Non-invasive beat to beat arterial blood pressure during non-REM sleep in obstructive sleep apnoea and snoring

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Abstract

Background **– Obstructive sleep apnoea, and possibly snoring, are associated with a poorly understood increase in cardiovascular mortality which may be explained by their effects on systemic blood pressure during sleep. This study compares changes in mean blood pressure during obstructive sleep apnoea and snoring without apnoeas with those in matched control subjects during non-REM sleep.**

Methods **– Eighteen men with obstructive sleep apnoea, 16 men who snored without apnoeas, and 34 control subjects matched for age, sex, obesity, smoking, and alcohol intake were studied. During polysomnography non-invasive mean blood pressure (Finapres) was recorded from each cardiac cycle during non-REM sleep and averaged over a 10 minute period. This was compared with the blood pressure during 10 minutes before sleep onset. The changes in the patients' sleeping blood pressure were compared with those in their individually matched control subjects.**

Results **– Compared with the control subjects the change in mean (SD) arterial blood pressure between being awake and asleep was higher during obstructive sleep apnoea (+6·5 (9) mm Hg *v* −2 (6·5), difference 8·5 (11)), and the rise from wakefulness to sleep in the obstructive sleep apnoea group was itself significant. The average mean arterial pressure was not raised in those who snored without apnoeas compared with either the control subjects or during wakefulness.**

Conclusions **– Average mean arterial pressure is higher during obstructive sleep apnoea than it is during wakefulness, while normal subjects show a fall in blood pressure at sleep onset. This sleep related rise in blood pressure may contribute to the excess cardiovascular morbidity and mortality experienced by patients with this condition.**

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Partial pharyngeal collapse during sleep causes snoring. Complete collapse causes asphyxia and leads to recurrent arousal – obstructive sleep apnoea. Approximately 17% of British men snore, and about one in 300 have severe obstructive sleep apnoea.[1] Compared with the normal population patients with obstructive sleep apnoea have an increased risk of cardiovascular disease[2,3] which is often ascribed to a higher daytime blood pressure. However, the relation between snoring, sleep apnoea, and a higher daytime blood pressure can be explained by confounding variables, and may not be a direct result of the respiratory disturbance during sleep.[4-6] During the night there are known to be repetitive rises in night time blood pressure during obstructive sleep apnoea[7] which produce a considerable disturbance from the normal sleeping pattern.[8] The overall effects of these night time changes have not been compared with well matched controls, and it is therefore unclear whether they just represent an increase in variability about a normal average or whether the blood pressure rises overall.

A study was performed using a non-invasive monitoring system to quantify the changes in mean blood pressure that occur during obstructive sleep apnoea and snoring without apnoeas, and the results were compared with those from well matched control subjects.

Methods

SUBJECTS

Eighteen men were drawn from 23 sequential cases starting treatment for symptomatic, sleep study proven, obstructive sleep apnoea, and 16 men with documented snoring were drawn from two sources: 10 were hospital referrals who had been shown to snore without apnoea during a previous sleep study, and six were from a prevalence study of snoring and sleep apnoea in the normal community[1] and had their snoring confirmed with two overnight domiciliary tape recordings. At least three weeks elapsed between these diagnostic sleep studies and entry into this study.

Each of the patients with obstructive sleep apnoea and the snorers was individually matched with a normal control who was found by a computer search of the records of over 3900 men attending three general practices. An adequate match was established when a subject/control pair had similar ages ±10%, body mass indices ±15%, smoking (smoker/non-smoker), and alcohol intakes (> or < 40 g alcohol per day). If, during a subsequent polysomnogram, a potential control for an obstructive sleep apnoea patient had more than five >4% dips in arterial oxygen saturation per hour of sleep, or a control for a snoring subject was shown to snore, another matching subject

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was sought. No subject asked to take part in the study as a control declined to do so.

