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Review Article

The role of flow limitation as an important diagnostic tool and clinical finding in mild sleep-disordered breathing

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ARTICLE INFO

Article history:
Received 2 July 2015
Received in revised form
5 August 2015
Accepted 17 August 2015
Available online 3 September 2015

Keywords:
Inspiratory flow limitation
Obstructive sleep apnea
Upper airway resistance syndrome
Preeclampsia
Cyclic alternating pattern

ABSTRACT

Obstructive sleep apnea (OSA) is defined by quantifying apneas and hypopneas along with symptoms suggesting sleep disruption. Subtler forms of sleep-disordered breathing can be missed when this criteria is used. Newer technologies allow for non-invasive detection of flow limitation, however consensus classification is needed. Subjects with flow limitation demonstrate electroencephalogram changes and clinical symptoms indicating sleep fragmentation. Flow limitation may be increased in special populations and treatment with nasal continuous positive airway pressure (CPAP) has been shown to improve outcomes. Titrating CPAP to eliminate flow limitation may be associated with improved clinical outcomes compared to treating apneas and hypopneas.

1. Introduction

Severity of obstructive sleep apnea (OSA) has been defined by the quantity of apnea and hypopnea events (i.e. the apnea/hypopnea index, or AHI) occurring per hour of recorded sleep. Early detection of these events was accomplished via the use of oronasal thermistors. However, this technique cannot assess for respiratory effort; which has been identified to cause frequent arousals from sleep due to intrathoracic pressure swings that occur with little or no detectable change in thermistor signals [1–3]. Encephalography (EEG) arousals occurring in the absence of apneas and hypopneas with evidence of increased intrathoracic pressure swings can be included with AHI to an index known as the respiratory disturbance index (RDI). Elevation of RDI without significant increase in AHI is suggestive of upper airway flow limitation and clinically can be diagnosed as upper airway resistance syndrome (UARS). The International Classification of Sleep Disorders has placed UARS in the diagnostic category of OSA disorders [4]; however UARS may be more challenging to diagnosis. Diagnosis requires evidence of intrathoracic pressure changes culminating in arousals, defined as a respiratory effort related arousal (RERA), versus significant quantifiable reductions in air flow seen in OSA [5]. While there is strong evidence highlighting the cardiovascular risk of OSA [6,7], it has been proposed that other forms of sleep

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Peer review under responsibility of Brazilian Association of Sleep.

http://dx.doi.org/10.1016/j.slsci.2015.08.003

disordered breathing (SDB) such as UARS can be correlated with excessive-daytime-sleepiness – EDS [8–10], long-term cardiovascular complications [11,12] and significant costs to society [13–15].

The finding of RERAs has increased the sensitivity of diagnosing SDB, especially in individuals with a high clinical suspicion without polysomnogram (PSG) data supporting a clear diagnosis of OSA. The reference measurement for respiratory effort and intrathoracic pressure is esophageal pressure monitoring [16]. Chervin et al. showed a decreased esophageal pressure nadir and less sleep time with esophageal pressure more negative than 10 cm of water after adenotonsillectomy in children, suggestive of improved upper airway resistance after this procedure [17]. In clinical practice, the usage of respiratory inductance plethysmography (RIP) is accepted for measurement of respiratory effort in place of esophageal pressure monitoring by measuring thoraco-abdominal excursion during breathing versus direct measurement of intrathoracic pressure [18]. The principle of diagnosing SDB beyond quantitative airflow reductions remains important for recognition of the full spectrum pathology.

Inspiratory flow limitation (IFL) can be observed as flattening of the flow tracing on PSG. Physiologically, IFL indicates absence of an increase in flow despite an elevation in negative intrathoracic pressure indicating increasing effort [19]. Condos described this phenomenon during his study when titrating continuous positive airway pressure (CPAP) to where the inspiratory flow was rounded rather than plateaued. The flattening of the inspiratory flow is related to resistance of the airway which can occur even with application of positive airway pressure [20]. The presence of inspiratory flow limitation is vital to the understanding of UARS and subsequently as a diagnostic tool for this population.

