decreased clearance is associated with higher mortality, which is important new information. Hopefully, the findings from this and previous studies will promote more prospective studies of therapeutic strategies aimed at increasing alveolar edema clearance in ALI/ARDS patients. For example, prospective studies could be designed to determine whether catecholamine treatment improves indirect measures of clearance (gas exchange and compliance), shortens ventilator days, and improves survival. The development of simpler and more accurate methods to assess changes in edema clearance will certainly facilitate such investigations.

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References


Oral Appliance Therapy for Obstructive Sleep Apnea
Finally Evidence You Can Sink Your Teeth Into

In the last decade there has been an explosion of interest in using oral appliances to treat obstructive sleep apnea (OSA). Based upon available evidence they generally have been recommended for the treatment of mild OSA or simple snoring (1, 2). Oral appliances are appealing because they are simple to use, reversible, portable, and appear to be quite safe (although long-term safety data are lacking). Anterior mandibular positioners are the most commonly used appliances and the best studied.

In 1997 a much debated paper was published in the British Medical Journal that reviewed the research evidence for the health consequences of OSA and the effectiveness of continuous positive airway pressure (CPAP) therapy (3). The authors concluded that the health effects of OSA were exaggerated and that the effectiveness of CPAP in improving health outcomes had been poorly evaluated. The state of the literature on oral appliance therapy was even more deficient with few controlled trials. Many clinicians and scientists did not agree with the overall conclusions of the article (4) but most agreed that further research was needed (5). The state of the CPAP literature has improved considerably since 1997 but the debate continues (6, 7).

The majority of published trials of oral appliance therapy are small, short term, and usually retrospective in design, without any control or comparison group. Many studies have poorly defined outcome criteria, usually subjective, and have a failure of all patients to have polysomnography at baseline and outcome. Most studies exclude patients with severe OSA and include patients who failed other treatment modalities, which introduces a significant source of bias. Many studies provide little detail of the actual appliance used, the method to select the optimal amount of mandibular protrusion, or even the timing of the outcome study. The nature and severity of side effects and complications are generally not reported. To date, important outcomes of therapy such as the impact on sleepiness and performance have not been systematically evaluated and predictors of treatment success are not known. Finally, no studies have reported objective compliance and only a few have reported subjective compliance.

An article in this issue of the Journal (pp. 1457–1461) is a major step forward in correcting many of the deficiencies of the published literature (8). Mehta and colleagues have conducted the first prospective randomized placebo-controlled crossover trial of an anterior mandibular positioner for the treatment of patients with symptomatic OSA. Previous crossover studies of oral appliances have compared them with CPAP (either in a randomized [9, 10] or nonrandomized [11] design) or to another oral appliance (12). The primary aim of this randomized study was to assess efficacy of an adjustable mandibular advancement splint (MAS) and secondarily to examine whether any anthropomorphic, polysomnographic, or radiologic characteristics could predict treatment outcome.

Twenty-eight patients received an adjustable oral appliance with full occlusal coverage. The placebo was the lower plate of the device that did not specifically alter mandibular position. All patients had an acclimatization period during which the mandible was incrementally advanced until symptoms resolved or maximum tolerated protrusion was obtained. Patients were then randomly assigned to treatment with the placebo followed by the MAS or treatment with the MAS followed by the placebo. The authors used a conservative definition of treatment success. They defined a complete response to be a reduction in apnea/hypopnea index (AHI) to < 5/h. A partial response was defined as an improvement in symptoms combined with a ≥ 50% reduction in AHI but the AHI remained > 5/h. Treatment failures were defined as having ongoing symptoms and/or a < 50% reduction in AHI. Compliance failure was defined as an inability of the patient to use the treatment. Other outcomes included the effects on sleep structure, oxygenation, and snoring and questionnaires evaluating snoring, quality of sleep, and daytime sleepiness.

The patients were typical of a population of OSA pa-
tients—middle aged, overweight, and mostly male. One important strength of this study is that it included patients who had a range of severity of OSA with AHI between 10 and 68/h. The placebo device had no impact on the AHI or on oxygen saturation. The MAS resulted in a partial or complete response in 15 patients or 62.5% (complete response in 9—37.5%). Other studies have used a cutoff of an AHI of 10/h to define treatment success and 71% of patients had a complete or partial response by this criteria. The MAS had beneficial effects on the amount of rapid eye movement (REM) sleep, snoring intensity and frequency, the number of arousals, and oxygenation. Patients tolerated the treatment well and reported improvements in sleep quality and daytime sleepiness. Side effects were few and there were no complications. They found four independent predictors of the treated AHI—neck circumference, baseline AHI, and two cephalometric variables. The predictive equation requires validation to see if it is generalizable to other patient populations.

This study provides confirmation of the efficacy of adjustable mandibular positioner therapy in some patients with OSA. They had good results in patients with more significant OSA (AHI ≥ 40) and many patients elected to continue on with MAS therapy as they had a good symptomatic response. Subjective response to the MAS was clearly superior to the objective response (reduction in AHI). The study suggests that the mechanism of action of oral appliances is mandibular advancement because the presence of an intraoral device without advancement showed no clinical benefit.

Long-term studies are still required that objectively evaluate performance and sleepiness and that monitor for complications that may not emerge for several years. Perhaps these authors will continue to follow these patients and report later on their long-term outcome. On the horizon for the field of oral appliance therapy is the introduction of a compliance monitor that will allow an objective determination of appliance usage. In addition, several investigators are developing systems that would allow overnight titration of oral appliances in the sleep laboratory. Results from this study support the use of this treatment in patients with symptomatic OSA as long as a follow-up sleep evaluation occurs.

Autoadjusting Continuous Positive Airway Pressure
What Can We Expect?

Since 1996, there have been technologies that allow automatic adjustment of continuous positive airway pressure (CPAP) for treatment of obstructive sleep apnea (OSA) (1–4). There are many factors that influence overnight pressure needs in a given individual, including sleep structure, sleeping position, physiological changes in nasal resistance, and fluctuations in body weight. Moreover, it has been assumed that a significant reduction in CPAP pressure may improve compliance with treatment due to a reduction in side effects or improvement in comfort, although there are nearly no data to support such an hypothesis until now (1–3).

Several parameters have been used to drive autoadjust CPAP, using either pressure or flow signals available inside the machine that allow the detection of apneas, hypopneas, snoring, and flow limitation. The forced oscillation technique (FOT) is a very promising concept allowing a continuous measure of upper airway (UA) impedance. A single threshold of impedance may be used to drive the device without any need to identify specific respiratory events (5).

In the first March issue of the Journal (pp. 652–657), Rand erath and coworkers evaluated an original autoadjusting CPAP system based on FOT (6). In a randomized crossover study, they compared the effects of autoadjusting positive airway pressure (APAP) and constant CPAP on sleep-disordered breathing, sleep structure, and treatment compliance in more than 50 patients over a 6–wk period.

Identification of sleep-disordered breathing was based on thermists placed under the CPAP mask, as a pneumotachometer inserted in the CPAP line might have altered the application of FOT. This method of measurement and a desaturation criterion of 4% make the scoring of hypopneas very insensitive (7)—specifically when looking at residual events while using CPAP. Scoring of respiratory events, however, was equally insensitive under both constant CPAP and APAP conditions.

Overall, APAP, driven by FOT, was effective in correcting respiratory disturbances and improving sleep structure (6), and it was comparable with published data on other intelligent CPAP systems (1–5, 8). The reduction in microarousals while