REPORT

Floppy Eyelid Syndrome and Obstructive Sleep Apnoea

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SUMMARY

Floppy Eyelid Syndrome and Obstructive Sleep Apnoea
Floppy eyelid syndrome (FES) is a relatively rare condition of unknown aetiology, commonly described in association with other systemic conditions, particularly with obstructive sleep apnoea – OSA (the most frequent and most significant sleep-related breathing disorder in terms of morbidity and mortality). It is characterized by an extremely enlarged and floppy upper eyelid which can be very easily everted (often spontaneously during sleep). The laterality of the disease corresponds to the side the patient sleeps on. The patient may also present with upper lid ptosis, lash ptosis or trichiasis, lower lid ectropion, chronic papillary conjunctivitis, and chronic corneal disorders. The aim of this study is to report this syndrome, which is often overlooked in eye clinics, and to summarize our experience with its diagnosis and treatment. The correct and early diagnosis of FES may be a clue to the correct diagnosis of, at the time of FES diagnosis, unknown OSA.

Key words: floppy eyelid syndrome, conjunctivitis, obstructive sleep apnoea, snoring
Čes. a slov. Oftal., 68, 2012, No. 1, p. 22-28

INTRODUCTION

Floppy eyelid syndrome (FES) is a disorder characterised by chronic papillary conjunctivitis, which practically does not respond to regular local therapy, and pronounced laxity of the upper eyelid. The upper eyelid is soft and easily evertable. Spontaneous eversion occurs especially during sleep. Affliction may be unilateral. In this case it mostly concerns the eyelid on the side on which the patient prefers to sleep. If both eyelids are afflicted, the patient usually sleeps on the stomach or alternates between both sides. The disorder mostly affects obese men in middle age (BMI – body mass index above 30). It is precisely these patients who are frequently associated with FES with obstructive sleep apnoea (OSA). This system involves intermittent and repeated obstruction of the upper respiratory tracts during sleep, which leads to arrests of breath (apnoeic or hypopnoeic pauses) and a subsequent decrease of saturation of haemoglobin by oxygen. Snoring and frequent micro-awakenings considerably disturb sleep patterns. During the day patients with OSA complain primarily of increased fatigue, somnolence, microsleeps and falling asleep during monotonous activity. It leads to a development of serious cardiovascular complications, frequently in connection with metabolic syndrome. Morbidity and mortality of these patients increases. Eye complaints, most frequently FES, can be an important guide to determining the correct diagnosis and subsequently also treatment of OSA.

FLOPPY EYELID SYNDROME

Definition

The term “Floppy Eyelid Syndrome” was first used in 1981 by Culbertson and Ostler (9) in the case of 11 obese men with a finding of a markedly lax upper eyelid, signs of papillary conjunctivitis on the tarsal conjunctiva and signs of chronic eye irritation. All of these patients stated spontaneous eversion of the upper eyelid upon minimal mechanical stimulus. They complained subjectively of non-specific eye complaints with the character of burning, stinging and lacrimation. If they had these symptoms only on one side, this was the side on which they preferred to sleep. Further publications followed in the English and German speaking literature focusing on this disorder, which was referred to in the English speaking literature as “Floppy Eyelid Syndrome” and in the German literature as “Das Syndrom des Schlaffen Oberlides” (26). Since this time FES has also been described in women, children, patients with diabetes, hypertension and mental retardation. For these patients, who did not meet the original criteria (obese men in middle age), a new term “Lax Eyelid Syndrome” was introduced. However, the majority of ophthalmologists do not differentiate between these two syndromes.

Clinical manifestations

Symptoms of FES can be highly variable. The most frequent complaints suffered by patients are: feeling of dry eyes, feeling of foreign body in eye, reddening, lacrimation, hazy vision and general “eye discomfort”. Patients sometimes state occasional reddening and swelling of the eyelids. These symptoms may be both unilateral and bilateral. In a targeted questionnaire patients may state spontaneous eversion of eyelids (especially during sleep). These eye complaints are frequently stated as a reason for repeated awakening during the night. The complaints are generally manifested more on the side on which patients prefer to sleep (28). Upon a clinical examination of patients with FES, we are initially struck by pronounced dermatochalasis and potentially also slight ptosis of the upper eyelid, which is generally on the side of the more

