

Cycling alternating and Alpha-EEG patterns may contribute to CPAP non-compliance among Sleep Apnea patients.

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Abstract: - CPAP compliance is a therapeutic challenge. Although there may be PSG evidence of control of OSA with a reduction in AHI, snoring, nocturnal awakenings, improved oxygen saturation, and reduced daytime sleepiness, some patients continue to report residual non-restorative sleep with marked daytime fatigue which might be associated with PSG evidence of cycling alternating pattern (CAP) and alpha electroencephalography pattern (alpha-EEG). CAP and alpha-EEG are markers of sleep instability and are associated with autonomic instability, non-restorative sleep, daytime fatigue, variable musculoskeletal pain, and cognitive issues with memory and concentration.. These markers of sleep instability do not generally respond longer-term to hypnotic medication and are a potential barrier to CPAP compliance. Patients with combined OSA and markers of sleep instability suffer from both sleepiness and fatigue and are more likely to erroneously deduce that CPAP treatment has not been of benefit and abandon treatment.

In this pilot study we identified 6 OSA patients with CAP and/or alpha-EEG, who were non-compliant with CPAP and who had abnormally high scores on an Adrenal Fatigue Questionnaire and have clinical evidence of low saliva cortisol throughout the day. On the Symptom Checklist-90 (SCL-90) patients reported moderate to excessive psychological distress with anxiety and depressive symptoms, on the Wahler Physical Symptoms Inventory there was evidence of marked physical fatigue and discomfort and elevated scores on the Epworth Sleepiness Scale. In addition to CPAP, these patients were treated with a multimodal approach addressing the physical, biochemical, bio-electrical and psychological factors. Subjective improvement in their sleep, improvement in their daytime sleepiness and fatigue, decrease in CAP and/or alpha-EEG, as well as higher rates of CPAP compliance were observed with this therapeutic approach.

Key-Words: - Obstructive sleep apnea, CPAP therapy, cycling alternating pattern, alpha EEG pattern, polisomnography, sleep medicine

1 Introduction and aims

Obstructive sleep apnea (OSA) is a common sleep disorder and the most frequent sleep-disordered breathing disease.[1] Globally, sleep disorders are a global major cause of mortality, morbidity and independent primary risk factor for cardiovascular and metabolic diseases, and for traffic accidents.[2] OSA is characterized by repeated episodes of apnea-

hypopnea during sleep, frequent night-time awakenings, and daytime sleepiness.[3] Continuous positive airway pressure (CPAP) is the treatment of choice.[3-6] Since the introduction of CPAP therapy, OSA, is a problem that is easy and inexpensively treatable while significantly improving the quality of life of users.[7] Despite the dramatic improvement of symptoms with this therapy, adherence of only 60–70% has been

reported worldwide.[4,5] CPAP compliance is a therapeutic challenge.[8] Although there may be polysomnographic (PSG) evidence of control of OSA with a reduction in apnea hypopnea index (AHI), elimination of snoring, reduction of nocturnal awakenings, improved oxygen saturation, and reduced daytime sleepiness, some patients continue to report residual non-restorative sleep with marked daytime fatigue.[8]

Some states of non-restorative sleep are associated with PSG evidence of cycling alternating pattern (CAP) and alpha electroencephalography pattern (alpha-EEG). CAP and alpha-EEG are markers of disturbed sleep and are associated with autonomic instability, non-restorative sleep, daytime fatigue (ie. lack of energy with inability to fall asleep), variable musculoskeletal pain symptoms, poor memory and concentration, and low or irritable mood. Often patients, who suffer from OSA with daytime symptoms of morning headache, poor memory and concentration, low or irritable mood, and sleepiness (ie. irresistible urge to fall asleep), may also suffer from the comorbid symptoms resulting from CAP and alpha-EEG sleep instability. In these patients, CPAP treatment may rectify their OSA symptoms, but leave them with the residual comorbid symptoms from CAP and alpha-EEG sleep instability and CPAP treatment may often exacerbate these symptoms. Some patients misunderstand that the reason for their continued non-restorative sleep and low energy is CPAP inefficacy, instead of other sleep comorbidities, such as CAP and alpha-EEG. These markers of sleep instability do not generally respond longer-term to hypnotic medication and are a potential barrier to CPAP compliance.[8]

Insomnia and other sleep disorders often coexist with OSA overlapping it. Patients with combined OSA and markers of sleep instability suffer from both sleepiness and fatigue and are more likely to erroneously deduce that CPAP treatment has not been of benefit and abandon treatment.

