REVIEW

Sleep apnoea in patients with heart failure: Part II: Therapy

Apnée du sommeil et insuffisance cardiaque: partie II: thérapeutique

Philippe Bordier*

Hôpital cardiologique du Haut-Lévêque, avenue de Magellan, 33604 Pessac cedex, France

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KEYWORDS
Sleep apnoea; Heart failure

Summary Nasal continuous positive airway pressure (CPAP) is generally recommended for the treatment of obstructive sleep apnoea. CPAP lowers the cardiovascular morbidity and mortality associated with severe obstructive sleep apnoea. At least 50% of patients presenting with chronic heart failure (HF) have sleep apnoea; a subset of these patients may have obstructive sleep apnoea and may derive a survival benefit from CPAP. However, this population is also prone to developing central sleep apnoea, Cheyne-Stokes respiration or both (CSA/CSR), for which CPAP lowers the apnoea-hypopnoea index only partially and for which the overall effect of CPAP on survival remains to be determined, particularly as it has been observed to increase the mortality rate in subsets of patients. Other treatments may prove effective in patients with chronic HF and CSA/CSR, although none, thus far, has been found to confer a survival benefit. New ventilatory modes include bi-level positive airway pressure and automated adaptive servoventilation, the latter being most effective against CSA/CSR. Measures that can alleviate CSA/CSR indirectly include beta-adrenergic blockers and renin-angiotensin-aldosterone system inhibitors, nocturnal supplemental oxygen and cardiac resynchronization therapy (CRT). The effects of theophylline, acetazolamide and nocturnal CO2 have also been studied. The second part of this review describes the applications and effects of therapies that are available for sleep apnoea in patients with chronic HF.

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MOTS CLÉS
Apnée du sommeil ;

Résumé La ventilation en pression positive continue (VPPC) par masque facial est généralement recommandée pour traiter l’apnée du sommeil obstructive (ASO). Ce mode de ventilation réduit la morbidité et la mortalité cardiovasculaires associées aux ASO sévères. Chez les sujets

* Fax: +33 5 56 04 38 49.
E-mail address: phiboldier@aol.com.

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Abbreviations

AHI: apnoea-hypopnoea index
HF: heart failure
CPAP: continuous positive airway pressure
CRT: cardiac resynchronization therapy
CSA: central sleep apnoea
CSR: Cheyne-Stokes respiration
LVEF: left ventricular ejection fraction
OSA: obstructive sleep apnoea
PaCO₂: partial pressure of carbon dioxide in the arterial blood
PCO₂: partial pressure of carbon dioxide

Introduction

Nasal CPAP is generally recommended for the treatment of OSA, including for patients presenting with cardiovascular disorders [1]. CPAP lowers the cardiovascular morbidity and mortality associated with severe OSA [2]. At least half of the patients who present with chronic HF have sleep apnoea; a subset of these patients may have OSA, i.e., greater or equal 50% of abnormal respiratory events during sleep are of obstructive pattern [3,4], and may derive a survival benefit from CPAP [5–8]. However, this population is also prone to developing CSA, CSR or both (CSA/CSR) [3,4], for which CPAP lowers the apnoea-hypopnoea index (AHI; defined as the number of apnoeas and hypopnoeas per hour of sleep) only partially. The overall effect of CPAP on survival remains to be determined, particularly as it has been observed to increase the mortality rate in subsets of patients with chronic HF and CSA/CSR [9,10]. Other treatments may prove effective in patients with chronic HF and CSA/CSR, although none, thus far, has been found to confer a survival benefit. New ventilatory modes include bi-level positive airway pressure and automated adaptive servoventilation. Measures that can alleviate CSA/CSR indirectly include beta-adrenergic block-
Sleep apnoea in patients with heart failure: Part II: Therapy

