

Severe Central Sleep Apnea Associated With Chronic Baclofen Therapy

A Case Series



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Baclofen, a gamma-aminobutyric acid-B agonist with muscle-relaxant properties, is widely used in patients with severe spasticity. In animals, baclofen has been shown to decrease respiratory drive. In humans, however, use of baclofen at the standard dose did not significantly impair sleep-disordered breathing in a susceptible population of snorers. Recently, there has been increasing interest in the role of baclofen for the treatment of alcohol dependence. We describe severe central sleep apnea (CSA) in four patients with none of the conditions commonly associated with CSA who were receiving chronic baclofen therapy for alcohol withdrawal. In one patient, baclofen withdrawal was associated with a complete resolution of CSA. Three patients were treated by adaptive servo-ventilation while continuing their treatment with baclofen. Given the increasing number of patients receiving baclofen for alcohol withdrawal treatment, physicians should be aware that these patients might be affected by severe CSA. Future studies are required to determine the mechanisms, prevalence, and treatment modalities of sleep-disordered breathing associated with baclofen usage. CHEST 2016; 149(5):e127–e131

KEY WORDS: alcohol dependence; baclofen; central sleep apnea

Baclofen is a gamma-aminobutyric acid (GABA)-B agonist with muscle-relaxant and antispasmodic properties. It is widely used for the relief of chronic severe spasticity in patients with spinal cord lesions or other neurologic disorders.¹ After titration from low doses, standard treatment includes daily oral administration of 40 to 80 mg, which is the commonly accepted maximum daily dosage of baclofen.² In animals,³ baclofen has been shown to decrease respiratory drive;

in humans, however, use of the standard dose of the drug did not significantly impair sleep-disordered breathing (SDB) in a susceptible population of snorers.⁴ In recent years, there has been increasing interest in the potential role of baclofen for the treatment of alcohol dependence using a dosage of 30 to 270 mg/d.^{5,6} We describe four cases of severe central sleep apnea (CSA) attributed to oral baclofen therapy for alcohol withdrawal.

ABBREVIATIONS: ASV = adaptive servo-ventilation; CSA = central sleep apnea; GABA = gamma-aminobutyric acid; SDB = sleep-disordered breathing

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Case Reports

Four male patients aged 46 to 70 years treated with baclofen 40 to 190 mg/d for alcohol withdrawal underwent overnight polysomnography (n = 2) or respiratory recording (n = 2) for symptoms of sleep apnea; these symptoms included snoring, nocturnal choking, and daytime sleepiness (Table 1). Their other medications included antidepressants (n = 4), neuroleptic agents (n = 1), and anxiolytic and hypnotic drugs (n = 3). None of the patients had a history of cardiac disease, and one patient had a history of stroke

(4 years earlier). Patients had a BMI between 29 and 31 kg/m². Analysis of arterial blood gas measurements while breathing room air showed no hypocapnia or hypercapnia, no marked hypoxemia, and no alkalosis. Scores on the Epworth Sleepiness Scale varied between 6 and 15. The Epworth Sleepiness Scale is a reliable and validated questionnaire for measuring daytime sleepiness in adults with a score from 0 to 24. A higher score indicates more daytime sleepiness. An Epworth score >10 is considered being sleepy. Scoring of sleep recordings according to recommended guidelines⁷

TABLE 1] Patient Characteristics

Characteristic	Patient No.			
	1	2	3	4
Age, y	47	46	53	70
Sex	Male	Male	Male	Male
BMI, kg/cm ²	29	30	31	31
History of cardiovascular diseases ^a	None	None	Stroke	None
Baclofen				
Dosage, mg/d	190	150	40	180
Duration of use, mo	60	9	10	3
Associated medications				
Opioids	None	None	None	None
Antidepressants	Venlafaxine	Paroxetine	Venlafaxine	Paroxetine
Anxiolytic/hypnotic agents	None	Alprazolam, zolpidem	Zopiclone	Zopiclone
Neuroleptic agents	None	None	Risperidone, loxapine	None
Arterial blood gas				
PaO ₂ , mm Hg	80	90	93	74
PaCO ₂ , mm Hg	42	37	37	42
pH	7.40	7.41	7.44	7.42
Epworth Sleepiness Scale score	15	9	6	10
Polygraphic data				
Apnea-hypopnea index, no./h	59	73	100	73
Apnea index, no./h	35	57	100	46
Central apneas, %	90	98	100	98
Mean oxygen saturation, %	94	94	93	91
3% ODI, no./h	38	26	62.1	81
T90, %	5.00	0.07	13.40	19.00
Cheyne-Stokes respiration	None	None	None	None
Total sleep time, min	365	248
N1 sleep, %	40	30
N2 sleep, %	10	65.5
N3 sleep, %	35	0
REM sleep, %	15	4.5
Arousal index, no./h	40	42

ODI = oxygen desaturation index; REM = rapid eye movement; T90 = percentage of recording time with oxygen saturation < 90%.

^aIncluding cardiac disease, heart failure, atrial fibrillation, and stroke.

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