Sleep Science and Practice

CASE REPORT

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Central sleep apnea in chronic heart failure with hypoxemia - treatment efficacy and hemodynamic effects of three different treatment modalities: a case report

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Abstract

Background The optimal treatment for central sleep apnea (CSA) depends on the underlying pathophysiology and should consider the potential for hemodynamic impairment when using positive airway pressure devices. While the long-term effects on overall cardiovascular outcome have been investigated for different device settings, the immediate hemodynamic consequences are not well understood. This is mainly due to a lack of hemodynamic monitoring during routine polysomnographic assessment. The application of most monitoring devices is either restricted by their invasiveness, e.g. in thermodilution, or cannot be used continuously like in echocardiography. Impedance cardiography (ICG), however, enables physicians to implement a continuous non-invasive monitoring of different hemodynamic parameters which can be useful in various clinical scenarios. In sleep medicine, the hemodynamic effect of initiating positive airway pressure treatment in patients with pre-existing heart failure should be of special concern.

Case presentation In this case report, we compare the efficacy of three different treatment modalities in a patient with CSA related to chronic heart failure considering the resolution of respiratory events on polysomnography (PSG). In addition, we outline the hemodynamic effects of each treatment device using ICG for non-invasive hemodynamic monitoring. Regarding the reduction of respiratory central events, long-term oxygen treatment (LTOT) and adaptive servoventilation (ASV) proved to be more efficient compared with automatic positive airway pressure (APAP). Hemodynamically, substantial differences of the cardiac performance were observed between the treatment devices. This especially applied to ASV which led to a pronounced drop in cardiac output.

Conclusion Our case report indicates that treatment of CSA may induce significant changes of hemodynamic parameters which would remain undetected during routine polysomnographic assessment. We conclude that non-invasive hemodynamic monitoring may be considered when positive airway pressure treatment is initiated in patients at risk of hemodynamic impairment.

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Keywords Central sleep apnea, Chronic heart failure, Automatic positive airway pressure, Adaptive servoventilation, Long-term oxygen treatment, Case report

Introduction

Central sleep apnea (CSA) is commonly classified as either primary (idiopathic) or secondary due to a potentially reversible state or disorder. Chronic heart failure can induce ventilatory instability leading to CSA in about one third of patients unselected for symptoms of daytime sleepiness (Javaheri 2012). The prevalence of CSA in chronic heart failure rises with increasing left ventricular systolic dysfunction and is associated with elevated left ventricular filling pressures, circulatory delay, and a higher sympathetic activity (Bradley et al. 2003). Pulmonary congestion activating stretch receptors and compensatory sympathetic activation can induce hyperventilation resulting in hypocapnia. A shift towards an increased pCO_2 sensitivity during sleep and a prolonged circulation time in patients with chronic heart failure can then lead to an impaired ventilatory feedback response presenting as the crescendo-descrendo breathing pattern of Cheyne-stokes respiration (Yumino and Bradley 2008). Hypoxemia increases the pCO_2 sensitivity of peripheral chemoreceptors causing a stronger ventilatory response and a more pronounced decrease of pCO_2 levels (Chowdhuri and Badr 2017). This predisposes patients with chronic heart failure and concomitant hypoxemia towards developing central sleep apnea.

Despite appropriate treatment of the underlying condition, many patients remain symptomatic experiencing reduced sleep quality and persistent daytime sleepiness. Different treatment devices including automatic positive airway pressure (APAP), adaptive servoventilation (ASV) and long-term oxygen treatment (LTOT) may be considered for the treatment of CSA. While their effect on cardiovascular morbidity and mortality has been investigated in large multicentre trials (Cowie et al. 2017; Bradley et al. 2005), the immediate hemodynamic consequences are not well understood. A method to perform continuous hemodynamic monitoring is provided by impedance cardiography (ICG) which strongly correlated with the reference method of transpulmonary thermodilution (Broomhead et al. 1997; Woltjer et al. 1996; Water et al. 2003).

By extending the routine polysomnography study (PSG) with ICG, we continuously monitored our patient for changes of the cardiac performance, e.g. of stroke volume, under different treatment conditions. Four electrodes were placed on the patient's neck and along the anterior axillary line of the chest wall to detect pulsatile thoracic impedance changes from which the device calculated the required hemodynamic parameters.

