# Decrease in blood pressure during continuous positive airway pressure treatment for obstructive sleep apnoea: still searching for predictive factors

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**High blood pressure (BP) and non-dipping 24-hour BP profile may help to predict BP decrease after obstructive sleep apnoea treatment by CPAP. However, specific, highly reproducible traits associated with BP responsiveness to CPAP must still be identified.** http://bit.ly/2LbS4uV

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A very large number of studies have highlighted complex relationships between obstructive sleep apnoea (OSA) and blood pressure (BP). It is now established that OSA can increase BP with peculiar characteristics during the day and at night. Diurnal BP may show a sustained increase and, sometimes, resistance to drug therapy. Nocturnal BP almost always shows an increased variability due to short repeated peaks after apnoeas, which may result in an increase in its average values. This explains the non-dipping BP profile often found in OSA when BP is monitored noninvasively over 24 h by ambulatory BP monitoring (ABPM) [1]. Since the nocturnal peaks occur at the resolution of apnoeas, it may be expected that abolition of apnoeas acutely reduces nocturnal BP variability and average BP levels, which may result in increased nocturnal BP dipping or in a switch from a non-dipping to a dipping pattern. However, things are not that simple. Acute continuous positive airway pressure (CPAP) in severe OSA decreased BP variability in non-REM (rapid eye movement) stage 2 and REM sleep, as expected, but did not affect mean nocturnal BP or baroreflex sensitivity [2].

Meta-analyses on the effects of medium- to long-term OSA treatment by CPAP have shown that BP on average responds with a little reduction during the day and a slightly larger reduction at night [3–6]. By contrast, single studies showed variable results due to a very high interindividual variability in the BP response to CPAP. Factors like normal baseline BP [6], mild respiratory disorders [4], low cardiovascular responsiveness to autonomic activation [7] or lack of sleepiness [8], may attenuate the effect of apnoea abolition or give rise to unexpected findings. For example, some authors have described a small increase in nocturnal BP in some OSA patients [9, 10], and hypothesised the existence of some "OSA phenotypes" with specific BP responses to CPAP [9]. Identification of such phenotypes would be helpful for better and individualised patient management. However, this study was small, and the data need confirmation in larger samples.

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In this context, new data provide additional information on the effects of CPAP according to the 24-h BP profile. In this issue of the *European Respiratory Journal*, Sapiña-Beltrán *et al.* [11] report a secondary analysis of data collected in the randomised controlled trial (RCT) of the "CEPECTA" cohort, consisting of subjects with a new diagnosis of systemic hypertension based on office BP measurements and OSA diagnosed as apnoea–hypopnoea index >15 events·h$^{-1}$. No patient was on treatment for hypertension during the study. Patients were randomised to active or sham CPAP treatment and underwent ABPM at diagnosis and after 12 weeks of OSA treatment [12]. The primary outcome of the original study was to assess changes in diurnal and nocturnal BP after CPAP. The results of intention-to-treat analysis showed significant but small decreases in mean 24-h and nocturnal BP after active treatment. Analysis restricted to patients with ABPM-proven hypertension or good compliance to CPAP treatment showed slightly greater effects.

In the study by Sapiña-Beltrán *et al.* [11], BP changes were separately analysed according to occurrence of dipping or non-dipping BP profile at baseline in the same patients as in the original study. At baseline, the dipping and non-dipping groups did not differ in 24-h BP values, but the non-dipping group had a significantly higher nocturnal BP. A significant difference in the response to CPAP treatment between the two groups was found for the 24-h and the nocturnal BP, which decreased only in the non-dipper group. Daytime BP did not decrease significantly in either group and altogether did not show a differential response. The results were similar when considering separately the patients with hypertension confirmed by the 24-h ABPM or the whole group of patients, which included a subgroup with normal 24-h ABPM profile, *i.e.* patients with white coat hypertension. The authors emphasise that their results were relevant to non-dipping hypertensive patients, which suggests that OSA patients with these characteristics could be a target for CPAP treatment, due to its significant beneficial effects on BP. It is unclear, however, how specific the described effect of CPAP for non-dipping hypertensive patients could be.

Many other authors have investigated changes in BP profile after CPAP treatment. The majority of studies described an increased BP dipping due to a preferential effect of CPAP on nocturnal rather than on diurnal BP [1], but many studies were small, uncontrolled or non-randomised. Among RCTs on the effects of CPAP on BP, in a recently published paper on normotensive subjects, Sapiña-Beltrán *et al.* [10] reported that the subgroup of their patients with a non-dipping 24-h BP profile significantly decreased their nocturnal BP, which could suggest that not only hypertensive, but also normotensive subjects tend to decrease their nocturnal BP if they are non-dippers. By contrast, a smaller RCT on hypertensive OSA subjects had shown that patients treated with CPAP showed a nonsignificant trend to turn their 24-h BP profile from non-dipping to dipping [13]. Moreover, of two RCTs on patients with resistant hypertension [14, 15], only one [14] showed significant changes in nocturnal BP and a significant increase in the number of dippers.

The current study by Sapiña-Beltrán *et al.* [11] has several strengths, *i.e.* the elegant RCT design, the completeness of the data, the considerable sample of patients and the lack of any interference from antihypertensive drug therapy. These characteristics could explain the differences between its results and the results of some (not all) previous studies. However, once we accept that hypertensive non-dipper OSA patients benefit from CPAP treatment, it remains uncertain how specific the BP response of these patients is. Studies comparing behaviour of patients with different diurnal and nocturnal BP and with different 24-h BP profiles could help to clarify if phenotypes with different BP responses really exist. In addition, given the complex pathophysiology of systemic hypertension, it is surprising that factors such as severity of nocturnal hypoxaemia or sleep fragmentation were seldom considered in analysis of results of RCTs. Interestingly, a study in patients with resistant hypertension and OSA identified some microRNAs predictive of the clinically positive response of BP to CPAP treatment [16].

The most recent guideline on treatment of OSA patients published by the American Academy of Sleep Medicine suggests using CPAP to treat hypertensive OSA patients, but gives this suggestion as conditional, due to the need for more evidence, especially concerning the selection of patients more likely to have a BP reduction [17]. More studies similar to that of Sapiña-Beltrán *et al.* [11] would be of high clinical interest to fill the gap in our knowledge and for better targeted OSA therapy. However, given the complexity of the problem, it seems appropriate to obtain 24-h BP pattern by ABPM in all OSA patients [18] and consider the effects of different OSA "traits" which can possibly modulate BP during sleep.

Conflict of interest: None declared.

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