Oral-appliance therapy obstructive sleep apnea-hypopnea syndrome

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Chapter 2

Obstructive sleep apnea-hypopnea syndrome management

Chapter 2.1

Treatment modalities for obstructive sleep apnea-hypopnea syndrome

This chapter is based on the following publications:

* Hoekema A, Wijkstra PJ, Buiter CT, van der Hoeven JH, Meinesz AF, de Bont LGM. Treatment of the obstructive sleep-apnoea syndrome in adults. *Nederlands Tijdschrift voor Geneeskunde* 2003;147:2407-2412.
* Hoekema A, Stegenga B, de Bont LGM. Efficacy and co-morbidity of oral appliances in the treatment of obstructive sleep apnea-hypopnea: a systematic review. *Critical Reviews in Oral Biology & Medicine* 2004;15:137-155.
* Hoekema A. Management of the obstructive sleep apnoea syndrome: more knowledge required for an optimal choice of treatment modality. *Nederlands Tijdschrift voor Geneeskunde* 2006;150:175-178.

Summary

The obstructive sleep apnea-hypopnea syndrome (OSAHS) is a common sleep-related breathing disorder characterized by disruptive snoring and repetitive upper airway obstructions. Its neurobehavioral consequences include excessive sleepiness, an increased risk of accidents, and an impaired quality of life. Cardiovascular consequences may include hypertension and an increased risk of ischemic heart disease, congestive heart failure, and stroke. In the management of OSAHS, clinicians may consider various conservative, non-invasive and surgical treatment modalities. Conservative measures and the correction of morphological airway abnormalities should be considered first. If these measures are not effective or not applicable, continuous positive airway pressure (CPAP) is currently regarded as the treatment of choice for, especially, moderate to severe OSAHS. However, due to the obtrusive nature of CPAP, the effectiveness may be compromised by poor therapeutic acceptance and adherence. Surgical interventions for OSAHS may roughly be classified as ablative soft tissue surgery and surgical interventions that aim at soft tissue repositioning by means of skeletal modifications. Based on the current level of evidence, most surgical interventions in OSAHS should generally be reserved for patients failing CPAP therapy. Pharmacological management of OSAHS is only warranted as supplementary treatment in specific patients. Over the past decade, oral-appliance therapy has emerged as a popular alternative to CPAP. However, methodological limitations of most trials studying this dental treatment modality make the precise indication for oral appliances indistinct. Additional studies are required evaluating: the indication, effects on neurobehavioral and cardiovascular outcomes, patient compliance and side-effects of oral-appliance relative to CPAP therapy.

OSAHS

The obstructive sleep apnea-hypopnea syndrome (OSAHS), a common sleep-related breathing disorder, is characterized by repetitive upper airway obstructions and disruptive snoring during sleep.[1,2] Upper airway obstructions in OSAHS can be either partial or complete and often result in (possibly severe) oxygen desaturations. When a complete or partial airway obstruction is manifested by a complete cessation or substantial reduction (*i.e.*, >50%) in oronasal airflow of at least ten seconds, the respiratory event is defined as apnea or hypopnea, respectively.[3] A moderate reduction in airflow (*i.e.*, <50%) of ten seconds or longer is also defined as hypopnea when associated with an oxygen desaturation (>3%) or brief awakening from sleep. Normal upper airway patency is usually re-established after an increased respiratory effort in response to hypoxia and hypercapnia (*i.e.*, abnormal increase in PaC_{O}^{2}).[4] The increased respiratory efforts result in brief awakenings from sleep (arousals) that usually go unnoticed by patients.[5] Recurrent arousals are associated with sleep fragmentation and a depletion of rapid-eye-movement (REM) and slow-wave sleep (*i.e.*, non-REM stage 3 and 4), ultimately resulting in excessive daytime sleepiness. Other consequences of sleep fragmentation include reduced neurocognitive functioning, an impaired quality of life, and an increased risk of motor vehicle and occupational accidents.[6,7] Haemodynamic consequences of upper airway obstruction include sustained periods of hypertension,[8] and an increased risk of cardiovascular disease including myocardial ischemia and infarction, cerebrovascular accidents and congestive heart failure.[9-12] Moreover, the available data suggest that OSAHS, especially when severe, is associated with an increased mortality.[13]

Definition and epidemiology

According to the recommendations of the American Academy of Sleep Medicine, OSAHS is defined by a combination of symptoms (*e.g.*, excessive daytime sleepiness) and laboratory findings.[3] Laboratory findings should demonstrate a respiratory disturbance index (RDI) of five or more obstructed breathing events per hour of sleep. These events include any combination of apneas, hypopneas, and respiratory effort related arousals (RERA's). By including RERA's in the index, the upper airway resistance syndrome, a condition with similar pathophysiology but lacking marked upper airway obstructions, is classified as OSAHS.[3] Since the detection of RERA's requires more sensitive diagnostic monitoring techniques, the number of obstructed breathing events is usually quantified by the number of apneas and hypopneas per hour sleep (*i.e.*, apnea-hypopnea index; AHI).[3] Based on the AHI, OSAHS may be classified as mild (AHI 5–15), moderate (AHI 15–30) or severe (AHI >30).[3] When the above stated recommendations are adopted, OSAHS can be diagnosed in 2% of women and 4% of middle-aged men in the

North-American population.[14] In the Dutch population, at least 0.45% of males aged 35 years or older have clinically significant OSAHS.[15] Nevertheless, it is estimated that in the general population approximately 80 to 90% of patients meeting the criteria of at least moderate severe obstructive sleep apnea remain undiagnosed.[16] Since untreated OSAHS is likely to deteriorate over time and rarely disappears,[17] this is of serious consequence for unrecognized patients.

