





## **EDITORIAL**

## Sleep apnea in focus

## A apneia do sono em foco

Obstructive sleep apnea (OSA) is characterized by repetitive episodes of partial or complete upper airway obstruction during sleep. The immediate or primary consequences of OSA occurs during sleep and include cyclic asphyxia (i.e. decreases in arterial oxygen + increases in arterial  $CO_2$ ), generation of excessive negative intrathoracic pressure against the occluded airways and fragmented sleep. <sup>1</sup> The daytime symptoms that may accompany OSA are multiple and include excessive daytime somnolence, tiredness, loss of quality of life and loss of memory. OSA may trigger a cascade of intermediate mechanisms that are potentially harmful to the cardiovascular and metabolic system, and include sympathetic over activity, systemic in ammation, alterations in blood pressure control, insulin resistance, endothelial dysfunction and atherosclerosis. <sup>2-4</sup> OSA may trigger or contribute to several diseases, including hypertension, diabetes and cardiac arrhythmias. All these intermediate mechanisms may help to explain the increased mortality associated with OSA that can be reverted with the treatment with continuous positive airway pressure (CPAP). <sup>5</sup> The prevalence of OSA in the general population varies according to the disease criteria and technology used to detect respiratory events. One recent epidemiologic study in the city of Sao Paulo, Brazil, found that OSA syndrome according to current guidelines (i.e. apnea hypopnea index AHI > 5 events/h plus symptoms or AHI > 15 events/h independent of symptoms) was 32.8 %.6 Despite the high prevalence of OSA and the several consequences if left untreated, it is estimated that 85% of the patients are not diagnosed.<sup>2</sup> In this issue of the Portuguese Journal of Pulmonology, 2 fundamental aspects of OSA regarding diagnosis and treatment were reported and deserves close attention.

The search for questionnaires that will help to diagnose OSA remains a major challenge in the field. The Berlin questionnaire is a popular one used to screen and stratify patients in low and high risk for OSA and is based on

questions organized in 3 categories related to snoring and witnessed apneas, daytime tiredness and the presence of hypertension or obesity. Patients who are positive in at least 2 categories are considered as having high risk for OSA.7 The Berlin questionnaire has been validated and is used in Brazil to estimate the prevalence of OSA among truck drivers. 8,9 It is important to note that the Portuguese language from Portugal and from Brazil do present several different expressions. For instance the words used for snoring in Portugal and Brazil are different. Therefore the validation of the questionnaire in Portugal is imperative. In the rst study, Vaz et al have validated the Berlin Questionnaire to the Portuguese language by using back translation methodology.<sup>10</sup> In addition the authors have prospectively applied the questionnaire to 95 consecutive subjects referred to sleep centre with suspected OSA. The authors concluded that being in the high risk group was not a good predictor of OSA and that therefore the Berlin guestionnaire is not an appropriate screening tool for a high risk population such as the patients referred to a sleep laboratory. Therefore, for patients with a high pre test probability of OSA, the questionnaire may add little information. We have recently evaluated the characteristics and clinical predictors of OSA in a series of 99 consecutive patients followed up in a hypertension unit. <sup>11</sup> The clinical parameters included age, gender, obesity, daytime sleepiness, snoring, Berlin Questionnaire, resistant hypertension, and metabolic syndrome. The Berlin Questionnaire revealed a high sensitivity but a low speci city to predict OSA. The common theme that arises from these studies is that several patients with OSA do not present the so called typical symptoms.

In another provocative study by Loureiro et al. published in this issue of the Portuguese Journal of Pulmonology, the authors described a case series of patients with OSA and hypertension that presented a rise in blood pressure after the treatment of OSA with CPAP. <sup>12</sup> These paradoxical blood pressure responses occurred in 30 out of 508 patients

0873-2159/\$ - see front matter ' 2010 Published by Elsevier Espaæa, S.L. on behalf of Sociedade Portuguesa de Pneumologia. All rights reserved.

treated with CPAP, representing therefore 5.9% of the population. The reasons for such ndings were not clear, particularly because compliance to CPAP therapy was good, and the authors were not able to find correlations between the rise in blood pressure and any variable such as the severity of sleep apnea. One possibility is that the authors made the option to focus on a subgroup of patients that presented a raise in BP. This phenomenon is known as regression to the mean, and is related to the fact that any variable that oscillates over time will present subgroups of patients that will oscillate to one direction, while others will present oscillations in the opposite direction. <sup>13</sup> It is possible therefore that in the subgroup of patients reported, CPAP treatment was coincidental and not related to the rise in blood pressure. It is also possible that the authors would have seen a significant fall in blood pressure after CPAP treatment if they had included all 508 patients treated with CPAP. This approach would reconcile the ndings of Loureiro et al. with the literature that has consistently shown a fall in blood pressure after the treatment of OSA with CPAP. On the other hand, this approach would still not answer the question of why a small proportion presents a paradoxical blood pressure response to CPAP therapy. Another possibility is that paradoxical BP responses after CPAP may be modulated by genetic factors, in a similar way to what has been reported with anti-hypertensive drugs. <sup>14</sup> Finally, another possibility is that in that 27 out of 30 patients were treated with automatic CPAP. At least one study showed that in contrast to xed CPAP, automatic CPAP was not able to decrease blood pressure nor markers of sympathetic activity in patients with OSA. <sup>15</sup> While, it is possible only to speculate why the paradoxical response occurred, this article sheds light on what is known as individualized medicine, that focuses on differences rather then similarities between patients. In conclusion, this issue of Portuguese Journal of Pulmonology contributes to the discussion of signi cant aspects of OSA screening and complications. Moreover, it calls our attention to the importance of recognizing and treating patients with OSA.

