Comparison of Positional Therapy to CPAP in Patients with Positional Obstructive Sleep Apnea

Samuel Krachman, Irene Swift, and Maria Elena Vega

Introduction

Obstructive sleep apnea (OSA) is prevalent in the general population, affecting 9 % of females and 24 % of males ages 30–60 years old [1]. When associated with daytime sleepiness, OSA syndrome is reported to be present in 2 % of females and 4 % of males in the same age range [1]. While treatment has always focused on trying to improve patient's symptoms, including daytime sleepiness and cognitive dysfunction, the recognition that OSA is an independent risk factor for a number of cardiovascular disorders has enhanced efforts to appropriately treat the disorder [2–5]. Treatment of OSA needs to be individualized, as there have been major problems with adherence and compliance with all forms of therapy that are presently used [6–10].

An important factor that affects airway patency is the posture of the patient (supine vs. lateral) [11–13] and may explain the entity known as positional OSA, where all or the majority of sleep-disordered breathing events occur while sleeping in the supine position. Positional OSA has been reported to be present in up to 50–60 % of all patients with diagnosed OSA [14–17]. As a result, positional therapy, directed at keeping the patient from sleeping in the supine position, is recognized as an important treatment option in selected patients with OSA [18]. In this chapter, we will discuss the definitions and pathophysiology behind positional OSA and focus on those studies that have compared positional therapy to continuous positive airway pressure (CPAP) therapy, which is considered by many as the primary treatment for OSA.

S. Krachman, D.O. (✉) • I. Swift, M.D. • M.E. Vega, M.D.
Division of Pulmonary, Critical Care and Sleep Medicine, Temple University School of Medicine, 3401 North Broad St, Philadelphia, PA 19140, USA
e-mail: samuel.krachman@tuhs.temple.edu

N. de Vries et al. (eds.), *Positional Therapy in Obstructive Sleep Apnea*,
DOI 10.1007/978-3-319-09626-1_31

Definition of Positional OSA

While positional OSA is reported as being prevalent, many studies defined positional OSA as simply a 50 % reduction in the AHI when sleeping in the non-supine position [14–17]. As a result, many patients still had an elevated AHI while non-supine, often in the range of mild-to-moderate OSA. More recently, Mador et al. [19] used a definition of normalizing the AHI to <5 in addition to a 50 % reduction and reported an overall prevalence of 27 % of all patients having positional OSA. Based on severity, this included 50 % of patients with mild OSA and 19 % of those with moderate OSA having positional OSA. Only 7 % of patients with severe OSA met their criteria for positional OSA. However, as it is defined, many patients with OSA have a positional component that would allow effective positional therapy to be considered as a primary or secondary therapy.

Pathophysiology for Positional OSA

Upper airway patency is normally maintained through a balance between anatomical and physiological forces that tend to collapse the airway and dilating forces that must be present in order to prevent collapse [11]. Major dilating forces include pharyngeal dilator muscle activation (including the genioglossus) and lung inflation-induced caudal traction on the upper airway that stiffens it and reduces collapsibility [11]. The two primary forces that tend toward upper airway collapse are the negative intraluminal pressure generated by the diaphragm during inspiration and the extraluminal pressure from tissues and bony structures surrounding the airway [11].

An important factor that has an effect on airway anatomy and size is the posture of the individual (supine vs. lateral), primarily due to the effects of gravity on airway tissues. When supine, the tongue and palatal structures move posteriorly due to gravity, and if this increase in tissue pressure is not offset by other dilating forces, upper airway collapse will occur [12, 13].