30 minutes [11]. However, this short-term study was performed in only a few patients presenting with chronic HF, in the absence of sleep apnoea and while they were awake. With non-permanent atrial fibrillation, the risk of myocardial intolerance of CPAP seems lower. One study reported fewer recurrences of atrial fibrillation after cardioversion in patients with OSA treated with CPAP, compared with in patients with untreated OSA [12]. Patients with chronic HF were not excluded and greater than 50% were in New York Heart Association functional class II, III or IV, with a mean LVEF of 52 ± 13%. After 12 months of treatment with CPAP, the only significant difference found between patients with and without recurrences of atrial fibrillation was correctly applied treatment in the latter group. While no adverse effect of CPAP has been reported, lack of compliance with treatment may be a challenging issue. Furthermore, in OSA, the severity of nocturnal O₂ desaturation seems to be an independent risk factor for the development of atrial fibrillation [13]. The restoration of proper O₂ saturation might therefore explain the lower rate of recurrence of atrial fibrillation associated with CPAP treatment.

Although CPAP acts via anatomical changes at the pharyngeal level, it may also correct CSA/CSR [9,10]. In chronic HF due to systolic or diastolic dysfunction, the left ventricular end-diastolic pressure is usually elevated. The insufflation of air by the CPAP device maintains a constantly positive intrathoracic pressure, narrowing the pressure difference between the left intraventricular and intrathoracic pressures [14—16]. The resulting decrease in left ventricular end-diastolic pressure facilitates the filling of the failing left ventricle and increases its stroke volume. In addition, by raising the intrathoracic pressure, CPAP decreases the venous return to the right heart and alleviates pulmonary interstitial and myocardial congestion. The decrease in left ventricular preload may also contribute to an increase in cardiac output. The improvement in cardiac performance in turn restores the central respiratory drive, which alleviates CSA/CSR [17]. Fewer apnoeas are associated with a decrease in sympathetic activity, fewer surges in heart rate and blood pressure, less peripheral vasoconstriction and a decrease in left ventricular afterload [16]. In addition, the decrease in apnoeic-hypopnoeic events produced by CPAP limits the number of dips in blood O₂ saturation, which may increase the cardiac output by relieving myocardial ischaemia.

In clinical studies, CPAP alleviated the manifestations of chronic HF, improved the cardiac loading conditions, increased LVEF and mitigated the severity of CSA/CSR [9,10,18], although these changes have not been observed systematically [9,10,19]. In contrast to OSA, the effects of CPAP on CSA/CSR in patients presenting with chronic HF are less prominent, in the order of a 40 to 60% decrease in apnoeic events [10,20,21].

Sin et al. reported a higher survival rate among patients with chronic HF and CSA/CSR treated with CPAP than among untreated patients [18]. However, in a similar patient population, the randomized CANPAP study found an early increase in mortality in the group of patients assigned to CPAP compared with untreated controls, perhaps because of a decreased cardiac output due to the effects of CPAP on left ventricular preload and filling; at 2 years, however, the death and transplantation rates were similar in both study groups [10]. In both the control and the CPAP-treated groups, mortality was due predominantly to progressive chronic HF and sudden death. A more detailed post-hoc analysis of the CANPAP study found that patients in whom the AHI had decreased below 15 after 3 months of CPAP had a greater increase in LVEF and a higher cardiac transplantation-free survival rate than the control group [9]. In that subgroup, LVEF increased by an average of 3.6% within 3 months, from a mean baseline value of 25.6% — an increase significantly greater (p < 0.001) than that observed in the group not treated with CPAP. In contrast, no significant difference was observed in LVEF and heart transplant-free survival, between the group of patients whose AHI had remained greater or equal to 15 after 3 months of CPAP and the control group. Therefore, when CPAP is prescribed for the management of CSA/CSR in patients with chronic HF, its effects on AHI need to be closely monitored during the first 3 months of treatment, and it should be discontinued if its effects are unapparent or weak.

Between 1998 and 2004, the death and cardiac transplantation rate in the combined CPAP and control groups of the CANPAP trial fell from 20 per 100 person-years to four per 100 person-years (p = 0.003) [10]. This profound decrease in the rate of the primary study endpoint, observed in both groups, was independent of CPAP, and attributable to changes in medications prescribed during the study. In particular, the proportion of patients treated with beta-adrenergic blockers and spironolactone increased from 58 to 86% (p < 0.001) and from 14 to 41% (p = 0.001), respectively, while the prescription of digoxin decreased from 72 to 36% (p = 0.002). The role played by pharmaceuticals in CSA/CSR will be further discussed later.