G. Lorenzi-Filhoª,\*, P. Rodrigues Gentaª, L.F. Dragerb

 <sup>a</sup>Laboratorio do Sono, Disciplina de Pneumologia Instituto do Cora<sup>a</sup>o (InCor), Hospital das Clnicas da Faculdade de Medicina da Universidade de S<sup>a</sup>o Paulo, S<sup>a</sup>o Paulo, Brazil
<sup>b</sup>Unidade de Hipertens<sup>a</sup>o, Disciplina de Cardiologia Instituto do Cora<sup>a</sup>o (InCor), Hospital das Clnicas da Faculdade de Medicina da Universidade de S<sup>a</sup>o Paulo, S<sup>a</sup>o Paulo, Brazil

\*Corresponding author. E-mail: geraldo.lorenzi@incor.usp.br (G. Lorenzi-Filho).

## References

- 1. Bradley TD, Floras JS. Obstructive sleep apnoea and its cardiovascular consequences. Lancet. 2009;373:82-93.
- Chobanian AV, Bakris GL, Black HR, Cushman WC, Green LA, Izzo JL Jr, et al; Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. National Heart, Lung, and Blood Institute; National High Blood Pressure Education Program Coordinating Committee. Seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. Hypertension. 2003;42:1206-52.
- Drager LF, Bortolotto LA, Lorenzi MC, Figueiredo AC, Krieger EM, Lorenzi-Filho G. Early signs of atherosclerosis in obstructive sleep apnea. Am J Respir Crit Care Med. 2005;172:613-8.
- Drager LF, Bortolotto LA, Krieger EM, Lorenzi-Filho G. Additive effects of obstructive sleep apnea and hypertension on early markers of carotid atherosclerosis. Hypertension.2009; 53:64-9.
- Marin JM, Carrizo SJ, Vicente E, Agusti AG. Long-term cardiovascular outcomes in men with obstructive sleep apnoea-hypopnoea with or without treatment with continuous positive airway pressure: an observational study. Lancet. 2005;365:1046-53.
- 6. Tu k S, Santos-Silva R, Taddei JA, Bittencourt LRA. Obstructive sleep apnea syndrome in the Sao Paulo epidemiologic sleep study. Sleep Med. 2010;11:441-6.
- Netzer NC, Stoohs RA, Netzer CM, Clark K, Strohl KP. Using the Berlin Questionnaire to identify patients at risk for the sleep apnea syndrome. Ann Intern Med. 1999;131:485-91.
- Moreno CR, Carvalho FA, Lorenzi C, Matuzaki LS, Prezotti S, Bighetti P, et al. High risk for obstructive sleep apnea in truck drivers estimated by the Berlin questionnaire: prevalence and associated factors. Chronobiol Int. 2004;21:871-9.
- 9. Lemos LC, Marqueze EC, Sachi F, Lorenzi-Filho G, Moreno CR. Obstructive sleep apnea syndrome in truck drivers. J Bras Pneumol. 2009;35:500-6.
- Vaz AP, Drummond M, Caetano Mota P, Severo M, Almeida J, Winck JC. Translation of Berlin Questionnaire to Portuguese language and its application in OSA identi cation in a sleep disordered breathing clinic. Rev Port Pneumol. 2011;17(2): 59-65.
- Drager LF, Genta PR, Pedrosa RP, Nerbass FB, Gonzaga CC, Krieger EM, et al. Characteristics and predictors of obstructive sleep apnea in patients with systemic hypertension. Am J Cardiol. 2010;105:1135-9.
- Chaves Loureiro C, Drummond M, Winck JC, Almeida J. Paradoxical reaction of blood pressure on spleep apnoea patients treated with Positive Airway Pressure. Rev Port Pneumol. 2011;17(2):53-8.
- 13. Bland JM, Altman DG. Regression towards the mean. BMJ. 1994;308:1499.
- 14. Liu J, Liu ZQ, Yu BN, Xu FH, Mo W, Zhou G, et al. Beta1adrenergic receptor polymorphisms influence the response to metoprolol monotherapy in patients with essential hypertension. Clin Pharmacol Ther. 2006;80:23-32.
- Patruno V, Aiol S, Costantino G, Murgia R, Selmi C, Malliani A, et al. Fixed and autoadjusting continuous positive airway pressure treatments are not similar in reducing cardiovascular risk factors in patients with obstructive sleep apnea. Chest. 2007;131:1393-9.