ANTHROPOMETRIC, SMOKING, AND ALCOHOL ASSESSMENTS

Height, weight, waist, hip and neck circumferences were measured while standing. The waist circumference was measured at the umbilicus, hip circumference was measured at the level of the iliac crests, and neck circumference at the level of the cricothyroid membrane.

POLYSOMNOGRAPHY WITH BEAT TO BEAT BLOOD PRESSURE RECORDING

Subjects had a full polysomnogram with the true mean blood pressure recorded from every cardiac cycle (beat to beat). Sleep was staged from the electroencephalogram (C2–A3), electro-occulogram, and electromyogram (Multi-Parameter Analysis Recorder 2/Medilog 9200, Oxford Medical Instruments, Abingdon, UK). Sleep was initially staged automatically using standard criteria,[9] and this was confirmed manually for those periods used for the blood pressure analysis. Respiration was monitored from rib cage and abdomen movements, arterial pulse oximetry (Biox 3700), and an infrared video and audio recording. Obstructive sleep apnoea was defined from the full polysomnogram using standard criteria, and snoring was identified from the audio channel of the video recording by the presence or absence of the typical pharyngeal vibratory sound. The assessments of respiratory and sleep state were completed before the blood pressure analysis. The severity of obstructive sleep apnoea was quantified by computer from the number of >4% dips in arterial oxygen saturation per hour of the record.[10] Arterial beat to beat true mean blood pressure was recorded from the third finger of the left hand using an infrared plethysmographic volume clamp method (Finapres; Ohmeda, Englewood, Colorado, USA, logged to a personal computer).[11]

Two 10 minute periods were selected for blood pressure analysis. One consisted of quiet electroencephalogram confirmed wakefulness before sleep onset, and the other consisted of non-REM sleep from the first or second non-REM period during which obstructive sleep apnoea, snoring, or normal respiration were occurring (according to the subjects' study group). These periods satisfied two criteria which were verified from the video recording: (1) body posture was the same in the two selected periods; and (2) the hand to which the Finapres was attached was at a similar hydrostatic level related to the heart during the two periods, and this did not change during the recording period.

The mean blood pressure was averaged over the two sample periods and the difference between the two periods calculated. The blood pressure calculations were performed by computer.

ETHICAL APPROVAL

The study was approved by the Central Oxford Research ethics committee, and subjects gave their consent in accordance with the requirements of the committee.

STATISTICAL ANALYSIS

The absolute mean blood pressure before sleep in the four groups was compared by analysis of variance. Paired t tests were used for the comparison of the mean blood pressure changes on falling asleep and to compare the changes in each of the study groups with their matched controls.

Results

SUBJECTS

Overall the study groups were not significantly different in age, body mass index, waist to hip ratio, smoking, and alcohol intake habits from their matched control groups. A difference which approached significance was seen in the neck circumference between the patients with obstructive sleep apnoea and their matched control subjects (table).

Six patients with obstructive sleep apnoea and two of their matched controls had been told they had high blood pressure. Of these patients three with obstructive sleep apnoea and one of the control subjects were taking antihypertensive medication. Four of the snorers had been told they had raised blood pressure (two were taking treatment), and only one control for a snorer was said to have a raised blood pressure and he was on antihypertensive medication.

SLEEPING BEAT TO BEAT BLOOD PRESSURE

The absolute mean (SD) Finapres blood pressure before sleep onset was similar in the four groups (obstructive sleep apnoea patients 73 (10) mm Hg, control subjects for sleep apnoea patients 72 (11) mm Hg, snoring subjects 73 (12·3) mm Hg, controls for snoring subjects 76 (9) mm Hg, $p > 0·5$ analysis of var-

