Obstructive sleep apnoea and stroke

Introduction

The obstructive sleep apnoea/hypopnoea syndrome is one of the most common and important medical conditions to be identified in the last 50 years. Around 2% of middle-age men and 1% of middle-age women have a combination of increased irregular breathing at night with daytime sleepiness, this combination being the hallmark of the obstructive sleep apnoea/hypopnoea syndrome (OSAHS; Table 1). There is now irrefutable evidence from placebo controlled randomised treatment trials that OSAHS results in not only daytime sleepiness but also impaired cognition, mood, quality of life, and driving performance and raised blood pressure. This article will focus on the inter-relationships between sleep apnoea and stroke, examining the evidence that each may cause the other.

OSAHS as a cause of hypertension

Early epidemiological investigation showed an increase in hypertension amongst snorers but confounding factors such as obesity, age, gender and alcohol makes interpretation of these observations difficult. The same was true of studies suggesting the association between OSAHS and hypertension. Dog model studies have shown that recurrent apnoeas can produce both night time and sustained daytime hypertension. Studies in rats indicate that intermittent nocturnal hypoxaemia can produce daytime hypertension even in the absence of upper airway obstruction.

More recent epidemiological studies in which strenuous attempts have been made to exclude confounders strongly suggest an association between sleep apnoea and daytime hypertension. Convincing evidence comes from the Wisconsin cohort study in which 1060 members of the working population had their breathing studied during sleep and were then followed-up. At the initial study, those found to have more than 25 apnoeas/h hypopnoeas/hr of sleep had a 2.9 fold increased chance of developing hypertension. The increase in risk of hypertension was greater in thinner patients who had abnormal breathing during sleep. At follow-up 4 years later, those with more than 15 apnoeas had a 2.9 fold increased chance of developing new hypertension independent of confounders. Other cross sectional studies in normal populations or OSAHS patients have also indicated a 1.4-7 fold increased risk of hypertension, once allowance has been made for other risk factors.

A careful case control study found that patients with OSAHS had a significantly higher blood pressure than matched control subjects, but that these increases were only significant during the sleeping period and in the afternoon (see Fig. 1). More direct evidence that OSAHS causes hypertension comes from two studies showing that CPAP therapy reduces 24 hr blood pressure by 10-15 mmHg. The decreases are greatest in those with significant nocturnal hypoxaemia, those with more than twenty 4% oxygen desaturations/hr of sleep having drops in mean 24 hr systolic and diastolic blood pressure of 5mmHg. Taken together, these studies convincingly indicate that OSAHS causes elevation of systemic blood pressure, which is most marked during the hours of sleep. Averaged over a 24 hr day, this increase may be relatively small but a 5mm fall in 24 hr diastolic pressure decreases stroke risk by around 40%.

OSAHS as a cause of stroke

As yet, there is no direct evidence of increased stroke rate in patients previously found to have OSAHS, although this has been suggested from uncontrolled studies. Several studies suggest that snoring is associated with an increased risk of stroke but these are complicated by potential confounders. Although some of these studies have relied on patients recall of snoring, and thus they may be criticised for possible ascertainment bias, longitudinal studies of population whose snoring history was recorded at baseline have also shown an increased frequency of stroke in snorers. A case control study has shown no increased frequency of irregular breathing during sleep in TIA patients compared to carefully matched controls, but this study could have been underpowered. It is thus impossible at present to conclude that upper airway narrowing during sleep is a significant cause of stroke, but the proven association between OSAHS and hypertension makes this highly likely.

Stroke as a cause of sleep apnoea

Numerous recent studies have shown that irregular breathing during sleep is very common after strokes and nocturnal breathing abnormalities are common after strokes (Table 2). This abnormality is commonest in the first few weeks with over half of all patients having increased apnoeas and hypopnoeas during sleep in the first few days after stroke. There is spontaneous resolution of the irregular breathing during sleep over the first 3 months in around 50% of these patients. These respiratory events comprise a combination of obstructive apnoeas and hypopnoeas along with central apnoeas and hypopnoeas, some of the latter in the form of Cheyne-Stokes respiration.

These data pose several unresolved questions. Firstly, does the increased irregular breathing after stroke contribute to inattention and sleepiness, which might impair the rehabilitation of the patient? There are several ongoing studies which have attempted to treat stroke victims who have increased irregular breathing with continuous positive airway pressure (CPAP) and examined outcomes thereafter. There is consensus that this is a very difficult group of patients to treat with CPAP but some groups feel that CPAP results in benefit while others found no major benefits. There are several ongoing studies further examining this question and their results should be awaited before all patients with stroke are screened for OSAHS and treated with CPAP.

Table 1. Clinical features of OSAHS

- Daytime sleepiness
- Impaired concentration
- Unrefreshing nocturnal sleep
- Nocturnal choking
- Nocturia
- Loud snoring

Table 2. Relationship of stroke and OSAHS

1. OSAHS causes hypertension and thus probably stroke
2. Stroke causes apnoeas and hypopnoeas
3. Unknown whether treatment of apnoeas and hypopnoeas after stroke helps outcome

"Several studies suggest that snoring is associated with an increased risk of stroke."
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CPAP instituted. It may be that the future development of less obtrusive therapy is easier for this often disabled group of patients to use and may make it feasible to treat OSAHS in this patient group. At present, the consensus is they are a very challenging group of patients to convince to use CPAP regularly and the benefits of therapy are unclear. Secondly, do these apnoeas and hypopnoeas and the associated blood pressure surges predispose to further strokes and thus a poorer prognosis? Again, there are no convincing data thus far, with studies underway. Thirdly, are these events purely irrelevant epiphenomena? There is no evidence that treating asymptomatic individuals with apnoeas and hypopnoeas is of any benefit to them, and thus there is no merit in screening all stroke patients for sleep breathing irregularities. However, at present, it would seem reasonable that patients with stroke who are sleepy and who are not noted to snore loudly should be screened for OSAHS and treated with CPAP where appropriate and feasible.

Further reading

References