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Brief communication

A clinical investigation of obstructive sleep apnea syndrome (OSAS) and upper airway resistance syndrome (UARS) patients

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Abstract

Objective: (i) Evaluation of the clinical differences and similarities presented by patients diagnosed as OSAS and UARS subjects. (ii) Evaluation of the ability of a sleep disorders specialist to dissociate the two syndromes based upon clinical evaluation.

Population: 314 subjects were included. They were referred to a sleep disorders clinic with complaints of loud snoring during a 3 month period.

Method: The evaluation consisted of: (i) Clinical interview and evaluation. (ii) Administration of validated questionnaires (Sleep Disorders Questionnaire and Epworth Sleepiness Scale). (iii) Establishment of clinical diagnostic and results of polygraphic recording.

Results: After clinical evaluation and polygraphic recordings (performed within 3 weeks of initial evaluation) patients were subdivided into two groups: 176 OSAS and 128 UARS. The misclassification of patients by specialists correlated with body mass index (BMI) measurement, with an over classification of patient as OSAS when a high BMI was noted and vice-versa for UARS. The only significant difference between OSAS and UARS patients was an older age and a wider neck circumference in the OSAS group than in UARS patients.

Conclusion: Clinical presentation including daytime sleepiness complaint and ESS score is similar for patients with and without drop of oxygen saturation below 90% during sleep. There was always a male predominance within both syndromes, but more women were diagnosed with UARS than with OSAS.

Keywords: Obstructive sleep apnea syndrome; Upper airway resistance syndrome; Clinical evaluation; Daytime sleepiness; Gender difference

1. Introduction

We previously reported that subjects who do not present with classic Obstructive Sleep Apnea Syndrome (i.e. subjects who have a respiratory disturbance index (RDI) below 5 events per hour of sleep and maintain oxygen saturation at 90% or above) can have clinical complaints and symptoms. We called this syndrome the 'Upper Airway Resistance Syndrome' [1,2]. Over the years, we have monitored many patients who experience non-apneic sleep disordered breathing using esophageal pressure (P_{es}) recording and EEG alpha arousals. We wondered if we could find a difference in complaints and symptoms on patients presenting with classic sleep apnea-hypopnea syndrome and those patients who did not meet the OSAS criteria but experienced an abnormal pattern of respiratory efforts. The abnormal respira-

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tory effort was indicated by P_{es} measurement, with cycling of esophageal pressure swings becoming more negative P_{es} at end inspiration until an interruption by an arousal concomitant with a decrease in effort indicated by P_{es} reversal (i.e. a less negative end inspiratory esophageal pressure).

We hypothesized that the overall clinical complaints would be similar with both syndromes but that the degree of complaint would be more marked with OSAS, with higher score at the ESS.

2. Methods

2.1. Population

All patients who were referred to the sleep clinic during a 3-month period for suspicion of sleep- disordered breathing, who were not disqualified by the following exclusion criteria, were included in the study.

- Presence of 'noisy breathing' related to laryngeal lesion.
- Presence of upper airway tumor.
- Presence of neuromuscular disease.
- Age under 14 years.
- Inability to complete a questionnaire in English.
- Inability to understand questions and complete scales (disorders such as Downs syndrome, or presence of other syndromes known to be frequently associated with mental retardation).
- Presence of congenital cranio-facial syndrome (Crouzon, Apert, Treacher-Collin, etc.).
- Gross obesity (greater than 33 kg/m^2).
- Living alone.
- Simple snoring.

Although one fifth of the patients were self-referred, we received a large number of referrals from the surrounding community, including physicians, specialists, and particularly oro-rhino-laryngologist, head and neck surgeons. The most commonly reported cause of consultation was 'loud and disruptive snoring'.

2.2. Protocol

All subjects underwent the same systematic evaluation. Subjects completed the following.

