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Respiratory function and complication related by obesity?

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Abstract: Obstructive sleep apnoea (OSA),with intermittent occlusion of the upper airway and oxygen desaturation during sleep, is due to compression by surrounding fat and perhaps inflammatory and central actions of adipokines. Complications of OSA include hypertension, heart failure and premature death. Snoring and day-time sleepiness are characteristic, and polysomnography demonstrates episodic awakening and desaturation. Continuous positive airway pressure (CPAP) ventilation at night greatly improves symptoms and prognosis. Obesity/hyperventilation syndrome (OHS) results from in adequate ventilatory drive and causes pulmonary hypertension and premature death. CPAP and weight loss can be helpful. Lung volumes are decreased due to mechanical restriction. Meanwhile, many young people, especially women,may use smoking as a means to limit weight gain. However, the benefits of stopping smoking undoubtedly outweigh any detrimental effects of post-cessation weight gain. Obesity has also been associated with an increased risk of developing childhood asthma in a number of prospective studies, but not others in the childhood.

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1. Introduction

Obesity adversely affects several aspects of respiratory function, partly through mechanical restriction of respiration, as well as poorly explained indirect effects. First of all, obesity is the most powerful risk factor for OSA,the association being attributed to central actions of leptin and other adipokines as well as compression by fat of the pharynx [1].OSA impairs the sufferer's quality of life and is implicated in the initiation and progression of hypertension and cardiovascular disease,notably heart failure [2]. Ultimately, OSA shortens life expectancy. Symptoms may be vague and pass unnoticed by the patient and physician alike, but timely diagnosis and treatment with continuous positive airway pressure (CPAP) can markedly improve quality of life and prognosis.A high index of suspicion is therefore required,and the characteristic history sought routinely. As with OSA, the diagnosis and treatment of obesity/hypoventilation syndrome (OHS) are often neglected. A high index of suspicion, coupled with a careful history, is required and the measurement of arterial oxygen and carbon dioxide tensions is diagnostic.

Obesity restricts expansion of the chest wall and downward movement of the diaphragm. As weight increases, all lung volumes decline, the great estimpact being on the functional residual capacity(FRC) and expiratory reserve volume (ERV). In adults, smoking is relevant to the management of obesity for several reasons. It enhances the risks of respiratory disease and also of lung malignancies, including some to which obesity also predisposes. The health risks of smoking and obesity appear tobe at least additive, and smoking may exacerbate various obesity-related abnormalities such as OSA, OHS and respiratory malignancies. Apart from a suggestion that it may predispose to childhood asthma, there is no evidence that obesity causes or worsens intrinsic lung disease.

2. Obstructive sleep apnoea (OSA)

OSA is characterized by episodes of partial and/or complete occlusion of the pharynx during sleep,leading to cessation of breathing for at least 10 seconds and sometimes for over a minute. Sleep is disturbed by restlessness, snoring, the typical prolonged apnoeic episodes,and recurrent awakening;

morning headache and daytime sleepiness and impaired concentration are also typical (Table 1, attached below). Obesity is the most important risk factor for OSA. The general prevalence of OSA in middle-aged men and women is respectively 4 – 9% and 1 – 2%, but this rises over 10-fold to40 – 70% in morbidly obese subjects whose BMI is 35 kg/m2. Furthermore, weight gain of 10%is associated with a 6-fold increase in the risk of developing OSA [3].Until recently, the association was attributed to excess fat in the neck compressing the upper airway. Morbidly obese men with OSA show a reduction in pharyngeal cross-sectional area that is proportional to surrounding fat deposition. Conversely, weight loss in obese subjects results in an increased pharyngeal area and a corresponding reduction in the severity of the OSA [4]. (Figure 1, attached below)

Interestingly, recent evidence implicates raised levels of pro-inflammatory adipokines, notably TNF-α and interleukin-6 (IL-6), released especially by visceral fat, in the development of OSA.Consistent with this suggestion, pilot studies using metanercept (a fusion protein that mimics the TNF-deactivating action of the soluble TNF-α receptor) have shown significant reductions in the frequency of apnoeic episodes and in daytime sleepiness in obese subjects with OSA [5]. Suggested pathogenic mechanisms include decreased respiratory drive (especially at night), inflammation of the upper airways and soft-tissue oedema [5].OSA is a serious condition that damages quality of life for the sufferers (and often their partner)and also increases morbidity and risk of premature death, especially from cardiovascular diseases [6]. Cardiovascular complications include hypertension, myocardial infarction and heart failure, for which OSA doubles the 5-year mortality rate from 12% to 24% [6, 7]. Deleterious effects of peri-odic deoxygenation and excessive cardiac loading from exaggerated inspiratory effort may contrib-ute [8].

Awareness of OSA among physicians is poor,and the diagnosis is often missed and treatment delayed. The diagnosis is based on the characteristic symptoms (see Table 1); the sleep history is often graphically provided by the patient’s partner. The Epworth Sleepiness Scale is useful for quantifying daytime symptoms [9]. A neck circumference of 42 cm in men and 38 cm in women is strongly predictive of clinically significant OSA. Sleep studies (polysomnography) are diagnostic, demonstrating both the apnoeic episodes (with increased inspiratory effort against a closed pharynx),and the resulting fall in transcutaneous oxygen tension. Once the diagnosis is established, the Apnoea/Hypopnoea Index (AHI), which quantifies sleep disruption and oxygen desaturation, is useful to determine the severity of the OSA [10].