A more specific measurement of the inherent structural collapsibility of the upper airway can be obtained by measuring the critical collapsing pressure (Pcrit), the nasal pressure at which the hypotonic or "passive" pharynx collapses and inspiratory flow is abolished [20]. In normal subjects, the Pcrit is lower (-6.5 ± 2.7 cm H_2O) as compared to snorers (-1.6 ± 1.4 cm H_2O) and those patients with severe OSA (2.5 ± 1.5 cm H_2O) [21]. Of significance is the effect of body posture on Pcrit in patients with OSA. In the lateral position, Pcrit has been found to be dramatically lower, by 2.0–2.9 cm H_2O, than noted while patients are supine, denoting a stiffer less collapsible airway in the lateral position [22–24]. Values while in the lateral position were at or significantly less than 0 cm H_2O (range from 0.3 to 2.9 cm H_2O) consistent with values seen in normal individuals or snorers [21]. These physiological changes noted in the upper airway based on positioning help explain the entity of positional OSA as well as why some patients can be effectively treated with just positional therapy.

CPAP Compliance Issues

CPAP therapy has been demonstrated to be very effective at correcting sleep-disordered breathing [25] and improving cognitive function and daytime sleepiness [26, 27]. However, compliance with CPAP therapy has been poor [6, 28, 29]. In the seminal paper by Kribbs et al. [6], only 46 % of the patients prescribed with CPAP met the criteria that they defined as regular use, which was >4 h/night for 70 % of the nights monitored. More recently, similar findings of poor compliance have been noted in studies that have compared in-lab vs. at-home sleep testing [30, 31]. Rosen et al. [30] noted no difference in compliance between in-lab (39 %) and at-home testing (50 %) when evaluated at 3 months using a similar definition of compliance of >4 h/night for 70 % of the nights evaluated. Kuna et al. [31] reported that only 49 % and 52 % of in-lab- and at-home-tested VA patients, respectively, used CPAP for >4 h/night at the end of 3 months. The reasons for the poor compliance that is seen with CPAP therapy are numerable and include the mask being uncomfortable and burdensome, intolerance to the pressure, side effects such as nasal congestion, and complaints of claustrophobia [32]. In addition, socioeconomic factors also appear to play a role [33, 34]. However, how important each of these factors are in determining CPAP compliance still remains unclear [7, 8]. What is clear is that when patients are not compliant with CPAP therapy, their OSA will go untreated if other forms of therapy are not sorted out by the patient or physician. As a result, patients are symptomatic and continue to have the cardiovascular risks associated with untreated OSA [2–5]. Therefore, it is important to consider effective alternative treatments in these patients, which may include positional therapy if they have positional OSA.

Types of Positional Devices

There have been a number of positional therapy devices that have been used over the years to try and maintain patients with positional OSA in the non-supine position during sleep. Probably, the oldest and most familiar of these devices is the simple tennis ball technique, where patients have a tennis ball sewn into the back of a T-shirt that they would wear at night [35]. Variants of the tennis ball technique have been used in a number of studies [9, 10] including those that have compared this technique to CPAP therapy in patients with positional OSA [36, 37]. Jokic et al. [36] compared CPAP to positional therapy using a backpack with a soft ball placed inside of it. The size of the ball in the backpack was 10×5.5 in., and it was made of semirigid synthetic foam. In another adaptation of the tennis ball technique, Skinner et al. [37] created the thoracic anti-supine band (TASB) (Fig. 1). The device consists of two cotton stockinette-covered pieces of foam rubber with Velcro attachments on each end. A polystyrene ball (8 or 10 cm in circumference) is inserted inside at the level of the sixth thoracic vertebra. The two short ends are draped over the shoulders and fastened with Velcro over the two long ends. In the only other study that has compared positional therapy to CPAP therapy in patients with positional OSA,

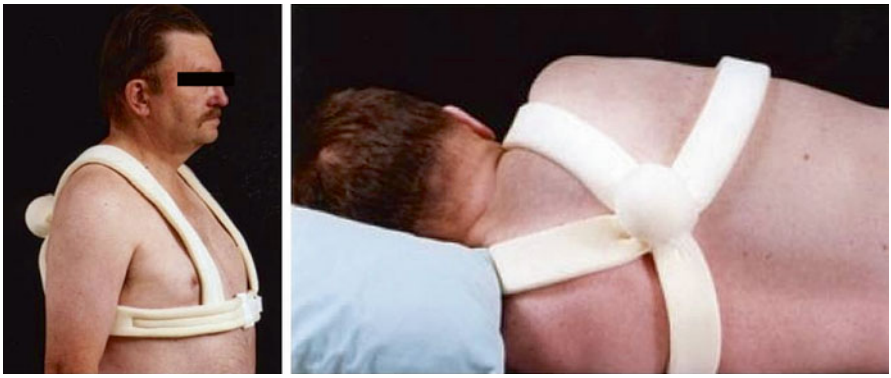

Fig. 1 Thoracic anti-supine band (TASB) (from [37], with permission)

