Patient histories suggest that obstructive sleep apnea syndrome (OSAS) is a progressive condition. To investigate whether this could be shown in data from sleep recordings, 42 patients with OSAS were retrospectively studied. All had undergone a screening recording of respiration movements and oximetry at least 6 months (average, 16 months) prior to a diagnostic polysomnogram including these parameters. No treatment was given in the meantime. In the first recording, mean oxygen desaturation index (ODI, average number of desaturations of >4 percent per sleeping hour) was 10; periodic, obstructive respiration movements occurred during (average) 36 percent of total estimated sleeping time, and mean nadir SaO2 was 85 percent. In the second recording, mean ODI was 21 (significant change, p = 0.0002), periodic respiration time was 61 percent, and nadir SaO2 was 80 percent (p = 0.0001, respectively). In 26 of 42 patients (62 percent), ODI had increased by >50 percent. Increases in ODIs and periodic breathing were significantly correlated to increases in body weight. There were, however, exceptional patients with considerable increases in respiratory disturbance despite weight loss. The greatest changes were found in the patients who had the highest apnea indices in the polysomnograms. Early treatment may therefore be justified, since a borderline case may change to severe OSAS in 1 to 2 years' time. Follow-up recordings of untreated patients are important.

\[ AHI = \text{apnea-hypopnea index}; \ BM = \text{body mass index}; \ ODI = \text{oxygen desaturation index}; \ OSAS = \text{obstructive sleep apnea syndrome}; \ SCSB = \text{screening recording of respiration and body movements by an apnea mattress} \]

There are indications that obstructive sleep apnea syndrome (OSAS) is a progressive disease. Lugaresi et al. have made a retrospective study based on histories of 118 patients. The typical patient was found to be a man who snored every night, who was in his 20s, and continuing with increasing loudness until the age of 40 years. His snoring then became intermittent, i.e., interrupted by silences at regular intervals. A few years after this, the patient also started to experience successively increasing daytime somnolence. Based on this information, Lugaresi et al. proposed that OSAS is a progressive disease which evolves from simple snoring. Kales et al. have interviewed patients with severe OSAS and described a similar clinical course.

The hypothesis of progression, however, has not been substantiated in data from sleep recordings. To investigate whether parameters reflecting respiratory disturbance increased over time, and, if so, at what rate, a retrospective study of patients with OSAS who had gone through two successive sleep apnea recordings was performed.

All patients referred because of clinically suspected OSAS first made a screening recording of respiration and body movements by an apnea mattress (SCSB) combined with ear oximetry. In this type of recording, obstructive sleep apneas are typically reflected as a periodic, diamond-shaped respiration movement pattern, accompanied by repetitive oxygen desaturations. SCSB oximetry recordings have been compared with simultaneously performed conventional polysomnograms and criteria for pathology established. Sleep time could be estimated with good accuracy in the SCSB recording by absence of gross body movements and occurrence of typical respiration movement patterns (overestimation of on average 18 min during 332 min of actual sleep in 77 patients, p<0.0001). Therefore, an oxygen desaturation index (ODI), i.e., the average number of significant desaturations per sleeping hour, could be calculated. Both ODI and percentage of periodic respiration movement time were well correlated with the conventional apnea index apnea \( \pm \) hypopnea index (AHI); p<0.0001, respectively. Since this validation study had not been completed at the time the present study comprises, all patients with any indication, weak or strong, of nocturnal upper airway obstruction in the first limited recording went on to a second diagnostic investigation.

