Obstructive Sleep Apnoea: Increasing Evidence of Cardiovascular Complications

Dr. David SC Hui  MBBS, MD (UNSW), FRACP, FRCPI (Lond, Edin, Glasg), FCCP, FHKCP, FHKAM
Associate Professor & Head of Division of Respiratory Medicine, Chinese University of Hong Kong, Prince of Wales Hospital, Sha Tin, NT, Hong Kong

Introduction
Obstructive sleep apnoea syndrome (OSAS) is a common form of sleep disordered breathing (SDB) characterised by repetitive episodes of partial or complete upper airway obstruction causing sleep fragmentation and symptoms. It is equally common among the middle-aged male Caucasian and HK Chinese populations with a prevalence of at least 4%. OSAS may cause disabling daytime sleepiness, impaired cognitive function, poor quality of life, and increase the risk of road traffic accidents. Sleep-induced loss of upper airway muscle tone and obesity are the major factors in the pathogenesis of OSAS. However craniofacial abnormalities may play an important role especially in the Asian populations. While Asian patients with OSAS are generally less obese than the Caucasian counterparts, craniofacial abnormalities such as a low hyoid bone and retro-position of the maxilla or mandible are common predisposing factors in the Chinese populations. Other predisposing factors in the pathogenesis of OSAS in adults include inappropriate use of benzodiazepine or alcohol (further reduction in muscle tone), endocrine causes such as hypothyroidism (macroglossia, mucopolysaccharide deposits in upper airway, myopathy, neuropathy) and acromegaly (macroglossia, central sleep apnoea), smoking (airway inflammation), and enlarged tonsils and adenoids (mechanical obstruction) in the paediatric cases.

Obstructive sleep apnoea and cardiovascular complications
In recent years, there are growing data linking SDB to cardiovascular complications. Several epidemiological studies have shown an independent association between SDB and hypertension after controlling for confounding factors such as age, body mass index (BMI), sex, alcohol and smoking. Patients with OSAS have increased ambulatory diastolic blood pressure (BP) both day and night and increased systolic BP at night compared to controls matched for age and BMI. The US Sleep Heart Health Study cohort has shown the effects of SDB on various manifestations of cardiovascular diseases, and relatively SDB was more strongly associated with reported stroke and heart failure than with coronary artery disease. A 7-year longitudinal study of otherwise healthy patients with OSAS has shown a higher incidence (56.8%) of at least one cardiovascular complication in patients incompletely treated than those effectively treated, who have a low incidence (6.7%) similar to the normal controls.

Cerebrovascular disease is an important cause of morbidity and mortality worldwide. Several overseas studies have reported a high prevalence of SDB predominantly of obstructive nature in patients following stroke in the acute phase and rehabilitation phase. A case-controlled study in HK has shown a high prevalence of OSA in Chinese patients admitted with acute ischaemic stroke (49% vs 24% in a control group). Two recent studies in Europe have shown that patients with both OSA and stroke have lower survival rates than those with stroke alone. Atherosclerosis of the carotid arteries is an important cause of ischaemic stroke. In recent years, carotid artery intima-media thickness (IMT), measured by B-mode ultrasound, has been shown to correlate with traditional vascular risk factors and may predict the likelihood of acute coronary events and stroke. In a study of 167 Japanese patients referred for screening of OSAS, Suzuki et al. have shown that the severity of OSA is independently related to the carotid artery IMT, and that the severity of OSA-induced hypoxaemia is more important than the frequency of obstructive events. The findings have been strengthened by a case-control study in Germany. OSARED-related arousals are closely linked to increases in sympathetic activity. A case-controlled study recently conducted in HK has shown that OSAS, through repeated episodes of arousals, may lead to platelet activation. Platelet activation is an important step in the pathogenesis of ischaemic stroke but its activity can be reduced by nasal continuous positive airway pressure (CPAP) treatment. In addition to hypertension, other mechanisms for the association between SDB and cardiovascular complications are not fully understood but there is strong evidence indicating a role for the sympathetic nervous system in the pathophysiological process. Multiple, potentially intertwined mechanisms are proposed to link OSA with chronic cardiovascular diseases, and these include tonic elevation of sympathetic neural activity, vascular endothelial dysfunction, oxidative stress,
inflammation, and metabolic dysregulation. In addition to cascades of increased vasoactive peptides and proinflammatory factors, repetitive surges of sympathetic activity may directly promote endothelial/vascular injury and enhanced coagulability. Platelet aggregability, increases in haematoctrit, fibrinogen levels, and blood viscosity may also predispose to clot formation and atherosclerosis in patients with OSAS.

