Conflicts of interest

The authors have no conflicts of interest to declare.

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CPAP treatment for catathrenia

Catathrenia is a rare, idiopathic sleep disorder classified as an isolated symptom of sleep-disordered breathing (SDB).[1] Its prevalence is unknown,[2] and its onset is usually in adolescence.[3] Affected individuals are frequently unaware of their problem, and family members or bed partners commonly report strange sounds while breathing during sleep.[1,3]

The hallmark of this disorder is a deep inspiration followed by prolonged expiration and a monotonous vocalization resembling groaning, usually during rapid eye movement sleep.[1]

No pharmacological treatments are available,[4] but some studies have shown partial or complete resolution of events with continuous positive airway pressure (CPAP) therapy, especially in patients with a SDB associated.[2,4,5]

The purpose of this study was to assess the effectiveness of CPAP treatment and a 6-month CPAP therapy in patients with catathrenia without SDB events associated.

We performed a prospective study of patients with catathrenia, diagnosed between 2008 and 2014, who underwent a CPAP titration PSG and subsequently initiated home CPAP therapy for 6 months. There were no exclusion criteria.

During anamnesis, the evaluated symptoms were: groaning, snoring, choking, apnea, daytime sleepiness (Epworth Sleepiness Scale [ESS]), headache, fatigue, and anxiety/depression. The diagnosis was based on an overnight polysomnogram (PSG). A catathrenia event was defined as a deep inhalation followed by prolonged exhalation, and a monotonous vocalization resembling groaning.[1] After the diagnostic study, patients underwent a CPAP titration PSG to correct catathrenia events. CPAP began at 4 cmH_2O and was progressively increased according to the type of respiratory events observed. In the presence of obstructive events, such as obstructive apnea or hypopnea, the pressure was increased by 2 cmH_2O every 15 min, and in the presence of snoring, respiratory effort-related arousals, and/or groaning episodes, it was increased by 1 cmH_2O every 15 min, until the events reduced in number or disappeared. Once the optimal pressure was achieved, CPAP was initiated at home with the established pressure. The patients were evaluated at 1 and 3 months of CPAP therapy, in the presence of their bed partner. During the evaluation, patients were questioned how they would classify their daytime complaints improvement (scale 0–100). After the first 3 months of CPAP therapy, they were contacted monthly by telephone to evaluate improvements over the remaining 3 months of therapy.

Eight patients were included. Five patients had abnormal sleepiness (ESS > 10). Six patients had symptoms of anxiety disorder and 7 were medicated with psycopharms (Table 1).

Catathrenia events during the diagnostic and CPAP titration polysomnograms are displayed on Table 2. Diagnostic PSG showed a mean respiratory disturbance index (RDI) of 2.8 ± 3.29 events/h, a mean apnea–hypopnea index of 1.2 ± 1.5 events/h. The mean number of catathrenia events was 39.3 ± 26.6. Patient #6 experienced a partial resolution of events, despite an increase in pressure up to 12 cmH_2O. This patient did not tolerate a higher pressure.

After 1 month of therapy, seven patients had significantly fewer moaning/groaning episodes and patient #6 reported a moderate reduction. After 3 months, seven patients reported complete resolution of nocturnal episodes and patient #6 reported maintenance of the moderate reduction achieved with the first month of therapy. An improvement in daytime complaints was reported by all patients (mean subjective improvement of 80/100). One patient maintained an abnormal sleepiness (ESS > 10). Complete resolution of events was maintained during the 6 months of follow-up, except for patient #6 who continued to exhibit partial improvement. This patient was subsequently treated with clonazepam for 6 months, but showed no additional improvements.

Although CPAP titration has been used in previous studies of catathrenia, its goal was to correct apnea, hypopnea, and flow limitation.[2,5] Other studies have reported an improvement in moaning/groaning with CPAP, but the majority of patients had associated SDB.[2,4]

Iriarte et al.[6] have argued that the pathological mechanism underlying catathrenia is mainly obstructive. Our results support this theory, as our patients responded to

Table 1 Demographic and clinical characteristics of patients.

