PTT is able to categorise central and obstructive respiratory events accordingly. Furthermore, PTT has showed its sensitivity to monitor marginal BP fluctuations during tidal breathing. Hence, preliminary results suggest that PTT can be a valuable OSAS screening tool for infants.

KEY WORDS
Noninvasive measurement, pulse transit time, obstructive sleep apnea, and sleep disordered breathing

1. Introduction

Obstructive sleep apnoea syndrome (OSAS) has been identified and described in children and infants [1-3]. The overall prevalence of OSAS affects about 2% of the pediatric population [1-2]. Currently, polysomnography (PSG) is the gold standard procedure for the study of sleep and breathing disorders, including for infants [3]. The clinical symptoms and PSG characteristics of OSAS for infants differ from those in children and adults [4]. Children with OSAS frequently exhibit a pattern of persistent and partial upper airway obstructions associated with gas exchange abnormalities. This characteristic is rather distinctive from the recurrent and discrete episodes of obstructions experienced by their adult [5-6] and infant [4] counterparts. The prevalence of infancy OSAS usually results from congenital facial anomalies and neurological abnormalities that involve muscle tone and upper airway control [7]. Unlike children and adults, sleep disordered breathing in an infant can present a unique threat to life like apnoea of prematurity and sudden infant death syndrome [4]. Overnight PSG study is usually recommended to investigate and monitor OSAS in infants. Considerable interest was generated in portable devices that can record a combination of cardiorespiratory parameters for home studies [8]. These recordings need to be useful for clinical assessments of respiratory events. However, few techniques can yet adequately assess respiratory variables for this purpose [9].

A cardio-respiratory measure known as pulse transit time (PTT) has been proposed as it shows promises to be practical for such purposes in adults. A significant correlation of oesophageal pressure variations induced by episodes of augmented airways resistance and PTT fluctuations between inspiration and expiration was established [10]. PTT is the time difference between the origins of a pulse wave in the left ventricle to its detection at a periphery. This technique is usually measured as the time delay between the R-wave on the electrocardiogram (ECG) and its subsequent arrival at the selected periphery. The principal velocity determinant by which these waves propagate is the compliance of the arterial wall. This compliance in turn, is highly dependent on the instantaneous blood pressure (BP) [11]. As the BP increases, this affects the geometric and mechanical properties of the arterial wall thus, leading to an increase in its stiffness. This can occur when there is an abrupt BP changes generated by high pleural pressure swings encountered during OSAS. During such occurrences, these pulse waves propagate faster and thereby decreasing the duration of PTT measurement [10-11]. Based on these findings, changes in PTT can reflect changes in respiratory efforts in infants during their sleep. Hence, the objectives of this study were (1) to determine the use of PTT to detect changes in respiratory efforts and (2) assess the capability of PTT to differentiate obstructive from central respiratory events in infants.
2. Materials and Methods

2.1. Polysomnography

Routine overnight PSG was performed in the sleep laboratory with parameters monitored that included electroencephalography (electrodes C3-A2 and O2-A1), left and right electrooculogram (LE-A2 and RE-A1), oronasal airflow tracing (via pressure transducer), AC-coupled respiratory inductance plethysmography (RIP) recording of chest and abdominal movement (Respirtrac Calibrator System, Ambulatory Monitoring Inc, Ardsley, USA), infrared photoplethysmography (PPG), heart rate calculation and oxygen saturation (SaO₂) by pulse oximetry (Novametrix Medical Systems Inc, Wallingford, USA). The studies were continuously observed by experienced PSG personnel and all readings were recorded by a commercial PSG system (Uniquant system, LaMont Medical Inc, Wisconsin, USA).

The contribution of the chest to tidal breathing may be limited in newborns due to its shape, high compliance and deformability. Studies have shown that 1 year of age or less, this contribution can be compromised [12]. Hence, inclusion of any respiratory sleep events is based on the pre-scoring of 2 blinded observers. For this study, an episode of obstructive apnoea was defined as a complete cessation of airflow with the presence of chest or/and abdominal wall movement. An obstructive hypopnoea had similar characteristics except that airflow was reduced by at least 50% from its baseline. During both types of event, the patient may exhibit paradoxical respiratory efforts. In this study, both were classified as obstructive event (OE). Central hypopnoea events were defined as a reduction of 50% or more in airflow proportional to the decrease in respiratory drive. While for central apnoea, it was the complete cessation in both airflow and respiratory drive. Similarly, they were regarded as central event (CE) in the context of this study.