In this case report, we compare the treatment response of a patient with chronic heart failure and hypoxemia to three different treatment modalities assessed by the SOMNOscreen™ polysomnography system (SOMNOmedics GmbH, Randersacker, Germany). We further outline the effect of each treatment device on hemodynamic parameters measured with the CardioScreen® 1000 impedance cardiograph (Medis, Illmenau, Germany).

Report of case

A 65-year-old female patient experiencing poor sleep quality, excessive daytime sleepiness, and shortness of breath grade 3 according to the mMRC scale presented to our sleep clinic. On physical examination, we noted edematous ankles, a body mass index (BMI) of 46.4 kg/m^2, a heart rate of 63/min., and a systemic blood pressure of 126/67 mmHg. Her past medical history included chronic heart failure with reduced ejection fraction, arterial hypertension, type 2 diabetes and hyperlipoproteinemia. Her home medications included olmesartan, torasemid, atorvastatin, metformin and metamizol. Pulmonary function testing revealed a mild restrictive ventilatory disorder with normal diffusion capacity. Blood gas analyses repeatedly showed hypoxemia and hypocapnia with respiratory alkalosis. The clinical signs of congestive heart failure were confirmed by an elevated NT-proBNP of 2257 pg/ml. On echocardiographic assessment, we observed a mildly reduced left ventricular ejection fraction of 48% with normal cavitary dimensions and no evidence of hemodynamically significant valvular pathologies.

Polysomnographic assessment was performed using the SOMNOscreen™ polysomnography system (SOMNOmedics GmbH, Randersacker, Germany). Airflow was measured with a thermistor and a nasal pressure transducer during the diagnostic night and with the pneumotachograph of the treatment device under therapeutic conditions. Thoracoabdominal breathing excursions were monitored with a respiratory induction plethysmograph. A finger clip oximeter was used to measure arterial oxygen saturation. Continuous blood pressure measurement was performed with the pulse transit time technique (Gesche et al. 2012). To enable hemodynamic monitoring with the impedance cardiography system two electrodes connected to two dual sensors were placed along the anterior axillary line of the chest wall (Fig. 1). The outer sensors create an alternating low amplitude current which is sensed by the inner sensors and is used to detect the change in thoracic impedance over time. For precision measurement of the cardiac cycle intervals an

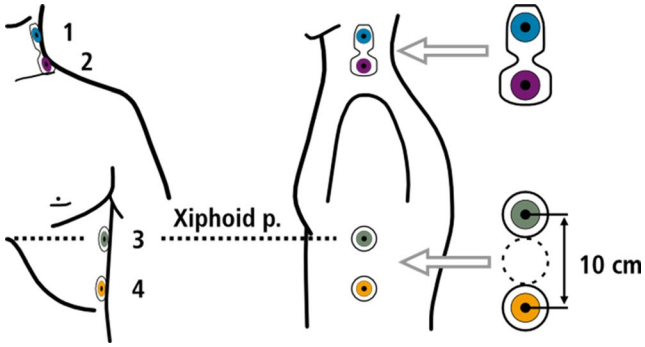

Fig. 1 Electrode placement of the impedance cardiography device

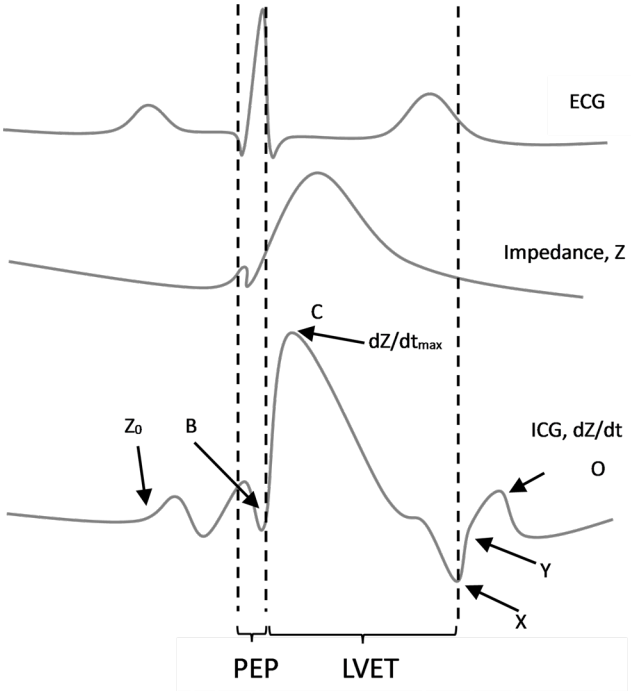

Fig. 2 Time course of the electro- and impedance cardiogram with its characteristic turning points and the derived systolic time intervals. *Abbreviations* B, opening of the aortic valve; C (dZ/dt_{max}), maximal systolic blood flow velocity; dZ/dt, maximal change in impedance; ECG, electrocardiogram; ICG, impedance cardiography; LVET, left-ventricular ejection time; O, closure of the mitral valve; PEP, pre-ejection period; X, closure of the aortic valve; Y, closure of the pulmonic valve, Z_0, baseline impedance