Mean (SD) characteristics of the study groups and their matched control groups

	Age	*Body mass index*	*Waist/hip ratio*	*Neck circumference (cm)*	*>4% SaO_2 dip rate*	*Smoking*	*Alcohol*
OSA patients (n = 18)	47·5 (10·0)	30·9 (5·7)	1·0 (0·06)	42·6 (3·7)	36 (17·2)	8/10	18/0
Controls (n = 18)	47·6 (8·9)	30·0 (5·1)	1·0 (0·05)	41·3 (3·3)	1·2 (1·3)	8/10	18/0
Significance	p > 0·9	p > 0·1	p > 0·5	p < 0·1	p < 0·0001	–	–
Snorers (n = 16)	48·3 (7·4)	28·1 (3·3)	1·0 (0·05)	41·3 (1·9)	2·1 (2·1)	6/10	15/1
Controls (n = 16)	47·6 (6·5)	27·7 (3·4)	0·9 (0·03)	40·5 (2·2)	0·7 (1·0)	6/10	15/1
Significance	p = 0·2	p > 0·4	p > 0·4	p > 0·2	p < 0·05	–	–

Differences between the subjects and their matched pairs were compared by paired t tests.
OSA = obstructive sleep apnoea.

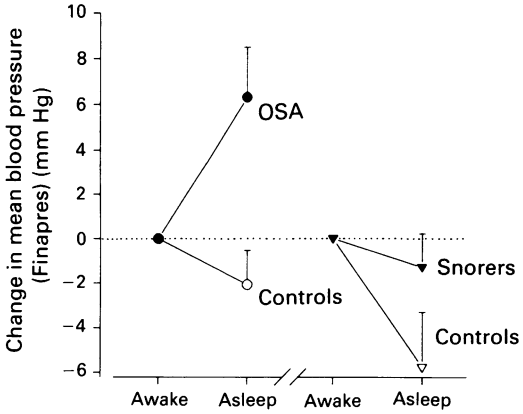

Figure 1 Mean (SE) change in beat to beat (Finapres) blood pressure between presleep quiet wakefulness and 10 minutes of non-REM sleep. OSA = obstructive sleep apnoea.

iance). The changes in beat to beat blood pressure from wakefulness to non-REM sleep are shown in fig 1. The average fall in mean (SD) blood pressure in the snorers was smaller than the matched controls. This difference approached but did not achieve formal significance (snorers −1·5 (6) mm Hg, controls −6 (9·8) mm Hg; difference 4·5 (10) mm Hg; 95% CI −1 to +10, p = 0·1, paired *t* test). The rise in blood pressure seen in the patients with obstructive sleep apnoea compared with their matched controls was significant (obstructive sleep apnoea patients +6·5 (9) mm Hg, controls −2 (6·5) mm Hg; difference 8·5 (11) mm Hg; 95% CI +3 to +14, p < 0·005, paired *t* test). The 6·5 mm Hg rise in blood pressure seen during obstructive sleep apnoea is itself significantly different from zero (95% CI +2 to +11, p < 0·01, paired *t* test).

Discussion

This study reports beat to beat blood pressure in patients with obstructive sleep apnoea, snorers, and carefully matched controls. During periods of sleep disrupted by obstructive sleep apnoea, non-REM sleep blood pressure was 8·5 mm Hg higher relative to the normal sleep in the control subjects, and 6·5 mm Hg higher than during quiet supine presleep wakefulness (p < 0·005, fig 1). Night time blood pressure was not significantly raised in the snorers when compared with their controls, although a difference which approached significance was seen.

Snoring and obstructive sleep apnoea are associated with obesity, smoking, and raised alcohol intake,[12] and some of these variables correlate with blood pressure.[13 14] In this study control subjects were matched for these confounding variables so that the effects of snoring and obstructive sleep apnoea could be examined in isolation. This proved difficult, and over 3900 records from general practice had to be searched to find the final 34 study pairs. This matching has produced groups which have very similar mean ages, body mass indices, and waist to hip ratios (table). A trend towards a difference in neck circumference between the patients with obstructive sleep apnoea and their matched controls was seen. This is presumably because neck size is a better predictor than general obesity for obstructive sleep apnoea.[15]

