Acta Otorrinolaringol Esp. 2009;**60(3):**202-7

Acta Otorrinolaringológica Española

www.elsevier.es/otorrino

REVIEW ARTICLE

Obstructive sleep apnoea syndrome in children

José A. Maltrana-García,* Mahfoud El Uali-Abeida, Laura Pérez-Delgado, Isabel Adiego-Leza, Eugenio A. Vicente-González, and Alberto Ortiz-García

Hospital Universitario Miguel Servet, Zaragoza, Spain

Received July 18, 2008; accepted November 26, 2008

KEYWORDS
Obstructive sleep apnoea;
Children;
Sleep disorders;
Surgical treatment;
Pharmacological treatment;
Leukotriene

Abstract
Obstructive sleep apnoea syndrome is a well-known clinical entity in adults but until now it has been less well studied in children. In recent years there has been a dramatic increase in the recognition of sleep disorders in children. Our goal is to analyze scientific data published in the last few years. We reviewed published articles regarding paediatric obstructive sleep apnoea syndrome and extracted the clinical symptoms, diagnosis and treatment options. In conclusion, the natural course and long-term prognosis of childhood obstructive sleep apnoea syndrome are not well-known and further studies are needed in this area.

PALABRAS CLAVE
Apnea obstructiva del sueño;
Niños;
Trastornos del sueño;
Tratamiento quirúrgico;
Tratamiento farmacológico;
Leucotrienos
Síndrome de apnea obstructiva en niños

Síndrome de apnea obstructiva en niños

Resumen
El síndrome de apnea obstructiva del sueño es una entidad bien conocida en adultos, pero hasta ahora ha sido menos estudiada en niños. Recientemente se ha producido un importante incremento en el reconocimiento de los trastornos del sueño en la etapa infantil. Nuestro objetivo es analizar los estudios científicos publicados en los últimos años. Hemos revisado artículos publicados acerca del síndrome de apnea obstructiva en edad pediátrica y hemos estudiado la sintomatología, el diagnóstico y las opciones de tratamiento. En conclusión, el curso natural y el pronóstico a largo plazo del síndrome de apnea obstructiva en la infancia no son bien conocidos, por lo que se necesitan más estudios en esta área.

*Corresponding author.
E-mail address: jamaltranagarcia@hotmail.com (J.A. Maltrana-García).

0001-6519/$ - see front matter

Introduction

Obstructive sleep apnoea syndrome (OSAS) is a frequent entity in the paediatric population, with significant morbidity and, in recent years, attracting increasing interest.

The first historical reference in children was made by William Osler in 1892, but it was not until 1976 that the first article was written by Guilleminault on OSAS in children.

Despite the growing literature published recently, as we shall see in this article, there are still significant gaps that must be studied properly.

In primary snoring (PS), there is a respiratory noise without accompanying apnoeas, hypoventilation, or hypoxemia. Nor are there alterations in the sleep pattern or any daytime symptoms. It is present in 7%10%of children.[1] The factors that predispose towards PS are the same as in OSAS, the most common being hypertrophy of the tonsils.

In the upper airway resistance syndrome (UARS), children snore and have a partial blockage of the upper airway, causing episodes of increased respiratory effort that end in a micro-awakening. They do not have apnoeas, hypopnoeas or gas exchange alterations, but they do have a disturbed sleep pattern.

OSAS is defined as a sleep-related breathing disorder characterized by a prolonged partial obstruction of the upper airway and/or intermittent complete obstruction (obstructive apnoea) that disrupts normal ventilation during sleep and its normal patterns. Concomitant symptoms include: habitual snoring at night, difficulty in sleeping, and/or behavioural problems during the day.[2]

The relationships between PS, UARS, and OSAS are not sufficiently clear at present. Some authors feel that these entities represent an evolution, with OSAS as the final stage.[3,4] It seems that the PS does not progress to OSAS in the short term,[5,6] but the call for long term studies is unanimous. Guilleminault et al[7] cast doubt over the existence of PS, since a health problem, however small, is always found on thorough investigation.

Although the prevalence of PSis 10%12%,[6,8] that of OSASis around 0.7%3%in most published studies.[1,6,9,10] The average age of onset of apnoea was 34 months, approximately, while that of PSis 22 months. The highest prevalence is observed between 2 and 8 years,[5] when the adenotonsillar tissue is bulkier relative to the size of the airway.

There are important differences in this disease depending on whether it occurs in children or in adults.[11] These differences are outlined in Table.