additional pulsoximetry sensor is attached to one ear lobe to record pulse volume curves using infrared light. Based on these blood flow dependent changes of the thoracic impedance and the electrocardiographic time intervals (Fig. 2), the software Cardio Vascular Lab calculates several hemodynamic parameters. For the purpose of our investigation, we limited our analysis to stroke volume, cardiac output and the systolic time intervals, namely pre-ejection period (PEP) and left-ventricular ejection time (LVET). While the duration of the PEP shows a negative correlation with sympathetic activity (Schächinger et al. 2001), a shortened LVET is related to a reduced left ventricular ejection fraction (Alhakak et al. 2021).

Diagnostic polysomnography (Fig. 3) revealed a respiratory distress index (RDI) of 67.9 h^{-1} mainly consisting of central events and occasional hypopneas (Table 1). The oxygen desaturation index (ODI) was 67.3 h^{-1} and the arousal index was 51.0 h^{-1}. The overall sleep efficiency as well as the percentage of both slow wave and REM sleep were reduced. Hemodynamic monitoring with ICG showed no evidence of hemodynamic compromise with values for stroke volume and cardiac ouput in the upper normal range (Table 2). Continuous blood pressure measurement revealed systemic arterial hypertension with an elevated pulse pressure during the entire sleep study.

The second sleep study with APAP (AirSense 10 AutoSet™, ResMed) showed a reduction of the RDI and the

