European Archives of Oto-Rhino-Laryngology (2019) 276:2611–2619
https://doi.org/10.1007/s00405-019-05545-y

MISCELLANEOUS

New-generation positional therapy in patients with positional central sleep apnea

L. B. L. Benoist[1,2] · P. E. Vonk[1] · N. de Vries[1,3,4] · H. C. J. P. Janssen[5] · J. Verbraecken[6]

Received: 20 May 2019 / Accepted: 3 July 2019 / Published online: 13 July 2019

Abstract

Purpose To evaluate the effect of a sleep position trainer (SPT) in patients with positional central sleep apnea (PCSA).

Methods A multicentre cohort study was conducted. Patients with symptomatic PCSA were included. Effectiveness, compliance and quality of life were assessed at 1- and 6-month follow-up.

Results Sixteen patients were included. Median AHI dropped from 23.4/h [12.9–31.2] to 11.5/h [7.2–24.5] ($p=0.044$) after 1-month SPT therapy and in patients who continued treatment, median AHI further decreased after 6 months to 9.7/h [3.4–27.6] ($p=0.075$). Median percentage of supine sleep decreased significantly from 37.6 [17.2–51.8] to 6.7 [0.7–22.8] ($p<0.001$), after 1 month, and to 6.8 [0.7–22.1] ($p=0.001$), after 6 months. Mean compliance over 1 and 6 months was 78.6 ± 35.3 and $66.0\pm33.3\%$, respectively. Epworth Sleepiness Scale at baseline was 9.5 [3.3–11.8] and did not significantly decrease after 1 month (11.0 [3.0–13.0]) and 6 months (4.0 [3.0–10.5]) follow-up. Functional Outcomes of Sleep Questionnaire remained stable within the first month. However, after 6 months, there was a significant improvement compared to baseline values, 15.9 [11.9–18.4] vs. 17.8 [14.3–19.2]; $p=0.030$.

Conclusion This is the first study on effects of positional therapy with a new-generation smart device in patients with PCSA after 1 and 6 months of follow-up. Results of this study show that the SPT is effective in reducing AHI and central AI, feasible in PCSA, and is associated with symptomatic improvement. While the working mechanism behind this effect remains speculative, the effect is positive and considerable.

Keywords Sleep-disordered breathing · Sleep apnea · Positional central sleep apnea · Positional therapy · Sleep position trainer

Introduction

Central sleep apnea (CSA) describes a group of conditions, which are characterised by a lack of respiratory effort leading to cessation of airflow during sleep. These events result in insufficient or absent ventilation and compromised gas exchange [1]. In contrast to obstructive sleep apnea (OSA), respiratory effort is not present during these respiratory events.

Various forms of CSA exist and they can be classified into two groups based on wakefulness CO2 levels: hypercapnic versus non hypercapnic CSA. Distinction between these subgroups is important, since understanding the underlying mechanism causing CSA is of paramount importance when making a decision in the type of therapy which is initiated in patients with hypercapnic CSA, an impaired ventilatory output is present during wakefulness, which worsens during sleep, resulting in sleep hypoventilation. Hypercapnic

✉ P. E. Vonk
p.e.vonk@olvg.nl

1 Department of Otolaryngology and Head and Neck Surgery, OLVG, Jan Tooropstraat 164, 1061 AE Amsterdam, The Netherlands

2 Department of Otolaryngology and Head and Neck Surgery, Erasmus University Medical Center, Rotterdam, The Netherlands

3 Department of Otolaryngology and Head and Neck Surgery, Antwerp University Hospital and University of Antwerp, Antwerp, Belgium

4 Department of Oral Kinesiology, ACTA, Amsterdam, The Netherlands

5 Sleep Medicine Center Kempenhaeghe, Heeze, The Netherlands

6 Department of Pulmonary Medicine and Multidisciplinary Sleep Disorders Centre, Antwerp University Hospital and University of Antwerp, Edegem, Antwerp, Belgium

CSA can result from opioid usage or obesity hypoventilation syndrome (OHS). The underlying pathophysiology for hypocapnic CSA differs from hypercapnic CSA. The majority of hypocapnic CSA patients suffer from congestive heart failure and Cheyne Stokes Breathing (CSB) with a typical waxing-and-waning breathing pattern followed by a central apnea [1–3]. These patients have an increased ventilatory response to carbon dioxide (PCO_2) [4]. As compared with OSA patients, most heart failure patients with CSA have less complaints of nocturnal awakenings, insomnia or excessive daytime sleepiness [5]. CSA due to hyperventilation not related to chronic heart failure, is called idiopathic CSA (ICSA). ICSA is less common and may constitute less than 5% of all patients referred to a sleep centre [1]. Furthermore, its aetiology and pathogenesis is still under debate [6].

The influence of body position on the severity of sleep apnea has been extensively investigated in patients with OSA. Cartwright defined a patient as having positional OSA (POSA), if the apnea–hypopnea index (AHI) in supine position is at least twice as high as in non-supine position [7]. Around 50–60% of patients with mild OSA are positional [8]. Occasionally, patients suffering from CSA–CSB have been reported with an increased AHI particularly in the supine position [9]. In ICSA, positional differences in AHI are not well understood and have only been illustrated in some case reports in the literature [10, 11]. While the gravitational effect in POSA is self-evident, the pathophysiological mechanism in positional CSA (PSA) is much less understood.

