Influence of sampling interval on the evaluation of nocturnal blood pressure in subjects with and without obstructive sleep apnoea

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ABSTRACT: Blood pressure (BP) variability during sleep is high in obstructive sleep apnoea syndrome (OSAS). How BP sampling interval affects the estimate of mean nocturnal BP in OSAS and control subjects was investigated.

Nine subjects with apnoea/hypopnoea index (AHI) <5 and 18 OSAS patients with AHI >30 underwent nocturnal polysomnography with beat-by-beat BP monitoring. Mean nocturnal BP was evaluated averaging: a) all systolic (Ps) and diastolic (Pd) BP values; b) Ps and Pd sampled every 5, 10, 15, 20, and 30 min. The sampling starting point was repeatedly shifted, and several mean BP estimates for each sampling interval were obtained. Differences (∆Ps and ∆Pd) between means obtained by sampling BP and by averaging all BP values were calculated.

In both groups ∆Ps and ∆Pd scatter increased as sampling interval increased; their variance was always higher in OSAS subjects (p<0.001). Over 95% of ∆Ps and ∆Pd were <5% of the beat-by-beat mean values at all sampling intervals in controls, but this occurred only at sampling intervals >10 min in OSAS subjects.

To conclude, for each blood pressure sampling time, a larger number of inaccurate nocturnal mean BP were obtained in obstructive sleep apnoea syndrome than in control subjects. Obstructive sleep apnoea syndrome subjects require more frequent blood pressure measurements to obtain a similar accuracy in nocturnal blood pressure evaluation.

Twenty-four-h blood pressure (BP) assessment is usually performed by ambulatory blood pressure monitoring (ABPM), which allows repeated BP measurements at regular intervals. Comparison of beat-to-beat BP measurements and sampled measurements was proved reliable in hypertensive subjects unselected for sleep problems [1]. In particular, nocturnal BP measurements taken every 30 min accurately reflected mean nocturnal BP calculated with continuous BP monitoring [2]. In addition, mean nocturnal BP did not differ if calculated on measurements taken every 15 or every 60 min [3].

Obstructive sleep apnoea syndrome (OSAS) is a condition characterized by the recurrence of episodes of upper airway obstruction during sleep, which are usually terminated by an arousal with heavy snoring, hyperventilation, and a sudden transient rise in heart rate and BP [4]. In addition to the repeated nocturnal BP augmentations, OSAS is often associated with diurnal hypertension [4]; available data about reversibility of systemic hypertension by long-term OSAS treatment are still contradictory [5–11]. Cardiovascular accidents, possibly linked to either diurnal or nocturnal high BP, are considered common complications of this syndrome and possible causes of death [12]. A correct evaluation of BP in OSAS could help to identify subjects at highest risk of cardiovascular complications and to better understand the effect of OSAS treatment on BP. However, in patients with OSAS the occurrence of apnoeas during sleep increases nocturnal BP variability [13], and in particular its short-term variability [14]. Therefore intervals between BP measurements as long as 30 or 60 min, commonly used for the assessment of mean nocturnal BP, could not be enough to warrant a correct assessment of mean nocturnal BP in these patients.

In this study, how the assessment of mean nocturnal BP is affected by different BP sampling rates in OSAS and in control subjects was evaluated.

Patients and methods

Eighteen patients, aged 47±6/9 (mean±sd) yrs, referred to our sleep laboratory for a strong suspicion of OSAS, and nine healthy subjects, aged 45±3/8 yrs were studied.

A standard nocturnal polysomnography was performed using a computerized system (Somnostar 4100; Sensormedics, Yorba Linda, CA, USA). At the same time BP was continuously monitored by a 2300 Finapres™ BP monitor (Ohmeda, Louisville, CO, USA). This device works with a dynamic servo set-point adjuster, frequently checking the
set-point during short interruptions of the BP recording in an automatic fashion [15]. The Finapres\textsuperscript{TM} was automatically turned off for 5 min every 40 min to avoid finger discomfort and local vascular or fluid changes that could alter estimation of BP. The BP signal was recorded on tape (TEAC XR-5000, Japan).