2.2. PTT Measurements

A stand-alone PTT system based on a microcontroller to continuously acquire the physiologic data from a single-lead ECG machine (S&W Medico, Teknik, Denmark) and PPG signals derived from the PSG oximetry. This system has an accuracy of 1ms for all taken measurements. The ECG signal was sampled at 1ms interval and a slope detection algorithm was used to determine the initial upstroke of the R-wave. A differentiator in firmware then detected the peak and a timer was initiated at this point. The PPG signal was also sampled at 1ms sampling period and a moving threshold detector was used to minimise the effect of baseline wander. The corresponding 25% of peak-to-peak amplitude was derived as suggested by Smith et al [10] in their similar studies to mark the arrival of the pulse wave at the peripheral. At this point, the timer was terminated and its count was stored as the PTT value. This system then outputs an analogue voltage signal to the PSG system so as to allow comparison of PTT with all other measured parameters over the study period.

2.3. Subjects and Experimental Protocol

This was a study that included 3 male and 1 female infants as subjects. Their age mean and standard deviation (SD) were 7.8 ± 1.9months (range 5-9 months). Their mean height and weight with their SD were 65.9 ± 14.0cm and 5.99 ± 1.55kg respectively. They were scheduled to undergo routine overnight PSG studies. Prior to any study, their parent was given the study purposes and procedures verbally. Informed consent was obtained prior to the study. Furthermore, institutional ethical approval was obtained for these studies. The accuracy of PTT measurements was verified against the corresponding readings of both the RIP and oronasal airflow measure of the PSG scorings. The RIP method usually detects increased respiration efforts through the de-synchronization of chest and abdominal movements, while airflow measurement is determined by changes in the respiration pressure at the nares. The only exclusion criteria in this study were infants with coexisting cardiac diseases. These diseases may affect the isometric contraction time of the left ventricle that forms a major part of the measured PTT. The confounding effects on PTT measure warrant these infants to be excluded from this study to avoid complications in results [12].

2.4. Data Analysis

PTT is a non-continuous respiratory effort measure since it is only available with each heartbeat. Therefore, PTT comparison needs to be based over several consecutive breaths to quantify any respiratory effort events [10]. In order to classify these events, the average PTT estimate for the duration of the event was computed. This is then compared against the baseline PTT value during tidal breathing that was prior to the event and with the same duration. Furthermore, the relative maximal decrease (%) in PTT was registered for all of these events. Only events that fulfilled the following criteria were considered in this study: (1) Respiratory events that were pre-scored by two blinded observers, (2) must last for more than 8 PTT readings and (3) no apparent motion artefacts can be observed. The latter criterion was achieved by monitoring the baseline stability of the PPG signals throughout the duration of each study. Statistical analysis was performed using SPSS version 10 for Microsoft Windows (SPSS, North Chicago, Illinois, USA). Differences between respiratory events of CE or OE with baseline tidal breathing were assessed by using the Student’s t-test for paired variants. Two-way analysis of variance was also used to test for differences between CE and OE from baseline. The mean, SD, mean % decrease and maximal % decrease in PTT in each event were also calculated. A value of p<0.05 was considered significant in this study.

3. Results

From the 58 valid respiratory events obtained, the mean PTT change (%), ± SD range (ms), maximal PTT decrease (%) and p value were shown in Table 1
accordingly. There were distinctive differences between events of tidal breathing, OE and CE. During OE, this exhibits a greater PTT decrease and wider SD ($p<0.05$) from its nominal values during its occurrence. On the other hand, CE displays negligible variation ($p>0.05$). Variations in PTT were expected even during tidal breathing as they reflected the changes in the respiratory drive of the infant during sleep.

In Figure 1, it can be observed that there was an increase in PTT variations. This may signify an increased negative intra-thoracic pressure generated in hope to overcome the obstruction. In CE, PTT variations became less prominent with a general reduction in respiratory drive as shown in Figure 2. The ribcage and abdominal component of the RIP in this example showed a cessation of breathing efforts as well as the termination of airflow. Without the ongoing breathing efforts, the nominal PTT variations due to the respiratory drive diminished. Interestingly, the $\text{SaO}_2$ value of the subject deteriorated with the progression of the prolonged CE. Worthy of note, a total of 32 respiratory events were rejected on the basis of motion artefacts.

