J. Sleep Res. (2009) 18, 337–341 Sleep disordered breathing

doi: 10.1111/j.1365-2869.2009.00734.x

Evolution of upper airway resistance syndrome

LUIZA JONCZAK[1], ROBERT PŁYWACZEWSKI[1], PAWEŁ ŚLIWIŃSKI[1], MICHAŁ BEDNAREK[2], DOROTA GÓRECKA[2] and JAN ZIELIŃSKI[2]

[1]Department of Diagnosis and Treatment of Respiratory Failure and [2]2nd Department of Respiratory Medicine, National Research Institute of Tuberculosis and Lung Diseases, Warsaw, Poland

Accepted in revised form 1 December 2008; received 4 March 2008

SUMMARY The question of whether upper airway resistance syndrome (UARS) is a distinct disease or an initial feature of obstructive sleep apnoea syndrome is still a matter of debate. We evaluated a retrospective group of UARS patients to determine the evolution of UARS over time and the relationship between clinical evolution and subjects' phenotype. Investigations were performed in 30 patients, in whom UARS was diagnosed between 1995 and 2000 by the use of full polysomnography (PSG) without oesophageal pressure (Pes) measurement. The time between initial and follow-up investigations was 6.6 ± 2.6 years. All subjects had full PSG with Pes measurement and completed a sleep questionnaire, including the Epworth Sleepiness Scale. In 19 subjects, PSG results were compatible with UARS. In nine subjects, obstructive sleep apnoea–hypopnoea syndrome (OSAHS) was diagnosed. In two subjects, PSG did not demonstrate breathing abnormalities. The mean ± SD apnoea–hypopnoea index in the UARS group was 1.5 ± 1.7 h^{-1} and 25.2 ± 19 h^{-1} in the OSAHS group ($P < 0.01$). The increase in body mass index (BMI) between initial and follow-up investigations in the UARS group was from 29.4 ± 4 to 31 ± 5.7 kg m^{-2} ($P = 0.014$) and in the OSAHS group from 30 ± 4.1 to 32.4 ± 4.7 kg m^{-2}($P = 0.004$). Amplitude of Pes swings during respiratory events was significantly higher in OSAHS than that in UARS ($P = 0.014$). Our results suggest that UARS is part of a clinical continuum from habitual snoring to OSAHS. Progression from UARS to OSAHS seems to be related to an increase in the BMI.

KEYWORDS obstructive sleep apnoea, oesophageal pressure, polysomnography, upper airway resistance syndrome

INTRODUCTION

Guilleminault *et al.* (1993) described a group of subjects whose main clinical symptom was excessive daytime sleepiness. On polysomnographic evaluation, these subjects presented with multiple arousals during sleep preceded by increased breathing effort without apnoea or hypopnoea. Continuous recording of oesophageal pressure (Pes) revealed multiple excessive breathing efforts during sleep terminated by arousals. Guilleminault *et al.* (1993) suggested that this conglomeration of symptoms and signs represented a distinct clinical entity, and named it 'upper airway resistance syndrome' (UARS). Publication was preceded by four earlier reports on the same type of patients (Guilleminault *et al.*, 1991, 1992; Stoohs and Guilleminault, 1990, 1991). Between 1993 and 2000, Wheatley (2000) found 20 original papers describing patients with UARS.

A questionnaire survey among pulmonary and sleep specialists performed in the United States in 1995 revealed that UARS was diagnosed in 60% of sleep laboratories, although in only a few was Pes recording performed to confirm the diagnosis (Phillips *et al.*, 1996).

The American Academy of Sleep Medicine (AASM) did not, however, recognize UARS as a separate disease. In 1999, the Academy proposed including UARS as a preclinical stage of obstructive sleep apnoea syndrome (OSAS) unless new

Correspondence: Jan Zieliński, Department of Respiratory Medicine, National Research Institute of Tuberculosis and Lung Diseases, ul. Płocka 26, 01-128, Warsaw, Poland. Tel.: +48 22 4312144; fax: +48 22 4312454; e-mail: j.zielinski@igichp.edu.pl

evidence confirming distinctness of the syndrome emerged (AASM Task Force, 1999). In 2005, AASM included UARS as an OSAS (AASM, 2005).

