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Impact of stepwise mandibular advancement on upper airway mechanics in obstructive sleep apnea using phrenic nerve magnetic stimulation

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ABSTRACT

Mandibular advancement devices (MAD) represent a potential treatment for obstructive sleep apnea (OSA). However, their mechanisms of actions are not completely understood. This study was aimed to explore the effects of MAD-induced mandibular protrusion on upper airway mechanics. 25 men commencing treatment for OSA with MAD were recruited. Phrenic nerve magnetic stimulation (PNMS) was used to measure flow/pressure relationship during progressive protrusion in three conditions (without MAD, MAD at minimum protrusion, and MAD at maximum tolerable protrusion). Pressures were recorded simultaneously at three different upper airway segments (naso-, velo-, and oro-pharynx). Without MAD, PNMS twitches induced flow-limitation at the velopharyngeal level in 19 subjects and six of them experienced a shift in the flow-limitation site to the lower segment with MAD at maximum protrusion. An association was found between having a velopharyngeal limitation site without MAD and the increase in maximum flow with the advanced MAD. These data suggest that mandibular advancement devices are acting predominantly at the velopharyngeal level.

1. Introduction

Obstructive sleep apnea (OSA) is a common disorder characterized by recurrent episodes of upper airway (UA) partial or complete closure during sleep. This is mainly due to combinations of anatomical and neuromuscular factors that lead to an imbalance between dilating and collapsing forces acting on the UA. The most effective treatment for OSA is continuous positive airway pressure (CPAP). However, because of its cumbersome nature, its clinical effectiveness is sometimes limited by poor patient tolerance. Mandibular advancement devices (MAD) represent an alternative treatment: these are designed to increase the UA size and reduce the occurrence of apneas, hypopneas, and snoring in patients with OSA (Marklund et al., 2012). MAD seems more easily accepted than CPAP but it is less effective to reduce the apnea hypopnea index (AHI) (Ferguson et al., 2006; Phillips et al., 2013). In OSA patients, various imaging methods have been used to visualize the changes in UA dimensions without and with MAD and several studies found important changes in airway size at the velopharyngeal level (Chan et al., 2010a, 2010b; Lowe et al., 2000; Ryan et al., 1999; Tsuiki et al., 2004). As the degree of mandibular advancement plays a crucial role in obtaining positive clinical response (Kato et al., 2000), most of these imaging studies were done after the titration period, which typically takes place over several weeks.

By generating a diaphragm contraction independently of neural activation of UA dilator muscles, phrenic nerve magnetic stimulation (PNMS) can mimic during wakefulness the flow-limitation phenomenon associated with UA closure during sleep (Series et al., 2000). We recently used this painless technique to test the hypothesis that baseline UA collapsing site(s) identified by PNMS could predict MAD efficacy (Bosshard et al., 2011). Considering that mandibular position is influenced by MAD even without protrusion and that MAD efficiency is influenced by the degree of advancement, we wanted to investigate the influence of MAD without and with advancement on UA mechanical properties. Therefore, the aim of the study was to assess the effect of the amount of MAD protrusion on UA mechanical properties using PNMS.

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2. Methods

2.1. Subjects

The protocol was conducted in 25 untreated male OSA patients in whom mandibular advancement was retained as treatment choice. Full baseline polysomnographic recordings (in lab or ambulatory) were performed to confirm the diagnosis. Recordings were scored according to standardized recommendations American Academy of Sleep Medicine (1999). The MAD treatment option was proposed using the selection criteria recommended in clinical practice: (a) adequate dental conditions, (b) absence of contra-indication related to temporo-mandibular joint conditions, (c) mild/moderate sleep apnea without severe daytime sleepiness that would require immediate effective treatment, or (d) CPAP failure due to intolerance, side effects or rebuttal. The internal review board of our institution approved this protocol and informed consent was obtained from all subjects.

2.2. Mandibular advancement device

The MAD used in the present study was from Thornton Adjustable Positionner (Airway Management Inc., Carrolton, TX). This device was chosen because the advancement could be easily adjusted using its external screw. In order to assess to what extent our study population was relevant for MAD in the treatment of their sleep apnea, MAD titration procedure was completed by one of the investigators (JFM), who was blind to the results of the PNMS experiment. Briefly, following the PNMS experiment, MAD was progressively advanced to obtain optimal clinical response based on the assessment of subjective (symptoms resolution, abolition of snoring, improvement in daytime sleepiness according to the Epworth Sleepiness Score) and objective (abbreviated home respiratory recording: Apnoea link, version 6.0, ResMed, Poway, CA) variables or until maximal tolerance. Following completion of the titration period, MAD efficacy was documented by a nocturnal respiratory recording (in lab or ambulatory).