Attempts to decrease the severity of OSA by influencing sleep position have been described since 1872, when Sullivan introduced a contraption which consisted of a bulky mass worn on the back preventing a person from turning on his back. Over the years, various other types of positional therapy (PT) have been suggested, including tennis balls and bulky pillows [8]. Although these techniques are effective in reducing the AHI, compliance is hampered by discomfort, resulting in disappointing long-term results [12]. Recent development have seen a new-generation PT device that was first studied by van Maanen et al. the Sleep Position Trainer (SPT) [13]. This device is worn around the trunk with a small sensor that measures sleep position and gives a soft vibration when the supine position is detected. The user is stimulated to react to the signal and to turn to a non-supine position. The sensor is optimised to do this effectively without disturbing the natural sleep pattern and to remain comfortable for patients to use. Short- and long-term results of the SPT showed a reduction in AHI combined with high compliance rates [14, 15]. PT can be used as a stand-alone therapy or can be combined with other treatments such as oral appliances or upper airway surgery [16, 17].

In patients with CSA, the most common treatment is positive airway pressure (PAP). Other treatment modalities include other forms of PAP therapy (i.e. adaptive servo ventilation, bilevel PAP), supplemental gases (i.e. oxygen therapy, carbon dioxide) and medications (i.e. acetazolamide or hypnotics) [2, 6]. Different mechanisms have been postulated why the lateral decubitus position is beneficial for avoiding central apneas [18–20]. Zahara et al. earlier prescribed an old-generation PT (positional pillow) in CSA, but results could not be reported since their patients refused further treatment [10]. Therefore, the aim of this pilot study was to determine the effectiveness of the SPT in patients with PCSA during 1-month and 6-month follow-up. We hypothesised that PCSA patients might benefit from PT in terms of reduction in central apneas, self-reported daytime sleepiness and quality of life, albeit that this has never been tested.

Methods

Study design

We performed a multicentre prospective pilot study including patients from three sleep centres in The Netherlands ($n=2$) and Belgium ($n=1$). Participating centres were: Department of Otolaryngology and Head and Neck surgery OLVG, Amsterdam, The Netherlands; Sleep Medicine Center Kempenhaeghe, Heeze, the Netherlands; and the Department of Pulmonary Medicine and Multidisciplinary Sleep Disorders Centre, Antwerp University Hospital and University of Antwerp, Antwerp, Belgium.

A consecutive series of patients with PCSA, confirmed by overnight polysomnography (PSG), between October 2013 and November 2015 were included. Patients used the SPT during a period of 6 months. A follow-up PSG was performed after 1 and 6 months of therapy usage. Self-reported daytime sleepiness and quality of life were evaluated at each visit using the Epworth Sleepiness Scale (ESS) and the Functional Outcomes of Sleep Questionnaire (FOSQ).

Patients

Patients aged 18 years or older with symptomatic PCSA were eligible for inclusion. Other inclusion criteria were the presence of a central AI of $\geq 20\%$ from total AHI, total sleep time in supine position between 10 and 90% and an AHI in non-supine position ≤ 15 events/h.

Exclusion criteria were: night or rotating shift work, muscular or joint problems in head, neck, shoulder or back area, simultaneous use of other treatment modalities for CSA or OSA, pregnancy, and coexisting non-respiratory sleep disorders that would influence functional sleep assessment. Patients with cardiovascular comorbidities were not excluded.

Definitions

PCSA was defined using a combination of the previously mentioned definition for CSA and Cartwright's criteria for POSA [7]: a central AI in supine position of at least twice as high as compared to the central AI in non-supine position. Furthermore, the patient should experience other sleep apnea-related symptoms, such as excessive daytime sleepiness, frequent awakenings or wakening up due to shortness of breath during sleep [21].

Successful treatment with the SPT was defined as a post-treatment AHI < 20 events/h along with a reduction of the AHI of at least 50% from baseline (responders). Treatment failure was defined as a post-treatment reduction in AHI from baseline of less than 50% (non-responders).

Obstructive apneas were defined as the cessation of nasal airflow for a period of 10 s or longer with continued respiratory effort. Hypopneas were scored whenever oronasal airflow reduced with ≥ 30% for at least 10 s and the oxygen saturation decreased ≥ 4% or more. Central apneas were defined as a cessation of airflow ≥ 10 s in the absence of any inspiratory effort. The apnea–hypopnea index (AHI) was then calculated representing the average number of apneas and hypopneas per hour of sleep [21].

Intervention

The SPT that was used in this study (SPT-DEV-PX-11.08, NightBalance, The Hague, The Netherlands) is a small sensor that has to be worn across the chest in a neoprene torso strap (Fig. 1). The device continuously measures body position during the night and gives a soft vibration when supine position is detected, to urge a patient to change body position.

Polysomnography

In Amsterdam, a PSG was performed using a digital polysomnography system (Embla A10, Broomfield, CO, USA).