We decided to investigate the clinical evolution of a retrospective group of patients with UARS diagnosed in our laboratory between 1995 and 2000 to add new evidence to the continuing debate on the place of UARS in the sleep-disordered breathing spectrum (Douglas, 2000; Guilleminault and Chowdhuri, 2000b; Guilleminault *et al*., 2000a, 2001, 2006; Loube and Andrada, 1999).

The aim of our study was to investigate: (1) the clinical evolution of patients with UARS over time; and (2) the relationship between clinical evolution and subjects' phenotype.

MATERIALS

From 1995 to 2000 in our sleep laboratory, 25 males and 5 females, aged 34–66 years (mean ± SD 54.1 ± 7.8), were diagnosed with UARS. The diagnosis was based on the original Guilleminault *et al*. (1993) description: typical clinical symptoms (snoring and excessive daytime somnolence) and apnoea–hypopnoea index (AHI) $< 5\ h^{-1}$. All patients presented with excessive daytime sleepiness, disrupted sleep and low AHI (Table 1). Periodic limb movement disorders were excluded. None of the subjects investigated accepted continuous positive airway pressure therapy.

In 2002, all subjects were contacted by letter inviting them for a new assessment as part of the study to evaluate the current status of their sleep-disordered breathing. All patients gave their informed consent. The time between initial assessment and current investigations averaged 6.6 ± 2.6 years. The protocol was approved by the institutional ethics committee.

Table 1 Comparison of initial investigation and follow-up investigation: Epworth Sleepiness Scale (ESS), body mass index (BMI) and polysomnography (PSG) variables

Variable	*Initial investigation (n = 30)*	*Follow-up investigation (n = 30)*
Age (years)	47.4 ± 7.9	54.1 ± 7.8
BMI (kg m^{-2})	29.7 ± 3.8	31 ± 5*
ESS (points)	15.1 ± 3.6	14.5 ± 5.2
AHI (per hour)	3.3 ± 2.6	8.6 ± 15*
ARI (per hour)	32.4 ± 15.1	35.1 ± 17.3
SaO_2 min (%)	87.5 ± 4.1	87.5 ± 5.4
SaO_2 mean (%)	93.1 ± 1.6	93 ± 2.6
T90 (%)	4.6 ± 8	8.4 ± 20.6*

*$P < 0.001$. AHI, apnoea–hypopnoea index; ARI, arousal index; SaO_2 min, minimal arterial blood oxygen saturation; SaO_2 mean, mean arterial blood oxygen saturation; T90, percentage of time spent in $SaO_2 < 90\%$.

METHODS

All subjects completed a sleep questionnaire that included the Epworth Sleepiness Scale (ESS) (Johns, 1992). All subjects underwent medical history checks, clinical evaluation and diagnostic nocturnal polysomnographic recording. The clinical evaluation included examination of the upper airway by an ear–nose–throat specialist.

Measurements

All patients underwent first full night polysomnography (PSG 1) with SomnoStar Alfa Series (SensorMedics Corporation, Yorba Linda, CA, USA) between 1995 and 2000 according to standard techniques. At that time, our sleep laboratory was not equipped to measure Pes. Measurements included central and occipital electroencephalograms (EEG), right and left electro-oculograms (EOG), submental and tibial electromyograms and electrocardiograms. Oronasal airflow was recorded by thermistor, thoracoabdominal movements by inductive plethysmography, snoring sounds by microphone taped above the larynx and arterial blood oxyhaemoglobin saturation by pulse oxymetry.

The second (follow-up) PSG (PSG 2) was performed during the current investigation and included, in addition, to a standard recording montage, the measurement of Pes. Pes was measured with a conventional 10-cm latex balloon catheter placed transnasally in the lower third part of the oesophagus. The balloon catheter was connected to a pressure transducer (143PC03D Honeywell, Freeport, IL, US) and recorded on line on one of the PSG channels.