This review on inspiratory flow limitation is intended to increase awareness of this entity, its diagnosis, and its clinical relevance. The current system using apneas and hypopneas does not capture all individuals who may be suffering from clinically significant respiratory disturbances during sleep. Often the most challenging cases faced by sleep medicine clinicians are patients with “normal” PSG findings despite presenting with symptoms consistent with OSA. With improved diagnostic measures and understanding of IFL, opportunities for successful treatment may follow.

2. Detection of IFL

Assessing for inspiratory flow limitation requires recognition of both flow and intrathoracic pressure changes [21]. A decrease in flow normally is accompanied by a compensatory increase in intrathoracic pressure. This is illustrated in Fig. 1 in the setting of differentiating a central and obstructive event via airflow and esophageal pressure monitoring [18]. Inspiratory flow limitation, which does not meet criteria for an obstructive hypopnea is illustrated in Fig. 2. Esophageal pressure monitoring, by demonstrating intrathoracic pressure changes before EEG arousal, remains key in the clinical diagnosis of UARS [9]. As esophageal pressure monitoring may be uncomfortable and is not practical for routine monitoring, different methods ofidentification are needed. Conventional pneumotachography has

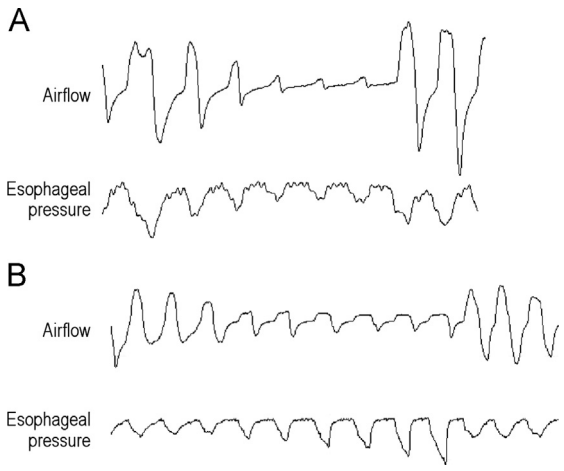

Fig. 1 – Airflow and esophageal pressure monitoring on PSG. (A) A central event with reduction in airflow without any change in esophageal pressure signal during the event. (B) A reduction in airflow with an increase in esophageal pressure for the duration of the event, indicative of an obstructive hypopnea. Flattening of the airflow signal can also be seen during the obstructive event suggestive of flow limitation.

demonstrated that plateaus on inspiratory flow waveforms correlate with elevated upper airway resistance [20–22]. Similar to esophageal pressure monitoring, routine application of pneumotachography is limited by discomfort with the monitoring equipment [22]. Respiratory-Inductance-Plethysmography – RIP-has also been shown to be effective for evaluation of upper airway resistance, however there is difficulty in ensuring an accurate tidal volume measurement when using this measure alone [23].

Many studies have been done assessing nasal cannula/pressure transducer system as a non-invasive assessment of IFL, in addition to its role in detection of hypopneas and apneas [2,3,21,22,24]. Ayappa et al. hypothesized that by assessing the contour of flow shape, rather than amplitude of signal, respiratory effort could be detected with similar accuracy to Pes. . Ayappa showed that assessment of RERAs via flattening of the waveform contour was nearly identical to the detection by Pes, with interclass correlation coefficient of 0.96 [24]. In addition, Hosselet showed that upper airway resistance is increased in flow limited breaths by as much as 387% [2].These results suggest that esophageal pressure monitoring may not be required in assessing for inspiratory effort, and that further evaluation of waveform contour via routinely applied nasal cannula/pressure transducer could reveal these very important events.

Comparison of different monitoring measures has been done since Ayappa's study showing promise of the nasal cannula/pressure transducer. Johnson et al. stimulated upper airway resistance in normal subjects with alcohol consumption and compared nasal cannula/pressure transducer with Pes, respiratory inductive plethysmography and a fourth method including a piezo-electrically treated stretch sensor adhered to the supraclavicular fossa. It was shown that nasal cannula/pressure transducer was superior to all tested modalities in detecting arousals secondary to increased upper airway resistance. Surprisingly, many events culminating in