Treatment of OSA requires specialist intervention. Continuous positive airway pressure(CPAP) ventilation during the night, delivered using a tightly-fitting mask over the mouth and nose, keeps the upper airway open; this dramatically reduces the frequency of apnoea and oxygen desaturation, with a striking improve-ment in symptoms and quality of life [8]. Blood pressure and cardiac function also improve, and life expectancy may be extended [8]. Weight loss also improves symptoms, but may require a long time to be effective. Some patients with structural abnormalities of the lower face or neck may be helped by surgical reconstruction, but operations to remove the uvula and redundant soft palate have now fallen out of favour.

3. Obesity/hypoventilation syndrome (OHS)

This rare condition, strongly associated with obesity, can occur alone or may develop secondarily to OSA. It has also been called the ‘Pickwickian Syndrome’ after Joe, the obese and hypersomnolent boy in Dickens’ The Pickwick Papers.OHS is due to inadequate ventilatory drive,presumably at the level of the respiratory centre, leading to severe hypoxaemia and ultimately hypercapnic respiratory failure. Associated features are pulmonary hypertension and right-sided heart failure (cor pulmonale), which are unexplained.Life expectancy is severely reduced: in one study,the 18-month mortality rate was 23%, compared with 9% among obese subjects without OHS[11]. The causes of ventilatory failure and the unresponsiveness to hypoxaemia and hypercapnia are not known. Postulated factors include respiratory muscle dysfunction,reduced respiratory drive and blunted chemo sensitivity to low oxygen and high carbon dioxide levels; ‘resistance’ to central actions of leptin has been implicated [12].As with OSA, the diagnosis and treatment are often neglected. A high index of suspicion, coupled with a careful history, is required and the measurement of arterial oxygen and carbon dioxide tensions is diagnostic. Treatment is by CPAP,to prevent apnoea and hypopnoea; non-invasive mechanical intervention, to alleviate daytime hypercapnia; and weight loss, which improves both pulmonary function and central ventilatory drive.

4. The indicators of Lung volumes related by obesity

Obesity restricts expansion of the chest wall and downward movement of the diaphragm. As weight

increases, all lung volumes decline, the greatest impact being on the functional residual capacity(FRC) and expiratory reserve volume (ERV), as shown in Figure 2. In one study, subjects with a BMI of 30 kg/m2showed reductions in FRC and ERV of 25 and 53%, respectively, compared with the values at a BMI of 20 kg/m2[13]. Cohort studies have demonstrated that vital capacity (VC) falls by 25 ml for each1 kg of excess weight [14]. With increasing weight, airway resistance increases, and forced expiratory volume in 1 second (FEV1) falls, possibly because small airway stend to close as lung volumes decline [13]. Reduced static lung volumes, together with enhanced respiratory drive, possibly in response to the increased mechanical loading of the chest wall and abdomen, can cause otherwise healthy obese people to feel breathless, especially when respiratory demand is increased through physical activity [14, 15].

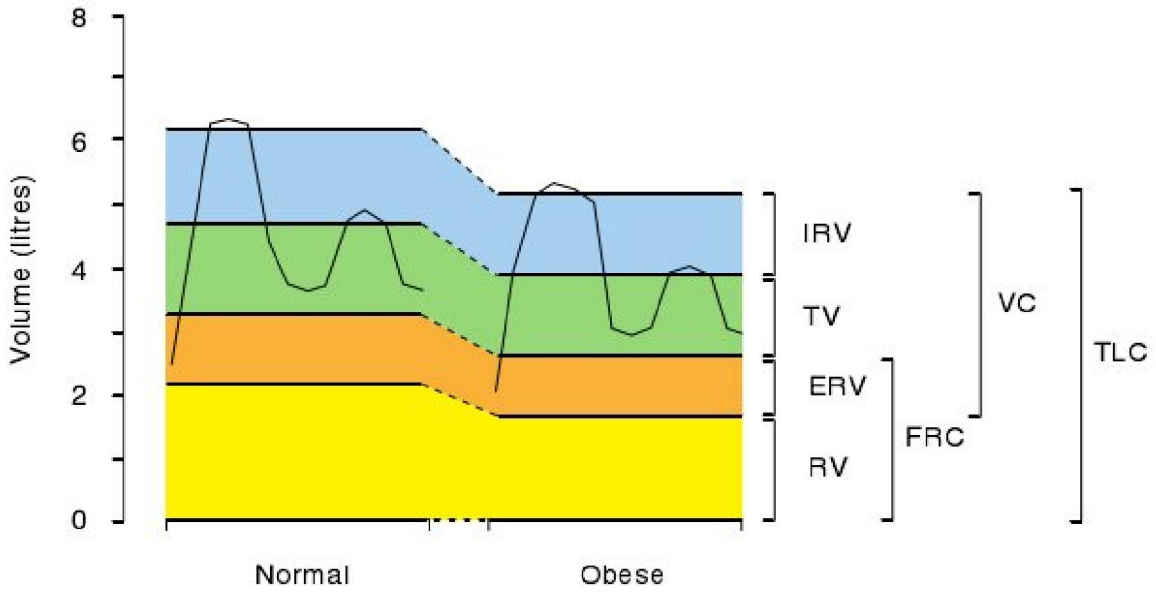

Figure 2 Impact of obesity on lung volumes.
ERV: expiratory reserve volume; FRC: functional residual capacity;IRV: inspiratory reserve volume; RV: residual volume; TLC: total lung capacity; TV: tidal volume; VC: vital capacity.

