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Sleep Medicine 5 (2004) 507–508

SLEEP MEDICINE

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Case report

Effectiveness of mirtazapine in the treatment of sleep apnea/hypopnea syndrome (SAHS)

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Received 14 February 2004; received in revised form 1 June 2004; accepted 3 June 2004

Abstract

Several drugs have been described as possible treatments for Sleep Apnea/Hypopnea Syndrome (SAHS) but the data available does not support their use. In an animal model of central apnea the use of mirtazapine produced a significant reduction of apneas. We present a male patient, 82 years old, with excessive daytime sleepiness and loud snoring during at least 10 years. An overnight polysomnography (PSG) revealed an apnea/hypopnea index of 54.9 events per hour of sleep with a minimum pulse oximetric saturation (SaO_2) of 78% and an arousal index of 40.4 per hour. A nasal CPAP titration in the second half of the night showed suppression of apneas with a CPAP level of 8 cmH_2O.

The patient refused to use the CPAP device and began with 15 mg of mirtazapine at bedtime. A second PSG performed after 3 months of mirtazapine showed a significant reduction in the apnea/hypopnea index (9.3 events per hour of sleep; 81% minimal oxygen saturation (SaO_2)). Clinically, the patient and his wife reported a clear reduction of excessive daytime sleepiness and an improvement in self-reported functioning and well-being without any important side effects.

This successful case appears to be the first report with mirtazapine in human SAHS and supports the need for an appropriate clinical trial with this drug.

1. Introduction

Nasal continuous positive airway pressure (CPAP) is the best treatment for the SAHS at present, especially in patients with moderate to severe SAHS [1].

CPAP has been demonstrated to be effective controlling the symptoms and decreasing the apneas and hypopneas, but the acceptance and compliance by patients is only partial [2]. In addition, as there is increasing evidence linking this syndrome to cardiovascular and cerebrovascular complications [3], it is important to find alternative therapies for these patients.

Serotonin-enhancing drugs have been tested as pharmacological treatments for SAHS due to their potential to stimulate respiration; however, the improvement has been found to be poor. Carley and Radulovacki [4] used mirtazapine, an antidepressant with 5-HT1 agonist as well as 5-HT2 and 5-HT3 antagonist effect, in an animal model of central apnea, achieving a significant reduction of apneas during NREM and REM sleep.

2. Case report

We present a male patient, 82 years old, body mass index (BMI) of 24.4 kg/m^2, with excessive daytime sleepiness and loud snoring over at least 10 years. An overnight PSG using standard wide criteria and including oronasal thermistor and nasal cannula pressure transducer (Alice 3; Healthdyne; Atlanta, GA) was performed in May 2002. This test revealed an apnea/hypopnea index of 54.9 events per hour of sleep (central apneas: 67; mixed apneas: 38; obstructive apneas: 6 and hypopneas: 18) (Table 1) with a minimum pulse oximetric saturation (SaO_2) of 78% and an arousal index of 40.4 arousals per hour. A nasal CPAP titration on the second

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doi:10.1016/j.sleep.2004.06.004

Table 1
Comparison of PSG variables on PSG basal, CPAP titration and with mirtazapine treatment

PSG variable	Basal PSG	CPAP titration	Mirtazapine treatment
Stage 1 (%)	73	53.2	29.8
Stage 2 (%)	27	34.8	62.9
Stages 3 and 4 (%)	0	11.9	0.8
REM (%)	0	0	6.5
Average oxygen saturation (%)	91	93	94
Lowest oxygen saturation (%)	78	83	81
Apnea/hypopnea index (N°/h)	54.9	14.3	9.3
Apnea Index (N°/h)	47.2	8.4	1
Obstructive apnea index (N°/h)	2.6	0	1
Mixed apnea index (N°/h)	16.2	0	0
Central apnea index (N°/h)	28.5	8.4	0
Hypopneas index (N°/h)	7.7	6	8.3
Mean event duration (s)	20.3	19.7	16.5

half of the night showed suppression of apneas with a CPAP level of 8 cmH_2O. The patient refused to use the CPAP device and in July 2003 began with 15 mg of mirtazapine at bedtime.

A second PSG performed in October 2003, after 3 months of mirtazapine, showed a significant reduction in the apnea/hypopnea index (9.3 events per hour of sleep; 81% minimal oxygen saturation (SaO_2)).

Clinically, the patient and his wife reported a clear reduction of excessive daytime sleepiness and an improvement in self-reported functioning and well-being. The BMI in October 2003 was 26 kg/m^2. Up to the last follow-up on January 17, 2004, with the same dosage of mirtazapine the patient was doing well and without any important side effects. He only complained of slight dryness of the mouth.

3. Discussion

It has been known for more than 25 years that central apneas can be seen in heavy snorers [5]; however, this case did show an unusually large number of central apneas. These central events are reduced by nasal CPAP; their underlying pathophysiology has been studied by Guilleminault et al. [6]. Schwartz and Rochemaure [7] reported improvement of obstructive apneas in Pickwickian patients using clomipramine, a tricyclic medication with aminergic reuptake blocking properties. Protriptyline was used in the 1980 s in loud snoring and mild sleep-disordered breathing, but because it produced impotence it was not use widely. The poor therapeutic effect obtained with more specific serotonin-enhancing drugs, such as fluoxetine and paroxetine [8,9], is probably due to a nonspecific stimulation of the serotoninergic system instead of the more selective action of mirtazapine [4]. A recent Cochrane review [10] of double-blind, randomized placebo-controlled trials of drug treatments for obstructive sleep apneas, found that protriptyline led to a symptomatic improvement but without any change in the apnea frequency.

The effects of mirtazapine in sleep, improving the efficiency and increasing the slow wave sleep, especially in depressed patients, have also been reported [11].

This successful case appears to be the first report with mirtazapine in human SAHS and supports the need for an appropriate clinical trial with this drug.

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