This was a full polysomnogram with simultaneous SCSB oximetry. No kind of treatment, not even advice concerning eating and drinking habits, was given until the second recording had been performed. Due to inadequate polysomnographic capacity, there could be a long interval between the two investigations. In this study, comparison has been made between the 2 SCSB oximetry recordings in all patients who had to wait at least 6 months.
METHODS

Sleep Recordings

A whole-night screening recording was made first. This comprised monitoring respiration and body movements by means of a static charge sensitive bed (SCSB), and arterial oxygen saturation (SaO₂, Biox III with an ear probe). The second investigation was a whole-night polysomnogram, including EEG, electro-oculogram, chin electromyogram, airflow (three-port thermistor), respiration movements, and ECG. Simultaneous to this, SCSB and oximetry were recorded at a separate strip chart recorder at slow paper speed in exactly the same manner as in the previous investigation. Body weight was noted at both recording sessions. The following values were always calculated and could therefore be used for comparison between the two SCSB oximetry recordings: (1) ODI, i.e., the number of desaturations of 4 percent or more divided by sleeping time in minutes divided by 60; (2) the percentage obstructive respiration movement time of total sleeping time; and (3) the lowest recorded, i.e., the nadir, SaO₂ value during sleep.

Statistics

All comparisons between identical variables from the two recordings were performed with the Wilcoxon signed rank test for pairs, except in the case of body mass indexes (BMIs), which were assumed to be of a Gaussian distribution. Hence, the paired t test was used.

Inclusion Criteria

Inclusion criteria were as follows: (1) an AHI above 5 in the polysomnogram; (2) at least 6-month interval to the preceding screening recording; and (3) no treatment given in the meantime.

Patients

Forty-two OSAS patients, 35 men and 7 women, mean age 55 years (range, 41 to 72 years) were included. They all complained of socially unacceptable snoring and daytime symptoms and were referred to an ear, nose, and throat specialist. Mean polysomnographic AHI was 23.5 (range, 6 to 55, t95 percent [confidence interval] 4.4).

RESULTS

The mean recording interval between the 2 investigations was 15.6 months (range, 6 to 32 months, t95 percent 1.5).

Mean sleep time in the first investigation, estimated from the SCSB recording, was 382.3 min (SD, 69.0). In the following polysomnogram, the sleep time was significantly shorter (average, 342.8 min; SD, 51.1; p = 0.0067).

In the first recording, the mean ODI was 10.1 (range, 1 to 31, t95 percent 2.4), with an increase to 20.9 (range, 2 to 63, t95 percent 5.0) in the second recording (p = 0.0002) (Fig 1). The ODI values were changed in 50 percent or more in 26 of the 42 patients (62 percent). The fastest rate of progression in ODI was from 4 to 56 in 15 months. Decreases of 50 percent or more occurred in 24 patients (57 percent), 20 of whom had similar increases in ODI. Decreases by 50 percent or more occurred in two patients only, in both cases with similar changes in ODI.

Mean nadir SaO₂ was 85.3 percent (71 to 92 percent, t95 percent 1.4) in the first recording, and 79.7 percent (56 to 92 percent, t95 percent 2.5) in the second (p = 0.0001).

Complete data for calculation of change in BMI was obtained in 39 patients. Mean BMI was 27.1 at the first recording, and 27.3 at the second. This change is not statistically significant. Individual changes in ODI and BMI were significantly correlated (p = 0.019, simple regression analysis). However, some patients had considerable increases in ODI despite the fact that they had not gained weight; they might even have lost some. The relationship between BMI and ODI changes is shown in Figure 2. Changes in BMI were also significantly correlated to changes in percentage of obstructive respiration (p = 0.028) and nadir SaO₂ (p = 0.010).

There was no statistically significant correlation

FIGURE 1. In the first recording of 42 patients, mean oxygen desaturation index (ODI) was 10 (7.7 to 12.5, 95 percent confidence interval). On average 16 months later, it had changed to 21 (15.9 to 25.9).

FIGURE 2. Correlation between changes in oxygen desaturation index (ODI) and body mass index (BMI) for 39 patients. p = 0.019, R² = 0.14.
between patients' ages and changes in indices of respiratory disturbance. It is, however, noteworthy that the largest increases in ODI occurred among the five youngest patients (younger than 45 years), whereas the six oldest patients (65 or over) exhibited minor changes only (Fig 3).