Sleep was staged according to standard rules [16]. Total time in bed (TIB), total sleep time (TST) and sleep efficiency (total sleep time/time in bed \times 100) were calculated. Apnoeas were considered as cessation of oronasal airflow lasting at least 10 s; hypopnoeas as reduction in the airflow signal lasting at least 10 s associated to a ≥3% oxyhaemoglobin saturation (SaO\textsubscript{2}) fall or followed by an arousal [16]. Apnoea plus hypopnoea frequency was calculated both per hour of sleep (AHI) and per hour of time in bed (AH/TIB).

The BP signal was acquired at a sampling rate of 200 Hz on a personal computer for off-line analysis. A program of analysis was developed using the Matlab software (Math Works Inc., Natick, MA, USA). After visual inspection of the BP signal to eliminate artefacts, systolic and diastolic BP values, in mmHg, were obtained, and mean nocturnal systolic ($P_s$) and diastolic ($P_d$) BP values were calculated: a) on all the recorded nocturnal heart beats; b) on single heart beats sampled every 5, 10, 15, 20, and 30 min. Mean values calculated averaging all nocturnal heart beats were considered "real" reference values, while mean values calculated averaging the single sampled heart beats were considered as "estimates". To account for effects of different starting points in the sampling, the starting point was shifted several times by one minute for every sampling interval so as to obtain, for each subject, up to 5, 10, 15, 20, and 30 mean estimated BP values, respectively, for the different sampling intervals (fig. 1). Due to the occurrence of autocalibrations, temporary turn-offs or artefacts on the Finapres\textsuperscript{TM} signal, the number of points actually sampled for the calculation of some mean values had to be lower than expected; a threshold of a minimum of 60, 30, 20, 15, and 10 points for the sampling intervals of 5, 10, 15, 20, and 30 minutes, respectively, for a mean BP estimate to be accepted was established. In all subjects and for all sampling intervals the number of mean nocturnal BP estimates and the number of points averaged for each estimate was always the same for systolic and diastolic values.

To evaluate the error due to each sampling interval, the following values were calculated:

\[
\Delta D = \text{mean estimated } P_s - \text{mean real } P_s
\]

\[
\Delta D = \text{mean estimated } P_d - \text{mean real } P_d
\]

\[
\Delta D\% = (\text{mean estimated } P_s - \text{mean real } P_s)/\text{mean real } P_s \times 100
\]

\[
\Delta D\% = (\text{mean estimated } P_d - \text{mean real } P_d)/\text{mean real } P_d \times 100
\]

Coefficients of variation of beat-by-beat $P_s$ and $P_d$ were calculated for every normal and OSAS subject. Mean±SD of $\Delta D$ and $\Delta D\%$ were calculated separately for the OSAS population and for the controls for each sampling interval. Differences in variance in $\Delta D$ and $\Delta D\%$ values at each sampling interval between the control and the OSAS group were evaluated by the F test. Differences in other variables were tested by two-tailed unpaired t-test or U-Mann Whitney test. Correlations between variables were evaluated by linear regression analysis. A $p<0.05$ was considered significant.

### Results

Control and OSAS groups did not differ in TIB and TST, while sleep efficiency was slightly, but significantly, higher in the OSAS group. AHI was on average very high in the OSAS group, although with a large range (47–144). Real mean BP values were higher in the OSAS group than in controls (table 1).

The number of mean nocturnal BP estimates and the number of points used for the calculations are shown in table 2. At all sampling intervals, there was no difference between groups in the mean number of points averaged per mean BP estimate or in the average number of mean BP estimates per subject. There was no correlation between the number of points used for the calculation of each mean BP estimate and the absolute values of $\Delta D$.

![Fig. 1. Schematic representation of the method used to sample blood pressure values.](image)