2.3. Measurements of UA mechanical parameters during phrenic nerve magnetic stimulation (PNMS)

During PNMS experiment, pharyngeal pressures were measured with a custom-made pressure-tipped catheter with three sensors (Gaeltec, Hackensack, NJ), which was inserted after local anesthesia (xylocaine 2% spray) of one nostril. The distance between the proximal and middle sensor was 4 cm and the distance between the middle and distal one was 3 cm. In order to determine its precise location, the catheter had centimeter marks. The proximal sensor was positioned under direct visualization 2 cm above the soft palate; consequently, the proximal sensor measured nasopharyngeal pressure, the middle sensor velopharyngeal pressure and the distal one, oropharyngeal pressure. Of note, during swallowing, dissociation between pressures reading for the sensor located above and the two sensors below the soft palate had to be observed. A plastic nasal stent (Nozovent; WPM International AB; Göteborg, Sweden) was inserted in the anterior nares to prevent nasal collapse. A nasal mask (Respironics, Murrysville, PA) was then placed over the nose with the catheter passing through a drilled hole. Occlusion of the mask opening during maximal inspiratory efforts was done to assess its airtightness. A heated pneumotachograph (model 112467-3850A, Hans Rudolf, Kansas City, MO) connected to the mask was used to obtain instantaneous flow. Pressures and flow signals were digitally recorded at 2 kHz (Digidata 1322, Axon Instrument, Foster City, CA) on a computer for real-time visualization.

2.4. Phrenic nerve magnetic stimulation procedure

Subjects were seated in a comfortable armchair in a semi-recumbent position and a molded pillow kept the head in a neutral position to ensure the same head positioning throughout the experiment. Bilateral anterior magnetic phrenic nerve stimulation was performed with two Magstim 200 stimulators (Magstim, Whitland, Dyfed, UK), connected to two 90° handle 45-mm eight-shaped coils, according to previously described technique (Mills et al., 1996; Series et al., 2000). Briefly, each stimulating coil was positioned anterolaterally over the anatomical landmark of the phrenic nerve in the neck. The optimal position and orientation of the coils were determined separately for each side by checking motor evoked potentials of costal diaphragmatic EMG response to the stimulation. These responses were obtained by using silver cup surface electrodes placed on the axillary line of the sixth to the eight right and left intercostal spaces (Demoule et al., 2003). Single pulse (approximately 1 ms duration) stimuli were delivered manually during end-expiration according to real-time pressures and flow traces with subjects breathing exclusively through the nose. Twitches were applied at end-expiration since we wanted to characterize UA mechanics free of phasic muscular activity and in order to control as precisely as possible for the confounding effects of lung volume and abdominal configuration on the output of phrenic stimulation (Verin et al., 2003a). Using this PNMS set-up, we previously demonstrated that UA dynamic properties significantly differed between OSA and non-OSA subjects (Verin et al., 2003b) and that therapeutic CPAP as well as oral appliance efficacy could be predicted during wakefulness (Bosshard et al., 2011; Verin et al., 2003a). Flow, pressures, and EMG responses to PNMS were recorded at 10 kHz on a second computer for off-line analysis (Digidata 1320, Axon Instrument, Foster City, CA).

2.5. Protocol

Once the MAD had been individually adjusted to an arbitrary optimal comfortable advancement by one of the investigators (JFM), subjects were asked to sleep at least two weeks with the device at this setting before completing the PNMS experiment. During PNMS experiment, the minimum magnetic stimulator output sufficient to induce clear flow-limited twitches was first determined (see next section). Thereafter, using this intensity, five stimulations were applied at baseline (without MAD) and then with MAD at minimum protrusion (the arbitrary optimal comfortable advancement). Finally, the device was slowly advanced until subject's maximum tolerance and five stimulations were triggered at this MAD setting. For each condition, a random inter-stimulus interval of several breathing cycles was maintained between twitches. At the end of the experiment, the device was reset to the dentist initial adjustment and the conventional titration procedure was initiated.

2.6. Analysis of flow-pressure responses to PNMS

Fig. 1 shows examples of PNMS twitches. Twitch-induced breathes were considered flow limited when instantaneous flow plateaued or decreased despite a persistent decrease in velo- and/or oro-pharyngeal pressures of at least 1 cmH_2O. Velo- and oro-pharyngeal pressures were referenced to nasopharyngeal pressures. Thus, velopharyngeal limitation was depicted when such a decrease in pressure occurred below the nasopharynx (Fig. 1A) and oropharyngeal limitation was depicted when such a decrease in pressure occurred below the velopharynx (Fig. 1B). From the above definition, for a given condition, patients could be classified as having velopharyngeal or oropharyngeal obstruction. For all twitches, maximum inspiratory flow (VI_{max}) and oro-/velo-pharyngeal