It has been observed that patients with CAP and alpha-EEG have a history of significant stressors (psychological and/or physical) and often exhibit marked anxiety. States of stress and high anxiety, stimulate the sympathetic nervous and increase adrenal output. It can be postulated that if these high-output states persist, their sleep quality is affected; possibly predisposing them to developing significant sleep instability with the presence of CAP and /or alpha-EEG and adrenal fatigue. Increased anxiety may also make it difficult for patients to tolerate the sensation of the CPAP mask on their face.

In our Sleep Clinics in Canada (<http://www.sleepwakeawareness.com>) and Venezuela (<http://www.clinicadelsueno.com.ve>, www.clinicadelsueno.es) we often face OSA patients who exhibit severe anxiety and some are non-compliant with their CPAP therapy. We perform a comprehensive assessment of our patients' sleep/wake health and administer a multimodal treatment approach assess, of which CPAP treatment for OSA is only one component. We have observed that insomnia and CAP and alpha-EEG are present in some patients with OSA and that is why we have designed this pilot study to assess the implications of these sleep disorders on CPAP non-compliance.

We have conducted this pilot study with the aim to: 1.- Identify/diagnose CAP and alpha-EEG patterns among CPAP non-compliant OSA sufferers, 2.- Identify stressors among these patients, 3.- Apply several questionnaires and test in order to reveal anxiety, depression and/or high adrenal output, and 4.- treat this patients with a multimodal approach regimen in order to improve compliance and ameliorate the CAP and alpha-EEE patterns.

This article is organized as follows: section 2, a brief review of OSA as a public health problem and its therapy with CPAP; section 3, a review of CAP and alpha-EEG and its association with OSA; section 4, the methodology followed in this pilot study is explained; in section 5 we present some preliminary results and conclusions.

2 OSA and CPAP therapy

OSA is a public health problem and a major cardiovascular risk factor.[3,5-7] Although it was beautifully described by Charles Dickens nearly 180 years ago[9], the syndrome of obstructive apneas during sleep was described in details in early 1970s. Only 20 years later, OSA became widely recognized as a widespread and significant issue of public health. A considerable portion of society, and even the medical community, do have not enough knowledge about this problem and its negative impact on health.[10] Coronary heart disease,[11] stroke,[12] hypertension,[13] arrhythmias (being atrial fibrillation the most frequent but not the only one),[14-15] sudden death,[16] stroke, heart failure,[17] pulmonary hypertension, renal failure, obesity, diabetes,[18] traffic and occupational accidents[6,19] are some medical problems among which OSA has been

attributed as an independent risk factor.[8] Our team (unpublished data) has also observed an epidemiological association between OSA and gastroesophageal reflux disease,[20] abdominal hernias,[21] polycythemia,[22] sexual dysfunction, erectile dysfunction,[23] overacting bladder,[24] enuresis, nocturia and urgency incontinence, seizures,[25] chronic headache,[26] anxiety, depression,[27] poor memory and concentration, and low or irritable mood, high intelligence level but also poor educational achievement[28] or job performance,[29] aging, perception of less attractiveness and beauty and other aesthetical problems, palpebral edema, small for gestational age, affected quality of life of bed partners,[30] divorces,[31] couple conflicts, hypercoagulability, deep venous thrombosis, pulmonary embolism,[32] musculoskeletal pain, fibromyalgia disease,[33] among many other medical, psychological and social problems.