Patient	Sex	Age (years)	BMI (kg/m^2)	Chief complaint	Onset of groaning	Other symptoms	Craniofacial examination	Psycopharms	ESS score
1	F	40	21.4	Groaning, excessive daytime sleepiness	Childhood	Choking, morning headache, panic attack,	Mallampati I, high narrow hard palate	Paroxetine	13
2	F	25	27.7	Groaning, fatigue	Childhood	Morning headache, panic attack	Mallampati I, deviated nasal septum	Ethyl loflazepate, trazodone	14
3	F	37	39.5	Groaning, snoring, choking	15 years of age	Depression	Mallampati II, long uvula	Paroxetine, Lorazepam, Trazodone	20
4	F	30	22	Groaning	Childhood	Tension headache	Mallampati II, tonsillectomy	Cloxazolam	11
5	M	31	26	Groaning	25 years of age	Morning headache and fatigue	Mallampati II, long uvula	–	4
6	M	32	27.2	Groaning, morning fatigue and headache	28 years of age	Apnea, depression	Mallampati I, High narrow hard palate	Sertraline, alprazolan	4
7	F	36	45.8	Groaning	26 years of age	Headache, fatigue, depression	Mallampati I	Alprazolam	3
8	F	34	18.2	Groaning	32 years of age	Choking, morning fatigue, anxiety	Mallampati I, high narrow hard palate, short uvula	Fluoxetine, alprazolam	14

F – female; M – male; BMI – body mass index; ESS – Epworth Sleepiness Scale.

Table 2 Catathrenia events and sleep characterization during the diagnostic PSG.

Patient	Diagnostic PSG										Titration PSG					After CPAP
	RDI	AHI	Min O_2 Sat	Mean O_2 Sat	Catathrenia events (total)	Catathrenia events during non-REM sleep	Catathrenia events during REM sleep	Minimum Duration (s)	Maximum Duration (s)	Clusters[a] (total)	Clusters duration (mean, s)	RDI	Peak CPAP used during titration (cmH_2O)	Catathrenia events under CPAP (total)	Minimum duration under CPAP (s)	Maximum duration under CPAP (s)	ESS
1	7	3.9	89	96	37	29	8	6	40	7	59	0.2	7	0	0	0	7
2	0.8	0.5	95	98	1	1	0	15	15	0	0	0.4	6	0	0	0	12
3	8.3	3.1	91	95	28	7	21	0.8	23	5	23	6.1	6	0	0	0	7
4	1.3	0.9	91	99	6	2	4	7	13	1	15	3.1	8	0	0	0	5
5	4.6	1.2	88	94	65	53	12	5	28	12	76	7	9	0	0	0	4
6	0	0	91	98	73	48	25	6	34	18	56	0.3	12	9	8	14	5
7	0.9	0	88	93	60	50	10	9	20	8	80	5	8	0	0	0	2
8	0.1	0	97	99	44	0	44	2	21	3	67	4.8	7	0	0	0	10

PSG – polysomnogram; CPAP – continuous positive airway pressure; RDI – respiratory disturbance index; AHI – apnea/hypopnea index; TST – total sleep time; REM – rapid eye movement; NREM – non rapid eye movement; N1, N2, N3 – sleep stages of NREM.

[a] A cluster was considered a series of at least 2 deep inspirations followed by prolonged expirations containing a groaning sound.

positive airway pressure. Vetrugno et al.[3] described a series of 10 patients with catathrenia and a normal RDI (as our patients) who had a post-inspiratory positive rise in endoesophageal pressure during events, higher than that observed in expiration in eupnoic breathing, suggesting an expiratory upper airway obstruction. One possible mechanism that might explain the response observed in our patients is subtotal closure of the glottis during expiration.[3]

Our patients presented some differences in relation to previous published series: there was a preponderance of women; OSA was absent and the majority of patients were sleepy. It is possible that patients with more severe SDB, catathrenia events were unnoticed or obscured by other respiratory sounds and therefore not detected. This may explain the lower prevalence in men and patients with OSA in our series. The higher frequency of young women is also probably related to the less severe SDB. As for sleepiness, it may be argued that it may be related to the concomitant psychiatric disorders and medications. Other sleepiness causes, recognized to contribute to sleep deprivation, were not analyzed in the present study. However, its improvement following efficacious catathrenia treatment suggest an association between both complaints and warrants further research. While no clear association has been demonstrated between catathrenia and psychiatric disorders,[1] they marked a bold presence in our study (7/8 patients). Examination by a psychiatric specialist with validated questionnaires would have provided a clearer idea of the presence of psychiatric disease in our patients. We believe CPAP treatment in patients with catathrenia without SDB events can improve nocturnal groaning episodes and daytime complaints. In a future research, laryngoscopy during sleep may help to elucidate catathrenia pathophysiology.[7]

Conflicts of interest

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Concomitant lung cancer and interstitial lung disease: A challenge in clinical practice

Dear Editor,

Lung cancer (LC) risk is increased in patients with interstitial lung disease (ILD) and sometimes both occur concomitantly.[1] LC incidence is increased 4.96-fold in patients with idiopathic pulmonary fibrosis (IPF) compared with the general population even after adjusting for age, gender and smoking habit.[2] Idiopathic interstitial pneumonias are also associated with increased LC risk and connective tissue disease-associated ILD (CT-ILD) may be a predisposing factor for pulmonary malignancy.[2]

A retrospective analysis of ILD patients diagnosed with LC at our centre in the past 5 years was performed. Characteristics of this cohort were described and outcomes were also reported.

