Oral-appliance therapy obstructive sleep apnea-hypopnea syndrome

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Chapter 1
General introduction

Introduction

In one of his famous novels *The Posthumous papers of the Pickwick Club* dating from 1837, Charles Dickens created a character named Joe, "a fat and red-faced boy, (often) in a state of somnolency and constantly snoring";[1]

The object that presented itself to the eyes of the astonished clerk was a boy—a wonderfully fat boy—habited as a serving lad, standing upright on the mat, with his eyes closed as if in sleep. He had never seen such a fat boy, in or out of a travelling caravan; and this, coupled with the calmness and repose of his appearance, so very different from what was reasonably to have been expected of the inflictor of such knocks, smote him with wonder.

"What's the matter?" inquired the clerk.

The extraordinary boy replied not a word; but he nodded once, and seemed, to the clerk's imagination, to snore feebly.

"Where do you come from?" inquired the clerk.

The boy made no sign. He breathed heavily, but in all other respects was motionless.

The clerk repeated the question thrice, and receiving no answer, prepared to shut the door, when the boy suddenly opened his eyes, winked several times, sneezed once, and raised his hand as if to repeat the knocking. Finding the door open, he stared about him with astonishment, and at length fixed his eyes on Mr. Lowten's face.

"What the devil do you knock in that way for?" inquired the clerk angrily.

"Which way?" said the boy, in a slow and sleepy voice.

"Why, like forty hackney-coachmen," replied the clerk.

"Because master said, I wasn't to leave off knocking till they opened the door, for fear I should go to sleep," said the boy.

With this characterization of Joe, Dickens provided one of the earliest accurate descriptions of someone with severe obstructive sleep apnea-hypopnea syndrome (OSAHS). Nowadays, OSAHS is considered a common sleep-related breathing disorder, affecting approximately 4% of male and 2% of female adults in the North-American population.[2] The condition is characterized by disruptive snoring and repetitive upper airway obstruction during sleep. In order to diagnose OSAHS a sleep registration (*e.g.*, polysomnography) should demonstrate five or more complete (apneas) or partial (hypopneas) upper airway obstructions per hour

sleep.[3] Patients have recurrent arousals from sleep as an attempt to restore upper airway patency. This results in activation of the sympathetic nervous system and sleep fragmentation.[4] Neurobehavioral consequences of sleep fragmentation include excessive sleepiness, an increased risk of accidents, and impairment of the quality of life.[5-8] Cardiovascular sequelae of OSAHS include hypertension and an increased risk of ischemic heart disease, congestive heart failure and stroke.[9-12] Because obesity is a risk factor for OSAHS, it should be considered a serious and increasing public health problem.[13,14]

Continuous positive airway pressure (CPAP) prevents upper airway obstruction by pneumatically "splinting" the upper airway during sleep. The effectiveness of CPAP in improving blood pressure and neurobehavioral outcomes has been demonstrated in randomized controlled trials.[5,8,15] Although CPAP is currently regarded as the treatment of choice,[8] poor compliance may compromise the effect of treatment due to its obtrusive nature.[16,17] Thus, there is a need for simpler treatments that match the effectiveness of CPAP therapy.

Over the past decade, oral-appliance therapy has emerged as an increasingly popular alternative to CPAP therapy.[18] An oral appliance aims at relieving upper airway obstruction during sleep by modifying the position of the mandible, the tongue, and pharyngeal structures. Although there are many studies that suggest a favorable effect of oral appliances, treatment is generally less effective than CPAP in relieving the upper airway obstructions.[19-21] Nevertheless, patients tend to prefer an oral appliance to CPAP in most randomized trials.[19,21] In addition, improvements of physiological and neurobehavioral outcomes, including blood pressure and quality of life, do not tend to differ between oral-appliance and CPAP therapy.[19,21] At present the specific role of oral-appliance therapy in OSAHS treatment is still uncertain.[18-20] Consequently, in clinical practice oral appliances are primarily restricted to patients unwilling or unable to comply with CPAP therapy.[20]

Aim of the thesis

The general aim of this thesis is to evaluate the specific role of oral-appliance therapy in the treatment of OSAHS patients. In the next chapters five main aspects related to the management of OSAHS with oral-appliance and CPAP therapy are explored.

Chapter 2 focuses on the different treatment options for OSAHS and reviews the current literature regarding oral-appliance therapy.

When treating OSAHS, clinicians may consider various non-invasive, surgical and pharmacological modalities. Treatment of OSAHS is preferably associated with minimal co-morbidity while optimally relieving symptoms. In Chapter 2.1 background information with respect to OSAHS is provided and the various treatment modalities for OSAHS are discussed.

The treatment of OSAHS with oral appliances has gained considerable popularity as an alternative to current modalities because of their simplicity and supposed reversibility. Despite a possible favorable outcome of oral-appliance therapy in the treatment of OSAHS, comparative studies regarding efficacy and co-morbidity of this dental treatment modality are relatively scarce. In Chapter 2.2 the available literature regarding the efficacy and co-morbidity of oral-appliance therapy for OSAHS is systematically reviewed.

Chapter 3 focuses on an alternative procedure for initiating CPAP therapy in OSAHS patients.

CPAP is currently recommended as the treatment of choice for, especially moderate to severe, OSAHS.[4] Determination of the effective positive airway pressure in a specific patient is usually a trade-off between the minimization of pressure-related side-effects and the prevention of upper airway obstruction during sleep. This procedure, known as CPAP titration, is routinely conducted by a technician in a sleep laboratory during polysomnography (manual CPAP titration).[22] Several alternatives for manual titration have emerged to shorten waiting lists for polysomnography and to improve cost-effectiveness of CPAP titration. A practical alternative for manual CPAP titration is titration without polysomnography during an afternoon nap (Nap-titration). In Chapter 3 it is evaluated whether Nap-titration is an appropriate procedure for the effective titration of CPAP in OSAHS patients.