Because the air is simply insufflated continuously, CPAP should a priori be ineffective in the absence of spontaneous respiratory efforts, as in CSA/CSR, although this may not be the case, as discussed earlier. Bi-level ventilation systems have been tested in CSA/CSR, as they can ventilate a patient in the absence of breathing efforts, corresponding to non-invasive assisted ventilation with a nasal or facial mask as well as CPAP [22,23]. In addition, if the pressure applied by CPAP during expiration is identical to that applied during inspiration, bi-level ventilation allows the setting of a low positive expiratory pressure for patients who are uncomfortable when exhaling against a high positive pressure. The spontaneous/timed mode is usually selected [22,23]. Bi-level ventilation in the spontaneous mode can be effective in OSA and is best implemented with a backup rate (timed mode) for CSA/CSR. For example, during spontaneous breathing, the patient is ventilated in an assisted mode at a fixed inspired pressure, which is two to three times lower and fixed during expiration. Should CSA/CSR occur, the ventilator switches, in a few seconds, to controlled delivery of the same pressures as during assisted ventilation and with a breathing rate preset at 12 to 15 breaths/minute. Upon the return of spontaneous breathing, assisted ventilation resumes. Bi-level ventilation has been found to be as effective as CPAP in alleviating CSA/CSR in patients with chronic HF [21—24]. In a study of 16 patients, a 14-day delivery of CPAP, set at 8.5 mbar, was compared with the delivery of bi-level ventilation, set at 8.5/3 mbar, each for 14 days [23]. AHI was similarly and significantly lowered, from 26.7 ± 10.7 at baseline to 7.7 ± 5.6 and 6.5 ± 6.6 by CPAP and bi-level ventilation,
Automated adaptive servoventilation

Nocturnal automated adaptive servoventilation with a facial mask is available for the treatment of CSA/CSR, and mixed and complex sleep apnoea. Its advantages are being studied, in particular in patients with chronic HF [19–21,24–26]. With a 91% decrease in central apnoeas in a single night, servoventilators have been found to be more effective than CPAP, bi-level ventilation and nocturnal O2 supplementation, for the management of CSA/CSR in patients with chronic HF [21]. Other small studies in patients with chronic HF have found unequivocally positive effects of servoventilators on CSA/CSR [20,24,25], mixed sleep apnoea [20] and complex sleep apnoea [20,24] in acute settings. The efficacy of servoventilators in the management of CSA/CSR has been confirmed at 1 month [26] and 6 months [19].

The physical characteristics of servoventilators are similar to those of CPAP or bi-level ventilation apparatuses. However, they include their own specific algorithms of assisted-controlled inspiration and controlled positive expiratory pressure. The algorithms are based on continuous, cycle-by-cycle measurements of ventilation amplitude and airflow pressure. A volume of air is delivered automatically through the facial mask, at a pressure that compensates for the incomplete tidal volume amplitude. The system smooths the CSR cycles, during which the ventilatory amplitude increases and decreases in phases separated by apnoea or hypopnoea. Therapeutic ventilation can begin with the default settings of the device manufacturer; for example, an end-expiratory pressure set at 5 cm H2O, sufficient to control any obstructive apnoea, and an inspiratory pressure support between 3 and 10 cm H2O. The support setting is the difference between end-inspiratory and end-expiratory pressures, with a minimum setting of 3 cm H2O and a maximum setting of 10 cm H2O. The default backup respiratory rate is 15 breaths/minute, above or below which the device tracks the patient’s spontaneous rate automatically [21,26]. Populations of patients with chronic HF and CSA/CSR in whom servoventilators have been tested, presented with a large majority of central respiratory events, as opposed to obstructive or mixed respiratory events [21,26].