- A validated questionnaire with 180 questions covering sleep disorders and health problems with a 5 point scale for each question [3], which they completed with help of other household members if needed.
- A clinical and sleep/wake medicine interview that confirmed the questionnaire responses and investigated further findings.
- The Epworth Sleepiness Scale [4].
- A clinical evaluation that included a cranio-facial investigation, determination of the neck circumference, and body mass index [5,6].

At the completion of the clinical evaluation, before performance of any polygraphic monitoring, the two physicians who examined and reviewed all cases were asked, based on their evaluation, to categorize patients as 'UARS' or 'OSAS'. The presence of snoring, even if loud and disruptive, was not sufficient to diagnose the subjects as having a syndrome (which supposes presence of symptoms, complaints and signs).

Following the clinician's evaluation and classification, the subjects were submitted to the following recordings, which were not scored or interpreted by the two physicians involved in the clinical investigation.

- A home recording with equipment previously used in research, Edentrace II® (Nelcor- Puritan-Benett, Eden Prairie, WI).
- A nocturnal sleep recording in the sleep laboratory.

The lab recording included EEG, C3/A2, C4/A1, O1/A1, EOG, chin and leg EMGs, and ECG (modified V2 lead). Respiration was monitored with naso-oral airflow (thermocouple), uncalibrated inductive plethysmography, esophageal pressure (after signal calibration before sleep onset), and oxygen saturation (Nelcor-pulsoximeter, San Leandro, CA).

The home recordings were performed to evaluate whether the presence of P_{es} monitoring or laboratory conditions had an impact on the respiratory disturbance index, and to investigate presence/ absence of snoring at home.

Home recordings were reviewed and scored for snoring, apneas, hypopneas, and SaO_2 drops $\geq 3\%$. Polygraphic recordings were scored following the Rechtschaffen and Kales criteria [7] and the ASDA atlas [8]. Apnea and hypopnea were scored following

Guilleminault's criteria (1982) [9]. The cut-off point for OSAS was a RDI ≥5 apnea and hypopnea per hour of sleep. UARS was labeled based upon the presence of 'crescendos' and abnormal respiratory efforts ending with arousals of 3 s or longer, if the abnormal features were seen in 10% or more of the recording time [1]. The scoring of abnormal respiratory efforts was made by visual inspection and also using a computerized system developed in collaboration with the Stanford University Department of Engineering and Computer Sciences that automatically determined the value of the peak end inspiratory esophageal pressure per each breath. The decision to classify a subject as OSAS or UARS was always based on the laboratory polygraphic recording.

3. Statistical analysis

Chi-square statistics were used to compare groups and symptoms reported in the questionnaire and at interview. Signs and scales results from OSAS and UARS subjects were compared by means of ANOVA procedure.

4. Results

The total group included 314 patients. One patient had to be excluded due to the loss of polygraphic data while transferring to optic disk. The results of the remaining 313 subjects are presented here. 304 patients were diagnosed with sleep-disordered breathing. The home recording did not modify the diagnosis based on the laboratory polysomnographic evaluation. Table 1 shows the gender and ethnic distribution. Compared to the 1990 census of population and housing, the ethnic distribution of patients in the sleep clinic is grossly similar to the actual population of Palo Alto and surrounding areas. There were more men than woman in both the UARS and OSAS groups, but there was a higher percentage of women diagnosed with UARS than OSAS. Also, all African-Americans were in the OSAS group.

Based on interviews, clinical evaluation, and ESS scores (data summarized in Tables 2–4), 131/176 subjects (74%) were properly classified as OSAS, and 81/128 (63.3%) subjects were appropriately classified as UARS by physicians. Forty-two UARS subjects (33%) were classified as OSAS. Forty-three (24.4%) OSAS subjects were classified as UARS. The patients' BMI influenced the sleep specialists, with patients ≥26 kg/m^2 more likely to have been classified as OSAS. All patients misclassified as UARS instead of OSAS had a BMI below 24.5 kg/m^2 (there was no difference in the overall symptom presentation in the misclassified subjects).

