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CLINICAL REVIEW

Obesity hypoventilation syndrome – The big and the breathless

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SUMMARY

Daytime hypercapnia that develops in morbidly obese individuals in the absence of concurrent lung or neuromuscular disease is referred to as the obesity hypoventilation syndrome (OHS). The characteristic polysomnographic (PSG) abnormality is marked sleep hypoxemia. Although the likelihood of hypoventilation increases with increasing body mass index (BMI), it is too simplistic to think of this disorder arising merely from chest wall restriction due to excess weight. Rather, this is a disorder which emerges when the compensatory mechanisms that normally operate to maintain ventilation appropriate for the level of obesity are impaired. OHS develops from a complex interaction between abnormal respiratory function, sleep disordered breathing and diminished respiratory drive. Irrespective of the mechanisms underlying the development of this disorder, early recognition of the problem and institution of effective therapy is important to reduce the significant clinical and societal repercussions of OHS. While therapy directed at improving sleep disordered breathing is effective in reversing daytime respiratory failure, it is not universally successful and information regarding longer term clinical outcomes is limited. Attention to weight reduction strategies are also necessary to reduce comorbid conditions and improve quality of life, but data regarding how successful and sustained this is in obesity hypoventilation are sparse.

Introduction

A substantial body of literature now exists highlighting the significant impact obesity has on upper airway function and the development of obstructive sleep apnea (OSA). More recently, the potential links between OSA and a range of cardiometabolic disorders have received considerable attention.[1] As obesity increases so do health problems, requiring greater utilisation of healthcare resources.[2,3] Current estimates suggest not only rising rates of obesity, but the emergence of an increasing population of morbidly obese (Body Mass Index: BMI $\geq$ 40 kg/m^2) and super obese (BMI $\geq$ 50 kg/m^2) individuals.[4]

Greater degrees of obesity have more significant consequences for the respiratory system. The most critical of these consequences is the development of alveolar hypoventilation and daytime respiratory failure (awake arterial carbon dioxide ($PaCO_2$) $\geq$ 45 mmHg) in patients with a BMI $\geq$ 30 kg/m^2. Termed obesity hypoventilation syndrome (OHS), this disorder is diagnosed after other possible causes of hypoventilation such as lung, neuromuscular or chest wall deformities have been excluded. The incidence of OHS rises significantly as obesity increases,[5] with a reported prevalence of around 10–20% in outpatients presenting to sleep clinics, to almost 50% of hospitalised patients with a BMI $\geq$ 50 kg/m.[26] The prevalence of OHS in the general population is unknown, as one of the major measures to identify this disorder (namely a raised $PaCO_2$ on arterial blood gas measurements) is not routinely performed in epidemiological studies. However, a current estimate suggests around 0.37% of the US population may have OHS,[7] equating to several hundred thousand individuals.[8] In light of the rapidly increasing numbers of individuals joining the ranks of the morbidly obese, and the significantly greater need they have for medical care, OHS needs to be considered as a significant clinical and societal problem. Unfortunately it is also one that is frequently overlooked,[6] despite the significant comorbidities[3,9] and higher hospitalisation rates these individuals experience.[3,6]

To breathe or not to breathe

The sources of respiratory abnormality in OHS have been categorised into three main areas: alterations in pulmonary function; changes in ventilatory control; and the presence of sleep breathing abnormalities. There is no doubt that obesity in its own right has a significant impact on each of these factors. However, the majority of morbidly obese individuals are able to compensate for the abnormalities imposed by their excessive weight, maintaining daytime eucapnia. Consequently, it appears that OHS emerges *only* when compensatory mechanisms fail or become overwhelmed.[10–13] It is important to realise that these various respiratory abnormalities

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Nomenclature

AHI	apnea hypopnea index
AVAPS	average volume-assured pressure support
BMI	body mass index
CPAP	continuous positive airway pressure
ERV	expiratory reserve volume
FEV_1	forced expiratory volume in 1 s
FRC	functional residual capacity
FVC	forced vital capacity
MVV	maximum voluntary ventilation
NIV	non-invasive ventilation
NREM	non-rapid eye movement sleep
OSA	obstructive sleep apnea
OHS	obesity hypoventilation syndrome
PAP	positive airway pressure
$PaCO_2$	partial pressure of carbon dioxide
PaO_2	partial pressure of oxygen
PEEPi	intrinsic positive end expiratory pressure
PSG	polysomnography
REM	rapid eye movement sleep
SpO_2	oxygen saturation, measured by pulse oximetry
SWS	slow wave sleep
TLC	total lung capacity
TST	total sleep time

do not occur in isolation, and that a complex interaction between pulmonary function, drive and sleep disordered breathing exists (Fig. 1).