The classic description of the snoring, obese patient with daytime drowsiness only corresponds to a small proportion of children, who are usually hyperactive during the day.[5,6]

The most frequent cause in children is adenotonsillar hypertrophy, while in adults the collapse is in the uvula, soft palate and posterior pharyngeal wall.

In adolescents and adults the phenomenon predominates in males, whereas in children the prevalence is equal in both genders.[5]

But more than total and cyclical obstructions, which are observed in adults, children present long-term partial obstructions (obstructive hypoventilation).[1,4] In contrast, desaturations are more important in children. For children the rate of pathological apnoeas[4,12] is >1, while in adults it is >5.

The treatment is not to control daytime symptoms in adults, but to avoid long term complications.[6]

For these reasons, today it is unclear whether OSAS in children is a different entity from that observed in adults.[5]

Predisposing factors

Factors that predispose to infant OSAS are those affecting the airways or their neurological control. Two main groups of factors can be distinguished: anatomical and functional. During inspiration an intense negative pressure is produced which collapses tissue inwards, counteracted by the action of the dilator muscles of the pharynx. Anatomical factors produce an increase in the resistance of the upper airway and functional factors affect the operation of the dilator muscles. Under normal conditions there is equilibrium between the negative inspiratory pressure, which tends to collapse the airway, and its relaxation by pharyngeal dilator muscles.

The most important anatomical factor is adenotonsillar hypertrophy, in addition to nasal obstruction, macroglossia, gastroesophageal reflux, obesity, surgery of the cleft palate, laryngomalacia, and craniofacial anomalies or genetic syndromes (achondroplasia and Apert, Beckwith-Wiedemann, Crouzon, Down, Pierre Robin, Treacher Collins syndromes, etc).

Moreover, the functional factor of greatest interest is pharyngeal hypotonia in REMphase, in addition to repeated infections of upper airways, neuromuscular disorders (muscular dystrophy, cerebral palsy), hypothyroidism, cerebrovascular affectations, medication and drugs.

The activity of dilator muscles is reduced in the REM phase, so childhood OSAS could be considered a disease of this stage of sleep.[6]

Many authors refer to the importance of this combination of structural and neuromuscular factors.[5,13] This idea is reinforced by the lack of correlation between the

Tabla Differences between children and adults

	Children	Adults
Age , years	2 6	45 55
Gender	M=F	M>F
Obesity	Infrequent	Frequent
Adenotonsillar hypertrophy	Infrequent	Very frequent
Daytime drowsiness	Normal	Altered
Sleep architecture	Variable	>10 s
Duration of pathological apnoeas	>1	>5
Pathological apnoea index	Infrequent	Frequent
Daytime behaviour	Hyperactivity	Cognitive alterations
Surgical treatment	AT	UPPP
Medical treatment	Occasional CPAP	CPAP
Tratamiento médico	CPAP ocasional	CPAP

AT indicates adenotonsillectomy; CPAP, continuous positive airway pressure; F, female; M, male; UPPP, uvulopalatopharyngoplasty.

adenotonsillar size and the severity of OSAS[14] and that it is not always cured after adenotonsillectomy (AT).

Symptoms

The most characteristic symptom during sleep is snoring, but respiratory pauses, restlessness with constant movement, sweating due to the respiratory effort, and enuresis can also be appreciated. During the day most children have no symptoms, although there can be behavioural disorders such as restlessness, hyperactivity, poor school performance, in addition to the typical symptoms caused by adenotonsillar hypertrophy.

There are many consequences of not diagnosing and treating OSAS in such vulnerable subjects, who are in the midst of physical and mental development.[8,10,15] Any degree of nocturnal hypoxia is detrimental to children in the process of neuropsychological development.[6]

Many children with OSAS have impaired weight and height and, as we shall see, will respond to appropriate treatment (growth hormone is affected in children with OSAS and PS).[16]

The cardiovascular system is also altered and an increase in blood pressure has been observed in these children, which can reach *cor pulmonale* in extreme cases.

The cognitive and behavioural changes sometimes presented by these children are important, and generally improve with appropriate treatment.[8]

Diagnosis

The diagnostic criteria for an adult cannot be extrapolated to a child. Another fundamental idea is that OSAS and PS can not be distinguished solely by clinical and physical examination.[10,17] Nor are there any pathognomonic signs.

Night-time polysomnography (PSG) is, without doubt, the reference standard for diagnosis of OSAS. However, its implementation and interpretation in children have not been standardized or evaluated for different age groups.[18] Nor are there studies correlating PSG results with clinical evolution; and the degree of abnormality that requires treatment is unknown.[5] Although there are studies with normal PSG values in children,[12] the diagnostic criteria of OSAS are not well defined. For the American Thoracic Society an apnoea-hypopnoea index (AHI) >1 per hour is diagnostic of OSAS. According to Harvey,[1] the disorder would be mild if 1>AHI<5/hour, moderate if 5>AHI<9, and severe if AHI>10 per hour.