OSA is the recurrent obstruction of upper airway due to the relaxation of oropharyngeal muscles during sleep. Total obstruction produce apnea and partial obstruction with limited airflow produce hypopnea associated with oxygen desaturation. The upper airway could be already narrowed (ie. Obesity, micrognathism, macroglossia) or wide enough but over relaxed (ie. Stroke, cerebral palsy). The resulting asphyxia, and all the physiological and pathophysiological compensatory mechanisms, are responsible for most of the pathological consequences that we have previously mentioned (ie. Cardiovascular and metabolic diseases). [3] These intermittent asphyxias generally ends when the patient wakes up, or has arousals, due to the central respiratory cerebral centre activation, disrupting sleep. This continuously interrupted/fragmented sleep creates a chronic state of disrupted, non-restorative and reduced sleep time, in addition to the pathophysiological factors explained above, can produce hypersomnia and cognitive and psychological problems (ie. Traffic accident, poor memory, and increased irritability). The intermittent Valsalva and Müller's manoeuvres, with their intermittent positive and negative intrathoracic pressure may contribute to hernias such as inguinal or hiatal, and gastroesophageal reflux.

It was only at the early 1980s, the number of publications about OSA began to rapidly grow; and this was because of the invention of CPAP therapy for this condition.[34] This landmark in

medical history sparked the understanding of the pathophysiology and the large scope of the health issues associated with OSA. CPAP is now the gold standard treatment for OSA, is a device which takes air from the environment and generates pressure that goes to the nose and/or mouth, through a hose and a mask, and works as a pneumatic splint. The pressurized air opens the otherwise obstructed oropharynx preventing asphyxia from occurring. The absence of hypoxia, hypercapnia, and all the compensatory mechanisms eliminates the cascade of events that configures the obstructive sleep apneas/hypopneas syndrome.

OSA can coexist with other sleep problems such as insomnia, jetlag, narcolepsy, sleep instability etc. If a patient with OSA who is adequately treated with CPAP manifests hypersomnia the day after a transatlantic flight it does not mean that the CPAP is not working but, rather, the jetlag is disrupting his/her sleep.



Fig 1. Nasal CPAP on an OSA patient

3 Cycling Alternating Pattern and alpha-EEG Pattern

CAP and alpha-EEG are markers of sleep instability and are associated with autonomic instability, non-restorative sleep, daytime fatigue, variable musculoskeletal pain symptoms, poor memory and concentration, and low or irritable mood. These markers of sleep instability do not generally respond longer-term to hypnotic medication and are a potential barrier to CPAP compliance.

Patients with combined OSA and markers of sleep instability suffer from both sleepiness and fatigue and are more likely to erroneously deduce that CPAP treatment has not been of benefit and abandon treatment.

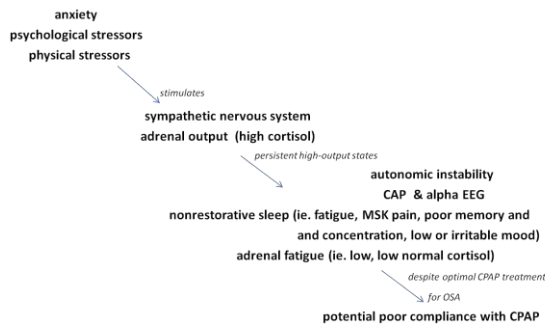


Fig 2. Proposed explanation of the role of CAP and alpha-EEG on CPAP non-compliance

It has been observed that patients with CAP and alpha-EEG have a history of significant stressors (psychological and/or physical) and often exhibit marked anxiety. States of stress and high anxiety, stimulate the sympathetic nervous and increase adrenal output. It can be postulated that if these high-output states persist, their sleep quality is affected; possibly predisposing them to developing significant sleep instability with the presence of CAP and /or alpha-EEG and adrenal fatigue. Increased anxiety may also make it difficult for patients to tolerate sensation of the CPAP mask on their face.