Alterations in pulmonary function

In morbid obesity, fat accumulation around the abdomen and chest wall imposes a significant load on the respiratory system such that lung volumes are reduced, while marked changes in respiratory system compliance and airway resistance contribute to a high work of breathing. Total lung capacity (TLC), expiratory reserve volume (ERV) and functional residual capacity (FRC) are all reduced, and these changes are more evident in OHS than eucapnic patients, even at similar levels of BMI.[12,14,15] This, in part, is due to the distribution of excess weight. A central pattern of obesity is associated with more severely compromised lung volumes than obese patients with a lower body obesity pattern.[16,17] Individuals with OHS have larger neck circumferences and higher waist: hip ratios than those with eucapnic obesity or OSA,[18] reflecting greater degrees of central obesity. Therefore larger reductions in lung volumes with OHS are not unexpected.

Breathing at low lung volumes significantly affects pulmonary mechanics,[19] reducing both chest wall and lung compliance,[19–21] while increasing airway resistance.[22] Respiratory system compliance has been shown to be around 20% less in eucapnic obese individuals compared to subjects who are of normal weight, and almost 60% less in patients with OHS,[20,23] with recent work suggesting this may be due to reduced lung rather than chest wall compliance.[19] By breathing at low lung volumes, small airway closure during exhalation is more likely, creating expiratory flow limitation and intrinsic positive and expiratory pressure (PEEPi).[24–26] This in turn increases the work of breathing by imposing a threshold load on the inspiratory muscles.[24,25,27] During spontaneous breathing at rest, patients with OHS have a significantly greater work of breathing than subjects of normal weight or eucapnic obese patients with OSA.[24,28] Adopting the supine posture creates further reductions in respiratory system compliance[20] and FRC,[26] while increasing expiratory flow limitation.[25] Upper airway resistance increases in the supine position in eucapnic OSA patients, while in those with OHS the increase in resistance is seen both in sitting and in lying.[29] These factors all contribute to the significantly higher work of breathing at rest seen in OHS patients compared to eucapnic obese individuals, which is increased further when the patient becomes recumbent for sleep.[28]

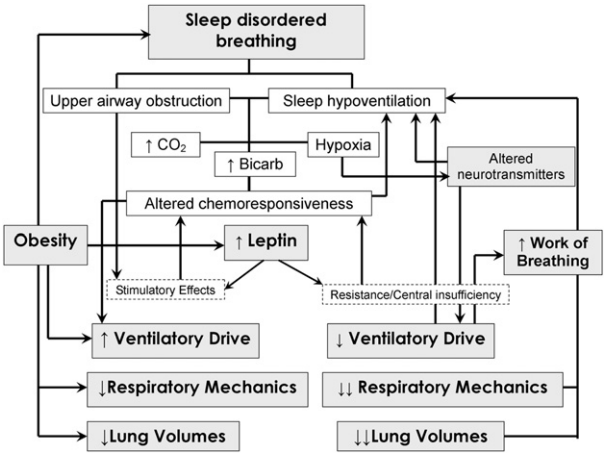

Fig. 1. Schema outlining the potential sources of respiratory abnormality that can occur in morbid obesity, and the complex interaction between these factors that may ultimately lead to the development of hypoventilation.

Low ERV also affects gas exchange, worsening ventilation-perfusion matching particularly in the supine position. Obese individuals adopt a pattern of breathing that is characterised by small tidal volumes and higher respiratory rates compared to non-obese.[30–32] This strategy is thought to optimise the O_2 cost of breathing, which is high in obesity,[33] but also increases dead space.[30] Consequently, hypoxemia is a common finding in both eucapnic obesity and OHS, but is significantly worse in the OHS group.[18]. Waist to hip ratio has been shown to have a significant impact on gas exchange, more so than actual weight or BMI,[34] and as this is frequently greater in OHS along with lower ERV, more derangement in oxygenation is not unexpected. However, greater exposure to longer periods of low oxygen levels during both wakefulness and sleep places patients with OHS at higher risk of developing hypoxia-related disorders such as pulmonary hypertension,[35] congestive heart failure and cor pulmonale.[3,9]

The performance of the respiratory muscles is impaired in OHS patients compared to morbidly obese subjects who remain eucapnic,[36,37] with further worsening in the supine position, especially in those with OHS.[38] One explanation put forward to explain this observation is a mechanical overstretching of the diaphragm by abdominal fat deposition rendering it less efficient.[38] Chronic hypoxia and hypercapnia, characteristic of OHS, could also contribute to poorer respiratory muscle function.[39] Maximum voluntary ventilation is lower in patients with OHS compared to eucapnic obesity, and strongly correlates with CO_2.[40] In studies of rats, the development of morbid obesity was associated with a thickening of the diaphragm[41] and an increase in its oxidative capacity, changes that would help maintain force and ventilation without inducing fatigue despite the high work of breathing from the added load.[42] It is unknown whether such remodelling occurs in human obesity and if there are differences between eucapnic and hypercapnic individuals. However, it is plausible that the reduced