Eleven patients were included [median age 68 (range 36 to 78) years; mostly men ($n = 9$; 81.8%)]. Almost all patients had smoking history (81.8%; ex-smokers $n = 7$; active smokers $n = 2$). The ILDs identified were CT-ILD ($n = 5$; 45.5%), combined pulmonary fibrosis and emphysema (CPFE) ($n = 2$; 18.1%), IPF ($n = 1$; 9.1%), sarcoidosis ($n = 1$; 9.1%), cryptogenic organising pneumonia ($n = 1$; 9.1%) and silicosis ($n = 1$; 9.1%). The most prevalent LC histological type was adenocarcinoma ($n = 5$; 45.5%), followed by squamous cell carcinoma ($n = 2$; 18.1%) and small cell carcinoma ($n = 2$; 18.1%). Most patients were diagnosed at advanced stages (IIIB and IV) ($n = 7$; 63.6%), mainly during clinical and radiological follow-up for the ILD. The tumours were predominantly in the peripheral lung fields, in relation to fibrotic areas. Median time from the onset of ILD to the onset of LC was 4 (range 0.3 to 249.7) months. Surgical resection was performed in 3 patients (27.3%) with stage IIA and IIIA LC; chemotherapy and/or radiotherapy were given to 6 patients (54.5%) with advanced disease (stage III and IV). One patient was refused for radiotherapy due to concern about the adverse effects and prognosis. Three patients (27.3%) had acute exacerbations of the ILD after LC treatment: 1 patient with CPFE and another with sarcoidosis presented acute exacerbation after radiotherapy and 1 patient with IPF presented acute exacerbation after chemotherapy with pemetrexed. Two of these patients died due to respiratory failure. Median survival time from the diagnosis of LC was 6.6 months (range 1.2 to 55.6). Three patients died due to progression of LC.

In our sample the majority of patients had a smoking history. Cigarette smoking is a recognised risk factor for the development of ILD[1] but the pathogenesis of LC in patients with ILD is still unclear. IPF has been considered a neoproliferative lung disorder since both IPF and cancer share similar pathogenic hallmarks such as genetic alterations, uncontrolled mesenchymal cell proliferation and tissue invasion behaviour, and dysregulated intracellular signalling pathways.[3]

The treatment choice for ILD patients presenting LC is a challenge to the physicians. In our sample some patients benefited from LC treatment but the pre-existence of ILD also influenced negatively the prognosis. Voltolini et al. showed that major lung resection in patients with early stage non-small cell LC and ILD was associated with increased postoperative morbidity and mortality, mainly in patients presenting lower preoperative FVC% and DLCO%. There was a higher postoperative mortality for pneumonectomy and lobectomy. No patients died after sublobar resection. Thus, anatomic surgical resections can be an option in appropriately selected LC-ILD patients.[4] When planning radiotherapy, it is important to determinate the radiation pneumonitis risk. A recent study showed that fatal radiation pneumonitis tended to be more common in patients with subclinical ILD and that the presence of extensive fibrosis on CT may be a contraindication for thoracic radiotherapy.[5] Stereotactic body radiation therapy (SBRT) could also be an option in LC-ILD patients because of its less invasive nature, nevertheless there is an increasing body of evidence suggesting that even SBRT can induce acute exacerbation of ILD. None of our patients were submitted to SBRT.

Chemotherapy plays an irreplaceable role against LC, but LC-ILD patients receiving chemotherapy may face risks of chemotherapy-related acute exacerbation of ILD. The question arises as to whether chemotherapy regimens are efficacious and safe for the co-morbidity population. So far, no consensus has been reached nor has enough evidence been presented to support an optimal treatment strategy for LC–ILD patients – these patients are usually excluded by most clinical trials and the relevant studies are largely single-armed. A previous meta-analysis performed to evaluate the safety and efficacy of chemotherapy in non-small cell LC–ILD patients suggested that chemotherapy might be an effective therapy for these patients, but it also might be associated with higher incidence of acute exacerbations of ILD.[6] Recently, the role of anti-fibrotic drugs in LC treatment was studied and the results were promising, opening new perspectives on therapeutic options for these complex patients.[7]