Table 1
Gender and ethnicity

	Total			OSAS			UARS		
	N	*A*[a] (%)	*B*[b] (%)	*N*	*A* (%)	*B* (%)	*N*	*A* (%)	*B* (%)
Total	304	100.0	100.0	176	58.0	100.0	128	42.0	100.0
Gender									
Men	231	76.0	76.0	139	46.0	79.0	92	30.0	72.0
Women	73	24.0	24.0	37	12	21	36	12	28
Ethnicity									
African American	10	3.3	3.3	10	3.3	5.7	0	0	0
Asian	22	7.2	7.2	8	2.6	4.3	12	3.9	9.4
Caucasian	254	83.5	83.5	147	48.4	83.5	107	35.2	83.6
Hispanic	22	7.2	7.2	11	3.6	6.2	7	2.3	5.5
Other	2	0.007	0.007	0	–	–	2	0.007	1.6

[a] Percentage compared to total group.
[b] Percentage compared to specific group (UARS or OSAS).

Table 2
Symptoms indicated in questionnaire and confirmed in interview

	UARS (%)	OSAS (%)
Snoring	100 ($n = 128$)	100 ($n = 176$)
Unrefreshing sleep	78.1 ($n = 100$)	80.1 ($n = 141$)
Daytime sleepiness	84.9 ($n = 107$)	85.8 ($n = 151$)
Memory problems	53 ($n = 68$)	55.7 ($n = 98$)
Morning headache	39 ($n = 50$)	51.1 ($n = 90$)
Nocturnal/morning dry mouth	87.5 ($n = 118$)	91.5 ($n = 161$)
Drooling at night	80.5 ($n = 103$)	81.8 ($n = 144$)
Reflux	30.5 ($n = 39$)	31.2 ($n = 55$)
Sleep walking	13.3 ($n = 17$)	8 ($n = 14$)
Bruxism	52.3 ($n = 67$)	50.6 ($n = 89$)
Nocturia ≥ 2	47.7 ($n = 61$)	48.9 ($n = 86$)

Tables 2–4 indicate that only two parameters, age and neck circumference, were significantly different in UARS and OSAS patients. Overall, OSAS patients were older and had a wider neck circumference than UARS group. Interestingly, in this sample there was no significant difference in mean BMI, in the arousal index at polysomnography, or in the ESS scores of patients diagnosed with UARS or OSAS.

Seven subjects (2% of the total group) were classified as having sleep-disordered breathing (5 UARS, 2 OSAS) based upon presence of loud, regular snoring and the complaint of daytime tiredness, fatigue, or daytime sleepiness and unrefreshing sleep. None of these diagnoses were confirmed by polygraphic recording, but six of the seven subjects were diagnosed with periodic limb movement syndrome and one with sleep-related gastroesophageal reflux, and snoring.

5. Comments

This study demonstrates that complaints and symptoms are similar in subjects labeled with OSAS and UARS, in spite of the absence of apneas or hypopneas with clear drops in SaO_2. A good specialist may be unable to predict the polygraphic findings, despite adequate clinical intake. However, our study did not attempt to investigate the specificity and sensitivity of a good but isolated clinical evaluation by a specialist, since we believe such investigation should be based on more than visual analysis of the polygraphic recording. Interestingly, seven subjects were also falsely considered with sleep-disordered breathing based on report of snoring and clinical symptoms and only the nocturnal polygraphic recording identified the health problem.

The fact that complaints and symptoms are similar in OSAS and UARS patients is not surprising since many different abnormalities of breathing during sleep lead to sleep disturbances and fragmentation. Sleep disturbance may be more common than previously recognized since our initial results suggest that an increase in respiratory efforts may trigger some cortical response. Research aimed at defining the cortical response threshold to breathing changes is necessary. We already have preliminary data indicating that sleep stages play a role in modulating this threshold [10]. Sleep states are most probably only one of the variables that play a role, and other factors will need to be better defined in the future.