Fig. 1 Sleep position trainer (SPT) SPT-DEV-PX-11.08 of NightBalance™

In Antwerp, an in-hospital attended PSG was performed (OSG, Rumst, Belgium) and in Kempenhaeghe, an in-hospital attended PSG was performed (Compumedics—Grael, Abbotsford, Australia). All PSG devices included electrodes that recorded an electroencephalogram (EEG) (FP2-C4/C4-O2, and in Kempenhaeghe F4-M1, C4-M1, O2-M1 and contralateral back-up), electro-oculogram (EOG), electrocardiogram (ECG) and a submental and anterior tibial electromyogram (EMG). Oxygen saturation was measured by finger pulse oximetry, while airflow was measured by a pressure sensor in a nasal cannula inserted in the opening of the nostrils and an oronasal thermocouple. Thoracoabdominal motion was recorded using belts containing piezoelectric transducers or respiratory inductance plethysmography. To differentiate between supine, prone, right lateral left lateral and upright positions, a position sensor (Sleepsense, St Charles, IL, USA) was attached to the midline of the abdominal wall. A portable registration device was used with multiple channels, for respiratory movements (thoracic and abdominal), airflow with heart frequency or ECG, oxygen saturation and a sleep position sensor. All signals were recorded with digital sampling, digital filtering, digital storage recording technology, permitting a sample efficiency of 90% and a sample rate up to 200 Hz. Storage was done on a PCMCIA flash card. A software program (Somnologica™studio, Broomfield, USA; DOMINO, SOMNOmedics GmbH, Randersacker, Germany; Brainlab RT, OSG, Rumst, Belgium and Compumedics' Profusion Software) was used to analyse the recorded data, which was manually checked and scored by experienced sleep technicians and in Kempenhaeghe double-checked by experienced ESRS-certified somnologists. All PSGs were scored according to the American Academy of Sleep Medicine (AASM) scoring manual (2012) [21].

Ethical considerations

In accordance with the Declaration of Helsinki, the study protocol was approved by the local Medical Ethical Committee. Informed consent was obtained from all participants. Data on study subjects were collected and stored anonymously to protect personal information.

Statistical analysis

Categorical and dichotomous variables were expressed as *n* (%). Skewed distributed data were expressed by their median and interquartile range [IQR]. Wilcoxon signed rank test was used to compare the respiratory parameters over time. *p* values > 0.05 were considered non-significant. Statistical analysis was performed using SPSS Statistical software (version 21.0, SPSS Inc., Chicago, IL).

Results

Patient characteristics

Sixteen consecutive patients (100% male; age 55.0 years [40.3–62.8]; BMI 27.5 kg/m^2 [24.1–29.5]) were eligible and included in the study. At baseline, four patients (25%) showed an AHI ≥ 5/h, eight patients (50%) an AHI ≥ 15/h and < 30/h, and four patients (25%) and AHI ≥ 30/h. Four patients were known with a cardiac medical history including myocardial infarction ($n = 1$), transient ischemic attack ($n = 1$), atrial fibrillation ($n = 1$) and coronary artery stenosis ($n = 1$). Ten patients were failures of PAP therapy before they were included in our study. We advised two patients (no. 5 and no. 8) to discontinue SPT therapy after 1 month since the AHI remained unchanged or even increased. Those patients were advised to restart PAP therapy. Table 1 demonstrates patients' characteristics. There was no change in BMI and neck circumference over time. Also, ESS and FOSQ questionnaire remained constant within the first month. However, after 6 months, there was a significant improvement in FOSQ scores ($p = 0.030$), compared to baseline values.

Respiratory indices

Total median AHI dropped from 23.4/h [12.9–31.2] to 11.5/h [7.2–24.5] ($p = 0.044$) after 1 month. At 1 month, two patients (12.5%) showed an AHI of < 5/h. In the majority of patients (56.3%), AHI decreased to < 15/h, two patients (12.5%) showed an AHI ≥ 15/h and < 30/h, and in three patients (18.8%) the AHI was ≥ 30/h. In those patients who continued using the SPT ($N = 14$), the total median AHI further decreased after 6 months to 9.7/h [3.4–27.6] ($p = 0.075$). In four patients (28.5%), this resulted in an AHI of < 5/h, in two patients (14.3%) AHI was < 15/h, five patients (35.7%) showed an AHI was between ≥ 15/h and < 30/h and in two patients (14.3%) the AHI was ≥ 30/h.

Total median central AI reduced from 9.4/h [6.4–11.8] to 2.5/h [1.0–5.4] ($p = 0.008$) after 1 month, and declined further to 0.9/h [0.1–11.9] after 6 months. Moreover, after 6 months of therapy, 46.2% ($n = 6$) of the patients were considered responders. During SPT usage, the median percentage of supine sleep decreased from 37.6 [17.2–51.8] to 6.8 [0.7–22.1] after 6 months, $p = 0.001$. Figure 2 shows the median percentage of supine sleep during the first month of follow-up. Other respiratory indices are presented in Table 2. Table 3 shows the main parameters per patient.

