Variability of Pulse Signal Frequency Obtained Using Nocturnal Pulse Oximetry in Patients with Sleep Apnoea/Hypoapnoea Syndrome

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ARTICLE INFO

Article history:
Received June 10, 2009
Accepted November 16, 2009
Available online 25 January 2010

Keywords:
Sleep apnoea syndrome
Measurement of central tendency
Heart rate
Diagnosis

ABSTRACT

Introduction: The measurement of central tendency (MCT) is a non-linear analysis technique which applied to second order differences diagrams enables the degree of variability to be quantified in a data series. In the present study an attempt is made to quantify and characterise the changes in heart rate obtained by pulse oximetry in patients with a clinical suspicion of sleep apnoea/hypoapnoea syndrome (SAHS) using the MCT and to evaluate its diagnostic use.

Patients and Methods: A total of 187 patients were included in the study, on whom a nocturnal polysomnographic and pulse oximetry study was performed. To evaluate the variability of the heart rate the MCT applied to graphs of second order differences obtained from the heart rate record.

Result: Patients with SAHS had a higher heart rate variability than patients without SAHS (0.449 vs 0.666, P<.001). In the multivariate analysis, the heart rate, the minimum saturation and the desaturation index of 4% were independently associated with the heart rate variability. As a diagnostic method, the MCT of the heart rate gives a sensitivity of 69.3%, a specificity of 77.6% and a diagnostic precision of 72.7%.

Conclusions: Patients with SAHS have a greater variability in heart rate during the night, evaluated by applying the MCT of the heart rate to diagrams of second order differences. As a screening method, the MCT applied to the heart rate has a moderate sensitivity and specificity.

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Introduction

Sleep apnoea/hypopnoea syndrome (SAHS) is a common condition characterised by recurrent upper airway collapsibility during sleep. These episodes of reduction or absence of air flow lead to characteristic modifications in both oxygen saturation and heart rate (HR).

Heart rate is a reflection of a subject’s cardiovascular state and increased HR has been associated with the presence of cardiovascular alterations and higher morbidity and mortality. In healthy subjects, heart rate shows complex fluctuations, tending to drop during sleep, especially the non-REM phase. Although the heart rate’s response to obstructive apnoeas can vary, patients with SAHS are normally considered to have a characteristic pattern of bradycardiac during sleep. These variations in heart rate seem to depend on alterations in the autonomic nervous system and the air flow. In this respect, modifications in heart rate have been considered to be a marker of autonomic arousals in patients with SAHS.

In recent years, the analysis of heart rate variability has aroused much interest, taking as a reference the electrocardiogram RR interval as a measure of autonomic control. However, few studies have tried to characterize heart rate behaviour in patients with SAHS using pulse oximetry and describe its diagnostic use in patients with a suspicion of SAHS. Most of these studies use linear processing techniques. Like other physiological signals, heart rate behaves in a complex, irregular way, even in healthy subjects, so non-linear techniques are probably more suitable for analysing it. Among this kind of procedures is the measure of central tendency (MCT) applied to diagrams of second order differences. Diagrams of second order differences are a very useful graphic method as they provide a rapid, visual analysis of the behaviour of a series of data. The graphs are centred on the origin, enabling the degree of chaos in a dataset to be evaluated. Thus, a diagram showing points clustered around the centre is associated with less variability of the series of data. MCT can be used to assess the second order diagrams objectively, enabling variability to be quantified. A low MCT value would imply greater variability of the signal analysed.

This prospective study aims to quantify and characterize the variability of pulse signal frequency obtained using pulse oximetry in patients with breathing disturbances during sleep, using measure of central tendency applied to diagrams of second order differences; we also aim to evaluate its diagnostic use with patients with a clinical suspicion of SAHS.

Patients and Methods

One hundred and eighty-seven subjects (147 men and 40 women) referred consecutively to the pneumology department at the Hospital Clínico Universitario in Santiago de Compostela with a clinical suspicion of SAHS were included in the study. All the subjects simultaneously underwent nocturnal polysomnography (Ultrason Network, Nicolet, Madison, WI, USA) and recording of heart rate and oxyhaemoglobin with a pulse oximeter (Criticare 504 oximeter, CSI, Wankeska, WI, USA), using a finger probe with a sampling frequency of 0.2Hz. The nocturnal polysomnography included the monitoring of electroencephalogram, electro-oculogram, oronasal flow by thermistor, thoracoabdominal movement, electrocardiogram, snoring and body position. Sleep was analysed following standard criteria. Apnoea was defined as the absence of air flow for over 10 s and hypopnoea as a noticeable reduction in air flow or chest wall movement, accompanied by a desaturation of over 3% or the presence of arousal. The apnoea/ hypopnoea index (AHI) was calculated by dividing the number of apneas and hypopneas by the number of hours of sleep. Patients were considered to have SAHS with an AHI over 10. All the patients were clinically stable while both studies were performed. SAHS was considered mild to moderate if the AHI was under 30, and severe when over 30. The polysomnography and pulse oximetry data were analysed independently.