Compared with the improvement in quality of life provided by CPAP in patients with common OSA, the effects of CPAP [10] or servventilation [19,24,26] in patients presenting with chronic HF and CSA/CSR are more modest. This is probably due to the mild or absent sleep apnoea-induced symptoms reported by these patients [19]. Trials are in progress to examine the effects of servventilation on the morbidity and mortality of patients with chronic HF and CSA/CSR. The impact of servventilation on cardiac function has been examined in a single randomized study of 25 patients [19]. After 6 months of treatment, a 6% increase in L VEF was observed in seven patients assigned to servventilation, as opposed to an approximately 3% decrease in six patients assigned to CPAP — a statistically significant difference. It is noteworthy that, in that randomized study, and in contrast to other studies in similar patient populations [9,10], CPAP was not associated with an increase in L VEF at 6 months [19].

The long-term compliance with this cumbersome and constraining therapy remains to be determined. The sensation of suffocation associated with a facial mask is a major issue in patients with chronic HF, whose original chief complaint is discomfort due to dyspnoea. In studies of CPAP for OSA, patient compliance was limited mainly by the mask and by local discomfort and complications.

Therapies with indirect effects on abnormal sleep-related respiratory events

When these therapies improve cardiac performance, they may alleviate sleep apnoea.

Medications for chronic congestive heart failure

The prominent effects of beta-adrenergic blockers and spironolactone on the survival rate of patients enrolled in the CANPAP trial [10] were reminiscent of earlier observations in patients with chronic HF treated with beta-adrenergic blockers, angiotensin-converting enzyme inhibitors and spironolactone, in whom the positive effects on morbidity and mortality became apparent after 3 to 6 months of treatment. A positive effect of angiotensin-converting enzyme inhibitors on sleep apnoea has been reported [27], as well as the alleviation of CSA/CSR by beta-adrenergic blockers in patients with chronic HF [28]. A mean AHI of 14 ± 11 was measured in 27 patients treated with carvedilol 5 to 10 mg/day, vs 33 ± 17 (p < 0.0001) in 18 similar
patients who did not receive a beta-adrenergic blocker. In another study, a decrease in mean AHI from 34 ± 13 before, to 14 ± 13 after 6 months of treatment with carvedilol 10 mg twice daily (p = 0.003), was measured in 16 patients [29]. In both studies, the decrease in AHI conferred by carvedilol was due to an alleviation of central apnoea. The alleviation of CSA/CSR conferred by these drugs might be viewed as a marker of their beneficial effects on the myocardium.

Nocturnal oxygen supplementation

A 45% decrease in the number of central apnoeic events has been reported in response to the acute delivery of O₂ (2 L/min) in patients with chronic HF who have sleep apnoea, with no effect on obstructive events [21]. As mentioned earlier, in that overnight study, the decreases in central apnoeas associated with CPAP, bi-level ventilation and servoventilation were 48, 76 and 91%, respectively. Another study in patients with chronic HF reported a 66% decrease in central AHI by CPAP, and a 70% decrease by O₂ delivered at 2 L/min, each for 3 months [30]. In that study, increases in LVEF and exercise capacity were treatment benefits conferred by CPAP, which were not observed in patients treated with O₂. After 3 months of nocturnal O₂ delivered at a rate of 3 L/min, AHI decreased from 21.0 ±10.8 to 10.0 ±11.6 (p < 0.001) [31] — a 50% decrease in CSA/CSR burden consistent with previous observations, which was confirmed recently [32]. Furthermore, in these same studies, LVEF increased after 3 months of O₂ supplementation from 34.7 ±10.4% to 38.2 ±13.6% (p = 0.002) [31] and from 27 ±9% to 37 ±10% (p < 0.01), respectively [32], and this was associated with a modest improvement in quality of life. This delayed effect of nocturnal O₂ is attributed to a higher cardiac performance, associated with fewer abnormal respiratory events of central origin. The delivery of sufficient supplemental O₂ [31] prevents or limits the dips in O₂ during apnoea, hypopnoea (Fig. 1) and secondary myocardial hypoxia. It also prevents the increase in myocardial O₂ demand due to the bursts of central sympathetic activity occurring at the end of obstructive or central respiratory events [14,15,33]. Suplemental nocturnal O₂ may also:

- limit myocardial reperfusion injury due to the oxidative stress caused by periodic hypoxia-normoxia occurring during sleep apnoea [34];
- increase partial pressure of carbon dioxide in the arterial blood (PaCO₂), which decreases the severity of CSA/CSR, because hypocapnoea is a key factor in its development [17,35];
- mitigate hyperventilation and shorten the circulation time in patients with chronic HF, limiting the severity of hypocapnoea;
- modulate the sensitivity of the chemoreceptors in the respiratory control system, interfering with the CO₂ and O₂ ventilatory drive;
- promote the formation of oxyhaemoglobin instead of carboxyhaemoglobin, which increases PaCO₂;
- counteract hypoxia, which participates in the prolongation of apnoea when vagal afferent activity is stimulated by pulmonary congestion, resulting in inhibitory respiratory reflex.

The ultimate health and survival benefits conferred by nocturnal O₂ supplementation in patients with chronic HF and sleep apnoea remain to be established.

Cardiac pacing

The results of an initial study suggesting that cardiac pacing might alleviate sleep apnoea [36] were not confirmed by a subsequent study, in which atrial overdrive pacing was delivered by dual chamber pacemakers implanted for the management of bradyarrhythmias, in patients presenting with OSA and without chronic HF [37]. During overdrive atrial pacing, the backup dual chamber pacing rate was programmed between seven and 20 bpm above the mean spontaneous nocturnal heart rate, for 24 hours and for 1 month. Furthermore, in a crossover study, 15 patients with OSA in absence of chronic HF who had no indication for cardiac pacing, derived no benefit from 1 night of overdrive atrial pacing [38]. In contrast, a decrease in AHI from 29.3 ± 12.1 to 12.3 ± 4.0 (p < 0.004) was measured after 1 week of overdrive atrial pacing in 7/19 (37%) patients presenting with OSA and no chronic HF [39]. These conflicting observations were not explained. Another study of 15 patients presenting with chronic HF and mixed sleep apnoea found a decrease in AHI from 41 ± 20 to 27 ± 15 (p < 0.005) in seven patients (47%) during nocturnal overdrive atrial pacing with a dual chamber system [40]. The patients in whom AHI had decreased had a greater proportion of central events than the patients in whom overdrive was ineffective. Importantly, that study, as well as another study that found no effect on OSA and mixed sleep apnoea conferred by up to 7 months of dynamic atrial overdrive pacing in patients with chronic HF [41], had recruited patients with clinical manifestations of OSA.

By contrast, all studies of the effects of CRT on CSA/CSR in patients with chronic HF have shown a significant decrease in AHI, 3 to 6 months after implantation of the system [42–47]. With respect to the effects of CRT on obstructive respiratory events, the results have been mixed, with either no change [42–44,46,47] or a decrease in AHI [48]. When CRT has alleviating effects on OSA in patients with chronic HF, it might be because the obstructive events are due to haemodynamic fragility instead of pure obstruction of the upper airways. After 3 to 6 months of CRT applied in patients presenting with sleep apnoea, the increase in LVEF ranged between 4 and 14% [42–48]. The improvement in cardiac function appeared to enhance the respiratory drive, an effect that may decrease the rate of abnormal central respiratory events, which, in turn, increases left ventricular contractility. A correlation has been noted between decrease in CSA/CSR and pulmonary arterial systolic pressure, and increase in LVEF after 3 months of CRT [47]. A decrease in AHI associated with CRT has also been observed in an acute setting [49].