The PSG recordings were scored manually using 30-s epochs following Rechtschaffen and Kales' (1968) criteria for sleep and wake determination and sleep staging. Arousals were defined as lasting more than a 3-s shift to alpha or theta EEG activity from a slower background frequency. Arousals were scored blind to respiratory events. Initial and second polysomnograms were scored and interpreted by the same investigators using exactly the same criteria.

Abnormal respiratory events were evaluated according to the standard criteria of the AASM Task Force (1999). Apnoeas were defined as a cessation of airflow for at least 10 s, and hypopnoeas as more than 50% decrease in airflow from baseline in amplitude of a valid measure of breathing during sleep for 10 s or more, associated with either an oxygen desaturation of >3% or an arousal. Respiratory events characterizing UARS were detected through analysis of a respiratory pattern showing a crescendo increase in Pes amplitude followed by an EEG arousal (Guilleminault *et al*., 1993). Pes crescendo was defined as an increase of more than 20% in inspiratory peak Pes amplitude (Pes_{max}) compared with baseline Pes (Pes_{min}), lasting 10 s or more, without apnoea and/or hypopnoea (AASM Task Force, 1999; Berg *et al*., 1997). An arousal was followed by an abrupt reduction of negativity of Pes amplitude and such episodes were not accompanied by significant oxygen desaturation.

Neck and abdominal circumferences were measured and the ESS was completed by all subjects.

Statistical analysis

Statistical analyses were performed with STATISTICA version 6.0 software (StatSoft, Tulsa, OK, USA, 2001). Quantitative data were described by the use of mean ± SD. Differences between group characteristics were analysed with the unpaired *t*-test. Pearson's method was used to analyse correlations between study variables. Tests were considered significant when $P < 0.05$.

RESULTS

Analysis of PSG 2 led us to separate the investigated subjects into three groups. In 19 subjects, PSG results were compatible with UARS. In nine subjects, obstructive sleep apnoea–hypopnoea syndrome (OSAHS) was diagnosed. They presented AHI $> 5\ h^{-1}$ and ESS > 9 points. The detailed PSG results in UARS and OSAHS patients are presented in Table 2.

In two subjects, PSG did not demonstrate sleep or breathing abnormalities. During follow-up time, the first subject lost 10 kg of body weight. The second subject also lost weight (2.5 kg) and completely changed his lifestyle. He resigned from a stressful manager's job and became a gardener. They both stopped snoring and excessive daytime sleepiness ceased. Both were excluded from further analysis.

The mean body mass index (BMI) was lower in UARS patients than that in OSAHS patients (31 ± 5.7 versus 32.4 ± 4.7 kg m^{-2}; $P = 0.034$). The increase in BMI between PSG 1 and PSG 2 was significant in both groups.

However, there was no correlation ($r = 0.24$, $P = 0.19$) between the change in weight and the change in AHI across the whole group over the follow-up period. The UARS subjects increased weight by (mean) 3.1 kg and OSAHS subjects by (mean) 6.2 kg.

The study group was subdivided into subjects who presented with normal body weight at entry (BMI ≤ 25) and subjects with BMI more than 25 kg m^{-2}. Three subjects had normal body weight at entry. Two did not gain weight and remained in the UARS group. One increased BMI from 21.8 to 25.6 kg m^{-2} (11 kg) and developed OSAHS. The remaining 27 subjects were overweight at entry (mean BMI, 30.5 kg m^{-2}). Two subjects lost weight and they had no symptoms and signs of UARS at follow-up. Of the other 25 subjects, eight of nine who were overweight at entry and continued to increase their weight during the follow-up period developed OSAHS; the rest remained in the UARS group.

The mean neck circumference was 42.3 ± 2.19 cm, and was almost identical in the UARS and OSAHS groups (42.2 ± 2.2 versus 42.5 ± 2.4 cm). The mean abdominal circumference was 105.5 ± 12.5 cm, and the difference between the UARS and the OSAHS groups was also not significant (103.3 ± 12.9 versus 108.5 ± 7.8 cm) ($P = 0.18$). Three males with normal body weight at entry had a neck circumference within normal limits at 40–42 cm (mean 40.6 ± 1.15 cm) and an abdominal circumference of 86–92 cm (mean 88.3 ± 3.21 cm). All overweight patients with OSAHS and 13 subjects with UARS had an abnormal abdominal circumference, mean 108.5 ± 7.8 cm and 109.7 ± 10.3 cm respectively.