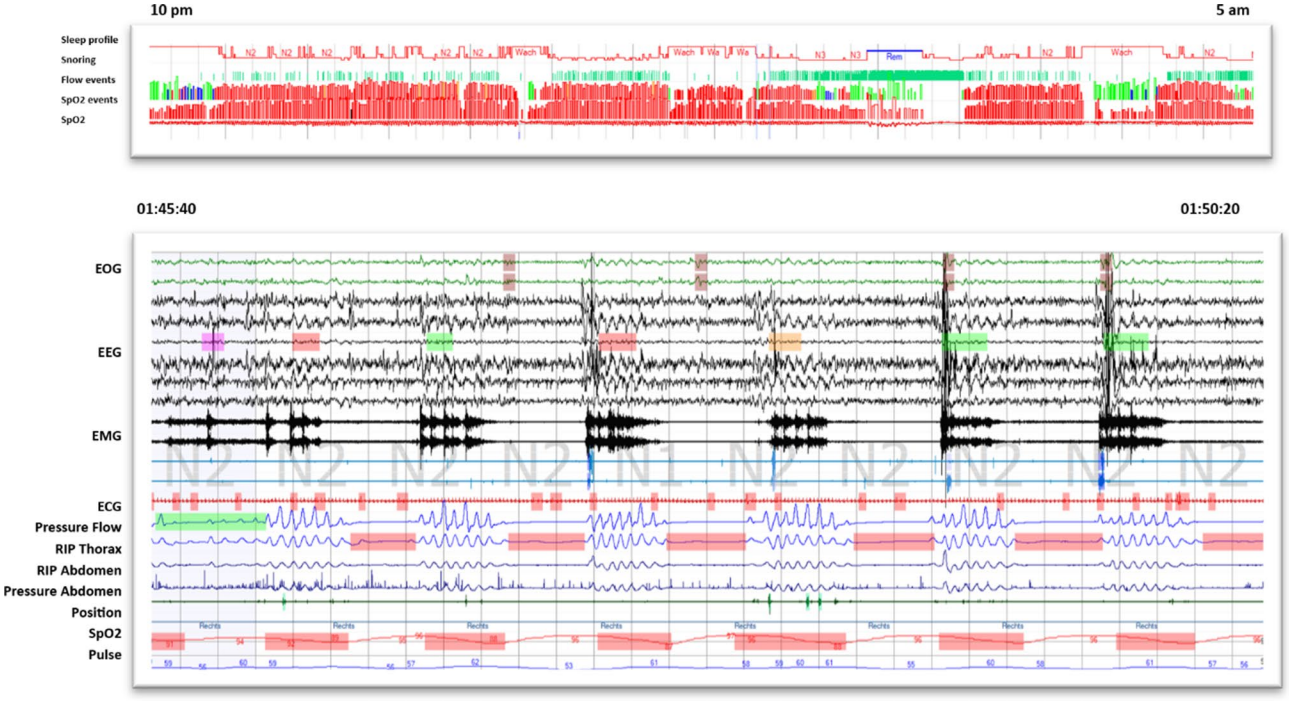

Fig. 3 Polysomnography showing Cheyne-Stokes breathing pattern under diagnostic conditions. *Abbreviations A*, auricular; C,central; ECG, electrocardiogram; F, frontal; EMG, electromyogram; EOG, electrooculogram; PLM, periodic leg movement; N, non-rapid eye movement sleep, O, occipital; RIP, respiratory inductance plethysmography, SpO2, oxygen saturation on pulse oximetry

Table 1 Polysomnographic results

	Dx	APAP	ASV	LTOT
RDI (events per hour)	67.9	37.9	5.8	6.3
central events (%)	83.9	81.8	1.7	-
obstructive events (%)	1.2	-	-	-
hypopneas (%)	12.2	16.1	98.3	100
mixed events (%)	2.5	-	-	-
ODI (events per hour)	67.3	34.2	6.4	0.2
Arousal index (events per hour)	51.0	12.9	10.9	12.8
TST (min)	310.3	315.5	354.0	349.0
Sleep efficiency (% TST)	69.0	73.2	85.6	84.7
Slow wave sleep (% TST)	21.1	55.2	46.5	38.8
REM sleep (% TST)	6.6	12.2	16.4	15.9

Results from baseline and subsequent polysomnographies. Dx, diagnostic; polysomnography; APAP, adaptive positive airway pressure; ASV, adaptive servo-ventilation; LTOT, long-term oxygen treatment; ODI, oxygen desaturation index; TST, total sleep time

Table 2 Hemodynamic parameters

	Dx	APAP	ASV	LTOT
SV (ml)	119,31 ± 22,78	111,41 ± 31,71	55,12 ± 7,17	100,82 ± 19,85
CO (l *min^{-1})	7,63 ± 2,62	6,89 ± 2,35	3,34 ± 0,67	5,82 ± 1,08
PEP (ms)	142,81 ± 25,23	168,62 ± 43,28	178,27 ± 23,65	159,52 ± 19,25
LVET (ms)	302,04 ± 25,23	240,49 ± 11,92	243,44 ± 16,85	295,09 ± 27,57
HR (min^{-1})	64,91 ± 18,73	62,01 ± 9,63	60,75 ± 7,18	57,03 ± 8,24
SBP (mmHg)	179,38 ± 8,74	140,19 ± 4,35	160,70 ± 5,77	143,82 ± 4,58
DBP (mmHg)	108,76 ± 8,38	88,47 ± 6,40	112,31 ± 6,37	100,38 ± 5,05
PP (mmHg)	70,62 ± 5,70	51,71 ± 4,11	48,39 ± 3,53	43,35 ± 4,33

Results from baseline and subsequent hemodynamic measurement. Dx, diagnostic; polysomnography; APAP, adaptive positive airway pressure; ASV, adaptive servo-ventilation; LTOT, long-term oxygen treatment; SV, stroke volume; CO, cardiac output; PEP, pre-ejection period; LVET, left ventricular ejection fraction; HR, heart rate; SBP, systolic blood pressure; DBP, diastolic blood pressure; PP, pulse pressure

ODI due to less frequent central events (Table 1). An improved sleep efficiency was associated with an increase of both slow wave und REM sleep. Hemodynamic monitoring showed a slight reduction of stroke volume and cardiac output as well as a significant drop of the systemic systolic blood pressure (Table 2). Regarding the systolic time intervals, a significant prolongation of the PEP occurred compared to diagnostic conditions.