Most studies of CRT and sleep apnoea have been performed without atrial overdrive pacing [42,44–47,49]. When atrial overdrive pacing was applied overnight after 6 months of CRT, in patients with OSA, it conferred no additional therapeutic benefits to those obtained with CRT [48]. Recently, a modest, though significant, additional decrease in AHI of central origin (23.8 ± 16.9 vs 21.5 ± 16.9; p < 0.01) was observed when nocturnal atrial overdrive pacing at
Figure 1. Nocturnal O₂ supplementation in chronic heart failure and sleep apnoea. Patient with an apnoea-hypopnoea index (AHI: number of apnoeas and hypopnoeas per hour of sleep) = 39.2, O₂ desaturation index (ODI: number of dips in O₂ per hour of sleep) = 35.4 and mean nocturnal blood oxygen saturation (SaO₂) = 90.7% on baseline nocturnal ventilation polygraphy. 1A and 1B. Baseline recordings, showing mixed and obstructive apnoeas, respectively, with profound dips in O₂. 1C and 1D. Recordings during 3 L/min of nocturnal O₂ supplementation; AHI = 4.5, ODI = 0.3 and mean nocturnal SaO₂ = 97.9%. 1C. Mixed residual apnoeas with very mild O₂ desaturation. The heart rate is stable in this pacemaker recipient, with pacing at a backup rate of 70 bpm. Pacemaker programming was similar during baseline polygraphy. This indicates that the elimination of O₂ desaturation during apnoeic events may suppress the autonomic nervous system instability. 1D. Prolonged, residual, abnormal respiratory event with obstructive hypopnoea progressing toward apnoea; note that the dips in O₂ remain shallow. ECG: electrocardiogram.
15 bpm was added after 3 months of successful CRT [43]. In that study, a decrease in central AHI was measured, from $33.6 \pm 14.3$ before, to $23.8 \pm 16.9$ during CRT ($p < 0.01$), before the addition of atrial overdrive pacing. It is noteworthy that neither the new onset nor the worsening of sleep apnoea has been reported during CRT [42–49]. While CSA/CSR in patients with chronic HF is not, in itself, an indication for CRT, cardiac desynchronization in the presence of CSA/CSR is a strong indication for implanting a CRT system, and the alleviation of sleep apnoea by CRT may be a valid criterion in the evaluation of the response to CRT [50].
Other therapeutic trials

In a randomized, crossover study of 15 patients presenting with chronic HF and CSA/CSR, theophylline, administered in an average dose of 3.3 mg/kg for 5 days (mean plasma concentration = 11 ± 2 mg/mL) decreased mean AH1 from 37 ± 23 during placebo treatment, to 18 ± 17 during active treatment (p = 0.001) [51]. This therapeutic effect was attributed to a theophylline-induced acceleration of the heart rate, a valid hypothesis as tachycardia is one of the main compensatory mechanisms activated by cardiac insufficiency. Theophylline also activates the central respiratory drive. Its systematic prescription is limited by a high incidence of adverse events, and, while its long-term effects on chronic HF are unknown, cardiac arrhythmias and sudden death associated with the use of theophylline have been reported previously.

Acetazolamide is a diuretic and respiratory stimulant used to treat idiopathic and high-altitude CSA. While other diuretics usually cause metabolic alkalosis, acetazolamide causes metabolic acidosis. The decrease in pH and [HCO3−] stimulates the chemoreceptors, eliciting respiratory compensation and hypocapnoea due to hyperventilation. The short-term effects of acetazolamide were tested for the treatment of CSA/CSR in 12 patients with chronic HF [52]. The drug was administered in a dose of 3.5 to 4.0 mg/kg, 1 hour before bedtime for 6 nights, with a goal of decreasing total venous CO2 by approximately 5 mmol/L, as evidence of its effect. This regimen was associated with a mean AH1 of 34 ± 20 versus 57 ± 28 during the administration of placebo (p = 0.002). Acetazolamide lowered the number of central apnoeas despite the persistence of hypocapnoea. Its administration was associated with a decrease in venous and arterial CO2 and an increase in arterial (H+) along with a decrease in pH and a decrease in arterial (HCO3−). It was hypothesised that the decrease in PCO2-driven apnoeic threshold was proportionally greater than the decrease in blood PCO2. In that study, other effects of acetazolamide, including diuresis and alleviation of pulmonary congestion, were minimal. As is the case with nearly all diuretics, acetazolamide increases the urinary excretion of potassium, and may cause life-threatening hypokalaemia, particularly in patients with chronic HF. The administration of acetazolamide raises other issues, such as the stimulation of the respiratory muscles and hyperventilation, which might accentuate the hypocapnoea observed in patients with chronic HF, who may already be hyperventilating. Furthermore, by inducing metabolic acidosis, acetazolamide may activate the sympathetic nervous system. Finally, because its long-term effects are unknown, acetazolamide cannot be recommended as a routine treatment.