Treatment

Nasal CPAP is the most effective treatment for OSAS with robust evidence in support of its efficacy in improving symptoms, cognitive function, and quality of life. Several randomised placebo-controlled studies have shown that nasal CPAP can reduce day and night BP in patients with OSAS. Pepperell et al have shown a 3.3 mmHg reduction in 24 hr mean systemic BP among sleepy OSAS patients with OSAS in the therapeutic vs the sub-therapeutic CPAP arm, and the beneficial effect of CPAP on BP was seen mostly in those with more severe OSAS.

Other favourable effects of CPAP include reduction of sympathetic activity and hypoxic/oxidative stress, with improvement of vasodilator response and endothelial function. In patients who are not able to tolerate nasal CPAP, dental appliance in the form of a removable splint can reduce day and night BP in patients with OSAS in the therapeutic vs the sub-therapeutic CPAP arm. The beneficial effect of CPAP on BP was seen mostly in those with more severe OSAS.

Other favourable effects of CPAP include reduction of sympathetic activity and hypoxic/oxidative stress, with improvement of vasodilator response and endothelial function. In patients who are not able to tolerate nasal CPAP, dental appliance in the form of a removable splint can reduce day and night BP in patients with OSAS in the therapeutic vs the sub-therapeutic CPAP arm. The beneficial effect of CPAP on BP was seen mostly in those with more severe OSAS.

References

4) Retroposition of the mandible or maxilla is a predisposing factor in Chinese patients with OSAS.
5) Patients with stroke and OSAS have lower survival rates than those with stroke alone.
6) Which of the following factors may predispose to OSAS?
   a) Sleep induced loss of muscle tone
   b) Obesity
   c) Craniofacial abnormalities
   d) Inappropriate use of alcohol
   e) All of the above
7) Which of the following treatment modalities is the most effective and evidence-based in improving symptoms such as sleepiness, cognitive function, and quality in OSAS?
   a) Mandibular advancement device
   b) Palatal surgery
   c) Weight reduction
   d) Nasal CPAP
   e) Sleep in lateral positions
8) Which of the following statements is INCORRECT concerning cardiovascular consequences in OSAS?
   a) Patients with severe OSAS have higher daytime and nocturnal BP compared to controls matched for age and BMI
   b) Central sleep apnoea is more common than Obstructive sleep apnoea in patients admitted with ischaemic stroke.
   c) Carotid artery intima-media thickness is increased in patients with OSAS compared to controls.
   d) Patients with OSAS not effectively treated have a higher incidence of developing cardiovascular complications
   e) Platelet activation is increased in patients with OSAS
9) Which of the following statements is INCORRECT concerning nasal treatment for OSAS?
   a) It can improve symptoms very effectively.
   b) It can reduce 24 hr mean blood pressure.
   c) It can improve endothelial function.
   d) It can increase activity of the sympathetic nervous system.
   e) It can reduce platelet activation.
10) In addition to improvement of symptoms, which of the following areas can dental device in the form of mandibular advancement splint improve in patients with OSAS?
    a) Platelet activation
    b) Systemic blood pressure
    c) Sympathetic activity
    d) Risk of car accidents
    e) Endothelial function

---

**ANSWER SHEET FOR MARCH 2005**

Please return the completed answer sheet to the Federation Secretariat on or before 31 March 2005 for documentation. 1 CME point will be awarded for answering the MCHK CME programme (for non-specialists) self-assessment questions.

**Obstructive Sleep Apnoea: Increasing Evidence of Cardiovascular Complications**

Dr. David SC Hui
MBBS, MD (UNSW), FRACP, FRCP(Lond, Edin, Glasg), FCCP, FHKCP, FHKAM
Associate Professor & Head of Division of Respiratory Medicine, Chinese University of Hong Kong, Prince of Wales Hospital, Shatin, NT, Hong Kong

Name: _____________________________________________________ HKID No. ___ ___ - ___ ___ ___ ___ X X (x)

Signature: _____________________________  Contact Tel No.:_________________________

---

**Answers to February 2005 issue**

**Changing Concept of Early Rheumatoid Arthritis**

1. (i) T  (ii) T  (iii) T  (iv) T  (v) F  3. (i) F  (ii) T  (iii) T  (iv) F  (v) F
2. (i) T  (ii) F  (iii) F  (iv) T  (v) F