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Review Article

Treatment of upper airway resistance syndrome in adults: Where do we stand?☆

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ABSTRACT

Objective: To evaluate the available literature regarding Upper Airway Resistance Syndrome (UARS) treatment. Methods: Keywords "Upper Airway Resistance Syndrome," "Sleep-related Breathing Disorder treatment," "Obstructive Sleep Apnea treatment" and "flow limitation and sleep" were used in main databases. Results: We found 27 articles describing UARS treatment. Nasal continuous positive airway pressure (CPAP) has been the mainstay therapy prescribed but with limited effectiveness. Studies about surgical treatments had methodological limitations. Oral appliances seem to be effective but their efficacy is not yet established. Conclusion: Randomized controlled trials with larger numbers of patients and long-term follow-up are important to establish UARS treatment options.

1. Introduction

The Upper Airway Resistance Syndrome (UARS) was first named by Guilleminault in 1993 [1] while investigating cases of excessive daytime sleepiness with no identified cause in adults. However, the respiratory pattern of increased upper airway resistance was previously identified in pre-pubertal children under the label "sleep-related respiratory resistive load" [2].

Since this first description, many authors have attempted to describe the clinical and polysomnographic features of UARS patients based on their experience, to find a definitive way to diagnose and finally treat them. In particular, during the last twenty years, the definition of UARS has varied (Table 1). Currently, UARS is subsumed under the diagnosis of Obstructive Sleep Apnea Syndrome (OSAS) by the American Academy of Sleep Medicine (AASM) (Berry AASM 2012) [3].

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Table 1 – UARS definitions.

Authors	Clinical criteria	Polysomnographic criteria	
Kristo et al., 2005 [47]	Excessive daytime sleepiness (ESS >10)	Pes ≤ - 12 cm H_2O	AHI < 5/hour, Arousal Index ≥ 10/hour, RERA ≥ 5/hour
Guilleminault et al. [7]	Excessive daytime sleepiness or fatigue	Pes and flow limitation by nasal cannula	AHI < 5/hour, RDI > 5/hour (RERA), Oxygen saturation > 92%
Loube et al., 2009 [48]	Excessive daytime sleepiness	Inductance plethysmogrhaphy Pes ≤ - 12 cm H_2O	AHI < 5/hour and RERA ≥ 10/hour
Stoohs et al., 2009 [49]	Excessive daytime sleepiness or fatigue	Flow limitation by nasal cannula	AHI < 5/hour and presence of RERA
Pépin et al., 2012 [6]	Excessive daytime sleepiness	Pes, flow limitation by nasal cannula	RERA as more than 50% of respiratory events

ESS: Epworth Sleepiness Scale, Pes: Esophageal pressure, AHI: Apnea / Hypopnea Index, RERA: Respiratory Event-Related Arousal, RDI: Respiratory Disturbance Index

Its diagnostic criterion is still not defined and some authors believe that UARS is part of a continuum between primary snoring and OSAS whereas others believe that it is a distinct syndrome from OSAS. Some authors support that both UARS and OSAS have the same symptoms and as their pathophysiology do not significantly differ from each other, UARS is not a distinct disease [4,5]. Nevertheless, other authors believe that UARS patients present different features than other Sleep related Breathing Disorder (SRBD) [6,7,8]. The most frequent symptoms are excessive daytime sleepiness, fatigue and sleep fragmentation. However, UARS patients also present significantly more often with sleep-onset and sleep-maintenance insomnia, postural hypotension, headaches, gastroesophageal reflux, irritable bowel syndrome, anxiety and alpha-delta sleep [9,10,11]. The proportion of women with UARS is also significantly higher than for OSAS [12]. Besides having some different clinical presentation, it has been suggested that UARS and OSAS differ from each other in terms of their sleep EEG and autonomic nervous system responses. Some authors believe that UARS patients have an increase in alpha rhythm and an over-activation of the autonomic nervous system [13].

UARS diagnosis is suspected in individuals with complaints of excessive daytime sleepiness or daytime tiredness, no OSAS and a polysomnographic study with respiratory parameters indicative of increased upper airway resistance, such as, flow limitation during sleep. They present arousals associated with increase in respiratory effort leading to sleep fragmentation and excessive daytime sleepiness. The polysomnographic studies of these patients also showed sequences of breaths with flow limitation, which were interrupted by abrupt arousals. Arousals were defined using American Sleep Disorders Center-American Academy of Sleep Medicine (AASM) [14,15] conventional criteria but were also described using the cyclic alternative pattern-CAP-atlas, [16] including the shorter duration arousals associated with abnormal increases of “Phase A2” and “Phase A3” of the CAP scoring system and with RERA [17]. The arousals associated with flow limitations were described as “respiratory event related arousals” (RERA) by AASM [14,15]. The polysomnography (PSG) pattern of “flow limitation,” introduced in 1991 [18] was further investigated and defined particularly in New York [19,20] as a sign of increased upper airway resistance to airflow.

Untreated UARS individuals can present low quality of life and cardiovascular consequences. Sleep and daytime symptoms, such as fatigue, insomnia and depressive mood, in untreated UARS usually increase over time [7]. The syndrome's characteristic esophagic pressure (Pes) negativity can cause a diastolic leftward shift of the interventricular heart septum and a consequent ventricular “collapse”. [21] The longlasting flow limitation episodes can induce a small increase in end-tidal carbon dioxide ($PetCO_2$) that can stimulate the sympathetic nervous system activity. This could cause hypertension, and cardiovascular and metabolic consequences. [6] Even an increase in inflammatory markers can happen in non-treated UARS individuals. [22]

In order to avoid the consequences mentioned above, a proper treatment should be offered to UARS patients. There are some treatment studies available in the literature, but most of these are case reports and case series. Nasal continuous positive airway pressure (CPAP) is one treatment option that has been evaluated as a therapy for UARS, and the available studies demonstrated that it can improve different aspects of the condition. CPAP treatment was associated with significant improvements in the excessive daytime sleepiness, numbers of transient arousals and abnormal upper airway resistance.1 Other types of treatments evaluated included oral appliances, nasal and palatal surgeries and maxillomandibular advancement. Long-term studies to evaluate treatment response will be helpful to better define this SBD.