Table 1 Symptoms of obstructive sleepapnoea (OSA).

Daytime symptoms	Nocturnal symptoms	Other symptoms
Excessive daytime sleepiness	Snoring	Decreased libido
Morning headaches	Recurrent awakening	Impotence
Impaired concentration	Restlessness, particularly the legs	
Depression	Nocturnal choking, gasping and snorting	
Irritability	Breathing cessation for over 10 s	

5. Impacts of smoking and obesity in adults

Smoking is relevant to the management of obesity for several reasons. It enhances the risks of respiratory disease and also of lung malignancies, including some to which obesity also predisposes. The health risks of smoking and obesity appear tobe at least additive, and smoking may exacerbate various obesity-related abnormalities such as OSA, OHS and respiratory malignancies [16]. Ultimately, the combination of smoking and obesity further shortens life expectancy: on average, obese smokers die between 5 and 13 years before their non-smoking counterparts [17,18].Smoking is associated with a lower fat mass and body weight, due partly to increased energy expenditure and decreased food intake through indirect and direct actions of nicotine. On average, middle-aged and older smokers have been shown to weigh 3-4 kg less than matched non-smokers, although weight differences are small (or non-existent) among adolescents and young adults [19]. The lower BMI and higher mortality among smokers are partly responsible for the low extreme of theU-shaped relationship between BMI and risk of death.

Conversely, smoking cessation often leads to weight gain. Several large prospective studies have shown that those who stop smoking gain on average 4-5 kg. Weight increase is more pronounced in women, younger subjects, Black people, heavy smokers and those whose initial weight is relatively low; overall, some 20% of those who stop smoking gain 10 kg or more [19]. This is due to increased energy intake (especially of sweet and fat-rich foods),together with loss of the catabolic actions of nicotine. Smokers commonly view weight gain as a serious consequence of stopping smoking, and it is probably a major disincentive for many; some young people, especially women,may use smoking as a means to limit weight gain.The benefits of stopping smoking undoubtedly outweigh any detrimental effects of post-cessation weight gain, and on balance, smoking cessation should take priority.

6. Impacts of obesity on respiratory complications in childhood

Adult obesity is associated with the obstructive sleep apnoea (OSA) syndrome, characterized by episodic obstruction of the upper airway, leading to blood oxygen desaturation and repeated arousals; disruption of valuable REM sleep results in daytime lethargy and somnolence. OSA is now being increasingly recognized among obese children [20, 21]. This is a potentially serious condition with evidence of increased left ventricular hypertrophy, pulmonary hypertension and risk of metabolic syndrome independent of BMI [22-24]. Also, reduced sleeping time during childhood may be an additional risk factor for obesity possibly through increased levels of the appetite-stimulating peptide, ghrelin thus potentially causing a vicious circle of worsening obesity and sleep deprivation [25].

Obesity has also been associated with an increased risk of developing childhood asthma in a number of prospective studies, but not others [26]. Some studies have shown that weight gain can antedate the development of asthma. Effect modification by sex may occur as some studies have shown effects of body mass index on asthma only among females. However, sex differences are not consistent. Several hypotheses have been proposed to explain the epidemiological associations including alterations in airway mechanics and immune responses, hormonal influences and genetic factors. There is evidence that obesity and overweight are associated with the development of asthma. Yet, the mechanisms underlying this relation are unclear. Weight reduction among asthmatic patients can result in improvements of lung function demonstrating the potential clinical impact of the findings [27].

7. Conclusion

Obesity and respiratory function or complication, what are the links? OSA,with intermittent occlusion of the upper airway and oxygen desaturation during sleep, is due to compression by surrounding fat and perhaps inflammatory and central actions of adipokines. Complications of OSA include hypertension, heart failure and premature death. Snoring and day-time sleepiness are characteristic, and polysomnography demonstrates episodic awakening and desaturation. CPAP ventilation at night greatly improves symptoms and prognosis. OHS results from in adequate ventilatory drive and causes pulmonary hypertension and premature death. CPAP and weight loss can be helpful. Lung volumes are decreased due to mechanical restriction. Meanwhile, many young people, especially women, may use smoking as a means to limit weight gain; otherwise the benefits of stopping smoking undoubtedly outweigh any detrimental effects of post-cessation weight gain. Obesity has also been associated with an increased risk of developing childhood asthma in a number of prospective studies, but not others in the childhood.

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