Daytime PSG is limited by the shorter time of sleep and duration of the REM stage.[5]

Night-time pulsioximetry can identify children at high risk. It is a good method to evaluate children with suspected OSAS and reduce the waiting list for a PSG. A nocturnal pulsioximetry with 3 or more desaturations <90% has up to 97% positive predictive value for OSAS in children without other health problems[19]. For other authors,[6] if the pulsioximetry is pathological and there is clinical suspicion of OSAS, then the diagnosis is practically complete. Depending on the severity of this test, it can indicate the urgency of treatment.[8,19] However, when this test is normal, it does not exclude OSAS (negative predictive value of 47%) and a nocturnal PSG would be required.

Other techniques, such as video and audio recordings at home, require further studies on their sensitivity and specificity.

There is no conclusion in the literature about the minimum degree of apnoeas and hypopnoeas that can be used as a clinical guide to indicate surgery.[4,13]

Treatment

Adenotonsillectomy is the treatment of choice for OSAS in children given that adenotonsillar hypertrophy is the anatomical factor most predisposing them to suffer this condition. With regard to adenotonsillectomy, the latest Cochrane Review[3] concludes that, because there are not enough double-blind studies, the effectiveness of AT needs more research. The available evidence suggests that AT is often effective in the treatment of OSAS, but further studies are required to compare the difference between applying AT or not. Other authors[20] also share the view that the benefit has not been well established in research-based evidence.

Because the most common aetiology is adenoid hypertrophy, it is logical to think that AT is the basis for the treatment of OSAS in children. It is the most effective and most widespread treatment among all surgeons and has approximately a 75% success.

A recent review article[21] states that AT is effective, with a cure rate (normalization of PSG) of 82.9%. In contrast, several papers cast doubt on the efficacy of isolated adenoidectomy.[4,8,9]

Frank et al, in 1983, were the first to use PSG to analyze the effect of AT on OSAS. Zuconi et al obtained a 100% cure in 29 children with AT and 0% in 5 children with isolated adenoidectomy. Multiple studies show the effectiveness of AT.[4,8,9,22,23] It has also been effective in obese children.[17] Research has been done on improving the clinical symptoms after AT in patients with normal PSG with respect to those not operated on[24] as well as the improvement of PS after AT.

Recent studies show the relationship between OSAS and growth hormone, and its improvement after AT.[25,26] In 41 children operated on with AT, Williams et al[27] noted an improvement in the percentile of weight in 75% of them. Nieminem et al,[16] in 70 children, reported an improvement in weight, height, and body mass index in those who had undergone surgery.

Another aspect which is studied is the improvement in hyperactive behaviour, emotional symptoms and, in general, the quality of life, according to the carers of children who had undergone AT.[28-32]

Despite these findings, AT is not effective in all cases. Children diagnosed with severe OSAS are those with the poorest cure rate after adenotonsillectomy.[33] Other studies[34,35] confirm the increased persistence of OSAS in obese children after surgery. Guilleminault et al[9,36] suggest that there are no reviews of the reason for the failure of AT and feel that this is due to not treating other craniofacial malformations simultaneously.

Suen, who achieved a cure rate of 85%, gives the absence of snoring after surgery a negative predictive value of 100% (if they do not snore, the treatment does not fail) and a

positive predictive value of 57%(if they snore, 57%will have a pathological PSG). Nieminem et al[4] also give a negative predictive value of 100% and believe there should be a reassessment after surgery if they continue snoring or if the preoperative AHI was high.

Unlike in adults, uvulopalatopharyngoplasty is a technique seldom used in children. It is used in neuromuscular diseases, cerebral palsy and cerebrovascular accidents. There are some published studies[37] with this technique in conjunction with AT in children with neurological disease and OSAS but they conclude that it is necessary to carry out more long-term monitoring. In another study,[38] improvement was observed in 15 children with cerebral palsy and Down syndrome.

Tracheotomy is used in neurological deficits and severe craniofacial abnormalities. It is usually maintained until the growth is complete or until there is some kind of surgery allowing removal of the cannula. However, while tracheotomy is a definitive treatment, the initial treatment with AT is a priority. Magardino et al[39] reported that, in 27 children with cerebral palsy, after carrying out AT in all of them, subsequent tracheotomy was only necessary in 4 of them.