Sleep instability is associated with chronic pain symptoms. Alpha EEG intrusions have been found in several sleep patients with fibromyalgia, but more recent controlled and quantitative scoring failed to support the notion that alpha EEG intrusions were pain or fibromyalgia specific. The current trend is to reassess such findings in the setting of mood alterations and sleep respiratory and movement events (e.g., apnea, Periodic Limb Movement Syndrome) and to reconcile them with the fact that patients with pain have arousals in clusters or in a sequence of phasic events, also termed the cyclic alternating pattern, defined as: repeated stereotyped EEG patterns lasting < 60 seconds and separated by time-equivalent intervals of background activity. Finally, a recent study has demonstrated that the reduction in heart rate variability during sleep of healthy subjects is absent in insomniac patients and patients with fibromyalgia. If such findings can be confirmed in patients with pain without mood alteration or respiratory-motor sleep disorders, this would add support to the notion that complaints of poor sleep in chronic pain are due to sleep instability, associated with maintenance of sympathetic activation and non-restorative function.”[35]

2.1 Signs and symptoms of adrenal fatigue

- Difficulty getting up in the morning (higher energy 10 am-2pm, low 300pm-400pm, better after evening meal)
- Debilitating fatigue not relieved by sleep
- Craving for salt or salty foods
- Lethargy (lack of energy)
- Increased effort to do everyday tasks
- Decreased sex drive
- Decreased ability to handle stress
- Increased time to recover from illness, injury, or trauma
- Light-headed when standing up quickly
- Mild depression, less enjoyment or happiness with life
- Variable musculoskeletal pain
- Increased premenstrual syndrome
- Symptoms increase if meals are skipped or inadequate
- Thoughts less focused, more fuzzy “fibro-fog”
- Memory less accurate
- Decreased stress tolerance, increased irritability

Adapted from: *Adrenal Fatigue: The 21st Century Stress Syndrome*, James L. Wilson, ND, DC, PhD

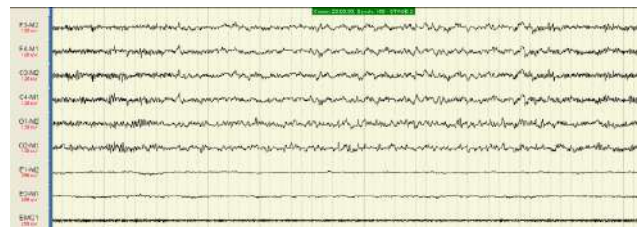


Figure 2 A 30 second epoch showing Periodic Alpha using a standard bilateral 6 lead, frontal, central and occipital EEG.

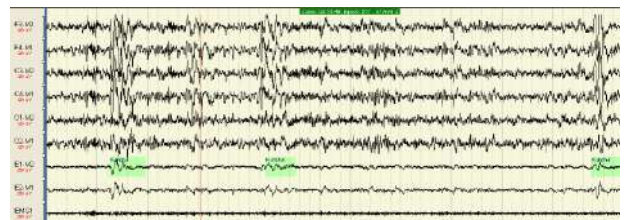


Figure 3. A one minute epoch showing Periodic K-Alpha using a standard bilateral 6 lead, frontal, central and occipital EEG.

Study Date: 09/14/2015

Time

Amplitude

9:00:01 AM 9:04:57 AM 9:05:00 AM 9:05:03 AM 9:05:06 AM 9:05:09 AM 9:05:12 AM 9:05:15 AM 9:05:18 AM 9:05:21 AM 9:05:24 AM 9:05:27 AM 9:05:30 AM 9:05:33 AM 9:05:36 AM 9:05:39 AM 9:05:42 AM 9:05:45 AM 9:05:48 AM 9:05:51 AM 9:05:54 AM 9:05:57 AM 9:06:00 AM 9:06:03 AM 9:06:06 AM 9:06:09 AM 9:06:12 AM 9:06:15 AM 9:06:18 AM 9:06:21 AM 9:06:24 AM 9:06:27 AM 9:06:30 AM 9:06:33 AM 9:06:36 AM 9:06:39 AM 9:06:42 AM 9:06:45 AM 9:06:48 AM 9:06:51 AM 9:06:54 AM 9:06:56 AM

F10 - [Ang]

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PARKING - (DMS15)

