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Obesity hypoventilation syndrome affects physical and mental health. Treatment should focus on weight loss but is aided by managing symptoms via non-invasive ventilation

Treatment of obesity hypoventilation syndrome

In this article...

- The impact of obesity on sleep-disordered breathing
- Pathophysiology of obesity hypoventilation syndrome
- Outline of the treatment options available

5 key points

1. The prevalence of obesity is a growing problem worldwide
2. Obese patients may have leptin resistance
3. Adipose tissue is a major contributing factor to compromising respiratory function
4. Volume-targeted non-invasive ventilation (NIV) is an alternative to standard bilevel NIV
5. The patient's ideal weight should be used when setting target tidal volumes

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Aside from being a health concern in itself, obesity can result in other serious health conditions. Some of these, such as cancer, can result in early death, while others, including sleep-disordered respiratory problems, can compromise patients' day-to-day quality of life and economic status. This article explores how obesity affects respiratory disorders and focuses on obesity hypoventilation syndrome. It outlines the pathophysiology and diagnosis of the condition, and explains how it can be treated with non-invasive ventilation.

A survey of obesity prevalence undertaken by Public Health England in 2014 shows an upward trend; this has far-reaching consequences on the health of individuals, from general sleep-disordered breathing to cardiovascular disease, and from diabetes to certain cancers, ultimately leading to premature death (PHE, 2014; Borel et al, 2012a). One consequence is obesity hypoventilation syndrome (OHS), which is defined as a combination of:

- Obesity;
- Hypercapnia (high levels of carbon dioxide in the blood in the day);
- Hypoxia (oxygen deficiency);
- Sleep-disordered breathing in the absence of other disorders that may cause hypoventilation, such as significant lung or respiratory muscle disease (Borel et al, 2012b; Mokhlesi et al, 2007).

OHS, commonly associated with obstructive sleep apnoea (OSA), is caused by upper airway obstruction, which results in recurrent apnoea as well as reduced air flow in the airways or hypopnoea (defined as shallow breathing or low respiratory rate), oxygen desaturations and frequent episodes of sleep arousal. It is estimated that 10-20% of patients with OSA may also have OHS (Mokhlesi et al, 2008). Box 1 outlines the characteristics of OHS.

Respiratory hypoventilation and sleep disorders are often unrecognised or underdiagnosed (Dabal and BaHammam, 2009). Simonds (2013) found that OHS often goes unrecognised until patients present with acute hypercapnic respiratory failure.

Pathophysiology

In people who are obese, adipose tissue mass in the abdominal and intrathoracic regions hinders the ability of the lungs to fully inflate, mainly by restricting the normal movement of the diaphragm during breathing. Adipose deposits also change the balance of elastic recoil between the chest and lung (Borel et al, 2012a); this reduces vital capacity (VC) – the maximum amount of air that can be inhaled and exhaled – and functional residual capacity (FRC), the amount of gas in the lungs at the end of an exhaled tidal volume. This reduction in VC and FRC due to excess adipose tissue distribution is a key cause of daytime hypercapnia in patients who are obese (Laaban and Chailleux, 2005; Resta et al, 2001).

In a study of 1,141 patients with OSA, Laaban and Chailleux (2005) found that those with hypercapnia had significantly higher weight and body mass index values and significantly lower VC, forced

A full face mask must be worn during the delivery of non-invasive ventilation therapy

Alamy

expiratory volume in 1 second (FEV1 – used to measure lung function and diagnose lung disease) and partial pressure of oxygen in arterial blood (PaO_2) values than patients with a normal level of carbon dioxide.

The following are all major factors that cause a change in physiological dynamics and the body's ability to maintain a normal level of carbon dioxide and haemostasis:

- Increased mechanical load;
- Restrictive lung impairment;
- Increased lung resistance;
- Reduced lung compliance;
- Progression to severe muscle weakness.

Neuro-hormonal abnormalities in patients who are obese are thought to be another cause of hypoventilation and subsequent hypercapnia (Mokhlesi et al, 2008). Leptin, a hormone that inhibits hunger, and therefore weight gain, has been found to be raised in obese patients and it has been suggested that they may be leptin-resistant (Myers et al, 2010). Tankersley et al (1998) found that hypoventilation could be related to leptin levels, and that raised levels of leptin and leptin resistance have also been associated with a reduction in respiratory drive and hypercapnic response in the absence of obesity.