The mean ± SD AHI in the UARS group was 1.5 ± 1.7 h^{-1} and was 25.2 ± 19 h^{-1} (range 11–73) in the OSAHS group ($P < 0.01$) (Table 2). There were no significant differences between the groups in the lowest nocturnal oxygen saturation and mean nocturnal oxygen saturation. The total time spent in desaturation ($SaO_2 < 90\%$), however, was significantly higher in the OSAHS group than that in the UARS group ($P = 0.01$) (Table 2).

Initial Pes measurements were performed in awakened subjects during quiet-breathing in both sitting and supine positions. In both positions, inspiratory Pes remained in the normal range, with mean −6.3 ± 2.2 cmH_2O (sitting) and −5.3 ± 2.9 cmH_2O (supine).

Table 2 Comparison of age, body mass index (BMI), epworth sleepiness scale (ESS) and respiratory polysomnography (PSG) variables in two groups: upper airway resistance syndrome (UARS) and obstructive sleep apnoea–hypopnoea syndrome (OSAHS) subjects [mean ± SD]

	UARS (n = *19*)			*OSAHS* (n = *19*)		
Variable	*PSG 1*	*PSG 2*	P	*PSG 1*	*PSG 2*	P
Age (years)	47.5 ± 7	53.5 ± 7		47.2 ± 9.7	54.9 ± 10.8	
BMI (kg m^{-2})	29.4 ± 4	31 ± 5.7	0.014	30 ± 4.1	32.4 ± 4.7	0.004
ESS (points)	14.9 ± 3.5	14.4 ± 5.3	NS	14.9 ± 4	15.5 ± 5.2	NS
AHI (per hour)	3.8 ± 2.9	1.5 ± 1.7	0.006	2.7 ± 1.7	25.2 ± 19	0.007
ARI (per hour)	34.1 ± 16.2	37.2 ± 18.5	NS	30.7 ± 13.9	34.9 ± 14	NS
SaO_2 min (%)	88.2 ± 4	88.7 ± 3	NS	86.1 ± 4.6	84.4 ± 8.1	NS
SaO_2 mean (%)	93.3 ± 1.9	93 ± 2	NS	92.3 ± 1.9	91.8 ± 3.6	NS
T90 (%)	4.2 ± 8.6	2.3 ± 6.2	NS	6.2 ± 7.5	22.2 ± 33.7	0.01

PSG 1, first polysomnography when UARS was diagnosed; PSG 2, second polysomnography with oesophageal pressure (Pes) measurement after (mean) 6 years of follow-up; AHI, apnoea–hypopnoea index; ARI, arousal index; SaO_2 min, minimal arterial blood oxygen saturation; SaO_2 mean, mean arterial blood oxygen saturation; T90, percentage of time spent in $SaO_2 < 90\%$; NS, not significant.

Table 3 Comparison of oesophageal pressure (Pes) measurements in two groups: upper airway resistance syndrome (UARS) and obstructive sleep apnoea–hypopnoea syndrome (OSAHS) subjects [mean ± SD]

Variable (cmH_2O)	*UARS* (n = *19*)	*OSAHS* (n = *9*)	P
Pes_{min}	−7.7 ± 3.5	−5.7 ± 3.4	NS
Pes_{max}	−15.2 ± 9.5	−19.7 ± 8.5	0.0421
ΔPes	9 ± 3.5	14 ± 5.9	0.014
exp_{min}	5.6 ± 3.1	4.8 ± 2.2	NS
exp_{max}	6.1 ± 3.2	5.7 ± 2.3	NS
Δ_{min}	13.2 ± 6.4	10 ± 5.5	NS
Δ_{max}	22.8 ± 9.3	25.4 ± 10.4	NS
T(s)	38.1 ± 8.2	34.5 ± 6.6	NS

Pes_{min}, inspiratory baseline oesophageal pressure at the beginning of the respiratory event; Pes_{max}, inspiratory peak of oesophageal pressure at the end of respiratory event; ΔPes, amplitude between baseline oesophageal pressure at the beginning of the event (Pes_{min}) and inspiratory peak (Pes_{min}); exp_{min}, expiratory pressure at the beginning of the event; exp_{max}, expiratory pressure at the end of the event; Δ_{min}, amplitude between Pes_{min} and exp_{min}; Δ_{max}, amplitude between Pes_{max} and exp_{max}; *T*, duration of episode; NS, not significant.