Fig. 2 Zzoma Positional Device (from [38], with permission)

Permut et al. [38] utilized the Zzoma Positional Device, which is 12×5.5×4 in. in size and made of lightweight semirigid synthetic foam (Fig. 2). It is contained in a backpack-type material with an associated Velcro elastic belt. The Zzoma Positional Device is worn on the back, with the elastic belts brought around each side of the patient and secured anteriorly (Fig. 2). The device, with its particular size and wedge-shaped design on both sides, keeps the patient positioned on their side and prevents him/her from assuming the supine position.

Comparison of Positional Therapy to CPAP Therapy

As of this point in time, there have only been three prospective studies that have compared positional therapy to CPAP therapy in patients with positional OSA (Table 1) [36–38]. Jokic et al. [36] in a randomized crossover study of 13 patients

Table 1 Comparison of positional therapy to CPAP therapy

Study	*N*	Length of study	Baseline AHI (events/h)	Effects on AHI	Effects on nocturnal oxygenation	Effects on sleep quality
Jokic et al. [36]	13	2 weeks	18 ± 5	CPAP and PD decreased AHI—but lower with CPAP	Lowest SaO_2 lower with PD	No difference in SE and TST
Skinner et al. [37]	22	1 month	23 ± 12	72 % with PD and 89 % with CPAP had an AHI < 10 events/h	Both PD and CPAP increased the mean SaO_2	No difference in SE and TST
Permut et al. [38]	38	1 night	13 ± 5	92 % with PD and 97 % with CPAP normalized AHI to <5 events/h	No change in mean SaO_2 with PD and increase with CPAP	No difference in SE but TST lower with CPAP

AHI apnea–hypopnea index, *PD* positional device, *SE* sleep efficiency, *TST* total sleep time

with mild-to-moderate OSA (AHI 17 ± 8 events/h) compared positional therapy using their soft ball in a backpack device to CPAP therapy after 2 weeks of using each treatment modality. Positional OSA was defined as an AHI during supine sleep that was two or more times the AHI during sleep in the lateral position. In addition, the AHI in the lateral position had to be <15 event/h, during a minimum duration of 1 h of sleep in the lateral position and the inclusion of at least 1 rapid eye movement (REM) period. In a cross-over designed study, Skinner et al. [37] compared their TASB to CPAP therapy in 22 patients with mild to moderately severe positional OSA (AHI 22.7 ± 12 events/h) after utilizing each treatment modality for 1 month. Positional OSA was defined as an AHI in the supine position that was greater or equal to twice the AHI in other positions. Permut et al. [38] compared the Zzoma Positional Device to CPAP therapy in a crossover designed study after 1 night of use in 38 patients with mild-to-moderate positional OSA (AHI of 13 ± 5 events/h). Positional OSA was defined on the baseline study as an overall apnea–hypopnea index (AHI) of ≥5 events/h with symptoms of excessive daytime sleepiness or an AHI of ≥15 events/h, with a 50 % decrease in the AHI in the non-supine position as compared to the supine position. Additionally, the AHI had to fall to <5 events/h in the non-supine position, and the patient must have slept in the lateral position for a minimum of 1 h during the baseline study.