Table 1. Sleep and blood pressure characteristics in the studied subjects

<table>
<thead>
<tr>
<th>Measurement</th>
<th>Controls</th>
<th>OSAS</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>TIB min</td>
<td>390±48</td>
<td>394±52</td>
<td>NS</td>
</tr>
<tr>
<td>TST min</td>
<td>301±55</td>
<td>325±52</td>
<td>NS</td>
</tr>
<tr>
<td>Sleep efficiency %</td>
<td>76.9±6.9</td>
<td>82.6±6.4</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>AHI</td>
<td>2.5±2.4</td>
<td>81.7±22.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>AH/TIB h⁻¹</td>
<td>1.9±1.9</td>
<td>67.7±19.9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mean real $P_s$ mmHg</td>
<td>118±20</td>
<td>140±15</td>
<td>&lt;0.005</td>
</tr>
<tr>
<td>Mean real $P_d$ mmHg</td>
<td>63±10</td>
<td>78±11</td>
<td>&lt;0.002</td>
</tr>
<tr>
<td>Beat-by-beat $P_s$ CV</td>
<td>0.06±0.01</td>
<td>0.16±0.02</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Beat-by-beat $P_d$ CV</td>
<td>0.07±0.01</td>
<td>0.20±0.03</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Data are shown as mean±SD. OSAS: obstructive sleep apnoea syndrome; TIB: time in bed; TST: total sleep time; AHI: apnoea/hypopnoea index; AH/TIB: apnoea/hypopnoeas per hour of TIB; Mean real $P_s$ and $P_d$: mean systolic and diastolic blood pressure calculated on all nocturnal heart beats; CV: coefficient of variation. NS: not significant.
and $D$ mean nocturnal time of 30 min was sufficient to obtain each sampling interval. In the control group, a sampling did not exceed a range of <2.5, 5, 7.5, 10, and 12.5% at as the sampling interval increased. However, variance of sampling rates, and their scatter increased progressively $D$ both groups, mean OSAS and control subjects are shown in figure 2. Within any subject.

In controls for each sampling interval ($p < 0.001$).

Figure 3 shows the frequency of $\Delta P_s$% and $\Delta P_d$% that did not exceed a range of ±2.5, 5, 7.5, 10, and 12.5% at each sampling interval. In the control group, a sampling time of 30 min was sufficient to obtain >95% of both mean nocturnal $P_s$ and $P_d$ estimates with an error ($\Delta P_s$% and $\Delta P_d$%) in the range ±5%. Conversely, in the OSAS group the sampling interval had to decrease to at least 10 min for a comparable level of accuracy; however, a sampling interval of 30 min was enough even in this group to obtain >95% of both mean nocturnal $P_s$ and $P_d$ estimates with an error in the range ±10%.

In the OSAS group, neither AHI nor AH/TIB were correlated to beat-by-beat $P_s$ or $P_d$ coefficients of variation; similarly, they were not correlated to mean $\Delta P_s$, $\Delta P_d$, $\Delta P_s$% or $\Delta P_d$%; expressed in absolute values.

**Discussion**

In non-OSAS subjects it has already been shown that BP sampling intervals of 30, or, sometimes, even 60 min are accurate enough to evaluate mean nocturnal BP values [1–3, 18]. In OSAS subjects, despite the well-known fact that BP during sleep has a much greater short-term variability than in normal subjects [14], similar intervals between nocturnal BP measurements have often been used when performing ABPM [7–11, 19–21], but the expected accuracy of the estimate of mean BP was not evaluated before this study.

The present aim was to evaluate to what extent ABPM may provide erroneous mean BP estimates due to an insufficient sampling rate. Rather than fully validating the use of ABPM in OSAS, this study regarded one of the aspects that influences the accuracy of ABPM in the assessment of mean BP, i.e. the length of intervals between BP measurements, in subjects with and without OSAS. In each of 18 OSAS and 9 control subjects several mean values of nocturnal BP were calculated, by sampling heart beats at different rates, and by changing repeatedly the heart beat from which sampling was started for each sampling rate. In this way the distribution of the difference between mean values obtained from sampled heart beats and from beat-to-beat measurements could be evaluated. This allowed to assess the probability to obtain values differing by more than predetermined thresholds from the real ones at different sampling rates. Such probability was found much higher in OSAS than in normal subjects.

In both OSAS and control subjects most mean BP estimates were close to mean real BP at all the tested sampling rates, but a very important difference between patients and controls was found in the scatter of the differences between estimated and real mean BP values: standard deviations of both $\Delta P_s$ and $\Delta P_d$ increased progressively as sampling interval was increased, as expected, while they remained about two-fold higher in the patients than in the controls at all the sampling intervals. This may have resulted from the higher BP variability in the patients. Since every apnoeic cycle is associated with a transient BP increase, the accuracy of mean nocturnal BP estimate could have been proportional to the rate of apnoeic and