During sleep, average maximum negative Pes demonstrated a wide variability in both UARS and OSAHS patients. The mean inspiratory peak Pes at the end of increased respiratory effort (Pes_{max}) was −16.2 ± 9.1 cmH_2O. It was higher in the OSAHS (−19.7 ± 8.5 cmH_2O) than that in the UARS group (−15.2 ± 9.5 cmH_2O) ($P = 0.042$). Two subjects without symptoms of UARS or OSAHS also had episodes of increased inspiratory effort, but fewer in the rest of the group (1.5 and 6.2 h^{-1}). Their mean Pes_{max} was −13.2 and −13 cmH_2O, slightly lower than that in UARS patients.

Pes amplitude (ΔPes) between baseline Pes at the beginning of the event (Pes_{min}) and inspiratory peak pressure (Pes_{max}) was also higher in OSAHS patients (mean 14 ± 5.9 cmH_2O) than that in UARS patients (9 ± 3.5 cmH_2O) ($P = 0.014$). In two subjects without breathing abnormalities, ΔPes was 5.9 and 3.9 cmH_2O respectively. There was no significant difference between groups in other variables (for details see Table 3).

The mean ESS in UARS patients was 14.5 ± 5.2 points, and 15.5 ± 5.3 in OSAHS patients ($P = 0.048$). In four UARS subjects, ESS score was <10 points. In PSG 2, however, they presented episodes of increased respiratory effort related to arousals. All subjects with OSAHS had an ESS score ≥10 points. Snoring was prevalent. In the UARS group, 84% of subjects and all subjects in the OSAHS group were habitual snorers.

DISCUSSION

We found that during 6 years of follow-up of the group, in patients diagnosed originally as having UARS, a significant number of the studied subjects developed signs of OSAS. Transition from UARS to OSAHS was related to a significant increase in the BMI. Our data support the opinion that UARS belongs to the clinical spectrum of OSAS.

Lugaresi *et al.* (1990), in a retrospective study of 118 patients with OSAHS, regarded the disease as a continuum, starting with heavy snoring. Increase in BMI led to the appearance of obstructive apnoea and correlated later with the AHI. A similar evolution could be observed in our study. Subjects with the highest increase in BMI developed signs of OSAHS. In subjects with a smaller increase in BMI, the clinical picture of the disease remained unchanged. In two subjects, who lost weight, snoring and daytime somnolence disappeared.

Guilleminault and Chowdhuri (2000b) presented new evidence supporting the hypothesis that UARS is a distinct clinical entity. Comparing UARS patients with OSAHS patients, they found that UARS patients presented with a different phenotype. UARS patients are characterized by 'Gothic' (high and narrow) hard palate and absence or early extraction of wisdom teeth. None of our subjects presented with such abnormalities.

Guilleminault *et al.* (2000a) investigated 176 OSHAS and 128 UARS subjects. In the OSHAS group, older age and a wider-neck circumference were significantly different compared to the UARS group. In this sample, there was no significant difference in mean BMI (UARS 28.2 4.1 versus OSHAS 29 3.7 kg m^2), arousal index and ESS.

Guilleminault *et al.* (2006) published a prospective study of 94 patients diagnosed with UARS between 1995 and 1998, according to a new definition of UARS based on AHI $< 5\ h^{-1}$ and oxygen saturation >92% throughout the night. Follow-up investigations performed for 43–69 months after initial evaluation showed that five subjects had AHI compatible with OSAHS, confirming their evolution from UARS to OSAHS (Guilleminault *et al.*, 2006). An increase in body weight was observed in all subjects. The majority of patients did not increase their weight significantly and were still in the UARS group.

