A 45-YEAR-OLD MAN WITH EXCESSIVE DAYTIME SOMNOLENCE, AND WITNESSED APNEA AT ALTITUDE

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Abstract
A sleepy man without sleep apnea at 1609m (5280 feet) had disturbed sleep at his home altitude of 3200m (10500 feet). In addition to common disruptors of sleep such as psychophysiological insomnia, restless leg syndrome, alcohol and excessive caffeine use, central sleep apnea with periodic breathing can be a significant cause of disturbed sleep at altitude. In symptomatic patients living at altitude, a sleep study at their home altitude should be considered to accurately diagnose the presence and magnitude of sleep disordered breathing as sleep studies performed at lower altitudes may miss this diagnosis. Treatments options differ from those to treat obstructive apnea. Supplemental oxygen is considered by many to be first-line therapy.

Case Report
A 45 year old man presents for evaluation of poor sleep, daytime somnolence, and morning headaches. His bed partner reports that he has loud snoring, gasping arousals, and frequent episodes of apnea. He is an obese man with diabetes, hypertension, rhinosinusitis, and gastroesophageal reflux disease who is a long time resident at 3200m (10500 feet). Polysomnography performed at 1609m (5280 feet) showed a normal apnea-hypopnea index (AHI) of 1.4. He spent less than one minute with an oxygen saturation (SaO2) less than 88%. Given the severity of his symptoms, a home cardiopulmonary sleep study was performed at 3200m (10500 feet). AHI was 39 non-supine and 56 supine. A representative portion of his study is shown in Figure 1. It demonstrates the absence of respiratory effort during apnea events, consistent with central sleep apnea from periodic breathing at altitude.
Figure 1. This is a representative example of breathing during sleep. The upper two channels show nasal (nasal flow) and oral air flow (thermistor). Respiratory effort signals in the abdomen and thorax are shown in the next two channels and oxygen saturation in the bottom tracing. A ten minute period of recording is displayed.

Discussion

Central apnea is characterized by recurrent episodes of apnea resulting from temporary loss of ventilatory effort. These episodes generally result from a strong dependence on the metabolic control of ventilation during sleep.\(^1\) Conditions inducing a reduced partial pressure of carbon dioxide in arterial blood (PaCO\(_2\)) can precipitate a central apnea, often associated with an arousal and leading to daytime somnolence.

At higher altitudes, the fraction of inspired oxygen (FiO\(_2\)) is the same as it is at sea level, but the barometric pressure and oxygen tension are less, so the partial pressure of oxygen in arterial blood (PaO\(_2\)) and SaO\(_2\) tend to be reduced. This tendency toward hypoxemia elicits a series of physiologic responses including increased alveolar ventilation, lowering the resting PaCO\(_2\), shrinking the gap between the resting PaO\(_2\) and the PaCO\(_2\) associated with apnea (the apnea threshold). People with sensitive chemoreceptors are more likely to develop periodic breathing at altitude. An increased ventilatory response to hypoxemia may reduce PaCO\(_2\) below the apnea threshold. The resultant apnea will eventually result in worsened hypoxemia, which will trigger hyperventilation setting up the oscillating pattern of apnea and hyperventilation typical of periodic breathing.\(^1\) Of note, these responses seem primarily related to hypoxemia rather
than low barometric pressure as they are present in simulated normobaric hypoxia equivalent to 2000m (6562 feet) altitude.²

Central sleep apnea encompasses multiple disorders including narcotic-induced central apnea, obesity-hypoventilation syndrome, Cheyne-Stokes breathing often seen with heart failure or cerebrovascular disease, and high altitude-induced periodic breathing. Periodic breathing at altitude has the pattern of apneic episodes with cycles of hypoxemia, subsequent hyperventilation, hypocapnia, and resulting apnea described above. The skeletal muscle atonia and reduced respiratory drive³ that normally occurs during rapid eye movement (REM) sleep typically terminates the periodicity by eliminating hyperventilation and restoring regular breathing. Thus, periodic breathing at altitude is seen primarily during non-REM sleep.⁴ This aberrant respiratory pattern may initially be beneficial at high altitude since the hyperventilation increases SaO2 by 2.9±1.5%, thus improving hypoxemia.⁴ In our patient, this potential benefit was overcome by a significant increase in sleep disturbance leading to sleep deprivation as well as mental and physical impairment.

Treatment options for periodic breathing at altitude include nighttime oxygen therapy, acetazolamide, and sedative-hypnotics. Supplemental oxygen breaks the apnea cycle by eliminating the hypoxemia that results in hyperventilation, hypocapnia, and apnea. Studies of supplemental oxygen at altitude have shown that subjects spend more time in deep sleep and have improvements in SaO2, tidal volume and AHI.⁵

Acetazolamide, a carbonic anhydrase inhibitor, induces a metabolic acidosis by urinary elimination of bicarbonate. This is thought to increase ventilation, left-shift the hypercapnic ventilatory response and thus reduce apnea events. Acetazolamide can significantly improve sleep disordered breathing and oxygen saturation during sleep.⁶ Sedative-hypnotic agents have also improved slow wave sleep at altitude without adversely affecting respiration or performance. This improvement is thought to be secondary to a decrease in wakefulness after sleep onset and improved sleep efficiency.⁷

This patient presented with classic symptoms of sleep apnea with a negative sleep study at 1609m (5280 feet), arousing clinical suspicion for periodic breathing at altitude. A repeat home sleep study revealed moderate to severe central sleep apnea. After treatment with oxygen and acetazolamide his symptoms significantly improved and repeat home monitoring demonstrated an AHI of 6. Treatment with oxygen alone resulted in improvement as well with an AHI of 13.

Central sleep apnea and periodic breathing are common causes of disturbed sleep at altitude. Symptomatic patients living at altitude should have a sleep study at their home altitude to accurately diagnose the presence and magnitude of sleep disordered breathing. Oxygen is considered by many to be first line therapy.

References


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**Abbreviation List:**

AHI - Apnea hypopnea index, the number of apneas or hypopneas per hour of sleep or recording

m – Meters

FiO2 – Fraction of inspired oxygen

PaCO2 - Partial pressure of carbon dioxide in arterial blood

PaO2 – Partial pressure of oxygen in arterial blood

REM – Rapid eye movement

SaO2 – Percentage of available hemoglobin that is saturated with oxygen