Patients previously diagnosed with autonomic neuropathy or autonomic dysfunction were excluded from the study, as were those with heart rate disorders. Seventeen point one percent had a history of cardiovascular disease. None of the patients included took anti-arrhythmic drugs. All the patients were stable while the polysomnography study was being performed. The study was approved by the ethics committee of the hospital.

Measure of Central Tendency

To quantify the variability of the pulse signal frequency obtained using nocturnal pulse oximetry, we used the measure of central tendency applied to diagrams of second order differences. Diagrams of second order differences are dispersion graphs centred on the coordinate origin. This kind of graph of the data obtained from a recording provides information quickly and visually about the dispersion (variability) of a series of analysed data. Thus, it is a very useful graphical tool for the analysis of biomedical data recordings. In this type of graph, the difference between two shifted versions of the signal under study is represented on each coordinate axis, which is why they are called second order differences. The MCT is used to numerically and objectively quantify the degree of dispersion of the data, which can also be visualised in the diagrams of second order differences. Both tools (graphical and numerical) are combined to characterize all the biological recordings, which in this case is heart rate (n). To do this, it is necessary to choose a circle with a fixed radius (r) around the origin, count the number of points inside the circle and normalize with regard to the total number of points. If the dispersion of the data in the diagram of second order differences is very high, that is, the points are scattered over the whole diagram, then a high percentage of them will fall outside the circle. This will give rise to a low MCT value, towards 0 (high variability). If, on the other hand, the dispersion of the data in the diagram is small and, therefore, the values tend to be concentrated around the coordinate origin, most of the data will be inside the circle. This will give rise to a high MCT value, towards 1 (low variability).

Selecting the right radius value (r) to calculate the MCT is very important. Generally, the radius selected depends on the type of data analysed. In our study the choice of radius for the circular area was made to look for the most significant differences between the groups of patients with and without SAHS. To do this, the MCT was calculated for each heart rate recording with different radii within a range determined by the nature of the data (from r = 1 to r = 10 in steps of 0.1). Then, the student test was applied and the radius giving the most significant differences between samples was chosen, which in our case was r = 1.5. Due to the length of the sleep recordings, to process the signals with the MCT, each of the recordings was divided into epochs of 200 samples, enabling several episodes of apnoea to be included in each epoch. Finally, an average was worked out, taking
Results

Nocturnal polysomnography made it possible to diagnose 59.3% of the subjects in the study with SAHS. The patients' clinical characteristics are shown in Table 1.

At the start of polysomnography recording, the patients with SAHS had a higher heart rate than those without SAHS (74.5 vs 69.3 bpm; p < 0.05). Figures 1 and 2 show characteristic diagrams of second order differences for heart rate of a subject without and with SAHS, respectively. In figure 1, the diagram shows a series of data with little variability, so the points are near to the origin (no SAHS). Figure 2 corresponds to a patient with SAHS and the diagram shows greater graphic dispersion of the heart rate values. Using the MCT with the second order diagrams makes it possible to evidence that the patients with SAHS have lower MCT values than those with SAHS (0.449 ± 0.225 vs 0.666 ± 0.168, P <.001) and therefore greater heart rate variability (Figure 3).

The MCT values for pulse frequency showed a negative correlation with: heart rate at the start of recording (r = −0.30, P <.001); AHI (r = −0.425, P <.001); desaturation index (DI) 4% (r = −0.426, P <.001); DI 3% (r = −0.408, P <.001); DI2% (r = −0.379, P <.001); mean saturation (r = 0.361, P <.001); minimum saturation (r = 0.460, P <.001); and the percentage of time at SaO2 below 90% (r = −0.324, P <.001). These correlations remain significant when adjusted for age and BMI. We found no relationship between the MCT for heart rate and either BMI or sex, but there was a positive relationship with age (r = 0.174). The patients with severe SAHS had greater variability with respect to those with mild SAHS (0.514 vs 0.413, P <.05).

In the multivariate analysis, the variables with the highest explanatory power of the MCT (variability) for pulse frequency were minimum saturation, the desaturation index 4%, and basal heart rate, which would explain 26.18% of the behaviour of the MCT value for heart rate.

Figure 4 shows the ROC curve for pulse frequency variability, used as a method to help diagnose SAHS. The best results are obtained with a cut-off point of 0.576, reaching a sensitivity of 69.3%, a specificity of 77.6%, a diagnostic accuracy of 72.7%, and with an area under the curve of 0.778 (CI 95% 0.712-0.836). The true positive rate was 3.10 (2-4.79) and the true negative rate was 0.39 (0.29-0.53) (Table 2).

In patients without SAHS, we found no differences between the false positives (CTM < 0.576 and AHI < 10) and the true negatives with regard to age (59.4 vs 51.6), BMI (27.7 vs 30) and AHI (2.03 vs 2.01), but we did find differences with respect to minimum saturation (87.4 vs 79.9) and desaturation index (0.87 vs 2.9) (P <.05). In patients with SAHS, those whose oximetry test gave false negative results showed significant differences with regard to the severity of AHI (31.5 vs 44), age (62.9 vs 56), minimum saturation (73.4 vs 68.1), and a lower desaturation index (11.3 vs 25.05).