Table 1 Characteristics of the study population

	Baseline $N = 16$	1 month $N = 16$	6 months $N = 14$	p value[a]	p value[b]
BMI, kg/m^2	27.5 [24.1–29.5]	27.0 [24.0–29.8]	26.6 [23.3–30.1]	0.893	0.205
Neck circumference, cm	41.0 [37.0–43.0]	40.5 [36.8–42.5]	41.0 [37.0–43.0]	0.999	0.248
ESS score (0/24)	9.5 [3.3–11.8]	11.0 [3.0–13.0]	4.0 [3.0–10.5]	0.373	0.084
FOSQ score	15.9 [11.9–18.4]	17.3 [13.8–19.2]	17.8 [14.3–19.2]	0.148	0.030*

Values are median [interquartile range], *$p < 0.05$

BMI body mass index, *ESS* Epworth Sleepiness Scale, *FOSQ* Functional Outcomes of Sleep Questionnaire

[a]Comparing baseline values with values after 1 month (Wilcoxon signed rank test)

[b]Comparing baseline values with values after 6 months (Wilcoxon signed rank test)

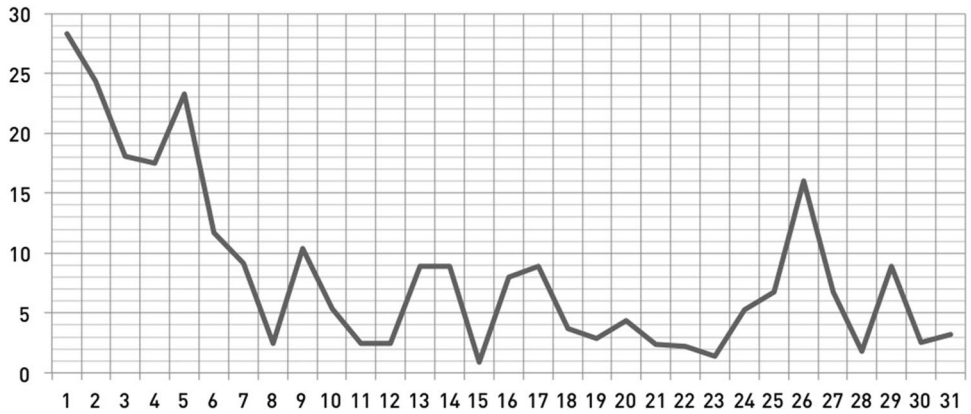

Fig. 2 Median percentage of sleep time in the supine position per night for the first month measured by the SPT. The first 9 days of the SPT therapy are part of the training program in which the SPT gradually decreases the number of times in which patients sleep on their back

Table 2 Respiratory indices during baseline and after 1 month and 6 months of follow-up

	Baseline $N=16$	$T=1$ month $N=16$	$T=6$ months $N=13$	p value[a]	p value[b]
Total AHI, events/h	23.4 [12.9–31.2]	11.5 [7.2–24.5]	9.7 [3.4–27.6]	0.044*	0.075
Total AI, events/h	14.4 [8.6–29.7]	6.2 [1.5–17.9]	5.0 [0.7–23.7]	0.041*	0.087
Total central AI, events/h	9.4 [6.4–11.8]	2.5 [1.0–5.4]	0.9 [0.1–11.9]	0.008*	0.152
Oxygen Desaturation Index, events/h	16.3 [5.5–23.8]	6.9 [3.5–17.6]	7.1 [2.0–18.1]	0.041*	0.182
Supine AHI, events/h	59.8 [42.2–76.5]	62.2 [15.0–79.5]	20.2 [0.0–36.2]	0.807	0.013*
Non-supine AHI, events/h	7.3 [2.1–11.8]	7.6 [4.1–15.2]	5.2 [1.9–21.8]	0.163	0.124
Supine central AI, events/h	21.0 [12.9–36.9]	9.6 [0.5–22.0]	0.0 [0.0–18.1]	0.079	0.081
Non-supine central AI, events/h	1.4 [0.9–3.1]	1.2 [0.1–3.8]	0.7 [0.0–5.1]	0.363	0.937
Percentage supine sleep	37.6 [17.2–51.8]	6.7 [0.7–22.8]	6.8 [0.7–22.1]	< 0.001*	0.001*
Total sleep time, h	6.7 [6.3–7.5]	6.9 [5.7–7.7]	7.0 [5.5–7.6]	0.717	0.600
Sleep efficiency, %	87.7 [72.3–92.4]	89.6 [79.6–94.0]	91.4 [78.1–95.0]	0.326	0.382
% REM	19.8 [16.1–23.1]	20.0 [12.7–22.4]	16.9 [11.8–26.4]	0.836	0.173
% Stage N1	5.7 [3.2–12.3]	7.4 [5.1–10.8]	6.9 [4.1–8.9]	0.918	0.917
% Stage N2	53.3 [45.0–58.0]	53.4 [44.9–59.7]	52.7 [49.7–60.3]	0.776	0.279
% Stage N3	19.3 [14.7–24.1]	20.7 [15.1–25.0]	21.3 [13.8–27.1]	0.717	0.917
Microarousal index, #/h	13.9 [3.1–35.9]	10.5 [5.4–16.5]	11.3 [5.6–15.9]	0.073	0.084
Positional change index, #/h	2.6 [1.9–3.7]	3.1 [1.8–5.7]	2.2 [1.2–4.8]	0.959	0.263
Minimal SpO_2 (%)	87.0 [84.3–88.0]	88.5 [86.3–91.0]	88.0 [86.5–90.5]	0.047*	0.062
Mean SpO_2	95.0 [93.5–96.0]	95.5 [95.0–96.0]	95.0 [94.0–96.0]	0.068	0.248
SpO2 < 90% (%TIB)	0.4 [0.03–2.03]	0.01 [0.00–0.28]	0.1 [0.0–0.3]	0.028*	0.171