**Table 2. – Characteristics of blood pressure samplings**

<table>
<thead>
<tr>
<th>Sampling interval min</th>
<th>No. of $P_s$ or $P_d$ values averaged/mean $P_s$ or $P_d$ estimate</th>
<th>No. of estimated $P_s$ and $P_d$ means/subject</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Controls</td>
<td>OSAS</td>
</tr>
<tr>
<td>5</td>
<td>69.2 (60–83)</td>
<td>71.2 (60–91)</td>
</tr>
<tr>
<td>10</td>
<td>34.3 (30–41)</td>
<td>35.5 (30–46)</td>
</tr>
<tr>
<td>15</td>
<td>24.2 (20–31)</td>
<td>24.0 (20–31)</td>
</tr>
<tr>
<td>20</td>
<td>17.1 (15–21)</td>
<td>17.5 (15–23)</td>
</tr>
<tr>
<td>30</td>
<td>11.8 (10–15)</td>
<td>11.8 (10–15)</td>
</tr>
</tbody>
</table>

Data presented as mean (range). $P_s$: systolic pressure; $P_d$: diastolic pressure; OSAS: obstructive sleep apnoea syndrome.

$\Delta P_s$, $\Delta P_s$% or $\Delta P_d$% for any tested sampling interval in any subject.

Mean $\Delta P_s$ and $\Delta P_d$ values for each sampling interval in OSAS and control subjects are shown in figure 2. Within both groups, mean $\Delta P_s$ and $\Delta P_d$ values were similar at all sampling rates, and their scatter increased progressively as the sampling interval increased. However, variance of both $\Delta P_s$ and $\Delta P_d$ was significantly higher in OSAS than in controls for each sampling interval ($p<0.001$).

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**Fig. 2. – Means and so of a) $\Delta P_s$ and b) $\Delta P_d$ values in control (□) and obstructive sleep apnoea (○) subjects for each sampling interval. $\Delta P_s$ and $\Delta P_d$: differences in mmHg between the mean nocturnal blood pressure values, respectively systolic and diastolic, obtained from sampled single heart beats and from all heart beats.
hypopnoeic episodes. In our group of patients, despite AHI and AH/TIB showed a large range of values, neither of them was correlated to $P_s$ or $P_d$ coefficient of variation; as a consequence, they were not correlated to the accuracy of BP estimates (evaluated by $\Delta P_s$, $\Delta P_d$, $\Delta P_s\%$, and $\Delta P_d\%$). These findings may be explained by the fact that BP variability does not depend only on the number, but also on the amplitude of BP swings. In fact, a large intersubject variability was shown in the amplitude of BP swings associated with apnoeic episodes, possibly related to factors such as age or $\text{Sa}_O_2$ fall [22].

The number of points averaged to calculate mean nocturnal BP estimates was similar among control and OSAS subjects. In both groups, within each sampling interval taken in consideration, no increase in the difference between estimated and real mean nocturnal BP was observed as the number of points averaged to calculate mean BP estimate decreased. Therefore, the threshold of number of BP points selected to accept mean BP estimates was appropriate to give an indication of the effect of various lengths between BP measurements, such as those used during ABPM, on the accuracy of nocturnal BP estimate in OSAS and non-OSAS subjects. Furthermore, even in the assessment of mean BP by ABPM occasional failures in BP measurements often occur: thus, the number of points we sampled for mean BP estimates at each sampling interval could reflect the number of measurements actually performed by ABPM when the same interval between measurements is set.

Two points about differences between the two groups deserve some discussion. First, BP was higher in the OSAS group: however, the larger scatter in mean BP estimates among the OSAS subjects was evident both when BP differences were evaluated in mmHg, and as percentage of the mean real values; this suggests that BP levels did not influence the results. Second, sleep efficiency was lower in the control group. More prolonged wakefulness periods may have caused an increase in BP variability, since in normal subjects BP variability is higher during wakefulness than during sleep [23]; a similar effect may have followed more frequent shifts between sleep and wakefulness; the increase in BP variability, in turn, may have decreased the accuracy of BP estimates. Therefore, for similar values of sleep efficiencies in normal and OSAS subjects, differences in mean nocturnal BP estimate accuracies could be slightly larger, but not smaller, than the ones found: this would not modify the conclusions about a much greater probability of inaccurate BP estimates by ABPM in OSAS than in normal subjects.