Sleep-Disordered Breathing

Many would consider the AHI as the most important parameter to be evaluated in regard to assessing the effectiveness of treatment in patient with OSA. That is also the case in regard to studies that have assessed patients with known positional OSA, including those that have compared positional therapy to CPAP therapy. Jokic et al. [36] noted that although 2 weeks of treatment with both their positional device and

CPAP decreased the AHI (from 18 to 10 and 3 events/h, respectively), the decrease with CPAP was statistically more significant and was associated with a normalization of the AHI (<5 events/h). Only 3 of the 13 patients (23 %) slept supine during their study night. Compliance as it relates to use of the positional device and CPAP was not assessed during the study. Skinner et al. [37] noted that both the TASB and CPAP decreased the AHI, from 23 to 12 and 5 events/h, respectively, with a significant difference noted between the two forms of therapy. Using a definition of successful treatment as an AHI of <10 events/h, treatment success was noted in 13/18 subjects using the TASB and 16/18 subjects using CPAP therapy. Supine sleep was significantly decreased but not completely eliminated with the TASB, with 6 % of the total sleep time spent in the supine position. Adherence with the TASB was based on a self-recorded diary, with a significantly higher adherence rate reported for TASB as compared to CPAP therapy. Permut et al. [38] noted that when compared to baseline, both the Zzoma Positional Device and CPAP therapy (mean 10 ± 3 cm H2O) significantly decreased the AHI, from 11 (9–15, 6–26) events/h to 2 (1–4, 0–8) and 0 (0–2, 0–7) events/h, respectively ($p < 0.001$), with a difference between the two treatments ($p < 0.001$). In addition, the Zzoma Positional Device was equivalent to CPAP (92 % vs. 97 %, respectively [$p = 0.16$]) at normalizing the AHI. The Zzoma Positional Device eliminated supine sleep in 37 of the 38 patients, with only a mean of 1 ± 4 % of total sleep time spent supine. However, the study was only an acute single night intervention, and more long-term results are being examined.

Nocturnal Oxygenation

Jokic et al. [36] noted no difference in mean SaO_2 between their positional device and CPAP therapy. However, the lowest SaO_2 during the night was lower with positional therapy as compared to CPAP. Skinner et al. [37] noted a clinically insignificant difference in mean SaO_2 during the night between CPAP and the TASB. In comparison, Permut et al. [38] noted the mean SaO_2 during the night was unchanged compared to baseline with the use of the Zzoma Positional Device, but was increased with CPAP therapy. In addition, there was an increase in the lowest SaO_2 during the night with both the Zzoma Positional Device and CPAP therapy, with no difference between the two treatment modalities. The percent of total sleep time with a $SaO_2 < 90$ % was significantly decreased compared to baseline with the Zzoma Positional Device and CPAP therapy.

Sleep Quality

Jokic et al. [36] demonstrated no difference in sleep quality between their positional device and CPAP therapy, as measured by total sleep time and sleep efficiency. In addition, the arousal index and sleep architecture were not different between the two

treatment modalities. Similar results were noted by Skinner et al. [37] when comparing the TASB to CPAP therapy, with no change in the total sleep time with either form of therapy as compared to baseline. In comparison, Permut el al. [38] noted that when compared to baseline, total sleep time did not change with the Zzoma Positional Device, but decreased with CPAP therapy. There was no change in sleep efficiency noted with either treatment, nor was there any change in the spontaneous arousal index. The sleep architecture, expressed as a percentage of total sleep time, including stage N3 and REM sleep, was not different as compared to baseline for either the Zzoma Positional Device or CPAP therapy.

Other Parameters

In regard to daytime sleepiness, Jokic et al. [36] noted a decrease in the Epworth Sleepiness Scale (ESS) after 2 weeks of therapy with both their positional device and CPAP therapy, but with no difference between the treatment modalities. In addition, similar sleep onset latencies were seen with both treatments as measured on maintenance of wakefulness (MWT) tests. Skinner et al. [37] noted a nonsignificant decrease in ESS with both their TASB and CPAP therapy at the end of 1 month.

Cognitive performance and quality of life changes have also been compared between positional therapy and CPAP therapy. Jokic et al. [36] found no difference in regard to these parameters between the two forms of therapy, and patient preference favored CPAP therapy in this study. Skinner et al. [37] noted no significant difference in any of the quality of life measures that they assessed when the results of their TASB and CPAP therapy were compared. Permut et al. [38] noted that 50 % of their patients preferred the Zzoma Positional Device, 34 % preferred CPAP therapy, and 16 % had no preference.