Values are presented as median [interquartile range], *$p < 0.05$

AHI apnea–hypopnea index, *AI* apnea index, REM rapid eye movement, *SpO_2* peripheral oxygen saturation, *TIB* time in bed

[a]Comparing baseline values with values after 1 month (Wilcoxon signed rank test)

[b]Comparing baseline values with values after 6 months (Wilcoxon signed rank test)

Compliance

Average usage of SPT was 5.8 ± 3.4 h/night at 1-month follow-up and 5.2 ± 2.8 h/night at 6-month follow-up. Mean compliance over 1 and 6 months defined as ≥ 4 h/night, ≥ 5 n/week and ≥ 4 h/night, ≥ 7n/week was 78.6 ± 35.3% and 66.0 ± 33.3%, respectively. Compliance data are presented in Table 4.

Discussion

To the best of our knowledge, this is the first pilot study evaluating the effects of PT with a new-generation smart device, the SPT, in a group of patients with PCSA. The concept of avoiding the supine position to cure or alleviate PCSA is simple, while the effect is positive and substantial. Why central apneas are present particularly (or to a higher extent) in the supine position and are absent or minor in the lateral position might be more difficult to comprehend.

Different mechanisms can be considered to explain this phenomenon. In ICSA as well as in CSB, about 20% of the central apneas are characterised by upper airway collapse that can develop due to passive collapse of the upper airway at the end of expiration [22, 23]. In specific phenotypes of CSA, upper airway collapse may occur more easily in the supine position, due to gravitational forces acting on the upper airway. Another explanation is an effect of the supine body position on pulmonary volumes, which is most relevant in patients with pulmonary congestion and an enlarged heart, with reduced buffer capacity to store oxygen and carbon dioxide. Moreover, lung volume changes have also been reported in healthy individuals, based on functional respiratory imaging [24]. Consequently, lower lung volumes facilitate ventilatory instability, finally resulting in a cycling breathing pattern. In accordance with this theory is the finding that increases in end-expiratory lung volumes were found during the ventilatory period in patients with CSB [25]. Evidence also suggests that right non-supine position may be more beneficial to avoid central apneas than left non-supine position in chronic heart failure. A better parasympathetic to sympathetic balance and lower norepinephrine concentrations have been reported in the right lateral decubitus position in patients with chronic heart failure [19, 20]. The mechanism is not completely elucidated, but it was

Table 3 Individual results during baseline and after 1 month and 6 months of follow-up

Patient no.	Relevant cardiac medical history	Opioid usage	CBS	AP failure	Total AHI (events/h)			Total central AI (events/h)			Central AI supine (events/h)			Central AI non-supine (events/h)		
					T = 0	T = 1	T = 6	T = 0	T = 1	T = 6	T = 0	T = 1	T = 6	T = 0	T = 1	T = 6
1	No	No	No	No	28.2	12.2	16.2	7.7	1.9	0.9	12.8	19.1	7.6	2.9	0.5	0.4
2	No	No	No	Yes	35.6	14.3	28.5	9.9	3.6	4.3	19.7	28.3	0.0	1.4	3.2	5.2
3	No	No	No	Yes	7.9	7.1	6.9	6.0	4.8	5.7	7.9	6.5	12.3	3.1	3.8	2.3
4	No	No	No	No	22.4	6.6	26.6	11.7	5.6	20.8	15.3	11.4	23.8	6.5	3.6	20.1
5	No	No	No	Yes	20.8	47.1	n/a	8.6	3.6	n/a	37.3	17.4	n/a	2.6	1.0	n/a
6	Yes	Yes	No	No	28.9	26.9	33.2	13.9	15.3	18.0	35.8	36.8	56.1	1.4	6.2	4.9
7	No	Yes	No	Yes	18.0	10.7	3.6	8.9	1.2	0.0	22.3	6.1	0.0	2.9	0.5	0.0
8	No	No	Yes	Yes	56.2	56.1	n/a	11.6	3.0	n/a	17.2	20.9	n/a	1.1	2.0	n/a
9	No	No	No	No	8.8	0.2	0.4	2.2	0.0	0.0	7.2	0.0	0.0	1.1	0.0	0.0
10	Yes	No	No	Yes	32.0	9.0	9.7	8.2	0.9	0.2	13.3	2.0	0.4	0.0	0.0	0.0
11	No	No	No	No	10.6	0.1	0.6	3.6	0.0	0.0	6.2	0.0	0.0	0.8	0.0	0.0
12	No	No	No	Yes	38.1	7.5	3.1	33.0	6.5	3.1	81.9	0.0	0.0	15.5	6.5	3.1
13	No	No	No	Yes	24.0	12.8	n/a	11.8	1.8	n/a	51.9	7.8	n/a	3.8	1.4	n/a
14	Yes	No	No	Yes	26.0	7.7	5.3	12.1	0.0	0.4	30.2	0.0	0.0	0.5	0.0	0.4
15	Yes	No	No	No	11.2	35.6	57.7	3.8	17.4	24.9	27.1	120	34.3	0.0	17.1	23.9
16	No	No	No	Yes	22.8	17.1	21.5	11.0	1.3	0.7	59.4	22.4	0.0	1.2	0.7	0.7