Chapter 4 focuses on the effects of oral-appliance and CPAP therapy on various neurobehavioral and physiological outcomes.

Although oral-appliance therapy is generally effective, specific indications for treatment are indeterminate.[18-20] Many patients prefer an oral appliance to CPAP, and physiological and neurobehavioral outcomes are not substantially different between these therapies.19,21 In Chapter 4.1 it is studied whether an oral appliance is not inferior to CPAP in treating OSAHS effectively.

Excessive sleepiness in OSAHS patients may adversely affect daytime performance and consequently, among other sequelae, influence driving performance.[23,24] Performance on driving simulators has been shown impaired in OSAHS patients.[25-29] Successful treatment with CPAP therapy generally results in improvements of simulated driving performance.[30-32] However, the effects of oral-appliance therapy on simulated driving performance have not been evaluated to date.[19] In Chapter 4.2 it is studied to what extent OSAHS patients have more difficulty with a monotonous simulated driving test when compared with control subjects, and the effects of oral-appliance therapy are compared with CPAP.

Cardiovascular sequelae of OSAHS may include hypertension and an increased risk of ischemic heart disease, congestive heart failure and stroke.[9,10] In patients without cardiovascular disease OSAHS is associated with an increased incidence of both

systolic and diastolic cardiac dysfunction and left ventricular hypertrophy.[33-38] This association is considered an important risk factor for developing cardiovascular disease. CPAP therapy has been shown to improve left ventricular structure and function in OSAHS patients without cardiac disease.[34-37] In addition, natriuretic peptides, which are believed to reflect the degree of left ventricular wall stress,[39] improved following successful CPAP therapy.[40] The effects of oral-appliance therapy on cardiac function are largely unknown.[19] In Chapter 4.3 left ventricular structure and function and natriuretic peptides in OSASH patients without cardiovascular disease are studied, and the effects of oral-appliance therapy are compared with CPAP.

In addition to various neurobehavioral and cardiovascular sequelae, OSAHS is associated with sexual dysfunction. Several studies have demonstrated erectile dysfunction and decreased libido in substantial proportions of male OSAHS patients.[41-45] Erectile dysfunction has been demonstrated to improve after successful treatment of OSAHS with CPAP therapy.[41,45] However, the effects of oral-appliance therapy on sexual function in OSAHS patients are unknown.[19] In Chapter 4.4 it is determined to what extent male OSAHS patients experience sexual dysfunctions compared with control subjects, and secondly the effects of oral-appliance and CPAP therapy on sexual functioning are evaluated.

Chapter 5 focuses on the possibilities to predict the outcome of oral-appliance and CPAP therapy.

Although there is evidence that oral-appliance therapy is effective for OSAHS, it is generally less effective in relieving upper airway obstruction when compared with CPAP therapy.[19-21] Conversely, many patients prefer an oral-appliance over CPAP therapy.[19] Therefore, predictors of treatment outcome are of importance for selecting suitable candidates that may benefit from either treatment. Although it has been reported that numerous clinical, polysomnographic and craniofacial variables correlate with increased effectiveness of oral-appliance therapy, predictors of treatment outcome are not reported uniformly.[46,47] As a result, the ability to predict treatment outcome and preselect suitable candidates for a specific treatment modality is still limited. In Chapter 5 the value of relevant clinical, polysomnographic and cephalometric variables is assessed to separately and jointly predict the outcome of oral-appliance and CPAP therapy.

Chapter 6 focuses on the application of oral appliances in specific cases.

Surgical treatment of OSAHS is principally aimed at enlarging airway dimensions and decreasing airway collapsibility.[48] Maxillomandibular advancement surgery has been suggested to be the most effective and acceptable surgical treatment for OSAHS.[49] Several different protocols for maxillomandibular advancement surgery in OSAHS patients are adopted. Despite this variety in treatment protocols, the precise indication for maxillomandibular advancement surgery in the management of OSAHS is undefined. In Chapter 6.1 the potential application

of oral-appliance therapy preceding maxillomandibular advancement surgery in the treatment of OSAHS patients is evaluated. Initial experiences with a new surgical protocol, in which oral-appliance therapy serves as a predictor for success of maxillomandibular advancement surgery, are reported.

Oral appliances that reposition the mandible (mandibular repositioning appliances) appear a viable treatment modality in the management of OSAHS.[19] However, in up to 34% of cases a mandibular repositioning appliance cannot be inserted because of dental limitations.[50] In the majority of cases there are an insufficient number of teeth to support and retain the appliance.[19,50] Several types of oral appliances have been described for managing OSAHS in edentulous patients.[51-56] Full-night application of these appliances is generally compromised by discomfort or poor retention in the upper or lower jaw. In order to stabilize and retain a mandibular repositioning appliance in the edentulous patient osseointegrated implants may be used.[51] However, no clinical studies of this technique have been reported to date. In Chapter 6.2 the initial experiences with an implant retained mandibular repositioning appliance in the treatment of edentulous OSAHS patients are described.

Chapter 7 discusses the main findings of the studies described in chapters 2 through 6 in broader context and draws general conclusions. This chapter will also provide suggestions for future research in oral-appliance therapy for OSAHS.

Chapter 8 provides a summary of the thesis in English and Dutch.

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