Obesity may cause a chronic inflammatory pathway that may lead not only lead to leptin resistance but to also insulin resistance and hypofunctioning of hypothalamic hormones related to circadian rhythm, causing sleep disorder breathing (Dabal and BaHammam, 2009; Zamarron et al, 2008; Hatipoglu and Rubinstein, 2003).

The more adipose tissue that is accumulated, the more challenging it is for the body to maintain a normal level of function. With a lower physical capability – that is, how patients breathe mechanically, and how they mobilise – added to the neurohormonal resistance to various hormones such as insulin and leptin – the pathway to physiological deterioration is set.

Reduced physical capability and exercise tolerance also affects patients socially and psychologically – they may experience a lack of social participation, decrease in activities of daily life, social isolation, unemployment and disability. In short, OSH may have far-reaching consequences affecting patients' physiological, social, financial and hormonal states (Fig 1).

Treatment

Non-acute OHS

Treatment of OHS involves several strategies, with a main focus on weight loss through diet and exercise. However, symptoms of acute/chronic hypercapnia and hypoxia with sleep-disordered breathing cause a downward spiral. Patients are generally lethargic, which is partly due to poor sleep quality, hypercapnia and the struggle to sustain physical exertion. Reducing the level of hypoventilation, hypercapnia and modulating associated sleep disorders is paramount to improving pulmonary function and sleep quality (Borel et al, 2012b).

Continuous positive airway pressure

In patients with primary OSA and OHS, treatment with continuous positive airway pressure (CPAP) has been shown to be successful (Mokhlesi et al, 2008; National Institute for Health and Care Excellence, 2008). CPAP uses a positive end-expiratory pressure (PEEP) to:

- Prevent alveoli from collapsing;
- Reduce atelectasis (collapsed lung);
- Open the upper airway.

Patients with simple sleep apnoea maintain a patent airway while sleeping, with less disruption to sleep patterns and fewer hypoxic periods. In addition, the reduced level of hypoxia achieved by using CPAP reduces the risk of stroke, diabetes and heart disease. With a better night's sleep, the patient often experiences less daytime tiredness and can be more active.

Bilevel non-invasive ventilation

In some patients with OHS, CPAP therapy may be sufficient, but in those with hypercapnia and hypoxia the work of breathing has diminished to such an extent that the respiratory muscles weaken and are at risk of further fatigue. In mild OSA, studies have shown that CPAP and bilevel non-invasive ventilation (NIV) can be equally effective at reducing daytime hypercapnia (Piper et al, 2008).

Bilevel NIV in OHS can provide both the inspiratory pressure and expiratory pressure to enable patients to:

- Reduce the effort required to breathe;
- Remove waste gases;
- Open up the airways.

Bilevel NIV has been shown to be effective in many studies of acute hypercapnic respiratory failure in chronic obstructive pulmonary disease (COPD) (Keenan et al, 2011). Carrillo et al (2012) found that patients who have OHS with hypercapnic respiratory failure could be treated using a similar bilevel NIV protocol to that used for patients with COPD; further to that, outcomes for patients with OHS were better than for those with COPD. Domiciliary bilevel NIV also improves gas exchange, daytime somnolence and quality of life, and reduces readmissions to hospital for patients with OHS (Piper and Grunstein, 2011).

Bilevel NIV devices use inspiratory positive airway pressure (IPAP) to provide ventilatory support, increasing patients' tidal volume when they inhale. Patients may trigger the device spontaneously to provide the IPAP or, if unable to do this, a timed breath may be delivered.

At the end of inspiration and start of exhalation, the device provides expiratory positive airway pressure (EPAP). This maintains a pressure to allow the alveoli to stay open; helping to prevent collapse of both the lower and upper airway, and allowing a gas exchange to take place and improve PaO2. The pressure level between the IPAP and the EPAP is known as pressure support; this can be adjusted to increase patients' tidal volume, which enables more of the carbon dioxide to be expelled, with the aim of reducing PaCO2.

There are risks with high pressures including pneumothorax, so patients should be closely monitored in the initial stages of therapy. They must wear a nasal or full face mask, which must be well sealed to make sure enough pressure is delivered. Patients can develop pressure ulcers on the bridge of the nose as a result of wearing the mask (Gregoretti et al, 2002) and wearing a mask can cause discomfort (Kramer et al, 1995). This leads to adherence problems, which, in turn, as Antonelli et al (2003) noted, reduces the duration of use. In patients with a long-term condition and domiciliary bilevel NIV, the overall effectiveness can be reduced.