Values are presented as median

CSB Cheyne Stokes Breathing, *PAP* positive airway pressure, *AHI* apnea–hypopnea index, *AI* apnea index

Table 4 Objective compliance and device usage

	1 month $N=15$	6 months $N=11$
Total nights of follow-up	35.0 [32.0–38.0]	188.0 [183.0–195.0]
Total nights of usage	32.0 [26.5–36.0]	181.0 [103.5–189.5]
Total nights with compliance > 4 h	23.6 ± 13.5	125.1 ± 64.0
Average hours of usage per follow-up night, h	5.8 ± 3.4	5.2 ± 2.8
Average hours of usage per used night, h	6.5 ± 2.4	6.6 ± 1.2
Compliance ≥ 4 h ≥ 7 n/week, % nights	69.7 ± 40.1	66.0 ± 33.3
Compliance ≥ 4 h ≥ 5 n/week, % nights	75.1 ± 39.7	78.6 ± 35.3

Values are presented as mean ± standard deviation or median [interquartile range]

suggested that in the right non-supine position, right atrial pressure may elevate due to increased hydrostatic pressure, with decreased venous return as a result. In addition, the hydrostatic pressure on the left ventricle may be less, contributing to reduced pulmonary congestion [26, 27]. This mechanism is in line with the findings of Pump et al. who found an increase in left atrial diameter and a simultaneous decrease in mean arterial pressure in the left lateral decubitus position, possibly by causing stimulation of low-pressure receptors and reduced compression of the inferior caval vein [18]. Whether this mechanism is applicable in ICSA is unproven, but subclinical cardiac alterations have been implicated in the pathophysiology of CSA [28]. However, given the fact that a change in sleeping position immediately influences central apnea frequency suggests a more rapid mechanism than a change in pulmonary congestion or a change in cardiac function, and supports the pathway of upper airway instability as the most relevant one [29]. Another interesting theory from Joosten et al. is related to airway shape [30]. They described that one of the key determinants of airway shape is lung volume, specifically functional residual capacity (FRC) and that parameters such as body position and BMI have been determined to influence FRC. In this study, they showed that supine dependent OSA patients demonstrate a significant decrease in FRC when moving from lateral to supine position, which could be a predisposing factor in the generation of upper airway obstruction. They also found that dynamic loop gain increases by a small but statistically significant amount when moving from the lateral to supine position [31]. It could be speculated in patients with PCSA that this could also be the underlying mechanism for the change in apnoeic events.

Since obstructive and central apneas often coexist, a cycling breathing pattern could also be induced due to hyperventilation provoked by repetitive obstructive events in POSA [32]. Last but not least, we have to be aware of misclassification of obstructive apneas as central events. Although this aspect has to be taken into account, the evidence was based on the use of mercury strain gauges and nasal thermistors [33]. We did overcome this problem using respiratory inductance plethysmography and nasal cannulas, which has sufficient reliability to classify central events [6].

Limitations

There are several limitation in this study. First, the aim of this study was to perform a pilot study, but the main limitation is our small cohort of patients. Although this is the first study to report on PT in CSA, the small sample size reduces the power of the results. Second, it must be kept in mind that (I) CSA is uncommon and that patients often suffer from coexisting obstructive respiratory events as well. PT has proven to be effective is POSA patients resulting in the possibility that the improvement of respiratory indices in this study are partly caused by a reduction in obstructive apneas. This can lead to an overestimation of the effect of PT in PCSA patients. Nevertheless, when analysing the effect on the central AI, a significant reduction was found after 1- and 6-month follow-up. Third, two patients (no. 5 and 8) were recommended to stop SPT therapy due to an increase in disease severity. When trying to explain the lack of effect of the SPT in these patients, several factors must be taken into consideration. Although, patient no. 5 showed an overall increase in total AI during follow-up, we did find a decrease in central AI. Consequently, total AHI could be increased due to an increase in obstructive apneas only. Furthermore, patient no. 8 was the only patient diagnosed with CSB. Although a previous study reported an increased AHI in supine position in patients suffering from CSA–CSB [9], this may indicate that patients with CSB need a different treatment approach. Last, four patients were known with a cardiac medical history. It is known that CSA is often related to heart failure and that proper treatment of the cardiovascular disease itself may improve CSA in those patients. This could have influenced our results.

Clinical relevance and future perspectives

As mentioned before, in patients with CSA, the most common treatment is PAP. Although this therapy has proven its effectiveness, one-third of all patients do not tolerate or refuse PAP [34, 35]. Based on the findings of this pilot study, treatment with new-generation PT devices seem to be a viable alternative and can be used as salvage therapy in patients who do not tolerate PAP. In the future, there is a demand for high-quality evidence from larger prospective studies, preferably using a control group to prove the effectiveness of PT in PCSA patients.

Conclusions

This is the first study on the effects of PT with a new-generation smart device in patients with PCSA during 1-month and 6-month follow-up. Results of this study show that the SPT is effective in reducing AHI and central AI and feasible in PCSA, and is associated with symptomatic improvement. While the working mechanism behind this effect remains speculative, the effect is positive and considerable.

Funding NightBalance provided the 16 SPT devices.