Applying ASV (Aircurve 10 ASV, ResMed) during the following night, we observed a resolution of central events with a further reduction of the ODI and re-establishment of physiological sleep cycles (Table 1). ICG monitoring however revealed a pronounced decrease

of hemodynamic parameters with values for stroke volume (55.12±7.17 ml) and cardiac output (3.34±0.67 l/min) below the normal range (Table 2). We therefore decided to perform another sleep study using LTOT with a continuous flow rate of 2 l/minute. Polysomnography showed a complete resolution of central events with a normal ODI and a physiological sleep profile (Table 1). Measurements of stroke volume and cardiac output were in the normal range. The systemic systolic blood pressure significantly decreased which was accompanied by a prolongation of the PEP and a lower heart rate (Fig. 1). Given a normalization of the polysomnographic parameters, the absence of hemodynamic impairment, and a subjectively good treatment tolerance, we prescribed LTOT for nocturnal application.

Discussion

The abovementioned symptoms of the patient presented were explained by the emergence of central sleep apnea due to congestive heart failure and concomitant hypoxemia. Although APAP led to an improvement of polysomnographic parameters, only ASV and LTOT could induce a complete resolution of central events. Hemodynamic monitoring however revealed a marked decrease of the cardiac performance for ASV compared to the diagnostic condition which was not observed for LTOT. The decrease of stroke volume and cardiac output was associated with a reduction of heart rate, SBP, PP, LVET and a prolonged PEP which could partly be explained by a reduced sympathetic tone due to less respiratory arousals.

While the long-term cardiovascular outcome of patients with chronic heart failure and central sleep apnea treated with ASV and positive airway pressure has been investigated in large clinical trials (Cowie et al. 2017; Bradley et al. 2005), the immediate hemodynamic impact of these treatment devices remains rather unclear. Our case report demonstrates the acute hemodynamic effect of different treatment modalities for central sleep apnea which is generally not part of the standard polysomnographic assessment. Considering the negative influence of ASV on cardiovascular mortality in patients with chronic heart failure and reduced ejection fraction, it has been hypothesized that ASV may reverse potentially beneficial compensatory effects of central sleep apnea (Naughton 2012). Apart from these long-term effects, our patient showed an immediate decrease of cardiac parameters under ASV conditions presuming that the treatment device may cause acute hemodynamic compromise in patients with chronic heart failure.

It should be noted that treatment related intrathoracic pressure (ITP) changes due to APAP and ASV may have a different effect depending on the pre-existing cardiac status. In general, elevations of ITP lead to a decrease of left ventricular pre- and afterload caused by a reduction of venous return and the transaortic (transmural) pressure gradient. While the effect on left ventricular preload may predominate in healthy individuals leading to a drop of cardiac output, a reduced afterload may have a stronger effect in some patients with chronic heart failure resulting in improved cardiac output (Singh and Pinsky 2018). However, these assumptions cannot be generalized to all patients with chronic heart failure as the response to ITP changes may also depend on left ventricular morphology. While the treatment associated decrease of transmural pressure may reduce left ventricular wall stress improving myocardial contractility in patients with eccentric hypertrophy, the drop of venous return may be detrimental in patients with concentric hypertrophy who show a stronger preload dependency (Grossmann et al. 1975).

In addition, our results demonstrate the efficacy of LTOT for CSA related to hypoxemia which prevented hypocapnia due to hyperventilation and thereby stabilized the respiratory cycle. This case report therefore indicates a necessity for hemodynamic monitoring in patients with chronic heart failure and CSA when positive airway pressure treatment is initiated.

Abbreviations

AHI	apnea hypopnea index
APAP	automatic positive airway pressure
ASV	adaptive servoventilation
BMI	body mass index
CSA	central sleep apnea
ICG	impedance cardiography
ITP	intrathoracic pressure
mMRC	modified medical research council
NT-proBNP	N-terminal pro b-type natriuretic peptide
ODI	oxygen desaturation index
PSG	polysomnography
REM	rapid eye movement
TST	total sleep time

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Author contributions

C.M. and J.K. conducted the hemodynamic and polysomonographic measurements and were responsible for data collection and analysis. C.M. wrote the manuscript and prepared tables and figures to illustrate the results. C.M., J.K. and D.D. discussed and interpreted the results. All authors approved the manuscript.

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Data availability

Primary data and material on which the analysed data presented in this work is based can be received by the corresponding author upon request.

Declarations

Ethical approval

Ethical approval was given by the Ethics Committee of Marburg University.

Informed consent
According to the Declaration of Helsinki, informed written consent was received by our patient.

Competing interests
The authors declare no competing interests.

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