Future Research

While CPAP compliance has been objectively evaluated in a number of studies [6, 30, 31], there are few studies that have evaluated positional therapy adherence and compliance, with most involving self-reported use or mailed questionnaires [9, 10, 37]. While some of these studies have suggested poor long-term use of positional therapy [9, 10], a more recent prospective study has reported a 3-month compliance rate of 74 % using actigraphy [39]. While this study suggests possible compliance rates that are better than those reported for CPAP therapy, it was uncontrolled. Similar types of studies need to be performed when positional therapy is directly compared to CPAP therapy using methods that allow objective assessment of use.

In addition to compliance, measurement of continued effectiveness should be better evaluated with the use of positional therapy. While some studies have repeated polysomnograms after 1–3 months of using a positional device to demonstrate the

device retains its ability to decrease or eliminate supine sleep, studies evaluating continuous nightly effectiveness have not been performed.

Finally, while CPAP therapy has been shown to decrease parameters associated with cardiovascular risk in patients with OSA, the effects of positional therapy on cardiovascular risk are presently unknown [40–44]. CPAP has been demonstrated to decrease endothelial dysfunction as measured by flow-mediated dilation and carotid intima–media thickness measurements [40–42]. In addition, CPAP therapy has been shown to decrease systemic inflammation as measured using biomarkers such as C-reactive protein [43, 44]. At the present time, it is not known whether positional therapy has a similar effect at decreasing cardiovascular risk.

Summary

A large percentage of patients with diagnosed OSA have positional OSA. While CPAP therapy is the most common form of therapy, compliance is poor, and other forms of therapy may be appropriate in these patients, including the use of effective positional therapy. Initial studies that directly compared positional therapy to CPAP therapy suggest that positional therapy can be considered as a primary therapy in patients with positional OSA. However, more long-term studies that use objective measurements of compliance and effectiveness should be performed. Whether positional therapy has the same beneficial effects on cardiovascular risk as seen with CPAP therapy awaits further study.

References

1. Young T, Palta M, Dempsey J, Skatrud J, Weber S, Badr S. The occurrence of sleep-disordered breathing among middle-aged adults. N Engl J Med. 1993;328:1230–5.
2. Nieto FJ, Young TB, Lind BK, et al. Association of sleep-disordered breathing, sleep apnea, and hypertension in a large community-based study: Sleep Heart Health Study. JAMA. 2000;283:1829–36.
3. Peppard PE, Young T, Palta M, Skatrud J. Prospective study of the association between sleep-disordered breathing and hypertension. N Engl J Med. 2000;342:1378–84.
4. Yaggi HK, Concato J, Kernan WN, Lichtman JH, Brass LM, Mohsenin V. Obstructive sleep apnea as a risk factor for stroke and death. N Engl J Med. 2005;353:2034–41.
5. Shahar E, Whitney CW, Redline S, Lee ET, Newman AB, Javier Nieto F, O'Connor GT, Boland LL, Schwartz JE, Samet JM. Sleep-disordered breathing and cardiovascular disease: cross-sectional results of the Sleep Heart Health Study. Am J Respir Crit Care Med. 2001;163:19–25.
6. Kribbs NB, Pack AI, Kline LR, Smith PL, Schwartz AR, Schubert NM, Redline S, Henry JN, Getsy JE, Dinges DF. Objective measurement of patterns of nasal CPAP use by patients with obstructive sleep apnea. Am Rev Respir Dis. 1993;147:887–95.
7. Weaver TE, Grunstein RR. Adherence to continuous positive airway pressure therapy. The challenge to effective treatment. Proc Am Thorac Soc. 2008;5:173–8.