Compliance with ethical standards

Conflict of interest Prof. Dr. N. de Vries is a member of the Medical Advisory Board of NightBalance. He is also an investigator of Inspire and Jazz Pharmaceutics, consultant of Philips, Olympus and the AE Mann Foundation. Prof. Dr. J. Verbraecken is a member of the Medical Advisory Boards of ResMed Narval and Bioprojet. He is also a consultant of Philips and Jazz Pharmaceutics, and an investigator of ResMed. All the other authors declare that they have no conflicts of interest or financial ties to disclose. Dr. L.B.L. Benoist, Dr. P.E. Vonk, and Dr. H.C.J.P. Janssen declare that they have no conflict of interest.

Research involving human participants All the procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all individual participants included in the study.

References

1. Eckert DJ, Jordan AS, Merchia P, Malhotra A (2007) Central sleep apnea: pathophysiology and treatment. Chest 131(2):595–607. https://doi.org/10.1378/chest.06.2287
2. Randerath W, Verbraecken J, Andreas S, Arzt M, Bloch KE, Brack T, Buyse B, De Backer W, Eckert DJ, Grote L, Hagmeyer L, Hedner J, Jennum P, La Rovere MT, Miltz C, McNicholas WT, Montserrat J, Naughton M, Pepin JL, Pevernagie D, Sanner B, Testelmans D, Tonia T, Vrijsen B, Wijkstra P, Levy P (2017) Definition, discrimination, diagnosis and treatment of central breathing disturbances during sleep. Eur Respir J. https://doi.org/10.1183/13993003.00959-2016
3. Yumino D, Bradley TD (2008) Central sleep apnea and Cheyne–Stokes respiration. Proc Am Thorac Soc 5(2):226–236. https://doi.org/10.1513/pats.200708-129MG
4. Xie A, Skatrud JB, Puleo DS, Morgan BJ (2001) Exposure to hypoxia produces long-lasting sympathetic activation in humans. J Appl Physiol (1985) 91(4):1555–1562. https://doi.org/10.1152/jappl.2001.91.4.1555
5. Muza RT (2015) Central sleep apnoea-a clinical review. J Thorac Dis 7(5):930–937. https://doi.org/10.3978/j.issn.2072-1439.2015.04.45
6. Randerath W (2017) Central sleep apnea: the problem of diagnosis. Sleep Med 34:224–225. https://doi.org/10.1016/j.sleep.2016.12.015
7. Cartwright RD (1984) Effect of sleep position on sleep apnea severity. Sleep 7(2):110–114
8. Ravesloot MJ, van Maanen JP, Dun L, de Vries N (2013) The undervalued potential of positional therapy in position-dependent snoring and obstructive sleep apnea—a review of the literature. Sleep Breath 17(1):39–49. https://doi.org/10.1007/s11325-012-0683-5
9. Sahlin C, Svanborg E, Stenlund H, Franklin KA (2005) Cheyne–Stokes respiration and supine dependency. Eur Respir J 25(5):829–833. https://doi.org/10.1183/09031936.05.00107904
10. Zaharna M, Rama A, Chan R, Kushida C (2013) A case of positional central sleep apnea. J Clin Sleep Med 9(3):265–268. https://doi.org/10.5664/jcsm.2496
11. DelRosso L, Gonzalez-Toledo E, Chesson AL Jr, Hoque R (2012) Positional central apnea and vascular medullary compression. Neurology 79(21):2156–2157. https://doi.org/10.1212/WNL.0b013e3182752cc9
12. de Vries GE, Hoekema A, Doff MH, Kerstjens HA, Meijer PM, van der Hoeven JH, Wijkstra PJ (2015) Usage of positional therapy in adults with obstructive sleep apnea. J Clin Sleep Med 11(2):131–137. https://doi.org/10.5664/jcsm.4458
13. van Maanen JP, Meester KA, Dun LN, Koutsourelakis I, Witte BI, Laman DM, Hilgevoord AA, de Vries N (2013) The sleep position trainer: a new treatment for positional obstructive sleep apnoea. Sleep Breath 17(2):771–779. https://doi.org/10.1007/s11325-012-0764-5
14. Ravesloot MJL, White D, Heinzer R, Oksenberg A, Pepin JL (2017) Efficacy of the new generation of devices for positional therapy for patients with positional obstructive sleep apnea: a systematic review of the literature and meta-analysis. J Clin Sleep Med 13(6):813–824. https://doi.org/10.5664/jcsm.6622
15. van Maanen JP, de Vries N (2014) Long-term effectiveness and compliance of positional therapy with the sleep position trainer in the treatment of positional obstructive sleep apnea syndrome. Sleep 37(7):1209–1215. https://doi.org/10.5665/sleep.3840
16. Benoist LB, Verhagen M, Torensma B, van Maanen JP, de Vries N (2016) Positional therapy in patients with residual positional obstructive sleep apnea after upper airway surgery. Sleep Breath. https://doi.org/10.1007/s11325-016-1397-x
17. Dieltjens M, Vroegop AV, Verbruggen AE, Wouters K, Willemen M, De Backer WA, Verbraecken JA, Van de Heyning PH, Braem MJ, de Vries N, Vanderveken OM (2015) A promising concept of combination therapy for positional obstructive sleep apnea. Sleep Breath 19(2):637–644. https://doi.org/10.1007/s11325-014-1068-8
18. Pump B, Talleruphuus U, Christensen NJ, Warberg J, Norsk P (2002) Effects of supine, prone, and lateral positions on cardiovascular and renal variables in humans. Am J Physiol Regul Integr Comp Physiol 283(1):R174–180. https://doi.org/10.1152/ajpregu.00619.2001