Redline et al. [11] published that African-Americans are at greater risk for OSAS than Caucasians. In

Table 3
Results of signs and scale scores evoking sleep disordered breathing[a]

	UARS		OSAS	
Variable	Mean ± SD	Range	Mean ± SD	Range
BMI (kg/m^2)	28.2 ± 4.1	18–33	29.0 ± 3.7	19–33
Neck circumference (cm)	38.2 ± 3.5	31–45	41.5 ± 4.2	32–49[b]
Age (years)	44.1 ± 13.2	14–81	50.3 ± 13.8	14–76[b]
ESS scores	11 ± 6.1	0–24	10.5 ± 5.0	0–24
No. of subjects with extractions of 4 wisdom teeth (%)	74.2 ($n = 95$)		73.3 ($n = 129$)	

[a] BMI = body mass index, ESS = Epworth Sleepiness Scale, SD = standard deviation.
[b] $P < 0.02$.

Table 4
Results of polygraphic recording[a]

Variable	UARS		OSAS	
	Mean ± SD	Range	Mean ± SD	Range
RDI (event/h)	2.5 ± 2.3	0–5	36 ± 26.1	5.5–186
Hypopnea index (event/h)	2.6 ± 1.6	0–5	15 ± 12	0–98
Apnea index (event/h)	0.49 ± 0.8	0–5	24.2 ± 22	4–100
NREM arousal Index (arousal/h)	18.8 ± 6.8		17.1 ± 9.2	
REM arousal index (arousal/h)	7.3 ± 3.3		5.1 ± 4.8	

[a] RDI = Respiratory disturbance index (number of apnea and hypopnea during total sleep time divided by 60).

our population, we found that all African-Americans seen in the clinic were in the OSAS group and none were in the UARS group. Does it suggest that African-Americans are at risk to develop OSAS faster that other ethnic groups? And if so, is this risk related to genetic factors, such as those involved in the development of upper airway mucosa or presence of obesity gene, or is it related to environmental factors, such as nutritional habits? These questions are yet to be resolved.

Our criteria for inclusion eliminated the non-complaining snorer from the investigation and some of them may have had abnormal findings at polygraphic recording. We acknowledge this problem, but we do not monitor subjects without complaints unless we are performing a general population survey. But, as found in the study, specialists may be misled by the presence of snoring and ignore the presence of another cause of sleep fragmentation, such as, periodic limb movement syndrome, based on clinical evaluation.

Also our inclusion criteria used a body mass index cut-off point of 33 kg/m^2. This is clearly within the range of obesity. We are well aware that obese patients with BMI $>$ 33 kg/m^2 will often have obstructive sleep apnea events as a co-morbid factor. But the choice of this cut-off point was based on sleep physiology. During REM sleep, the known physiologic muscle atonia will occur. This will affect respiratory muscles and will lead, particularly on a supine obese patient, to many changes, such as, flattening of the diaphragm and impact on chest bellows. We did not want to have questions on the origin of the complaint and symptoms and on the role of co-morbid association on the studied factors.

There is always a gap between research findings and clinical integration. Usage of some types of equipment monitoring breathing during sleep should be recognized as limited and not completely adequate. This is the case for thermocouples and thermistors. Some scales, such as the Epworth Sleepiness Scale should also be revised in an effort to increase specificity and sensitivity. Some simple testing procedures are highly sufficient to affirm pathology and the need for treatment, but at other times, more sophisticated tests are needed. This short note emphasizes the need to adjust our approach to sleep disordered breathing. Prescription of certain treatments should not be based solely upon the presence or absence of a certain apnea or RDI number. The clinical presentation and examination must also be taken into consideration.

Finally, our study does not address the question of the differences and similarities in the pathophysiology underlying the two clinical syndromes. There are indications that the microstructure of nocturnal sleep is different in UARS and OSAS [12] and patients with OSAS present more important drops in oxygen saturation with their abnormal breathing events than UARS patients. But further research is needed to understand the exact relationship between the two clinical entities.

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