8. Sawyer AM, Gooneratne NS, Marcus CL, Ofer D, Richards KC, Weaver TE. A systematic review of CPAP adherence across age groups: clinical and empiric insights for developing CPAP adherence interventions. Sleep Med Rev. 2011;15:343–56.
9. Oksenberg A, Silverberg D, Offenbach D, Arons E. Positional therapy for obstructive sleep apnea patients: a 6-month follow-up study. Laryngoscope. 2006;116:1995–2000.
10. Bignold JJ, Deans-Costi G, Goldworthy MR, Robertson CA, McEvoy D, Catcheside PG, Mercer JD. Poor long-term compliance with the tennis ball technique for treating positional obstructive sleep apnea. J Clin Sleep Med. 2009;5(5):428–30.
11. White D. Pathogenesis of obstructive and central sleep apnea. Am J Respir Crit Care Med. 2005;172:1363–70.
12. Olson L, Fouke J, Hokje P, Strohl K. A biomechanical view of the upper airway. In: Mathew OP, Saint'Ambroggio G, editors. The respiratory function of the upper airway. New York: Marcel Dekker; 1988. p. 359–90.
13. Fouke J, Strohl K. Effect of position and lung volume on upper airway geometry. J Appl Physiol. 1987;63:375–80.
14. Cartwright RD. Effect of sleep position on sleep apnea severity. Sleep. 1984;7:110–4.
15. Cartwright R, Ristanovic R, Diaz F, Caldarelli D, Alder G. A comparative study of treatments for positional sleep apnea. Sleep. 1991;14:546–52.
16. Oksenberg A, Silverberg DS, Arons E, Radwan H. Positional vs. nonpositional obstructive sleep apnea patients: anthropomorphic, nocturnal polysomnographic, and multiple sleep latency test data. Chest. 1997;112:629–39.
17. Akita Y, Kawakatsu K, Hattori C, Hattori H, Suzuki K, Nishimura T. Posture of patients with sleep apnea during sleep. Acta Otolaryngol. 2003;550(Suppl):41–5.
18. Epstein LJ, Kristo D, Strollo PJ, Friedman NF, Malhotra A, Patil AP, et al. Clinical guideline for the evaluation, management and long-term care of obstructive sleep apnea in adults. J Clin Sleep Med. 2009;5:263–76.
19. Mador MJ, Kufel TJ, Magalang UJ, et al. Prevalence of positional sleep apnea in patients undergoing polysomnography. Chest. 2005;128:2130–7.
20. Schwartz AR, O'Donnell CP, Baron J, et al. The hypotonic upper airway in obstructive sleep apnea: role of structures and neuromuscular activity. Am J Respir Crit Care Med. 1998;157:1051–7.
21. Gleadhill IC, Schwartz AR, Schubert N, Wise RA, Permutt S, Smith PL. Upper airway collapsibility in snorers and in patients with obstructive hypopnea and apnea. Am Rev Respir Dis. 1991;143:1300–3.
22. Boudewyns A, Punjabi N, Van de Heyning PH, De Backer WA, O'Donnell CP, Schneider H, Smith PL, Schwartz AR. Abbreviated method for assessing upper airway function in obstructive sleep apnea. Chest. 2000;118:1031–41.
23. Penzel T, Moller M, Becker HF, Knaack L, Peter JH. Effect of sleep position and sleep stage on the collapsibility of the upper airways in patients with sleep apnea. Sleep. 2001; 24:90–5.
24. Ong JSL, Touyz G, Tanner S, Hillman DR, Eastwood PR, Walsh JH. Variability of human upper airway collapsibility during sleep and the influence of body posture and sleep stage. J Sleep Res. 2011;20:533–7.
25. Gay P, Weaver T, Loube D, Iber C. Evaluation of positive airway pressure treatment for sleep related breathing disorders in adults. Sleep. 2006;29:381–401.
26. Stradling JR, Davies RJ. Is more NCPAP better? Sleep. 2000;23 Suppl 4:S150–3.
27. Antic NA, Catcheside P, Buchan C, Hensley M, Naughton MT, Rowland S, et al. The effect of CPAP in normalizing daytime sleepiness, quality of life and neurocognitive function in moderate-severe OSA. Sleep. 2011;34:111–9.
28. Engleman HM, Martin SE, Douglas NJ. Compliance with CPAP therapy in patients with sleep apnoea/hypopnoea syndrome. Thorax. 1994;49:263–6.
29. Reeves-Hoche MK, Meck R, Zwillich CW. Nasal CPAP. An objective evaluation of patient compliance. Am J Respir Crit Care Med. 1994;149:149–54.