19. Fujita M, Miyamoto S, Sekiguchi H, Eiho S, Sasayama S (2000) Effects of posture on sympathetic nervous modulation in patients with chronic heart failure. Lancet 356(9244):1822–1823. https://doi.org/10.1016/S0140-6736(00)03240-2
20. Miyamoto S, Fujita M, Sekiguchi H, Okano Y, Nagaya N, Ueda K, Tamaki S, Nohara R, Eiho S, Sasayama S (2001) Effects of posture on cardiac autonomic nervous activity in patients with congestive heart failure. J Am Coll Cardiol 37(7):1788–1793
21. Berry RB, Budhiraja R, Gottlieb DJ, Gozal D, Iber C, Kapur VK, Marcus CL, Mehra R, Parthasarathy S, Quan SF, Redline S, Strohl KP, Davidson Ward SL, Tangredi MM, American Academy of Sleep M (2012) Rules for scoring respiratory events in sleep: update of the 2007 AASM Manual for the Scoring of Sleep and Associated Events. Deliberations of the Sleep Apnea Definitions Task Force of the American Academy of Sleep Medicine. J Clin Sleep Med 8(5):597–619. https://doi.org/10.5664/jcsm.2172
22. Vanderveken OM, Oostveen E, Boudewyns AN, Verbraecken JA, Van de Heyning PH, De Backer WA (2005) Quantification of pharyngeal patency in patients with sleep-disordered breathing. ORL J Otorhinolaryngol Relat Spec 67(3):168–179. https://doi.org/10.1159/000086572
23. Jobin V, Rigau J, Beauregard J, Farre R, Monserrat J, Bradley TD, Kimoff RJ (2012) Evaluation of upper airway patency during Cheyne–Stokes breathing in heart failure patients. Eur Respir J 40(6):1523–1530. https://doi.org/10.1183/09031936.00060311
24. Leemans G, Ides K, Van Holsbeke C, Vissers D, Vos W, De Backer W (2013) The influence of posture on airway structure and function in healthy subjects. Eur Respir Soc
25. Brack T, Jubran A, Laghi F, Tobin MJ (2005) Fluctuations in end-expiratory lung volume during Cheyne–Stokes respiration. Am J Respir Crit Care Med 171(12):1408–1413. https://doi.org/10.1164/rccm.200503-409OC
26. Hazebroek EJ, Bonjer HJ (2006) Effect of patient position on cardiovascular and pulmonary function. In: Whelan RL, Fleshman JW, Fowler DL (eds) The SAGES manual of perioperative care in minimally invasive surgery, 1 edn. Springer, Berlin, pp 410–417. https://doi.org/10.1007/0-387-29050-8
27. Martin-Du Pan RC, Benoit R, Girardier L (2004) The role of body position and gravity in the symptoms and treatment of various medical diseases. Swiss Med Wkly 134(37–38):543–551. https://doi.org/10.4414/smw.2004/37/smw-09765
28. Solin P, Jackson D, Roebuck T, Naughton M (2002) Cardiac diastolic function and hypercapnic ventilatory responses in central sleep apnoea. Eur Respir J 20(3):717–723
29. Hanly PJ (2009) Impact of sleeping angle on the upper airway and pathogenesis of Cheyne Stokes respiration. Sleep 32(11):1412–1413
30. Joosten SA, Sands SA, Edwards BA, Hamza K, Turton A, Lau KK, Crossett M, Berger PJ, Hamilton GS (2015) Evaluation of the role of lung volume and airway size and shape in supine-predominant obstructive sleep apnoea patients. Respirology 20(5):819–827
31. Joosten SA, Landry SA, Sands SA, Terrill PI, Mann D, Andara C, Skuza E, Turton A, Berger P, Hamilton GS (2017) Dynamic loop gain increases upon adopting the supine body position during sleep in patients with obstructive sleep apnoea. Respirology 22(8):1662–1669
32. Galetke W, Ghassemi BM, Priegnitz C, Stieglitz S, Anduleit N, Richter K, Randerath WJ (2014) Anticyclic modulated ventilation versus continuous positive airway pressure in patients with coexisting obstructive sleep apnea and Cheyne–Stokes respiration: a randomized crossover trial. Sleep Med 15(8):874–879. https://doi.org/10.1016/j.sleep.2014.02.012
33. Boudewyns A, Willemen M, Wagemans M, De Cock W, Van de Heyning P, De Backer W (1997) Assessment of respiratory effort by means of strain gauges and esophageal pressure swings: a comparative study. Sleep 20(2):168–170
34. Rotenberg BW, Murariu D, Pang KP (2016) Trends in CPAP adherence over twenty years of data collection: a flattened curve. J Otolaryngol Head Neck Surg 45(1):43
35. Verbraecken J, Willemen M, Wittesaele W, Van de Heyning P, De Backer W (2002) Short-term CPAP does not influence the increased CO. Monaldi Arch Chest Dis 57(1):10–18