In our observation, the UARS subjects increased weight by (mean) 3.1 kg and OSAHS subjects by (mean) 6.2 kg. We did not find a correlation between changes in BMI and AHI. In two subjects, the second PSG did not show sleep or breathing abnormalities and they lost body weight during the follow-up period. Only three subjects had normal body weight at entry. Two did not gain weight and remained in the UARS group. One increased BMI from 21.8 to 25.6 kg m^{-2} (11 kg) and developed OSAHS.

Friberg *et al.* (1998) hypothesized that a progressive lesion in the afferent and/or efferent nerve pathways in this reflexogenic mechanism, caused by the snoring trauma, is a contributory factor to the collapsibility and obstruction of the upper airway seen in patients with OSAHS. Kimoff *et al.* (2001) found that non-apnoeic snorers and OSAHS patients had similar abnormal-pharyngeal sensitivity of receptors compared with normal subjects.

The difference in average maximum negative Pes observed between UARS and OSAHS in our study was significant. In

other studies comparing UARS with OSAHS patients, the difference in Pes values was not significant (Guilleminault *et al*., 2001; Loube and Andrada, 1999; Pelin *et al*., 2003). There is common agreement that respiratory effort is comparable in OSAHS and UARS patients. Only Guilleminault and Chowdhuri (2000b) suggested that in UARS patients, the internal respiratory load is exquisitely sensitive therefore allowing the patient to wake up in response to a small increase in inspiratory effort.

Rees *et al*. (2000), comparing UARS patients and asymptomatic subjects, showed that there was no significant difference in frequency of either flow limitation or resistive events between the two groups. Pleural pressure swings at resistive event termination were, however, significantly more negative in the UARS group (mean −15 versus −11 cmH_2O, $P = 0.02$), and the number of cortical arousals associated with resistive events was higher in the UARS patients (median 10 versus 3 h^{-1} sleep; $P = 0.02$).

Our study has several limitations. The first PSG was performed without Pes measurement as at that time we were not equipped to record Pes during sleep. All patients, however, complied with the UARS diagnostic criteria that we used (Guilleminault *et al*., 1993): excessive daytime sleepiness, elevated EEG arousal index and normal respiratory disturbance index of fewer than five events per hour of sleep. In addition, all patients were heavy snorers. Another important limitation is that we measured airflow using a thermistor, a method replaced by a nasal cannula pressure transducer, which is much more sensitive in detection of breath amplitude.

A further limitation is short total sleep time, which did not allow us to perform a valid analysis of sleep and could also influence the results of sleep-disordered breathing analysis.

CONCLUSIONS

Our findings suggest that UARS is part of a clinical continuum from habitual snoring to OSAHS. Progression from UARS to OSAHS seems to be related to increase in the BMI.

ACKNOWLEDGEMENTS

The authors give special thanks to Dr Anne Jones for essential and editorial advice during manuscript preparation. The study was supported by the Polish State Committee for Scientific Research Grant no. 3 PO5D 107 24.

REFERENCES

American Academy of Sleep Medicine. *ICSD-2, The International Classification of Sleep Disorders*, 2nd edn. Diagnostic and coding manual. American Academy of Sleep Medicine, Westchester, 2005.

American Academy of Sleep Medicine Task Force. Sleep-related breathing disorders in adults: recommendations for syndrome definition and measurement techniques in clinical research. The Report of an American Academy of Sleep Medicine Task Force. *Sleep*, 1999, 22: 667–689.

Berg, S., Nash, S., Cole, P. and Hoffstein, V. Arousals and nocturnal respiration in symptomatic snorers and nonsnorers. *Sleep*, 1997, 20: 1157–1161.

Douglas, N. J. Upper airway resistance syndrome is not a distinct syndrome. *Am. J. Respir. Crit. Care Med.*, 2000, 161: 1413–1416.