Etiopathogenesis

It is assumed that both anatomical and neuromuscular factors contribute to the pathogenesis of upper airway obstructions in OSAHS.[18] However, other variables, such as lung volume and individual variability in ventilatory control, may also be of significance.[2] The increased risk of OSAHS in males has been attributed to gender differences in upper airway morphology (*e.g.*, fat distribution and craniofacial dimension) and protective effects of female hormones on upper airway patency.[19,20] This latter hypothesis is confirmed by the fact that menopausal state entails a risk for developing OSAHS.[17] Although OSAHS prevalence is shown to increase with age,[21] it is unclear whether this can be attributed to an accumulation of cases or to an increase in incidence. OSAHS also appears to be more common in several endocrine disorders like hypothyroidism, acromegaly, Cushing's syndrome and diabetes mellitus.[22] Other risk factors for OSAHS include familial aggregation and Afro-American racial origin.[23,24] Besides gender and age, obesity is probably the most important risk factor for OSAHS.[25] It is hypothesized that obesity influences breathing during sleep by inducing hypoxemia, and altering (upper) airway structure and function.[26] Various anatomical abnormalities of the bony and soft tissue structures of the head and neck may also compromise the upper airway during sleep. Whether related to a genetic syndrome or not, these abnormalities include craniofacial abnormalities (*e.g.*, micrognathia), macroglossia, adenotonsillar hypertrophy and palatal enlargement.[27,28] Moreover, a compromised nasal passage due to allergic rhinitis, acute upper airway infection or a anatomical abnormality (*e.g.*, a deviated nasal septum, conchal hypertrophy or nasal polyps) has been identified as risk factor for OSAHS.[29] Finally, several intoxications may predispose to upper airway obstruction during sleep, including the use of tobacco, alcohol and respiratory depressant- or sedative medication.[2]

Diagnostic examination

Diagnosing OSAHS is primarily the expertise of ear, nose and throat surgeons, pulmonologists and neurologists. Anamnesis of symptoms and evaluation of risk factors constitute the first step in confirming the diagnosis. The physical investigation of suspected patients should also compromise visual inspection of the upper airway reaching from the external nasal valves up to the vocal cords. Inspection should be aimed at identifying morphological abnormalities that

TABLE 1. Prevalence, risk factors and differential diagnosis of the obstructive sleep apnea-hypopnea syndrome.

Prevalence
- North-American population: 2% of women and 4% of middle-aged men
- percentage of undiagnosed patients: estimated at 80-90%
- Dutch population: minimum of 0.45% in males aged 35 years or older

Risk factors
- obesity
- male gender
- menopause
- increased age
- anatomical abnormalities: craniofacial abnormalities, macroglossia, adenotonsillar hypertrophy, palatal enlargement
- compromised nasal passage: deviated nasal septum, nasal polyps, conchal hypertrophy, alar insufficiency, acute upper airway infection, allergic rhinitis
- endocrine disorders: hypothyroidism, acromegaly, Cushing's syndrome, diabetes mellitus
- familial aggregation of obstructive sleep apnea
- intoxications: alcohol, tobacco use, respiratory depressant- or sedative medication

Differential diagnosis
- primary snoring
- chronic hypoventilation syndromes
- central sleep apnea syndrome
- Cheyne-Stokes respiration
- narcolepsy
- sleep deprivation
- periodic limb movement disorder
- alcohol & drug abuse

may compromise airflow in the upper airway during sleep. In most cases, this is performed by means of flexible nasendosopy. In clinical practice, upper airway imaging techniques including cephalometry and computed tomography or magnetic resonance imaging are of limited value in the physical and diagnostic investigation of OSAHS patients.

Despite its labor-intensive character, full-night polysomnography is regarded as the standard diagnostic technique for OSAHS.[2] This comprehensive sleep registration, either performed in a sleep laboratory or ambulatory in a home setting, generally incorporates recording of an electroencephalogram, electro-

TABLE 2. Treatment modalities for the obstructive sleep apnea-hypopnea syndrome.

Conservative measures
- weight reduction
- regulation of sleeping position
- abstain from: alcohol, tobacco and respiratory depressant- or sedative medication
- improvements in "sleep hygiene"

Medical techniques
- continuous positive airway pressure (CPAP)
- bi-level positive airway pressure (BiPAP)
- oral appliances: mandibular repositioning appliances, tongue repositioning appliances
- other: nasopharyngeal intubation, nasal dilator, stimulation of the hypoglossal nerve

Surgical management
- correction of anatomical abnormality or a compromised nasal passage
- ablative soft tissue surgery: uvulopalatopharyngoplasty (UPPP), somnoplasty
- skeletal modifications: genioglossal advancement, hyoidthyroidpexia,
- maxillomandibular advancement surgery
- tracheotomy
- surgical treatment of obesity

Pharmacological management
- antidepressants: tricyclic and serotonergic agents
- other: wake promoting agents (*e.g.*, modafinil), steroid treatment (*e.g.*,medroxyprogesterone), treatment of endocrine disorder (hypothyroidism, acromegaly)

oculogram, chin electromyogram, snoring, thermistor, electrocardiogram, pulse oximetry and an tibilais anterior electromyogram. Polysomnography allows for assessment of sleep architecture and quantification of upper airway obstructions, arousals and oxygen desaturations. Other diagnostic instruments may be needed to provide additional information with regard complaints of sleepiness. Although a standard technique for measuring sleepiness is not available at present, the Epworth sleepiness scale is probably the most adequate and inexpensive test of all.[30] The Epworth sleepiness scale is a simple, self-administered questionnaire in which patients rate their propensity to fall asleep in eight different situations. Scales that objectify sleepiness include the multiple sleep latency test and the maintenance of wakefulness test.[3]

Differential diagnosis

OSAHS should be differentiated from the central sleep apnea syndrome, Cheyne-Stokes respiration, and several other conditions characterized by excessive sleepiness including narcolepsy, sleep deprivation, periodic limb movement disorder, chronic hypoventilation syndromes, and alcohol or drug abuse.[3] Moreover, OSAHS should be distinguished from primary snoring, which is associated with a physiological number of airway obstructions and the absence of OSAHS-related symptoms. The prevalence, risk factors and differential diagnosis of OSAHS are summarized in Table 1.

Treatment modalities

When treating OSAHS, clinicians may consider various non-invasive, surgical and pharmacological modalities. The treatment of OSAHS is preferably associated with minimal co-morbidity while optimally relieving symptoms and reducing morbidity and mortality.[31] The various treatment modalities for OSAHS are discussed in the next sections (Table 2).

Conservative measures

Conservative measures constitute the correction of a medical problem or a lifestyle, which possibly affects OSAHS-symptomatology. Positive effects of weight reduction in obese patients confirm the reversibility of overweight as a risk factor for OSAHS.[32,33] However, on a long-term basis weight loss is often difficult to achieve and not always effective in obese patients.[34] Sleep deprivation or fragmentation may also predispose to OSAHS.[35] Therefore, if appropriate, OSAHS patients should be encouraged to improve their "sleep hygiene" (*e.g.*, improvements in sleep-wake patterns and avoidance of stimulants in the evening).[36] Patients with "supine dependent" upper airway obstructions may be successfully treated by changing their sleeping position from supine to lateral or more upright.[37-39] Furthermore, if applicable, patients should be advised to abstain from alcohol, tobacco and respiratory depressant- or sedative medication (*e.g.*, opiates or benzodiazepines).[2] Although conservative measures usually require additional treatment of OSAHS, they should always be considered due to their facilitating effect.

Continuous positive airway pressure

When conservative measures are not applicable or effective, OSAHS patients are preferably treated with continuous positive airway pressure (CPAP).[40] The introduction of CPAP has been of great significance in the management of OSAHS patients.[41] Prior to CPAP, symptomatic patients were nearly always treated with a tracheotomy. CPAP pneumatically splints the upper airway during sleep by means of a flow generator that is connected to an (oro)nasal mask (Figure 1).[42]

Before the effective positive airway pressure may be determined (CPAP-titration), the nasal passage of patients should be evaluated and if required (surgically) improved.[43] Although there are no widely accepted guidelines on the standardization of CPAP-titration, treatment should be aimed at the near elimination of upper airway obstructions and a normalization of oxyhemoglobin saturation and sleep architecture.[43-45] Since discontinuation of treatment usually results in a rapid recurrence of upper airway obstructions and symptoms,[46] CPAP therapy is generally a lifelong requisite. Because of the predisposing effect for upper airway obstruction, increases in weight or the consumption of alcohol may cause that the prescribed CPAP pressure is no longer sufficient.[47] Recently, automatic-CPAP devices have been introduced to overcome these problems. Automatic-CPAP devices non-invasively detect signs of upper airway obstruction and increase pressure to maintain upper airway patency and decrease pressure if no signs of airway obstruction are detected.[43,48] Because the precise value and indication of automatic-CPAP is still undefined, routine use of these devices in the treatment of OSAHS patients is not warranted.[2,43]

Although a placebo effect has been demonstrated, CPAP therapy is known to improve excessive daytime sleepiness, quality of life, depression and neurocognitive performance of patients substantially.[40,45,49,50] Because of controversial findings, the precise effects of CPAP therapy on cardiovascular function is still an area of debate.[40,49] However, a favorable effect of treatment on hypertension is reported most uniformly in literature.[51] If therapy is not successful or requires excessively high pressures, CPAP with reduced expiratory pressure may be used (*i.e.*, bi-level positive airway pressure [BiPAP]).[43]

Side effects of CPAP, although rarely severe, are frequently observed in the initial period of use.[52,53] Beside possible discomfort for patient and partner, side effects predominantly relate to the (oro)nasal mask. Optimizing comfort of the mask is therefore crucial for a successful outcome of therapy. Moreover, CPAP may also cause nasal congestion, rhinorhea, sneezing and mucosal drying of the upper airway.[52,53] Most of these complaints can be adequately treated with either antihistaminics, inhalation steroids or (heated) humidification of the inhaled air.[2,52]

CPAP should be considered when conservative measures are not applicable or when additional treatment is required.[40] Based on the current level of evidence CPAP therapy is recommended as treatment of choice for especially moderate to severe OSAHS.[2,40] Poor compliance has been suggested to be the major drawback of therapy, with patients troubled by more side effects generally being less compliant.[54] Best compliance is usually seen in patients with severe OSAHS or substantial daytime sleepiness.[53,55] Patient counseling and adequate relief of side effects may optimize therapeutic compliance when initiating therapy.[43] Individuals

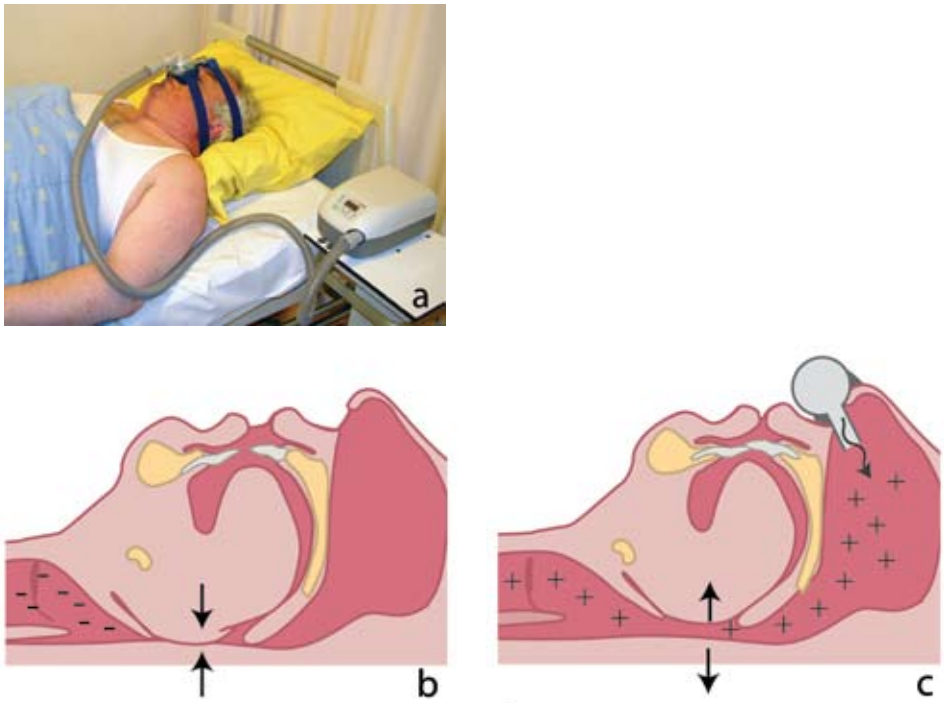

FIGURE 1. Continuous positive airway pressure therapy.

(a) patient in bed wearing a nasal mask connected to a continuous positive airway pressure (CPAP) device; (b & c) illustration of the mechanism of action in CPAP therapy: (b) retropalatal and retrolingual airway obstruction during sleep as a result of negative upper airway pressure during inspiration; (c) preventing upper airway obstruction by pneumatically splinting the upper airway during sleep by means of CPAP therapy (Figure adopted from; Hoekema A, Wijkstra PJ, Buiter CT, van der Hoeven JH, Meinesz AF, de Bont LGM. Treatment of the obstructive sleep-apnoea syndrome in adults. *Ned Tijdschr Geneeskd* 2003;147:2407-2412).

failing or refusing CPAP and patients with clearly reversible morphological airway abnormalities are candidates for alternative treatment.[2] Moreover, since results of CPAP in mild to moderate and asymptomatic OSAHS patients may be compromised by poor compliance,[46,56,57] alternative treatment may also be considered in these patients. If CPAP or bi-level positive airway pressure is not effective in a patient with an acute and life-threatening OSAHS, tracheal intubation or a tracheotomy should be contemplated.[43]

Surgical management

In general, surgical interventions for OSAHS are only indicated when a non-surgical intervention, such as CPAP, fails. Notable exceptions to this rule are clearly reversible morphological airway abnormalities (Table 1). When an anatomical

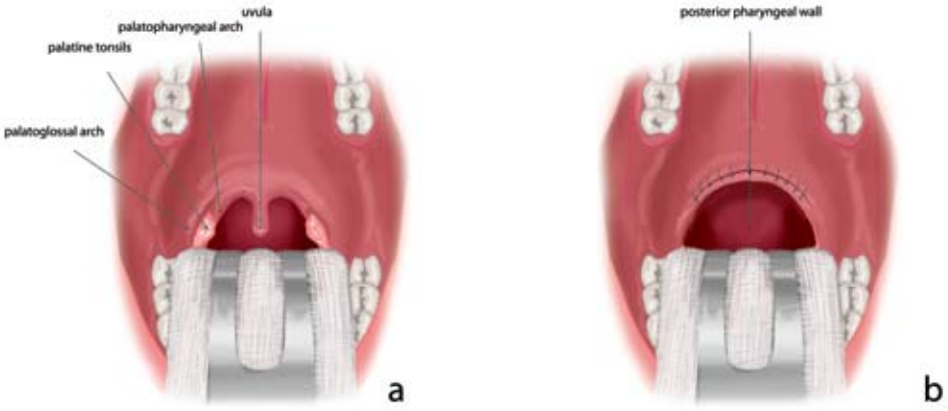

FIGURE 2. Uvulopalatopharyngoplasty.

A uvulopalatopharyngoplasty (UPPP) involves a resection of the uvula and the posterior portion of the soft palate, recontouring of the palatopharyngeal and palatoglossal arch and (if present) removal of the palatine tonsils. Intraoral view before (a) and after (b) UPPP (Figure adopted from; Richard W, den Herder C, de Vries N. Surgical treatment of obstructive sleep-apnoea syndrome. *Ned Tijdschr Geneeskd* 2005;149:1193-1196).

abnormality (*e.g.*, enlarged tonsils or adenoids) or a compromised nasal passage hinders upper airway patency, surgical correction may be indicated.[17,58] Although adenotonsillectomy or surgical correction of a compromised nasal passage usually fails to (completely) correct OSAHS in adult patients,[59] these interventions should always be considered because they facilitate in the treatment of OSAHS with other modalities (*e.g.*, CPAP). Other surgical interventions for OSAHS may roughly be classified as ablative soft tissue surgery (*e.g.*, uvulopalatopharyngoplasty or somnoplasty) and surgical interventions that aim at soft tissue repositioning by means of skeletal modifications (*e.g.*, genioglossal advancement, hyoidthyroidpexia or maxillomandibular advancement surgery) (Table 2).

An uvulopalatopharyngoplasty (UPPP) involves a resection of the uvula and redundant palatal, tonsillar and mucosal tissues (Figure 2). For a considerable time UPPP has been the most popular surgical procedure in the treatment of OSAHS patients. Despite its initial popularity, it has been shown that approximately 40% of OSAHS patients are successfully treated with a UPPP.[59] Long-term results are no more successful because relapse occurs in a significant proportion of initial successfully treated patients.[60] Moreover, recent employed techniques for correcting retropalatal airway obstruction, like laser-assisted uvulopalatoplasty or radiofrequency volumetric tissue reduction (*i.e.*, somnoplasty) of the soft palate, have also been disappointing in the treatment of OSAHS.[61,62] Somnoplasty uses controlled, low-power radiofrequency energy to create one or several submucosal

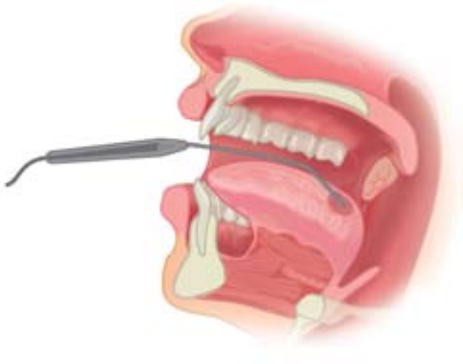

FIGURE 3. Somnoplasty.

Somnoplasty for the treatment of retrolingual airway obstruction: somnoplasty uses controlled, low-power radiofrequency energy to create one or several submucosal volumetric lesions. Over a period of six to eight weeks, the lesions are naturally resorbed, reducing tissue volume and stiffening remaining tissue in the desired area (Figure adopted from; Richard W, den Herder C, de Vries N. Surgical treatment of obstructive sleep-apnoea syndrome. *Ned Tijdschr Geneeskd* 2005;149:1193-1196).

volumetric lesions. Over a period of six to eight weeks, the lesions are naturally resorbed, reducing tissue volume and stiffening remaining tissue in the desired area. This method has not only been used for correction of the soft palate, but also for the correction of enlarged turbinates or relief of retrolingual airway obstruction (Figure 3).

More encouraging results have been obtained with surgical interventions that aim at soft tissue repositioning by means of skeletal modifications, including genioglossal advancement, hyoidthyroidpexia or maxillomandibular advancement surgery.[63,64] In genioglossal advancement the tongue is put under anterior traction by performing a limited parasagittal mandibular osteotomy and subsequent advancement of the genioid tubercle (Figure 4). In addition to genioglossal advancement a hyoidthyroidpexia is often performed. The latter procedure intends to enlarge the retrolingual airway by anterior fixation of the hyoid bone following the release of selected infra- and suprahyoid muscles (Figure 5). Maxillomandibular advancement provides maximal enlargement of the retrolingual and some enlargement of the retropalatal airway by means of a Le Fort I osteotomy of the maxilla and a bilateral sagittal split osteotomy of the mandible (Figure 6). In patients with a pronounced mandibular retrognathia, a bilateral sagittal split osteotomy of the mandible may suffice.

The chance of successful treatment of OSAHS following a UPPP or hyoidthyroidpexia in unselected patients is usually smaller than following CPAP therapy. The chance

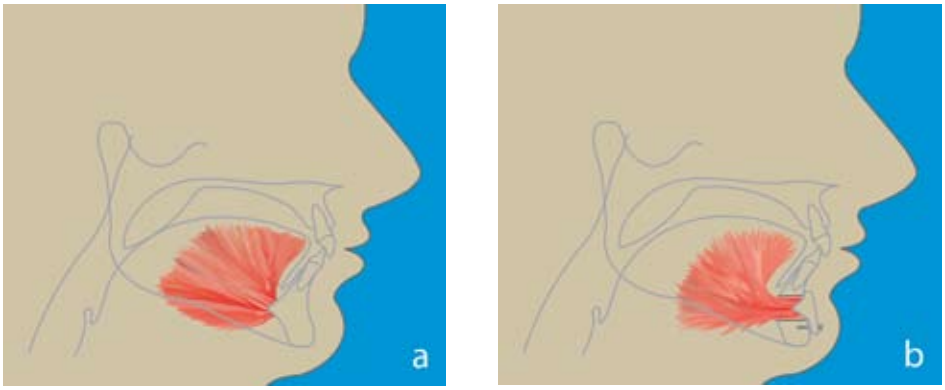

FIGURE 4. Genioglossal advancement.

In genioglossal advancement, the tongue is put under anterior traction by performing a limited parasagittal mandibular osteotomy and subsequent advancement of the genioid tubercle. Illustration of sagittal view before (a) and after (b) genioglossal advancement.

of success usually increases when a surgical procedure is selected based on the patient's specific level of upper airway obstruction (*i.e.*, retropalatal or retrolingual) or by combining several of the surgical interventions in one procedure.[65,66] By performing a UPPP, genioglossal advancement and/or hyoidthyroidpexia according to such a surgical protocol, successful management of OSAHS has been reported in approximately 60% of patients.[63] Maxillomandibular advancement surgery is successful in approximately 90% of treated patients and thereby comparable to CPAP therapy in terms of effectiveness.[63,67] One of the possible advantages of surgical management of OSAHS is that treatment efficacy is not dependent on adherence like in CPAP therapy. It should however be noted that studies evaluating surgical interventions in OSAHS generally incorporate methodological deficits.[68] Most studies do not employ a concurrent control group and usually report on findings of selected patient populations. Further bias is introduced with the use of divergent criteria of success, which impede a reliable comparison with CPAP therapy. Therefore, in clinical practice most surgical interventions for OSAHS are reserved for patients who are "nonresponsive" or "nonadherent" to CPAP therapy.

Despite considerable co-morbidity a tracheotomy, which results in a bypass of the upper airway, is probably the most predictable and effective surgical intervention for OSAHS.[63] Although gastric restrictive and bypass procedures are increasing in popularity, the limited experience in OSAHS patients and the morbidity and mortality associated with these procedures restrict their application to selected cases only.[69] Because OSAHS is associated with an increased operative risk,[70] anaesthesiological precautions and treatment according to protocol are requisite

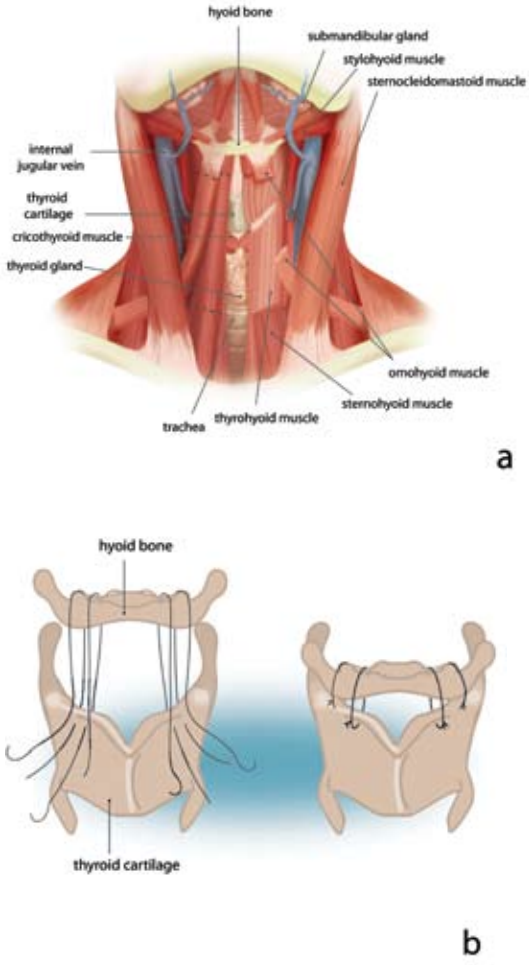

FIGURE 5. Hyoidthyroidpexia.

A hyoidthyroidpexia is aimed at enlarging the retrolingual airway. During this procedure selected infra- and suprahyoid muscles are dissected (a) whereupon the hyoid bone is mobilized in an anterior direction and permanently sutured to the thyroid cartilage (b) (Figure adopted from; Richard W, den Herder C, de Vries N. Surgical treatment of obstructive sleep-apnoea syndrome. *Ned Tijdschr Geneeskd* 2005;149:1193-1196).

with all surgical interventions in OSAHS patients.[71] The practice parameters of the American Sleep Disorders Association also provide recommendations for the surgical management of OSAHS patients.[72]

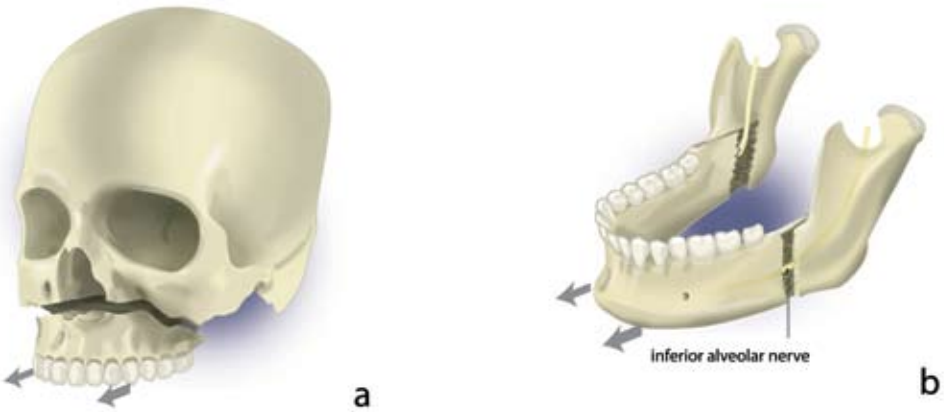

FIGURE 6. Maxillomandibular advancement surgery.

Maxillomandibular advancement surgery provides enlargement of the retrolingual and some enlargement of the retropalatal airway by means of a Le Fort I osteotomy of the maxilla (a) and a bilateral sagittal split osteotomy of the mandible (b) (Figure adopted from; Rosenberg AJ, Damen GW, Schreuder KE, Leverstein H. Obstructive sleep-apnoea syndrome: good results with maxillo-mandibular osteotomy after failure of conservative therapy. *Ned Tijdschr Geneeskd* 2005;149:1223-1226).

Pharmacological management

Various pharmacological agents have been deployed in the treatment of OSAHS (Table 2). Beneficial effects of tricyclic antidepressants and serotonergic agents have been reported in literature.[73,74] However, widespread use of these agents in OSAHS patients is mainly constrained by anticholinergic side effects and limited overall efficacy. In selected patients with persisting complaints of excessive sleepiness despite (adequate) OSAHS treatment, wake-promoting agents like modafinil may be beneficial.[75] Contrary to the suggested protective effect of sex-hormones in OSAHS pathogenesis, steroid treatment (*e.g.*, medroxyprogesterone) is generally only worth considering in patients with wake respiratory failure.[74] Thyroxin may be successful for the management of OSAHS patients with hypothyroidism.[76] However, in acromegalic patients additional treatment of OSAHS is usually required following the pharmacological suppression of growth hormones.[77] In clinical practice, pharmacological management of OSAHS is generally only indicated as supplementary treatment in selected cases.

Medical techniques

Medical techniques other than CPAP or oral appliances (see next section) are rarely used in the treatment of OSAHS patients. Treatment with nasopharyngeal intubation or mechanical dilation of the anterior nasal valve is usually associated

with poor tolerance and inadequate results, respectively.[78,79] However, promising results have been obtained following the stimulation of specific upper airway musculature during sleep. Especially, unilateral electrical stimulation of the hypoglossal nerve by means of an implanted electrode has been successful in the management of OSAHS.[80] However, for the clinical situation durable and reliable stimulation systems are required.

Oral appliances

Over the past decade, dental devices have become a popular alternative in the treatment of OSAHS.[81] These intra-oral devices, commonly known as oral appliances, relieve upper-airway obstruction during sleep by modifying the position of the mandible, tongue, and pharyngeal structures. Although several types of oral appliances are distinguished (Table 2), mandibular repositioning appliances (MRA's) are used most commonly in clinical practice. Mandibular repositioning appliances secure the mandible in an anterior position by means of an intraorally retained brace construction (Figure 7).[81]

