Effects of Long-term Nasal Continuous Positive Airway Pressure Treatment in Patients with Obstructive Sleep Apnoea Syndrome

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Metabolic Outcomes of Continuous Positive Airway Pressure Therapy

Nasal continuous positive airway pressure (nCPAP) is considered the first-choice treatment for patients with obstructive sleep apnoea syndrome (OSAHS) because it induces a reduction in nocturnal respiratory events, alleviates daytime sleepiness and improves quality of life.1 Some studies suggest that nCPAP may reduce morbidity and mortality2 and cardiovascular morbidity.3 Treatment with nCPAP reduces sympathetic activity,4 diminishes platelet activation and aggregation and normalises oxidation of low-density lipoprotein (LDL) particles,5 as well as decreasing the production of reactive oxygen species in neutrophils and monocytes.6 Circulating levels of C-reactive protein (CRP), fibrinogen and interleukin (IL)-6 are elevated in apnoeic patients and decrease significantly with nCPAP.7 The pro-inflammatory cytokines may not always be the only specific cause of the pathogenesis of sleep apnoea; however, some clinical data strongly indicate that IL-6 levels are elevated in patients with OSAHS, but not in patients who present with obesity alone.8

The baseline level of CRP in large-scale prospective studies9,10 is an independent predictive marker of future myocardial infarctions, strokes, cardiovascular deaths and incidences of peripheral arterial disease. Therefore, as well as being an active pathogenic agent, CRP level is a risk factor for atherosclerosis. Decreases11,12 in CRP levels in OSAHS patients become evident when CPAP has been used for in excess of four hours per night. However, the authors of these studies have concluded that CRP levels are unlikely to depend on OSAHS itself and may be associated with obesity.

Recently,13 patients with newly diagnosed non-smoking OSAHS without co-morbidities or on a medication course have been studied at baseline and during the follow-up period. Serum cardiovascular risk factors – i.e. high-sensitivity CRP, homocysteine, total cholesterol, triglycerides, high-density lipoprotein cholesterol (HDL-C), LDL cholesterol, apolipoprotein A-I (ApoA-I) and apolipoprotein B (ApoB) – were measured at baseline and six months after CPAP application. Patients have been classified into three groups according to CPAP use: group 1 (n=20), good compliance (>4 hours use per night); group 2 (n=19), poor compliance (<4 hours use per night); and group 3 (n=14), refusal of CPAP treatment. This study concluded that good compliance to CPAP treatment lowers the serum levels of cardiovascular risk factors, indicating a beneficial effect on the overall cardiovascular risk. Eventually, nCPAP14 reduces serum levels of inflammatory cytokines (tumour necrosis factor [TNF]-α, IL-6), probably lowering the risk of atherosclerosis.

Based on the experimental data above, and if extrapolating these findings to our data in OSAHS patients, we are inclined to speculate that the restoration of oxygenation and the prevention of associated oxygen desaturation with CPAP therapy can potentially result in improvement of the metabolic profile. This is achieved through mechanisms involving the downregulation of inflammatory cytokines, while at the same time altering cellular responses to hypoxia and disrupting inflammatory pathways. A large study of well-defined patients investigating the effect of CPAP treatment on lipid biosynthesis and cytokine-mediated tissue injury is urgently needed.

The diagnosis and treatment of OSAHS should be considered as part of the management of diabetes, hypertension and congestive heart failure, which are core aspects of primary care medicine. Sleep laboratory testing can be used as an objective insight into the patient’s pulmonary, cardiac, neurological, endocrine, cognitive and psychiatric status.

While searching the literature regarding the effect of CPAP therapy on blood gas – specifically hypercapnia and hypoxia – the results of a retrospective cohort study15 have demonstrated that in hypercapnic patients with OSAHS, adherence to PAP is an important modifiable predictor of improvements in arterial carbon dioxide pressure (PaCO2) and arterial oxygen pressure (PaO2), and its benefit plateaus between five and seven hours of daily therapy.

In a randomised, placebo-controlled study using a three-arm placebo-controlled design,16 nocturnal oxygen supplementation and CPAP treatments improved psychological symptoms. OSAHS patients (n=38) were monitored for two nights with polysomnography and then randomised to two weeks of therapeutic CPAP, placebo CPAP or O2 supplementation. As CPAP normalises both sleep disruption and oxyhaemoglobin desaturation, the mechanism of psychological symptom improvement is unclear.

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Finally, long-term nCPAP treatment re-establishes a physiological relationship between chronic lack of sleep and metabolic disorders and can improve nocturnal melatonin plasma levels, which play a crucial role as a mediator between the thermoregulatory arousal systems and sleep-promoting properties.

### Problems and Compliance with Continuous Positive Airway Pressure Therapy

Compliance with nCPAP therapy for the treatment of OSAHS is far from perfect, as is often the case for therapies for chronic diseases. Compliance has been defined as the use of CPAP therapy for >4 hours per night on 70% of the observed nights. A short-term follow-up of OSAHS patients demonstrates that CPAP-use patterns fall into two groups of patients: those with an average usage time >6 hours per night and those with an average usage time <3.5 hours per night. Long-term objective follow-up has demonstrated that approximately 68% of OSAHS patients continue to use their CPAP therapy after five years.

Nursing support and intensive education programmes have also been shown to improve compliance. Simple interventions such as weekly phone calls and mailings may improve compliance, especially when they are performed in the initial weeks of therapy. In general, increased intensity of patient education or the frequency of health-provider contact improves CPAP therapy adherence. Several studies have demonstrated that the addition of heated humidification improves the symptoms of nasal congestion and increases objective CPAP use.

A recent randomised trial study of 100 individuals (96 men) ranging from 32 to 81 years of age demonstrated that improved adherence to CPAP treatment in participants with OSAHS encourages a better cognitive behavioural therapy (CBT) intervention. All patients carried out one-hour CBT interventions (including a video of real CPAP users) plus usual treatment (mask-fitting and information) or usual treatment only. Questionnaires measuring self-efficacy, social support and expectancy screening as predictors of peripheral artherosclerosis, JAMA, 2001;285:2481–5.