For this study blood pressure has been measured by an infrared volume clamp method – the Finapres.[11] This system accurately follows the changes in arterial pressure seen during the Valsalva manoeuvre, the Müller manoeuvre, and atrial fibrillation,[16] as well as obstructive sleep apnoea.[17 18] However, because of progressive changes in arterial pressure along the vascular tree,[16 19] and the hydrostatic effects of hand position,[20] its exact readings differ from brachial artery pressures. For these reasons results from this method are best presented as changes from baseline[16] as they are in this study. The criteria for the selection of periods for blood pressure analysis (see methods) were designed to avoid the hydrostatic effects of posture or hand position changes. Within these constraints the Finapres provides an accurate record of blood pressure changes during the selected period, and does this without disturbing sleep. The non-invasive nature of this method has obvious advantages in the ethical study of normal subjects and, being painless, may disrupt sleep less than invasive cannulation.

This study has found that blood pressure is raised by obstructive sleep apnoea during non-REM sleep when compared with quiet presleep wakefulness. Previous studies of night time blood pressure in sleep apnoea have used either ambulatory cuff measurement systems[21–23] or invasive arterial monitoring to gain beat to beat data, but have not compared their findings with matched control subjects.[7 24] This report is the first to quantitate the average blood pressure change by comparing it with carefully matched control results. The blood pressure changes of obstructive sleep apnoea are extremely rapid (fig 2) and this is unsuited to intermittent cuff measurement. During obstructive sleep apnoea blood pressure can vary by more than 50 mm Hg over 10–15 seconds after each apnoea (approximately once a minute). Intermittent cuff readings which take half a minute to complete are a poor way of documenting such changes. Secondly, ambulatory blood pressure systems deliver an arousing stimulus during their measurement cycle. Arousal from sleep in response to this stimulus will halt obstructive sleep apnoea and so immediately change the sleeping blood pressure profile. Thirdly, the process of such arousal itself disturbs blood pressure, and it has been suggested this may distort night time ambulatory blood pressure recordings.[25] Finally, the blood pressure abnormality quantified in this study was emphasised by deliberately selecting periods of continuous obstructive sleep apnoea. Patients with moderate obstructive sleep apnoea will have periods of sleep undisturbed by apnoeas, and ambulatory cuff recordings during these periods would dilute the effect of the sleep apnoea.

One possible confounding explanation for the apparent rise at sleep onset might be that some of the patients with obstructive sleep apnoea had an unusually low blood pressure

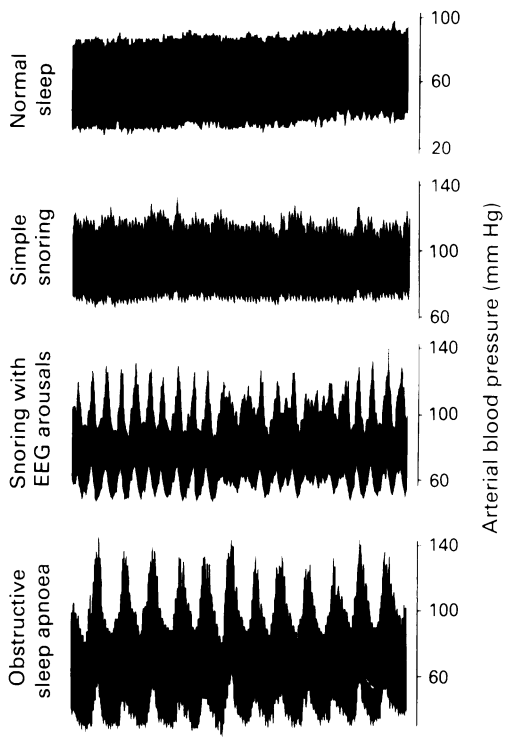

Figure 2 Blood pressure profiles in normal sleep, snoring without arousals, snoring with repetitive arousals but no apnoea, and obstructive sleep apnoea. Each cardiac cycle is represented as a vertical line joining the systolic and diastolic pressures with no space left between cardiac cycles. Each trace represents about 10 minutes recording.