The mechanism of action in oral-appliance therapy appears to be related primarily to an increase in upper airway dimensions during sleep. Beside anatomical changes, the mechanism of action in MRA therapy has also been attributed to a stabilization of the position of the mandible and hyoid bone and an increased muscle activity in the upper airway during sleep.[82] In patients with mild to moderate OSAHS, oral-appliance therapy is reported successful in 50 to 70% of cases.[81] Therapy appears less successful in patients with severe disease. Several crossover trials comparing CPAP and oral-appliance therapy have demonstrated similar improvements in symptomatology and quality of life.[83] CPAP is generally more effective in relieving upper airway obstructions. Conversely, many patients prefer an oral appliance to CPAP therapy.[40,83] Not only have oral appliances been shown more effective than uvulopalatopharyngoplasty,[83] therapy has also been demonstrated highly successful after failure of this surgical procedure.[84] Because an improvement of symptoms does not implicate a normalization of the number of upper airway obstructions (*i.e.*, AHI <5), the effects of oral-appliance therapy should always be verified by a sleep registration (*e.g.*, polysomnography).[81]

In the initial period of use, patients commonly report tenderness of the teeth and jaws, gum irritation, excessive salivation or xerostomia.[85] Problems of discomfort and salivation are usually mild and acceptable with most symptoms subsiding when treatment is continued.[86,87] On the long-term MRA therapy may result in (permanent) alterations in the dental occlusion.[83] The precise long-term effects of therapy on the stomatognathic system are, however, largely unknown. Treatment with an MRA should not be contemplated in case of extensive periodontal disease and dental decay, and restrictions in mouth opening or advancement of

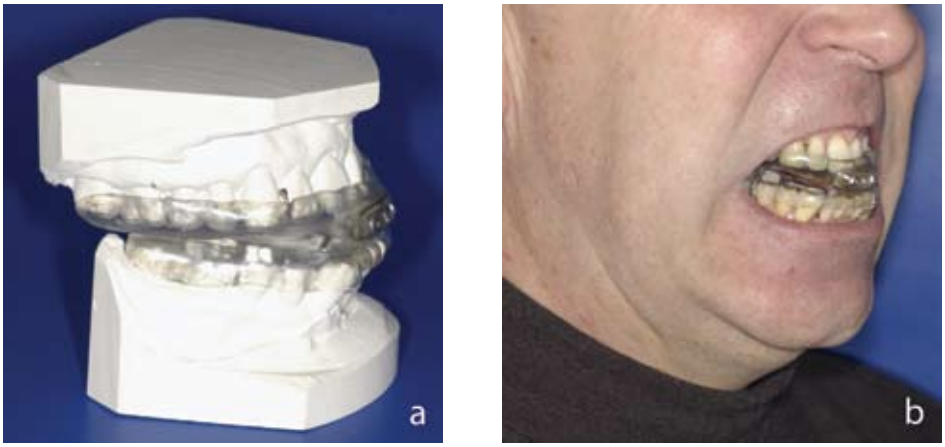

FIGURE 7. Mandibular repositioning appliance.

(a) Mandibular repositioning appliance (MRA) placed on plaster casts following the construction in a dental laboratory; (b) patient while wearing the MRA, the appliance secures the mandible in an anterior position (Figure adopted from; Hoekema A, Wijkstra PJ, Buiter CT, van der Hoeven JH, Meinesz AF, de Bont LGM. Treatment of the obstructive sleep-apnoea syndrome in adults. *Ned Tijdschr Geneeskd* 2003;147:2407-2412).

the mandible. Relative contraindications for treatment include active temporo-mandibular joint disorders or an insufficient number of teeth to support and retain the appliance. According to recommendations of the American Sleep Disorders Association from 1995, oral-appliance therapy should be considered in patients with primary snoring or mild OSAHS who do not respond to or are not appropriate candidates for behavioral measures (*e.g.*, weight loss or regulation of sleeping position).[85] In moderate to severe OSAHS, the recommendation is to consider oral-appliance therapy when patients do not tolerate or refuse CPAP, and when patients are no candidate for or refuse surgical intervention. Recent reports demonstrating the effectiveness of oral appliances in moderate and severe OSAHS probably necessitate redefinition of these recommendations.[88]

Epilogue

Since the first scientific descriptions of OSAHS in the mid-sixties, treatment of this sleep-related breathing disorder has evolved to a multidisciplinary approach. Where formerly symptomatic OSAHS patients could only be treated with a tracheotomy, clinicians currently have the disposal over a great variety in treatment options. It may seem obvious that a choice for a specific or combination

of conservative, non-invasive or surgical treatment modalities is tailored to the individual patient's characteristics and needs. Against this line of thought, it should be stated that for implementation of most of the treatment modalities as primary intervention for OSAHS there is insufficient scientific evidence. When conservative measures or the correction of morphological airway abnormalities are not successful or indicated, CPAP therapy is currently the evidence-based standard for OSAHS treatment. Consequently, many of the treatment alternatives for OSAHS are used as secondary intervention. As CPAP therapy requires wearing an obtrusive device, patients may abandon or adhere poorly to therapy. Especially this is the case in milder and asymptomatic variations of OSAHS. Against this background, oral appliances may serve as an adequate treatment alternative. Before the specific role of oral-appliance therapy in the management of OSAHS may be defined, additional studies are required evaluating the indication, effects on neurobehavioral and cardiovascular outcomes, patient compliance and side-effects relative to CPAP therapy.

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