PARKING - (DMS15)

PARKING - (DMS15)

NADA PRESSURE

AIRFLOW

CHEST

ABDOMEN

SpO2

230.0

10.0

79.0

97.0

9:00:01 AM 9:04:57 AM 9:05:00 AM 9:05:03 AM 9:05:06 AM 9:05:09 AM 9:05:12 AM 9:05:15 AM 9:05:18 AM 9:05:21 AM 9:05:24 AM 9:05:27 AM 9:05:30 AM 9:05:33 AM 9:05:36 AM 9:05:39 AM 9:05:42 AM 9:05:45 AM 9:05:48 AM 9:05:51 AM 9:05:54 AM 9:05:57 AM 9:06:00 AM 9:06:03 AM 9:06:06 AM 9:06:09 AM 9:06:12 AM 9:06:15 AM 9:06:18 AM 9:06:21 AM 9:06:24 AM 9:06:27 AM 9:06:30 AM 9:06:33 AM 9:06:36 AM 9:06:39 AM 9:06:42 AM 9:06:45 AM 9:06:48 AM 9:06:51 AM 9:06:54 AM 9:06:56 AM

We selected 30 patients with OSA, who were not compliant with their CPAP therapy. After assessing the reason for their withdrawal of therapy, we excluded those patients, who stopped the CPAP usage because reasons others than medical (ie. Economical, those who were not willing to use it, those who preferred to try another therapy). Ten patients were ruled out. We performed another PSG on those patients, who complained that CPAP was “not effective”, “it did not work as before”, or those who stated that somnolence and fatigue were unchanged or even worse than before using CPAP. A specific algorithm for CAP and alpha-EEG analysis was used.

traditional Chinese Medicine. Neuro Emotional Technique (NET)
<http://www.netmindbody.com/>

- 4) Psychological: psychodynamic psychotherapy.

5 Preliminary results, conclusion and recommendations

5.1 Sample case

This is a sample of one of the cases. Patients characteristic were similar. Results will be published elsewhere.

CASE 1 "I'm sleepy all the time...I can't get anything done"

47 YO woman, BMI 31, maintenance insomnia, history of snoring, day time sleepiness, restlessness in legs at night, pain in her neck, shoulders, back and feet, issues with memory and concentration, depressed mood, history of anxiety

Rx: zopiclone 7.5 mg qhs, citalopram 20mg OD, pramipexole 0.5mg qhs, synthroid 0.125 mg.

Diagnostic PSG: AHI 23.8, REM events/ hr 17.7, Sleep Efficiency 85.8, Min SaO₂%, 87 NREM, 85 REM, Total PLMS/ hr 24.3, Alpha-EEG score 3, Periodic EEG arousals/ hr 24.3, CPAP Titration PSG: CPAP 7 cm H₂O, AHI 2.4, REM events/ hr 4.6, Sleep Efficiency 80.0, Min SaO₂ 95 NREM, 94 REM, Total PMLS/ hr 27.6, Alpha-EEG score 3, Periodic EEG arousals/ hr 32.5.

5.2 Results

One patient was lost to follow-up. The remaining 5 patients showed improved compliance with CPAP when managed with a multimodal approach. They reported subjective improvement in their sleep, feeling more refreshed upon awakening and improvement in their daytime sleepiness and fatigue, as well as daytime functioning. There was also an improvement in the scores of self-report inventories. In 2 of the patients there was PSG evidence of a decrease in CAP and/or alpha-EEG.

5.3 Conclusions and recommendations

These preliminary findings warrant further investigation and offers potential avenues for treatment of patients with both OSA associated sleepiness and sleep instability associated non-restorative sleep and fatigue.

Education regarding differentiating the treatment effects of CPAP and the untreated clinical

symptoms of sleep instability is needed. As well, assessment and treatment of underlying adrenal fatigue, mood and anxiety disorders, and life stressors must be considered. Activities which enhance parasympathetic nervous system tone (ie. yoga, tai chi, swimming, and meditation) and systematic CPAP mask desensitization may improve compliance.

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