Table 1

| Characteristics of the patients included in the study, grouped by those with or without sleep apnoea/hypopnoea syndrome (SAHS) |
|------------------|------------------|------------------|------------------|------------------|
|                  | Overall sample (n=187) | No SAHS (n=76) | SAHS (n=111) | P           |
| Age, years       | 57.9 (12.8)        | 57.6 (12.9)     | 58.3 (12.9)     | ns          |
| BMI, kg/m²       | 29.5 (5.5)         | 28.4 (6.012)    | 30.5 (4.9)       | .03        |
| AHI              | 24.6 (1.7)         | 20.4 (2.36)     | 40.1 (19.6)      | .001       |
| COPD, %          | 22.5%             | 26.3%           | 19.8%           | ns         |
| Males, %         | 78.6%             | 69.7%           | 84.7%           | .02        |
| Heart rate       | 72.6 (13.3)        | 69.3 (12.4)     | 74.5 (13.5)      | .02        |
Discussion

The main finding of our study is that patients with SAHS have greater variability of nocturnal pulse signal frequency obtained using pulse oximetry than patients without SAHS, and therefore show greater dispersion in diagrams of second order differences. Even at rest, healthy subjects can show variability in their heart rate, depending on different factors such as age, body position, breathing rate and vagal tone. Sleep, especially in the early stages, involves changes in heart rate activity. In patients with SAHS, the presence of apnoeas produces relative bradycardia and vasodilation, followed by an increase in heart rate and vasoconstriction, which could explain the greater variability in pulse frequency shown by these patients.13

Despite its importance, heart rate behaviour in patients with SAHS has not been clarified.16 In our study basal heart rate, the desaturation index (4%) and minimum saturation were found to be the main parameters independently associated with heart rate variability measured by non-linear methods, although they can only explain 26.18% of this variability. For Zwillich,17 bradycardia is a common phenomenon in apnoeas, their duration and the increase in oxyhaemoglobin desaturation being factors determining its onset. Guilleminault found that there is a close relationship between the duration of apnoeas and bradycardia phenomena.4 However, other authors place a great deal of importance on arousals. Haba Rubio15 found that variations in heart rate and the plethysmographic waveform of the pulse do not differ with regard to the type of apnoea, but rather with regard to the duration of the arousals associated with them. Likewise, Guilleminault describes that, in patients with upper airway resistance syndrome, apnoeas accompanied by arousals have a greater tachycardic effect, even if there is only a small reduction in blood oxygen saturation.18

As in the study by Sumi,19 we also evidenced a relationship between heart rate with the AHI and the different desaturation

Table 2
Diagnostic use of applying the measure of central tendency to heart rate (diagnostic threshold=0.576)

<table>
<thead>
<tr>
<th>Statistics</th>
<th>Value</th>
<th>CI95%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity</td>
<td>69.3</td>
<td>60.8-77.9</td>
</tr>
<tr>
<td>Specificity</td>
<td>77.6</td>
<td>68.3-87.0</td>
</tr>
<tr>
<td>Diagnostic accuracy</td>
<td>72.7</td>
<td>66.3-79.1</td>
</tr>
<tr>
<td>Predictive positive value</td>
<td>81.9</td>
<td>74.1-89.7</td>
</tr>
<tr>
<td>Predictive negative value</td>
<td>63.4</td>
<td>53.7-73.2</td>
</tr>
<tr>
<td>Positive likelihood ratio</td>
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<td>2.004-4.799</td>
</tr>
<tr>
<td>Negative likelihood ratio</td>
<td>0.395</td>
<td>0.291-0.535</td>
</tr>
</tbody>
</table>

Figure 2. Diagram of second order differences showing the pulse signal frequency of a patient with SAHS. Each axis represents the difference between two shifted versions of the signal under study: \( x(n) \) is the original pulse frequency recording; \( x(n+1) \) is the pulse frequency recording after the time origin is shifted one sample; \( x(n+2) \) is the pulse frequency recording after shifting the time origin 2 samples.

Figure 3. Box graphs showing the differences between the values of the measure of central tendency (MCT) of the heart rate (HR) in patients with or without sleep apnoea/hypopnoea syndrome (SAHS).

Figure 4. Diagnostic efficacy curve to evaluate the presence or absence of SAHS using the value for the measure of central tendency (MCT) of heart rate (HR) obtained using nocturnal pulse oximetry. The symbol ◆ represents the optimal decision threshold.
and the minimum saturation. As a technique to help diagnose SAHS, the MCT of the heart rate gives moderate sensitivity and specificity. Using non-linear techniques like the MCT can help provide us with a better understanding of the dynamic behaviour of bio signals, beyond the limited information provided by traditional statistical methods.

**Funding**

Project funded by the Autonomous Government of Castilla y Leon and Carlos III Health Institute.

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