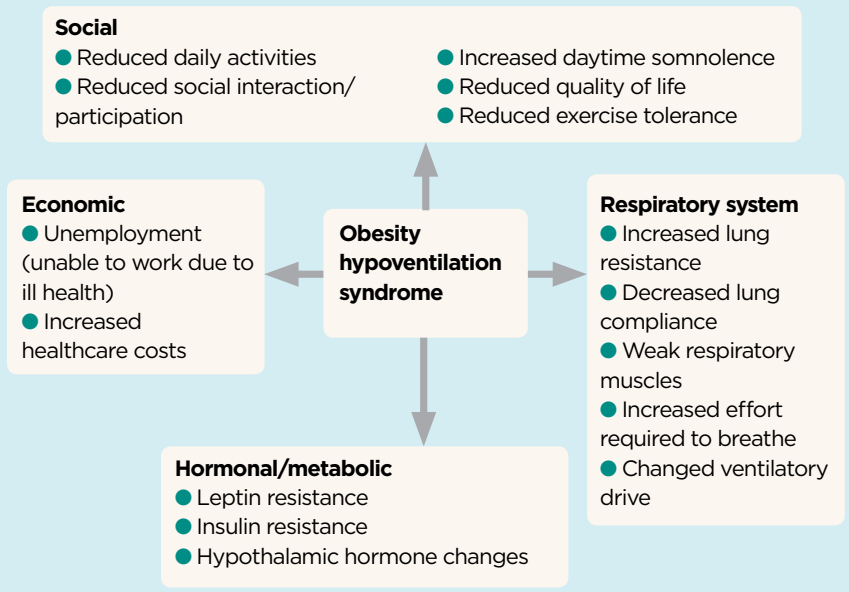
Average volume-assured pressure support

An alternative to standard bilevel NIV is average volume-assured pressure support (AVAPS). This is a volume-targeted mode of

BOX 1. CHARACTERISTICS OF OHS

- Obesity: body mass index >30kg/m² (range for a healthy weight is 18.5-24.9kg/m²)
- Daytime hypercapnia, or elevated levels of carbon dioxide in the blood (normal range 4.6–6.1kPa)
- Hypoxaemia (normal range PaO_2 12-14.6kPa)
- Sleep-disordered breathing in the absence of other disorders that may cause hypoventilation, such as significant lung or respiratory muscle disease (Borel et al, 2012a; Mokhlesi et al, 2007)

FIG 1. **EFFECTS OF OHS**



ventilation, also known as volume targeting by bilevel NIV (Janssens et al, 2008). Traditionally there have been two standard methods of delivering ventilator support:

- Via a pressure-controlled device, such as bilevel NIV – with this mode of ventilation there may be insufficient tidal volume delivered at times due to poor lung compliance and restrictive lung disease;
- By using a volume control device to ensure a target tidal volume is delivered to the patient – this may result in adverse consequences in terms of how much pressure is generated.

AVAPS is a hybrid of these two modes and aims to delivery a guaranteed tidal volume (Windisch et al, 2005).

Evidence suggests that volume targeting can improve the control of nocturnal hypoventilation and result in a significant decrease in transcutaneous carbon dioxide ($PtcCO_2$), a method of non-invasive monitoring carbon dioxide via a probe placed on the skin, with the effect of normalising $PtcCO_2$ during sleep. Claudett et al (2013) found that patients who received AVAPS quickly reached the IPAP levels needed to maintain assured tidal volume. Hypoventilation was corrected, with consequent improvements in alveolar ventilation.

Conclusion

There is significant evidence that obesity rates are increasing and many obese patients have both sleep-disordered breathing and hypoventilation syndrome as a direct result. Managing the various problems associated with obesity is complex – hypoventilation and hypercapnic respiratory failure are a major problem.

Several studies have demonstrated that NIV using positive pressure can reduce carbon dioxide levels and reverse hypercapnic respiratory failure, as well as improving sleep-disordered breathing. New modes of ventilation such as AVAPS may have a place in helping to control OHS through the use of assured volume-targeted pressure support. Through respiratory support, patients may have a better quality of sleep, reduced hypercapnia and hypoxia, and improved activities of daily living. **NT**

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