30. Rosen CL, Auckley D, Benca R, Foldvary-Schaefer N, Iber C, Kapur V, Rueschman M, Zee P, Redline S. A multisite randomized trial of portable sleep studies and positive airway pressure autotitration versus laboratory-based polysomnography for the diagnosis and treatment of obstructive sleep apnea: the HomePAP study. Sleep. 2012;35(6):757–67.
31. Kuna ST, Gurubhagavatula I, Malslin G, Hin S, Hartwig K, McCloskey S, Hachadoorian R, Hurley S, Gupta R, Staley B, Atwood CW. Noninferiority of functional outcome in ambulatory management of obstructive sleep apnea. Am J Respir Crit Care Med. 2011;183:1238–44.
32. Pepin JL, Leger P, Veale D, Langevin B, Robert R, Levy P. Side effects of nasal continuous positive airway pressure in sleep apnea syndrome: study of 193 patients in two French sleep centers. Chest. 1995;107:375–81.
33. Platt AB, Field SH, Asch DA, Chen Z, Patel N, Gupta R, et al. Neighborhood of residence is associated with daily adherence to CPAP therapy. Sleep. 2009;32(6):799–806.
34. Simon-Tuval T, Reuveni H, Greenberg-Dolan S, Oksenberg A, Tal A, Tarsiuk A. Low socio-economic status is a risk factor CPAP acceptance among adult OSAS patients requiring treatment. Sleep. 2009;32(4):545–52.
35. Kavey NB, Blitzer A, Gidro-Frank S, Korstanje K. Sleeping position and sleep apnea syndrome. Am J Otolaryngol. 1985;6(5):373–7.
36. Jokic R, Klimaszewski A, Crossley M, Sridhar G, Fitzpatrick MF. Positional treatment vs continuous positive airway pressure in patients with positional obstructive sleep apnea. Chest. 1999;115:771–81.
37. Skinner MA, Kingshott RN, Filsell S, Taylor DR. Efficacy of the 'tennis ball technique' versus NCPAP in the management of position-dependent obstructive sleep apnoea syndrome. Respirology. 2008;13:708–15.
38. Permut I, Diaz-Abad M, Chatila W, Crocetti J, Gaughan J, D'Alonzo GE, Krachman SL. Comparison of positional therapy to CPAP in patients with positional obstructive sleep apnea. J Clin Sleep Med. 2010;6(3):238–43.
39. Heinzer RC, Pellaton C, Rey V, Rossetti AO, Lecciso G, Haba-Rubio J, Tafti M, Lavigne G. Positional therapy for obstructive sleep apnea: an objective measurement of patients' usage and efficacy at home. Sleep Med. 2012;13(4):425–8.
40. Lattimore JL, Wilcox I, Skilton M, Langenfeld M, Celermajer DS. Treatment of obstructive sleep apnoea leads to improved microvascular endothelial function in the systemic circulation. Thorax. 2006;61(6):491–5.
41. Ip MS, Tse HF, Lam B, Tsang KW, Lam WK. Endothelial function in obstructive sleep apnea and response to treatment. Am J Respir Crit Care Med. 2004;169(3):348–53.
42. Imadojemu VA, Gleeson K, Quraishi SA, Kunselman AR, Sinoway LI, Leuenberger UA. Impaired vasodilator responses in obstructive sleep apnea are improved with continuous positive airway pressure therapy. Am J Respir Crit Care Med. 2002;65(7):950–3.
43. Shamsuzzaman ASM, Winnicki M, Lanfranchi P, Wolk R, Kara T, Accurso V, Somers VK. Elevated C-reactive protein in patients with obstructive sleep apnea. Circulation. 2002;105:2462–4.
44. Guo Y, Pan L, Ren D, Xie X. Impact of continuous positive airway pressure on C-reactive protein in patients with obstructive sleep apnea: a meta-analysis. Sleep Breath. 2013;17(2): 495–503.