A strongly significant correlation ($p = 0.0001$) existed between AHI in the second recording and changes in ODI. There were also significant correlations with changes in obstructive respiration time and nadir SaO$_2$ ($p = 0.0323$) and $p = 0.0037$, respectively.

**DISCUSSION**

The results of this study support the hypothesis that OSAS is a progressive condition. It also shows that there is a rapid progression in many cases. It must, however, be remembered that our patients suffered from daytime symptoms already at entrance into the study. In the report of Lugaresi et al., it was noted that the rate of progression appeared to increase once the patient had begun to experience daytime somnolence.

It was noticeable that the largest increases in ODI were seen among the youngest subjects in this study. In the oldest age group (older than 65 years), there were minor or no certain indications of progress. It has been shown that indices of respiratory disturbance may be increased in clinically healthy elderly subjects. Bliwise et al. have also found that slight increases in indices of sleep-related respiratory disturbance may occur in healthy middle-aged and elderly volunteers. One explanation for lack of progress in the elderly patients in this study, therefore, is that the OSAS diagnosis may not have been correct. Instead, the respiratory disturbance detected might reflect a normal aging process. However, four of these six patients were subsequently treated with uvulopalatopharyngoplasty or continuous positive airway pressure and three did benefit from treatment as shown by normalization of subsequent recordings and relief from symptoms.

Patients with large increases in BMI appear to be especially at risk for rapid progression. However, some patients showed marked increases in ODI, etc., in the absence of weight gain. Also, mean values of indices of respiratory disturbance increased significantly between the two recordings for the whole patient group, despite the fact that this was not the case with mean BMI. This indicates that other factors must play a part in the evolution of OSAS. Body position was not recorded in the present investigations, and it is possible that some patients had signs of increased respiratory disturbance because they spent more of their sleeping time on their backs in the second recording. The fact that increases in ODI and periodic breathing were positively correlated to BMI speaks against this as a major causative factor, since increased weight should not make the patient more disposed to sleep in the supine position. Another reason for worsening of a respiratory disturbance could be increased alcohol intake, but to our knowledge, the patients in question did not change their habits in this respect during the study period. In two recent biopsy studies it has been shown that there are signs of neurogenic damage in upper airway muscles of OSAS patients. Patients with constant snoring and fewer apneas had similar, but less marked, changes. In another recent study, it was found that OSAS patients had impaired temperature sensitivity in the oropharynx. Such lesions to both motor and sensory nerves could, for example, be caused by snoring-induced vibrations. Local neurogenic damage to the hands is known to occur in people who work with vibrating tools. The increased negative intrathoracic pressure that occurs in snoring, even in the absence of proper apneas, might also cause mechanical damage to the nerve endings by stretching the upper airway soft tissue. A nightly repeated injury of this type could well explain the progressive nature of OSAS. Spreading neurogenic damage would cause impaired muscle function with concomitantly decreasing ability to maintain the upper airway patency during sleep, when muscle tone is normally reduced.

The patients with the highest apnea indices on the polysomnograms, ie, those who were regarded as the most severe cases, also had the most marked increases in ODI and periodic breathing over time. This implies that a mild case may change to a severe one in 1 to 2 years, especially if the patient is young and/or prone to weight increase. The results of this study therefore suggest that it may be important to treat OSAS early. It has been an issue of debate whether patients with mild to moderate disease, ie, apnea index of 5 to 20, should receive active treatment. Such patients have not been found to have increased mortality, and it is not clear whether there is an increased risk of cardiovascular disease if obesity and other confounding factors are controlled. But since there may be rapid progression, it could well be pertinent to give active
treatment before this happens. It has been shown that uvulopalatopharyngoplasty often fails in severe cases, and it is usually not possible to discontinue continuous positive airway pressure therapy even if the patient loses weight. If treatment is given early, before the disease has developed into a severe stage, the chances of cure might improve. At any rate, the results of the present investigation stress the importance of follow-up recordings, also in patients considered borderline before a primary consultation.

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