The supplementation of inhaled air by CO2 during sleep-alleviated CSA/CSR in patients with chronic HF, an observation related to the key role played by hypocapnoea in CSA/CSR [53]. In that study, the effects of inhaling room air, CO2 or O2 mixtures were studied in ten patients during stage 2 of a single overnight sleep study. Once the patient was asleep, air was delivered through a facial mask coupled with a three-bag system allowing the selection of one of the three gas mixtures. In a first trial, 10 minutes after the onset of central apnoea, a mixture of 4% CO2, 21% O2 and 76% N2 was delivered. The fraction of inspired CO2 was increased slowly until central apnoeas and hypopnoeas were suppressed. The CO2 inhalation was continued for at least 10 minutes before switching the circuit to room air for 10 minutes. Thereafter, random trials of CO2− or O2-enriched gas mixtures were separated by 10 minutes of room air inhalation. O2 was administered in a sufficiently high concentration to increase blood O2 saturation to the level reached during CO2 inhalation. When the patients were not in stage 2 sleep, the system was switched to room air. Transcutaneous PCO2, closely correlated with PaCO2, was measured continuously. In the baseline, awake state, arterial PaO2 was 89.8 ± 18.5 mmHg and PaCO2 was 34.3 ± 5.1 mmHg. AH1 during room air was 38.7 ± 17.0 versus 2.3 ± 2.9 during CO2 inhalation (p < 0.0001). Only six patients underwent both CO2 and O2 inhalation trials, in whom a significant 38% decrease (9.4 ± 7.0) in the apnoea index occurred during O2 inhalation, compared with room air inhalation, which was less pronounced than the 100% decrease (24.9 ± 7.3) caused by CO2 inhalation. Although the inhalation of O2 decreased the apnoea index, it had no significant effect on AH1, indicating either an absence of effect on hypopnoeas, or the progression from apnoeas to hypopnoeas. The time occupied by central respiratory events was 82.9 ± 10.1% during inhalation of room air versus 6.1 ± 9.5% (p = 0.01) during CO2 inhalation and 84.5 ± 17.1% during O2 inhalation. The main value of these studies pertain to the physiopathology of CSA/CSR in chronic HF and the role played by hypocapnoea; the routine therapeutic use of supplemental CO2 is not currently recommended. CO2 supplementation may stimulate the sympathetic system prominently, which is undesirable in patients with chronic HF. While increasing the fraction of inspired CO2 by increasing the space of the mask-tube of ventilatory devices is a simple manoeuvre, it is neither suggested nor currently available in clinical practice.

Conclusions

The therapeutic options available for the alleviation of sleep apnoea in patients presenting with chronic HF are summarized in Fig. 2. Their ability to decrease AH1 is either unpredictable or partial, and, except in the case of OSA, evidence of their effect on morbidity and mortality in this patient population is lacking. The modest improvements in cardiac performance that might be observed during the treatment of sleep apnoea in patients with chronic HF are unlikely to systematically prolong life. In addition, the tolerance of systems using a nasal or facial mask remains a frequent complicating factor, justifying the consideration of all available options in each individual patient.

Conflicts of interest

None.
Figure 2. Treatment algorithm for sleep apnoea (SA) in patients with heart failure (HF). SA is considered to be obstructive (OSA), central (CSA) or mixed according to the predominant type of apnoea and hypopnoea. ACEI: angiotensin-converting enzyme inhibitor; CSR: Cheyne-Stokes respiration; CPAP: continuous positive airway pressure; CRT: cardiac resynchronization therapy.

References