<table>
<thead>
<tr>
<th>Events</th>
<th>$n$</th>
<th>$\Delta$ (%)</th>
<th>SD (ms)</th>
<th>Max $\Delta$ (%)</th>
<th>$p$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tidal</td>
<td>58</td>
<td>-</td>
<td>5.13</td>
<td>3.57</td>
<td>-</td>
</tr>
<tr>
<td>OE</td>
<td>10</td>
<td>4.95</td>
<td>13.10</td>
<td>14.92</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>CE</td>
<td>48</td>
<td>1.72</td>
<td>2.47</td>
<td>2.90</td>
<td>&gt;0.05</td>
</tr>
</tbody>
</table>

Table 1: Results of respiratory events

4. Discussions

From this study, PTT measurement can be used as a simple supportive technique in assessing respiratory effort changes in infants during sleep. The results obtained shows that PTT has shown its ability to differentiate respiratory events accordingly. PTT fluctuations have shown their correlations with abnormal changes in respiratory efforts detected by both RIP and oronasal airflow in the PSG studies conducted. During normal sleep, it can be observed that there were marginal PTT fluctuations and this can be depended on their BP fluctuations during tidal breathing. Trinder et al [13] reported that these breath-based BP changes may be due to the mechanical effects of changing intra-thoracic pressure and lung volume, thereby affecting the cardiac preload and afterload. Furthermore, they suggested that oscillations of venous return and cardiac output caused by periodic rises and falls in ventilation and pleural pressure during tidal breathing may also lead to BP fluctuations. From the results attained, the marginal PTT fluctuations observed during tidal breathing signified the ability of PTT to monitor even small changes in respiratory efforts.

It can be seen in this study that PTT measurement has the required sensitivity to detect BP fluctuations. PTT not only has the ability to monitor changes in respiratory efforts, but also shows the potential to differentiate CE from OE. Moreover, PTT was sensitive enough to distinguish hypopnoeic respiratory events. It has been established by other studies that there is an inverse correlation between changes in BP and PTT values [10-11]. Based on these studies, a parallel relationship of PTT variations with changes in respiratory efforts can be drawn. The preliminary results from this study have shown that PTT can discriminate respiratory events
accordingly. However, PTT by itself is non-quantitative. In order for PTT to assess changes in respiratory effort, it should be compared to its baseline history prior to each event. Classification of respiratory events is clinically important for both future pathological studies and their distinct treatment [10].

PTT technique is not a perfect measure and has its limitations. Although PTT measurement can be a simple and non-invasive alternative to estimate changes in respiratory efforts, it is a rather crude technique. Hence, PTT can only be part of a simplified screening system for the investigation of OSAS in infants. As there can be differences in BP and vascular compliance in individuals, their corresponding transit time can vary [14-15]. Hence, PTT value is useful when it was observed over a period of time on an individual basis. Furthermore, PTT may not reflect true variations of respiratory efforts in subjects with coexisting cardiac diseases. These diseases can affect the isometric contraction time in response to changes in respiratory efforts or arousals causing false changes in PTT value [10]. More importantly, the major limitation of PTT is motion artefacts caused by either movement from the chest wall affecting ECG signals or at the periphery interfering with the PPG signals. These may cause a shift in PTT baseline and may be incorrectly regarded as the occurrence of arousals or changes in respiratory drive. Moreover, at the termination of an OE, arousals can usually occur that can lead to bodily movements [10]. However, artefacts of this nature are common in all non-invasive measurement and the inclusion of motion detection can minimise this artefact-mediated error.

5. Conclusions

From this study, PTT has shown its potential to be able identified OSAS in infants. PTT has the advantage of being relatively simple to implement and non-invasive. PTT has shown not only its ability to detect changes in respiratory efforts, but also differentiate CE from OE in the absence of motion artefacts. Furthermore, marginal BP fluctuations during tidal breathing can be monitored by PTT. Identifying hypopnoeic events in infants during sleep is also possible using this technique. Hence, it can form as part of a simplified screening package for OSAS investigation. PTT technique does have its flaws, but with appropriate technological developments, this can improve its suitability in respiratory studies for infants.

References: