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Transcutaneous carbon dioxide during sleep-disordered breathing

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ABSTRACT

Respiratory drive is tightly controlled by the carbon dioxide levels. We tested the hypothesis that sequences of sleep apnoea (obstructive, central or mixed), hypopnoea and flow limitation are characterized by different levels of transcutaneous CO_2 ($PtcCO_2$). Polygraphic recordings ($n = 555$) from patients with suspected sleep-disordered breathing (SDB) were retrospectively screened to find sequences (5 min or 10 events) of both SDB and steady breathing. Eighty-eight SDB sequences from 44 patients were included and $PtcCO_2$ and SpO_2 values were collected. $PtcCO_2$ values during sequences were normalized by setting wakefulness level as 100%. In terms of $PtcCO_2$, apnoea sequences with central component (central ($n = 7$) and mixed ($n = 3$) apnoea) did not differ from wakefulness (102.0% vs 100%, $p = 0.122$) whereas obstructive apnoea (105.8%, $p < 0.001$) and hypopnoea did (105.4%, $p < 0.001$). $PtcCO_2$ during flow limitation was higher than that during any other sequence, including steady breathing (112.2% vs 108.4%, $p = 0.022$). Continuous $PtcCO_2$ monitoring during sleep adds to the understanding of different SDB phenotypes.

1. Introduction

Recording the arterial oxyhaemoglobin saturation (SaO_2) during sleep is a standard method to monitor the effect of sleep-disordered breathing (SDB) on arterial oxygen content. Monitoring the carbon dioxide during sleep is technically more demanding and its interpretation more complex. Therefore, the carbon dioxide is less frequently monitored during standard polysomnography (PSG) and its physiology less understood. Since carbon dioxide has important physiological roles including controlling pH and local perfusion through nitric oxide production (Lavi et al., 2003), better understanding of carbon dioxide physiology during sleep is needed.

Carbon dioxide is usually measured to detect hypoventilation during sleep (Pautrat et al., 2015). Gold standard is the arterial partial pressure of carbon dioxide ($PaCO_2$), but repetitive samples are difficult to obtain during sleep. Therefore, surrogate measures are used. End-tidal carbon dioxide ($PetCO_2$) provides breath-to-breath measurement, but low tidal volumes or mouth breathing can distort the results. Transcutaneous carbon dioxide ($PtcCO_2$), which reflects both ventilation and perfusion at the periphery (Stock, 1988; Clark et al., 1992), is not directly affected by mouth breathing or mask ventilation, but slow response time affects the timing in the analysis of individual respiratory events (Janssens et al., 1998; Kesten et al., 1991). Comparison between these different methods is difficult since they measure carbon dioxide at different sites and different phases of CO_2 production, diffusion, buffering or transport. Therefore, one CO_2 signal should not only be used as an estimate of another, since each signal has value in its own right. The $PtcCO_2$ signal is closest to the CO_2/pH environment at the tissue level, which in many clinical situations would be more useful than $PaCO_2$, if understood and interpreted accordingly.

We previously introduced the concept of $PtcCO_2$ plateau, defined as steady level of $PtcCO_2$ associated with steady breathing

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during sleep (Rimpilä et al., 2014). This plateau was shown to differentiate two phenotypes of upper airway flow limitation. The aim of the present study was to assess: (1) whether $PtcCO_2$ measurement is sensitive enough to detect differences between SDB types and (2) if so, how the $PtcCO_2$ levels associated with different phenotypes of SDB relate to the $PtcCO_2$ levels measured during wakefulness and the plateau $PtcCO_2$ during sleep. We hypothesized that each breathing type has a distinct $PtcCO_2$ level.

2. Methods

2.1. Ethical approval and patients

Initially, 555 cardio-respiratory sleep recordings with $PtcCO_2$ measurement performed between June 2005 and May 2007 in Tampere University Hospital, Tampere, Finland, were used for the study. All patients had previously been studied according to the standard clinical practice, without any modification for research purposes. Approval of the institutional ethics committee was therefore not required according to Finnish legislation.

2.2. Measurements

The cardiorespiratory recordings included overnight measurement of arterial oxyhaemoglobin saturation from pulse oximetry (SpO_2), nasal flow (prongs), anterior tibial electromyography (EMG), body position, respiratory efforts (uncalibrated thoracic and abdominal respiratory inductance plethysmography) and snoring (piezoelectric sensor) (Somnologica, Medcare Flaga hf, Reykjavik, Iceland). The partial pressures of CO_2 and O_2 were measured transcutaneously with a dual sensor, (TCM4, Radiometer, Copenhagen, Denmark). Device was calibrated with fixed gas composition (CO_2:7.5%, O_2:20.9%, N_2:71.6%) before sleep studies. The sensor was attached to upper chest next to sternum and warmed up to 43.0 °C, at which temperature the sensor was kept in the same location for the duration of the night. Online recording of the digital output of the TCM4 device with custom written software (TCM4ebm by Jussi Virkkala) ensured full synchronization and integration of the $PtcCO_2$ signal with Somnologica. Background information such as age, gender and BMI were collected from patient records. Arterial blood gas values were not available.

2.3. Design

This study is a database analysis of cardiorespiratory sleep recordings from patient population with suspected SDB. The study consisted of two phases. First, screening of the patient population for SDB sequences and normal breathing, and second the analysis of the effect of different types of SDB sequences on $PtcCO_2$ and SpO_2 levels. A recording was included to the study if all of the following sequences were identified: (1) a sequence of undisturbed normal breathing during evening wakefulness, (2) a sequence of steady breathing with minimal flow-limitation during sleep, and (3) one or more sequence(s) of cyclic SDB (central, mixed and obstructive apnoea or hypopnea). After inclusion, the $PtcCO_2$ traces were uncovered and recordings with insufficient $PtcCO_2$ quality: detached sensor or air leak within sensor, extremely low (below 3.0 kPa) or high (above 7.0 kPa) levels, suspicion of excessive overnight signal drift (more than 1.0 kPa difference between evening and morning wakefulness) or incomplete signal (morning/evening values missing), were excluded.

2.4. Sequence selection

Unfiltered nasal pressure signal, nasal flow signal with square root transformation and signal from snoring sensor were used to score the breathing. Wakefulness sequence with normal breathing was identified in the beginning of the recording, before lights-off mark. Sequences of steady breathing with minimal flow-limitation were characterized by breathing with stable amplitude and frequency and selected from period between wakefulness in the evening and clear awakening in the morning. Minimal flow-limitation (the inspiratory flow contour is not completely round) without snoring, and absence of major body movements were required to ensure that the sequence occurred during sleep. Episodes with waxing and waning patterns were not accepted. When more than one sequence of steady breathing was identified, the one with greatest stability was selected.

Inspiratory flow-limitation sequence with or without snoring was also included in the analysis when present. Identification of flow-limitation was based on typical inspiratory peaks and flattening of the inspiratory flow (Aittokallio et al., 2001), associated with signs of increased respiratory effort on the thoraco-abdominal belts.

Sequences of cyclic SDB events, repeating with similar pattern, were scored by using the following criteria: (1) the sequence length should be five minutes or more, or contain ten or more similar individual events; (2) the consecutive events within the sequence had to resemble each other in terms of their length and respiratory pattern. At least 50% of the respiratory events had to have the same classification (central, mixed, obstructive or hypopnea). Sequences were classified according to their most frequent event type. The respiratory events were scored apnoea, if they had a 90% reduction in inspiratory amplitude for a minimum duration of ten seconds. Episodes of hypopnoea were required to have 30% reduction in inspiratory amplitude for a minimum duration of ten seconds with no desaturation criteria. However, desaturation of 3% or more was noted when present. For the purpose of the study, one representative sequence of each type from each patient was included to the analysis. In the case of several candidate sequences the one with greatest stability and highest proportion of events with same classification was selected.

2.5. Data analysis

There is marked inter-individual variation in the $PtcCO_2$ readings (Fukui et al., 1993). Therefore, instead of comparing the absolute levels of the $PtcCO_2$ during various types of SDB, we analyzed the differences between sequences using either absolute ($\Delta PtcCO_2$, kPa) or relative (%) scales by fixing the $PtcCO_2$ levels observed during wakefulness as zero kPa or 100%. Additionally, the relative $PtcCO_2$ levels (%) during sequences were also compared when the $PtcCO_2$ during steady breathing with minimal flow-limitation was set to 100%.

Pre-event SpO_2 levels (SpO_2 start) and desaturations related to individual respiratory events in sequences with cyclic nature were determined and average values were used in the analysis. For stable sequences (wakefulness, steady breathing and flow limitation) median values were used. Once the final study population was confirmed the apnoea–hypopnoea-indices (AHI) were determined according to the latest consensus statement with the exception of arousal criterion for hypopnoea, which could not be used (Berry et al., 2012). Leg movements and PLM were scored according to the WASM criteria (Zucconi et al., 2006) with the exception that leg movements occurring within ten seconds on both sides of apnoea termination were considered to have an association and were excluded from the PLM index.

2.6. Statistical methods

The effect of gender on $PtcCO_2$ values was tested with Mann–Whitney *U* test and the effect of age with univariate ANOVA.