Friberg, D., Ansved, T., Borg, K., Carlsson-Nordlander, B., Larsson, H. and Svanborg, E. Histological indications of a progressive snorers disease in an upper airway muscle. *Am. J. Respir. Crit. Care Med.*, 1998, 157: 586–593.

Guilleminault, C. and Chowdhuri, S. Upper airway resistance syndrome is a distinct syndrome. *Am. J. Respir. Crit. Care Med.*, 2000b, 161: 1412–1413.

Guilleminault, C., Stoohs, R. and Duncan, S. Snoring: daytime sleepiness in regular heavy snorers. *Chest*, 1991, 99: 40–48.

Guilleminault, C., Stoohs, R., Clerk, A., Simmon, J. and Labanowski, M. From obstructive sleep apnea syndrome to upper airway resistance syndrome: consistency of daytime sleepiness. *Sleep*, 1992, 15(Suppl. 6): S13–S16.

Guilleminault, C., Stoohs, R., Clerk, A., Cetel, M. and Maistro, P. A cause of excessive daytime sleepiness. The upper airway resistance syndrome. *Chest*, 1993, 104: 781–787.

Guilleminault, C., Black, J. E., Palombini, L. and Ohayon, M. A clinical investigation of obstructive sleep apnea syndrome (OSAS) and upper airway resistance syndrome (UARS) patients. *Sleep Med.*, 2000a, 1: 51–56.

Guilleminault, C., Do Kim, Y., Chowdhuri, S., Horita, M., Ohyon, M. and Kushida, K. Sleep and daytime sleepiness in upper airway resistance syndrome compared to obstructive sleep apnea syndrome. *Eur. Respir. J.*, 2001, 17: 838–847.

Guilleminault, C., Kirisoglu, C., Poyares, D. *et al*. Upper airway resistance syndrome: a long-term outcome study. *J. Psychiatr. Res.*, 2006, 40: 273–279.

Johns, M. W. Reliability and factor analysis of the Epworth Sleepiness Scale. *Sleep*, 1992, 15: 376–381.

Kimoff, R. J., Sforza, E., Champagne, V., Ofiara, L. and Gendron, D. Upper airway sensation in snoring and obstructive sleep apnea. *Am. J. Respir. Crit. Care Med.*, 2001, 164: 250–255.

Loube, D. L. and Andrada, T. F. Comparison of respiratory polysomnographic parameters in matched cohorts of upper airway resistance and obstructive sleep apnea syndrome patients. *Chest*, 1999, 115: 1519–1524.

Lugaresi, E., Cirignotta, F., Gerardi, R. and Montagna, P. Natural history of heavy snorers disease. In: M. Partinen and C. Guilleminault (Eds) *Obstructive Sleep Apnea Syndrome. Clinical Research and Treatment*. Raven Press, New York, 1990: 25–36.

Pelin, Z., Karadeniz, D., Ozturk, L., Gozukirmizi, E. and Kaynak, H. The role of mean inspiratory effort on daytime sleepiness. *Eur. Respir. J.*, 2003, 21: 688–694.

Phillips, B., Collop, N. and Strollo, P. Controversies in sleep disorders medicine. *Chest*, 1996, 110: 1597–1602.

Rechtschaffen, A. and Kales, A. *A Manual of Standardized Terminology, Technique and Scoring System from Sleep Stages of Human Subjects*. Public Health Service, Government Printing Office, Washington DC, 1968.

Rees, K., Kingshott, R. N., Wraith, P. K. and Douglas, N. J. Frequency and significance of increased upper airway resistance during sleep. *Am. J. Respir. Crit. Care Med.*, 2000, 162: 1210–1214.

Stoohs, R. and Guilleminault, C. Obstructive sleep apnoea syndrome or abnormal upper airway resistance during sleep? *J. Clin. Neurophysiol.*, 1990, 7: 83–92.

Stoohs, R. and Guilleminault, C. Snoring during NREM sleep: respiratory timing, esophageal pressure, and EEG arousal. *Respir. Physiol.*, 1991, 85: 151–167.

Wheatley, J. R. Definition and diagnosis of upper airway resistance syndrome. *Sleep*, 2000, 23(Suppl. 4): S193–S196.