accentuated finding (fig. 1). The eyelids are very lax in the vertical and horizontal direction (fig. 2a, b). Upon minimal pulling in an upwards direction the eyelids spontaneously evert and there is a perceptibly soft and yielding tarsus (fig. 3). Another clinical symptom which we find in patients with FES is "lash ptosis" (20). This concerns a twisting of the eyelids in various directions and a loss of their parallel positioning, probably as a consequence of loss of support of the tarsus and orbicular muscle. A typical, though diagnostically misleading finding is also chronic papillary conjunctivitis, in particular a "velvety" appearance of the tarsal conjunctiva of the upper eyelids. Damage to the cornea may also result as a consequence of long-term persistence of the disorder. The prevalence of punctate keratitis is stated in as many as 45% of cases (10). In rare cases more serious corneal complications may occur – non-healing corneal defects, recurring erosions, deep neovascularisation and subepithelial scarring of the cornea (13, 28). The clinical picture may also include unstable lacrimal film and manifestations of dry eye syndrome (22). The clinical eye symptoms which have been described in connection with FES are summarised in table 1.

Pathophysiology

Since 1981, when this syndrome was first described, several hypotheses have been submitted concerning the origin of FES. Culbertson and Ostler (9) assumed that spontaneous eversion of the upper eyelid during sleep causes mechanical trauma and leads to the occurrence of papillary conjunctivitis, keratinisation of the conjunctiva and change of elasticity of the tarsus. They based this theory on the observation that the finding was worse on the side on which the patient preferred to sleep. This theory was also confirmed by Mazal (26) in his own observations. Later genetic predisposition was also considered, in particular abnormality of collagen and elastin (36). Suspicions have also been expressed of a relationship between hyperglycaemia and FES (15). The greatest attention at present is being devoted to relationship between FES and OSA (in particular the possible influence of systemic hypoxia). Suspicions have been expressed that eversion of the eyelid and its mechanical compression against the pillow occurs during sleep due to disturbed sleep and numerous hypopnoeic and apnoeic pauses. As a consequence of this, ischemia of the eyelid tissue takes place, followed by reperfusive damage thereto (10, 22) after the release of compression against the pillow (during micro-awakening). Ischemic-reperfusive damage to the eyelid tissue is then contributed to also by systemic hypoxia. The cornea comes into contact with the pillow, and mechanical damage of the cornea may occur. This mechanism is schematically demonstrated in fig. 4. This theory is in accordance with the fact stated above, that FES is generally more accented on the side on which the patient prefers to sleep. We have recorded this fact several times also on our own patients (fig. 5).

Histopathological findings have demonstrated that the structure of collagen in the eyelid is normal. However, a reduced quantity of elastin has been demonstrated in the tarsal

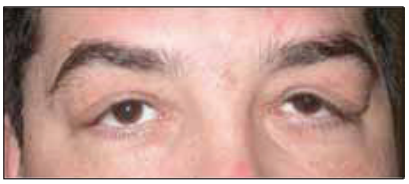

Fig. 1. Pronounced dermatochalasis to twisted buckling of eyelids in patient with severe FES and OSA, finding more accentuated on left side

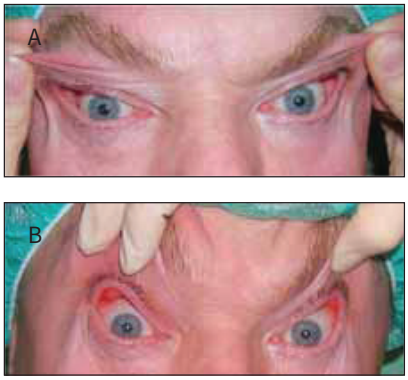

Fig. 2. Very lax upper eyelids in horizontal (a) and vertical (b) direction

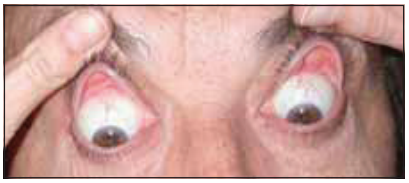

Fig. 3. Upon slight pulling upwards the eyelids spontaneously evert, tarsus is soft and yielding

Table 1. Clinical eye manifestations described in connection with FES

Dermatochalasis
Lax eyelid
Soft yielding tarsus
Semi-ptosis of upper eyelid
Papillary conjunctivitis
Lash ptosis
Trichiasis
Ectropium
Chronic blepharitis
Meibomitis
Punctal keratitis
Corneal neovascularisation
Corneal erosion
Corneal ulcer
Pseudopterygium

FES and with shallow eye sockets (1). The most attention recently has been paid to the possible relationship of FES and OSA towards normotensive glaucoma, open angle glaucoma and optic neuropathy (3, 7, 37). It is assumed that the stated clinical units could be a form of manifestation of chronic systemic ischemia, which occurs during episodes of sleep apnoea.

Fig. 4. Theory of origin of FES upon OSA – eversion of the eyelid occurs during disturbed sleep, with mechanical compression against pillow, ischemia and subsequently reperfusive damage, cornea comes into contact with pillow

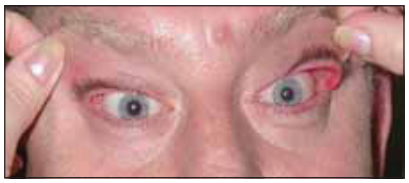

Fig. 5. Asymmetrical FES (more on left side) in patient with OSA, who mostly sleeps on left side

Fig. 6. Typical predisposition towards fat deposit in the neck area in obese patient with OSA

plates and in the surrounding area of the adjacent tissue (36). The remaining fibre of the elastin showed ultrastructural abnormalities and increased expression of elastin-degrading enzymes (MMP-7, MMP-9). On the basis of these finding the assumption was expressed that chronic mechanical stress (repeated eversion and compression of the eyelid) leads to "up-regulation" of elastolytic enzymes (matrix metalloproteinases) and subsequent degradation of elastic fibres. The result of this process is extremely increased laxity of eyelids. Very lax eyelids then have insufficient contact with the eyeball, which leads simultaneously with dysfunction of the meibomian glands and abnormalities of the lacrimal film to manifestations of keratoconjunctivitis, or even more serious damage to the cornea.

Associated eye disorders

A number of works have been published which dealt with the relationship between FES and other eye disorders. Attention has been devoted to the relationship between keratoconus and FES, the mutual association of these two disorders is stated in 1-17% of cases (10, 12, 20). One case of spontaneous luxation of the eyeball has been described in a patient with

Associated general disorders

The association of FES and obstructive sleep apnoea has been unequivocally demonstrated (28). Cases of remission of FES after successful therapy of OSA have been described in the literature (29). A higher frequency of occurrence of FES has also been observed in patients with other sleep disorders, but to a far lower degree. FES has also been described in mentally retarded patients (6). In this case the cause of pronounced laxity of the eyelids is considered to be repeated "rubbing" of the eyelids, which causes mechanical trauma of the eyelid tissue. We have recorded this "mechanical" theory of the origin of FES in practice in two of our patients. The first patient with mental retardation had clear symptoms of floppy eyelid syndrome, which was more accentuated on the left side. The cause was evidently repeated rubbing of the eyes, which we witnessed repeatedly, and which was also confirmed by the patient's mother. In the second case this concerned a patient with bilateral total ptosis of the eyelid upon paresis n. III following a neurosurgical procedure. The patient over a long period "unstuck" one of her eyelids, or lifted it by hand. The eyelid was markedly lax and showed all the signs of floppy eye syndrome – in comparison with the other side, where the finding was within the norm.

In a small number of cases this syndrome has been described in patients with psoriasis, with disorder of the conjunctival tissue (Marfan syndrome, pseudoxanthoma elasticum, Ehler-Danlos syndrome), or in patients addicted to cocaine. The systemic disorders which have been described in patients with FES are summarised in table 2.

Therapy

Therapy of FES can often be onerous. Symptomatic therapy consists primarily of abundant local application of lubricants in the form of drops, gels or greases. We recommend that patients cover the eyes during the night, most preferably with an eye patch. With regard to the fact that this syndrome is frequently overlooked and patients are listed under a diagnosis of chronic keratoconjunctivitis of various origin, in the anamnesis we encounter repeated local application of antibiotics, lubricants, non-steroid antiphlogistics or steroid preparations, mostly without general success. Local therapy has a rather supportive effect in this

Table 2. General disorders associated with FES

Obstructive Sleep Apnoea syndrome
Obesity
Hypertension
DM
ICHS
Cerebrovascular disorders
Mental retardation
Psoriasis
Disorders with hyperextensibility of skin and hypermotility of joints
Atopic eczema
Pachydermoperiostosis
Acne rosacea
Menkes syndrome
Corneal ulcer
Pseudopterygium

syndrome, and is very important before the actual definitive solution of the problem, which consists of therapy of OSA (if present) and also of a surgical procedure on the eyelids.

A whole range of surgical procedures have been described for treatment of FES. Partial tarsorraphy, frequently used in the past, is no longer used, or used only in exceptional cases for this syndrome. The basis of the surgical solution at present is horizontal shortening of the upper eyelid in its full thickness. A whole range of surgical procedures have been published (14, 24, 34). The most widely used techniques are presented in the following summary:

1. Hexapentagonal wedge resection of the upper eyelid in its lateral and medial part ranks amongst the standard, frequently used procedures in horizontal shortening of the eyelid. Nevertheless, the cosmetic effect is not entirely ideal. In particular the vertical scar, which is perpendicular to the fold of the skin, may have a highly undesirable effect. As a result other modified procedures have been developed.
2. Wedge resection with a shift in the temporal part of the eyelid is a more complex surgical procedure, nevertheless it has a markedly superior cosmetic effect.
3. The modified procedure according to the German authors Kluppel and Sundmacher consists of horizontal shortening of the eyelid up to 50%

of its width, an oval resection of the tarsus in the full thickness of the eyelid and subsequent excision of excess skin. This procedure is recommended only in severe cases. Upon this method of solution it is necessary also to be aware of the danger of hypercorrection.

OBSTRUCTIVE SLEEP APNOEA SYNDROME

Definition

According to the International Classification of Sleep Disorders, obstructive sleep apnoea (OSA) is classed amongst sleep-related respiratory disorders (32). Sleep apnoea is defined as an occurrence of arrests of breath during sleep (apnoeic and/or hypopnoeic pauses), with a duration of at least 10 seconds and which repeat more than five times per hour of sleep. It simultaneously causes awakening or awakening reactions. Apnoea means an interruption of the flow of air through the nose or mouth. Hypopnoea is a transitory restriction of the breathing volumes by at least 50% of the normal value, mostly with a decline in saturation of haemoglobin by oxygen by at least 3%. Apnoea is considered obstructive if breathing exertion persists within its duration – breathing exertion is not present in central apnoeas (38). OSA ranks amongst the most frequent and significant respiratory disorders during sleep from the perspective of morbidity and mortality.

Pathophysiology

From the perspective of pathophysiology, this represents a disorder of local neuromuscular reflexes in maintaining pharyngeal flow. A repeated collapse of the upper respiratory tracts occurs during sleep. Transitory obstruction during snoring is caused by a slackening and "suction" of the walls of the oropharynx, with interruption or restriction of the flow of air (apnoeic or hypopnoeic pauses) and a subsequent reduction in saturation of haemoglobin by oxygen, which results in transitory hypoxemia. The triggering cause of apnoea may be an anatomical obstacle in the area of bone structures or soft tissues (hypertrophy of tonsils, enlargement of uvula, extension of soft palate, fat deposit beneath the hypopharynx mucous membrane, macroglossia, in children most frequently adenoid vegetation).

One of the most significant causes of hypertrophy of soft tissues is obesity (23). The depositing of fat predominantly in the upper half of the body increases the external pressure on the pharyngeal wall, and influences the collapsibility of the respiratory tracts (fig. 6). The collapse of respiratory tracts may be on the level of the soft palate, the root of the tongue, or multilevel. The position of lying on the back also predisposes the patient to OSA by gravitational methods and causes a shift of the tongue in a backwards direction (11). Various studies have also shown that the pathophysiology of OSA is genetically predetermined, and have demonstrated a positive family anamnesis of OSA as an important risk factor (35).

The occurrence within the population is stated by various authors most often within the range of 2-9%, with a predominance of men. Although OSA was traditionally regarded as a disorder which affects men, a prevalence is ever increasingly being determined also in women, primarily after menopause (43). There is a higher recorded prevalence of OSA in patients with hypertension (30 – 83%), heart failure (12 – 53%), ischemic heart disease (30 – 58%) and stroke (43 – 91%) (8).

Clinical manifestations

The clinical picture has a varying degree of seriousness. The consequences of this sleep disorder are manifested also during an awakened state. The symptoms can be divided into night and day symptoms. Night symptoms are typified by snoring, apnoeic/hypopnoeic pauses during sleep, awakening with a feeling of shortness of breath, gasping for air during awakening reactions, micro-awakenings, disturbed sleep, and nocturnal polyuria, nocturnal perspiration and heart arrythmia may occur. Day symptoms most frequently include hypersomnia and falling asleep during monotonous activities as a result of sleep fragmentation. Typical symptoms are microsleep, morning fatigue with a feeling of sleep deficit or lack of rejuvenation from sleep, headaches and a feeling of dryness in the mouth and throat. Lapses of concentration occur, as well as deterioration of working performance, depressive mood and potential sexual dysfunctions.

Night sleep deprivation, recurrent hy-

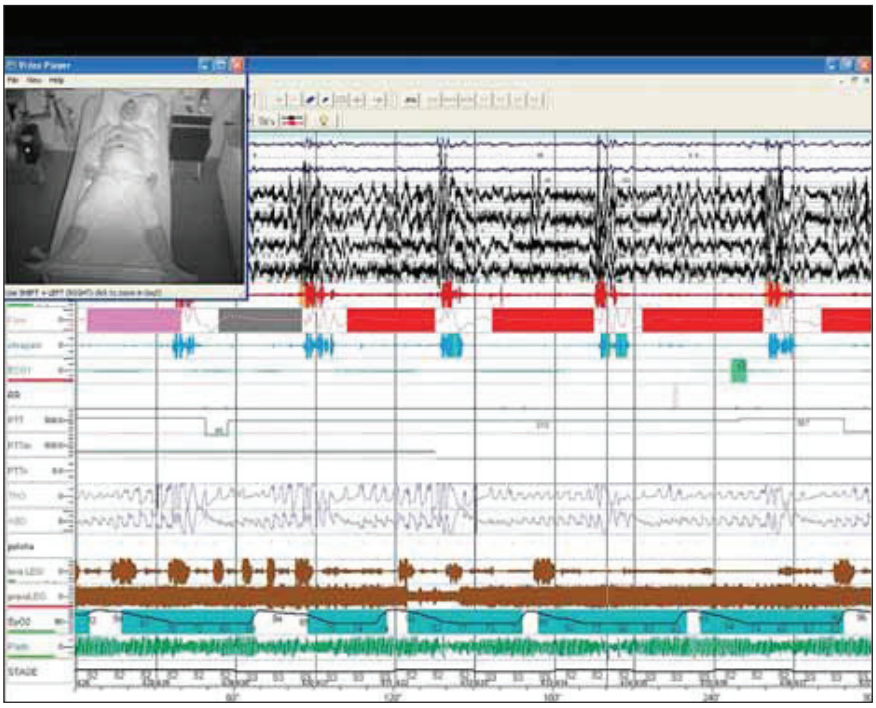

Fig. 7. Five-minute part of recording of video polysomnography – in the left corner of the recording on the screen is a patient who is recorded by a camera in infrared light. The first two rows are the EOG recording, lower is the EEG recording (highlighted red lines indicated micro-awakening). There follows the row of air flow with perceptible arrests of breath – apnoeic pauses (indicated by red rectangles). Between the apnoeic pauses, snoring is indicated in blue. In the lower part of the recording, the decrease in saturation of blood by oxygen is indicated in blue-green – evident decrease to 62% SaO_2.

poxia and activation of the sympathetic nervous system during the course of sleep may have undesirable metabolic and cardiovascular consequences (8, 40, 31). OSA causes endothelial dysfunction and accelerates the onset of atherosclerosis (16). The results of numerous studies have convincingly demonstrated an independent linkage of OSA and hypertension. This linkage is also supported by studies which demonstrate a drop in blood pressure during treatment by CPAP (2, 5, 17). A high percentage of patients (up to 40%) with resistant primary hypertension have undiagnosed sleep apnoea (4). Today OSA is considered one of the frequent causes of secondary hypertension, nocturnal hypertension and pharmacoresistant hypertension

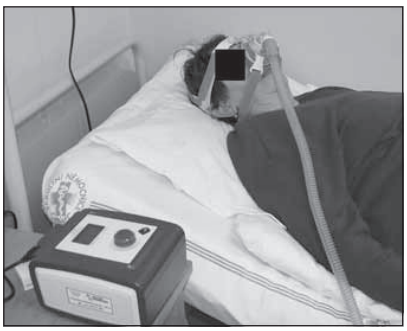

Fig. 8. Treatment of OSAS using a continual positive airways pressure machine

(5). Ischemic heart disease (IHD), heart arrhythmia and heart failure also occur more frequently in the case of OSA (40). Up to four times higher occurrence of strokes is described in these patients than in the rest of the population, as a result of a lower supply of oxygen to the CNS during apnoeic pauses (42). It is demonstrated that OSA increases mortality in the case of stroke (33). Further studies demonstrate that treatment of CPAP reduces the risk of jaundice, new stroke and death is in these patients (25). Numerous works also describe the linkage of OSA and metabolic syndrome (21).

DIAGNOSIS

The diagnosis is based on anamnestic data and questionnaire investigation with quantification of daily somnolence and subsequent polysomnographic examination in a sleep laboratory during the course of nocturnal sleep. The gold standard and most precise examination is full polysomnography (PSG). Parallel recording of electroencephalography (EEG), electromyography (EMG) and eye movements – electrooculography (EOG), which assist designation of the phase of sleep also takes place during this examination. Breathing sounds are also registered and recorded, and the patient is recorded on a video camera in infrared lighting (fig. 7). Upon the use of polysomnography there is a possibility, in contrast with limited polygraphy, to record micro-awakenings (32).

Therapy

Therapy is always complex. First of all are regime measures, in which one of the most important susceptible risk factors for OSA is reduction of mass. There follows conservative therapy – most frequently CPAP – continuous positive airway pressure. This represents continuous pressure applied b a nasal (or less frequently full face) mask into the respiratory tracts (fig. 8). This pressure prevents vibration and constriction of the slackened walls of the oropharynx. CPAP acts as a “pneumatic splint” in the respiratory tracts. Another possibility is surgical therapy, which is indicated in the case of a removable anatomic obstacle. Surgical procedures, today frequently performed using laser, can be divided into the area of the nose and nasopharynx, the area of the velopharyngeal channel and the retrobasilingual area (19). In indicated cases stomatosurgical procedures are performed.

DISCUSSION AND CONCLUSION

Floppy eyelid syndrome is a disorder which is very frequently overlooked or treated for long periods under another diagnosis. Despite the latest observations its pathophysiology remains to a large extent unknown. For clinical practice its demonstrated association with obstructive sleep apnoea is very important. In 2005 McNaab (30) analysed 50 patients with FES and determined that 96% of them had symptoms of OSA. In his previous study he determined that those patients with OSA who also had clinical manifestations of OSA had a larger number of apnoeic pauses during sleep and diminished saturation of haemoglobin by oxygen. In 2006 Karger et al. (18) confirmed his hypothesis. On the basis of current observations it is therefore possible to conclude that the majority of patients with FES suffer from OSA. However, this linkage does not apply in reverse (27). Only a part of patients with OSA have clinical manifestations of FES – and these are mostly patients with more severe manifestations of OSA, thus with a higher risk of morbidity and mortality. Each patient with diagnosed FES should undergo a polysomnographic examination in a sleep laboratory in order to exclude the possibility of OSA. If OSA is diagnosed in a patient, it is recommended first of all to apply continuous positive airways pressure (CPAP) to the patient. This treatment prevents the constriction of the slackened walls of the oropharynx during sleep and thus prevents the occurrence of apnoeic pauses, the decrease in saturation of haemoglobin by oxygen and numerous micro-awakenings. If OSA is not treated there is a high probability that even despite successful surgical therapy of FES there will in time be a recurrence of eye complaints. By contrast, upon successful therapy of OSA there may be a regression of eye complaints. Conservative therapy of FES is important, in more severe cases however surgical solution is necessary. According to our experiences with the patients with FES we have treated at our outpatient clinic, the most frequent problems which caused patients to seek the attention of an ophthalmologist were: lacrimation, reddened eyes (especially following injury), stinging and repeated inflammations of the conjunctiva. Patients with FES frequently also attend the clinic for ocular plastic surgery with a request for correction of dermatochalasis. Our experiences with the correction of dermatochalasis in patients with already diagnosed and treated apnoea are good, we have not recorded any postoperative complications. We have been forced to perform more extensive surgical correction of the upper eyelids (wedge resection with shift in temporal part of eyelid) on only one patient. This was a patient with untreated severe OSA. Eye complaints (spontaneous eversion of eyelids during sleep, repeated inflammations) caused the patient to seek medical attention and subsequently led to the determination of the correct diagnosis of OSA. After treatment of OSA and surgical correction of the upper eyelids the eye complaints were corrected. The patient evaluated the greatest benefit to be a return to normal life – without microsleeps, fatigue or lapses of concentration during the day.

Timely diagnosis and treatment of OSA can significantly improve patients’ quality of life. Thanks to its curing of excessive snoring which disturbs others, this also increases the quality of life of the patients’ partners. The fundamental pillar of successful treatment remains timely diagnosis. This requires close interdisciplinary co-operation and a good level of informedness about this issue.

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