when awake and a normal blood pressure when asleep. The blood pressure of these subjects would then seem to rise on falling asleep. The very similar absolute Finapres blood pressure before falling asleep suggests this is not so. The subjects studied here have also had their blood pressure recorded using an all day ambulatory method. Full details of these recordings are being reported elsewhere.[26] However, these ambulatory results also show no significant daytime blood pressure difference between the study groups, and there is no correlation between the average daytime mean ambulatory blood pressure and the change in Finapres blood pressure on falling asleep among the patients with obstructive sleep apnoea ($r = 0{\cdot}02$, $p > 0{\cdot}9$, Pearson's correlation coefficient).

The mechanisms of the changes in sleeping blood pressure in obstructive sleep apnoea remain contentious, and several different mechanisms are probably active. The falls in pleural pressure which accompany each obstructed inspiratory effort tend to increase intrathoracic blood volume by changing cardiac loading conditions. This could provide a volume load to be released at the end of the apnoea, raising blood pressure. However, where cardiac output has been measured during the blood pressure rise it has been shown to fall which makes this mechanism of doubtful significance.[27] Other factors which may also be important include arousal from sleep[28] and, perhaps, hypoxaemia (although studies which have used supplemental oxygen to prevent hypoxaemia during obstructive sleep apnoea have found this does not greatly change the blood pressure profile[17 29]). The relative importance of these different mechanisms is discussed in detail elsewhere.[30] During the periods of obstructive sleep apnoea sampled for this study all of these factors were present, and even some of the periods of snoring without frank apnoeas were fragmented by snoring induced arousals.

This study only reports results from non-REM sleep since it proved impossible to find periods of REM sleep where the subject's posture was identical to that of the presleep wakefulness control period. This was because REM sleep tends to occur towards the end of the night when the subject had usually changed sleeping position. This limitation may be of significance since it has been suggested that blood pressure may behave differently in obstructive sleep apnoea during REM sleep.[6]

In this study sleeping blood pressure was higher in snorers without apnoeas than in matched controls, but this did not achieve formal significance. This differs from a report from Mateika *et al*[31] in which snoring seemed clearly to elevate blood pressure. This difference is probably a result of study group selection. In our study 36% of the snorers were drawn from the normal community, while Mateika *et al*[31] examined subjects from a specialist sleep clinic. Snoring can cause recurrent arousal from sleep,[32] perhaps triggered by the effort of breathing through a partially collapsed pharynx.[33] Thus, the more severe the snoring, the more fragmented sleep is likely to be. Arousals induced by snoring cause blood pressure rises similar to those of obstructive sleep apnoea (fig 2). Sleeping blood pressure disturbance will therefore be greater if the snoring population studied is drawn from a sleep clinic where snoring is likely to be more severe and hypersomnolence one of the presenting symptoms.

Patients with untreated obstructive sleep apnoea have an increased morbidity and mortality from vascular causes.[34] The night time blood pressure changes seen in this study could contribute to this mortality, particularly since night time blood pressure seems to be an independent predictor of vascular disease in essential hypertensives.[35] Assessing the size of any such risk is difficult. The blood pressure disturbances of sleep disturbed by breathing abnormalities are pulsatile (fig 2), which may be more damaging than the sustained rise of essential hypertension. However, sleep disordered breathing only disturbs blood pressure during the night while essential hypertension often affects the whole 24 hour period. If the average mean night time blood pressure rise of about 9 mm Hg seen in this study can be equated with a 3 mm Hg rise over 24 hours (a night being about eight hours), then a risk estimation might be possible. A 3 mm Hg blood pressure rise increases the risk of a stroke by about 20%, and the risk of coronary heart disease by about 13% above that of the normal population.[36]

In conclusion, this study has found that obstructive sleep apnoea raises sleeping blood

pressure when compared with normal sleep in control subjects or quiet supine wakefulness. This rise in sleeping blood pressure may contribute to the excess vascular morbidity and mortality experienced by patients with this disorder.

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