

# Long-Term Effectiveness of Oral Appliance versus CPAP Therapy and the Emerging Importance of Understanding Patient Preferences

Commentary on Doff et al. Oral appliance versus continuous positive airway pressure in obstructive sleep apnea syndrome: a 2-year follow-up. *SLEEP* 2013;36:1289-1296.

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The two most common therapies used to treat obstructive sleep apnea (OSA) are: (1) continuous positive airway pressure (CPAP), and (2) mandibular advancement splints (MAS), which are the most commonly used oral appliance. These therapies differ in efficacy, cost, comfort, and side effects. Physicians typically select CPAP as the primary treatment since it is the most effective option in reducing the apnea-hypopnea index (AHI). For patients who consider the benefits worth the negatives and become adherent users of CPAP, this is the most appropriate course of action. However, the remaining 30% to 50% of patients for whom the discomfort, noise, and other negatives outweigh benefits become non-adherent to CPAP. Untreated OSA is associated with increased risks of strokes,<sup>1</sup> myocardial infarction,<sup>2</sup> motor vehicle crashes,<sup>3</sup> reduced work performance, and increased occupational injuries.<sup>4</sup> The economic burden related to untreated OSA is substantial, accounting for billions of dollars per year. In non-adherent CPAP users, a critical clinical question is whether to focus efforts on strategies to improve patients adherence to CPAP, or to instead treat patients with MAS?

The study by Doff and colleagues<sup>5</sup> in this issue of *SLEEP* provides important evidence on the relative efficacy of CPAP and MAS to address this question. In a 2-year randomized trial of 103 patients, they found that in an intent-to-treat analysis for mild to severe OSA patients, there was no statistical difference between the proportion of patients obtaining successful treatment (56% vs 60% in non-severe, and 50% vs 75% in severe for MAS and CPAP, respectively). The study also did not find any statistical difference between the treatments in terms of Epworth Sleepiness Scale, FOSQ-score, and the SF-36. In fact, the only difference identified between treatments was in the AHI and the lowest oxyhemoglobin saturation.

The findings of the trial by Doff et al.<sup>5</sup> build on an emerging evidence base. For example, a recent non-concurrent cohort study confirmed this finding, where the authors followed 208 control subjects compared to 254 severe OSA; 177 patients were treated with CPAP and 72 with MAS over a mean period of 5 years. They found MAS to be an equally effective therapy in reducing the risk of fatal cardiovascular events in patients

with severe OSA when compared to CPAP.<sup>6</sup> There are various trials showing that despite the presence of residual apneas and the inferior efficacy of MAS compared to CPAP in the reduction of AHI, MAS presents similar health outcomes as presented with surrogates to cardiovascular disease such as blood pressure,<sup>7,8</sup> endothelial function,<sup>9</sup> and microvascular reactivity.<sup>10</sup> They hypothesize that this is because the suboptimal efficacy with MAS therapy is counterbalanced by the superior adherence relative to CPAP, resulting in similar effectiveness of both treatments. Phillips and collaborators compared CPAP to MAS in a large randomized, controlled, crossover trial of moderate to severe OSA patients over a 3-month trial period.<sup>11</sup> This study evaluated 24-hour blood pressure measurements and found a non-inferiority of MAS compared to CPAP. Further, the treatments were found similar in terms of sleepiness and driving simulator performance. Both treatments improved quality of life on a disease-specific questionnaire, although MAS was superior to CPAP for improving four general QOL domains.

A limitation of the study by Doff et al.<sup>5</sup> is that only 62 of the 102 original participants completed the 2-year follow-up. A concern is that a greater number of patients withdrew from MAS in comparison to the CPAP arm (47% vs 33%). However on further scrutiny, it appears this difference was not due to adherence, but mostly due to a subgroup of patients with a higher BMI where MAS treatment is less effective. BMI is a consistent predictor of MAS efficacy, to the point where Gagnadoux and collaborators<sup>12</sup> describe a BMI greater than 35 kg/m<sup>2</sup> as a contraindication for MAS therapy. Another limitation of study<sup>5</sup> is lack of an objective assessment to measure adherence with MAS therapy. Vanderveken and collaborators<sup>13</sup> evaluated a recently developed micro-sensor in 51 patients over a period of 3 months, and their results illustrated the safety and feasibility of objective measurement of MAS adherence.

If the emerging evidence suggests MAS is an effective alternative therapy for OSA, the next question is how and when to determine if a patient should receive CPAP or MAS? Conventional wisdom suggests that patients failing to adhere to CPAP after a trial period should be offered MAS. But how long a trial period, and at what level of adherence? However, this is unknown and somewhat subjective. There is also a concern that non-adherent users will be lost to the system instead of returning for MAS,<sup>14</sup> frustrated that their preferences were not initially taken into account. An alternative and increasingly promoted approach in the wider medical literature is to conduct a "preference diagnosis" at the initial decision to determine which option is appropriate for each patient.<sup>15</sup> This requires

Submitted for publication July, 2013

Accepted for publication July, 2013

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providing patients with information about benefits and harms for options, determining which of these matter most to the patient, and engaging the patient in conversation and deliberation to identify the option that best matches their informed preferences.<sup>16</sup> Patient decision aids, the focus of significant funding in the Affordable Care Act in the US, are the predominant mode for implementing this patient-centered approach to treatment decision-making.<sup>17</sup>

While there is a lack of preference studies in the OSA literature, the recent crossover study by Phillips et al. gives some insight into the impact of such an approach in OSA.<sup>11</sup> They found that in retrospect, nearly half of patients preferred MAS and importantly, adherence to both CPAP and MAS were higher in patients who preferred the corresponding options (personal communication). The implications of an effective patient-centered approach is a future with significantly more patients adherent to OSA therapy, be it CPAP or MAS, and consequently better health outcomes for OSA patients as a whole.

In summary, the current literature increasingly supports MAS as an effective alternative to CPAP except for extremely and morbidly obese persons. Future studies focused on long-term comparative effectiveness outcomes that include objective measures of adherence as well as the consideration of informed patients' preferences for treatment are required for the comparisons between CPAP and MAS treatment. Such studies may generate evidence to help the patient and physicians choose the therapy that is most acceptable to improving the patient's health and quality of life.

#### CITATION

Almeida FR. Long-term effectiveness of oral appliance versus CPAP therapy and the emerging importance of understanding patient preferences. *SLEEP* 2013;36(9):1271-1272.

#### DISCLOSURE STATEMENT

The authors have indicated no financial conflicts of interest.

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