Several studies on 24-h BP by ABPM in OSAS have recently been published. Some of them were aimed at assessing the effect of long-term treatment on BP levels [6–11]; in only one of these studies was a 15 min sampling time used for nocturnal BP [6], while in the others a

![Fig. 3. - Percentage of measurements with $\Delta P_s\%$ (a,b) and $\Delta P_d\%$ (c,d) not exceeding ±2.5, 5, 7.5, 10, and 12.5%. a) and c) in the whole sample of controls; b) and d) in the whole sample of obstructive sleep apnoea subjects. $\Delta P_s\%$ and $\Delta P_d\%$ = differences between the mean nocturnal blood pressure values, respectively systolic and diastolic, obtained from sampled single heart beats and from all heart beats, expressed as percentage of the mean values calculated on all heart beats. Different symbols indicate different sampling intervals; ◯ : 5 min; ◇ : 10 min; ◆ : 15 min; ◊ : 20 min; + : 30 min.](image-url)
30-min [7, 9–11] or 60-min sampling time was chosen [8, 21]. Inconsistent results have been reported, not only from paper to paper but also among patients of single studies. Other studies investigated how often OSAS patients could be considered "nondippers" [24]; also in this case BP sampling intervals of either 15 [25, 26], 30 [11, 19, 20], or 60 min [21] were used. Although the differences among the findings of the studies did not appear related to the chosen sampling rate, a too long interval between measurements may have contributed to the inconsistencies of some results.

Before considering any estimated value as acceptable, it should be kept in mind what degree of accuracy is expected from the measurement, and what is the probability that the measurement reaches the required accuracy. For example, if an error within 10% mean nocturnal BP in a single night is required with a ≥95% probability, both in normal and in OSAS subjects a 30-min sampling interval would be accurate enough. However, if an error within 10% is required in the assessment of the difference between mean nocturnal BP of two different nights, then the highest error within each nocturnal measurement must be kept within ±5%, because the variance of the difference between two random variables is equal to the sum of the variances of each variable; in order to have the same probability that this threshold is not overcome, in normal subjects the 30-min sampling interval would remain accurate enough, providing further evidence that a 30-min interval between nocturnal measurements is adequate for non-OSAS subjects, while in the OSAS subjects the sampling interval should decrease to at least 10 min.

The authors are aware that too frequent BP measurements during ABPM may cause sleep disruption [27–30] that, according to some Authors, in normal subjects [29] as well as in snorers [30] may cause an increase in BP with an alteration particularly in the evaluation of the systolic values. According to the following data collected by the authors, consequences of cuff inflations on sleep structure and BP behaviour may be much less important in severe OSAS subjects than those reported in non-OSAS subjects. In five OSAS subjects (age 40–57 yrs, AHI 71–83) ABPM measurements were taken every 15 min during polysomnography. A small hose was placed under the cuff and connected to a pressure transducer: the signal recorded during compression and decompression of the hose allowed to exactly identify when the cuff was inflated and deflated. Because of the effect of apnoeic cycles in causing arousal, the independent arousing effect of cuff inflation (that usually lasted more than one apnoea with the following arousal) was difficult to detect. As ABPM-induced arousals the occurrence, during or immediately after the BP measurement by the ABPM device, of: a) a change in breathing pattern due to prolonged awakening; b) a shortening of apnoea following cuff inflation with a smaller SaO2 fall compared to the preceding apnoeic cycles (∆SaO2 >3%) were considered. Altogether, 141 BP measurements were automatically performed. Among them, 19 occurred during wakefulness and a stable breathing pattern. Of the remaining 122 measurements, 20.5%, (range per subject: 16–32%) were classified as contributing to the occurrence of arousals or awakenings: all except two, were identified just by small reductions in SaO2 falls, while apnoeas continued to recur. The much lower rate of cuff inflation-related arousals in these subjects than in those previously studied [27, 29, 30] may be interpreted as a consequence of a high resistance to arousing stimuli in severe OSAS, due to a high degree of sleepiness. Therefore, despite the objective difficulty in assessing the arousing effect of cuff inflations when apnoeas recur continuously during sleep, the data indicate that the frequency of BP measurements by ABPM in severe OSAS subjects should be kept higher than in normal subjects, and that the results of this study can be taken in consideration before settling the interval between BP measurements during ABPM in these subjects.

Conclusions

Sampling interval heavily affects the probability to obtain accurate estimates of mean nocturnal blood pressure values, especially in obstructive sleep apnoea syndrome. In severe obstructive sleep apnoea syndrome, an accuracy in mean nocturnal blood pressure evaluation similar to normal subjects requires a shorter blood pressure sampling interval than in normal subjects. The selection of an appropriate sampling interval should be based on the degree of accuracy that is required in the assessment of blood pressure in each subject.

References

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