Orthodontic treatment can be a complementary aid in the treatment of OSAS. It mainly uses rapid maxillary distraction (RMD) anchored to 2 molars and pressure is applied to separate the upper jaw and widen the nostrils.[9,40] A recent Cochrane review concluded that there is insufficient evidence to confirm its effectiveness.[41]

In terms of craniofacial surgery, some studies show that tracheotomy can be avoided.[42,43] It is usually not done until the age of 10-13 years. In addition to success in the resolution of OSAS,[44-46] others achieve removal of catheters.[47-49] Wittenborn et al[50] achieved extubation in 14 of 17 patients after surgery in the neonatal period. There are basically 2 techniques: mandibular distraction and maxillomandibular advance.

The paediatric post-operative risk, in the range of 0%-1.3% increases up to 27%in cases of OSAS. In a study with 2315 patients,[51] 6.4% had post-operative complications, such as oxygen desaturation, pneumonia, pulmonary oedema, pneumothorax, etc. Children under 3 years of age had a significantly greater risk. Patients with severe OSAS and those with concomitant medical illnesses have a higher respiratory risk.[52] In fact, the severity of the PSG is an important predictor of complications after AT.[15,53] Walker et al,[54] in a study in 2002, describe the criteria for hospital stay in the paediatric intensive care unit for children with adenotonsillectomy due to OSAS.

Continuous positive airway pressure (CPAP) has proved to be a safe device to treat OSAS in children, although it is not approved by the FDA for children under 30 kg[5,55]. Its use in children was described for the first time in 1984. It is used as primary therapy in craniofacial anomalies, neuromuscular disorders, genetic syndromes, obesity, and bone dysplasias which are not cured after AT, and is an alternative to tracheotomy,[56] as well as when there is a contraindication to surgery or minimal adenotonsillar tissue.[57] Furthermore, it can be used as a "bridging procedure" while facial growth is being completed and until craniofacial surgery can be carried out. The effectiveness is demonstrated in multiple studies with success rates of 80%-90%,[58,59] and in children under 2 years.[60] Some authors are observing, not without some alarm, that many indications, in as much as 2 out of every 3 patients, are due to obesity in children.[55] The most serious, albeit infrequent, side effects are facial hypoplasia and hypoventilation.

Pharmacological treatments have not been evaluated in controlled clinical trials[18]. The use of systemic steroids has been tested, but no beneficial effects have been demonstrated.[10,61] Topical nasal steroids have been shown to be beneficial. Broullette et al[62] applied fluticasone in 13 children during 6 weeks, which decreased the number of apnoeas and hypopnoeas, compared with 12 children who received placebo.

In recent years, an increase of leukotriene receptor LT1R and LT2R has been demonstrated in adenoid tissue and tonsils of children with OSAS, to levels significantly higher than in healthy patients[63] and patients with recurrent tonsillitis.[64] An increase of C-reactive protein was also found in serum of children and adults with OSAS,[65] and even an increase[66] of inflammation mediators in exhaled air in children with AHI>5. Some of these systemic inflammation markers, such as interleukins 6 and 10 and C-reactive protein, which are high in these children, return to normal levels following surgery.[67,68] In a study by Goldbart et al,[65] after 16 weeks of treatment with montelukast (a leukotriene receptor antagonist), the adenoid/ nasopharynx size ratio was reduced and the AHI improved significantly. In another study[69] from 2006, montelukast was combined with a nasal steroid to treat AT-resistant OSAS; it concludes that it may be a valid alternative to CPAP in mild cases, because the more severe cases (AHI>5) which do not respond to surgery are treated with CPAP. It is in this group of patients with AHI of 1-5 where it appears that this drug has a relevant role.

Many authors agree that there is an immune-inflammatory component in OSAS.[63,69,70] Goldbart et al[64] believe that perhaps the vibration of the airways could produce these inflammatory changes. It could be that this inflammatory component may cause failure after AT in some cases of OSAS, and that these anti-inflammatory treatments may be used in cases of mild OSAS which are waiting for other therapies. It has been observed in another study[71] that the administration of antibiotics in children with OSAS and tonsillar hypertrophy produced a temporary improvement, not significant, but which was not enough to bypass surgery.

Evolution

There are still many questions regarding the evolution of this entity. The natural course and long-term prognosis of childhood OSAS is still unknown. Nor is it known whether it is a precursor of OSAS in adults or if they are two different conditions affecting different populations. Moreover, it is difficult to ascertain what degree of severity and what type of respiratory disorder are clinically significant to warrant treatment.

Conflict of interests

The authors have indicated there is no conflict of interest.

References

1. Balbani AP, Weber SA, Montovani JC. Update in obstructive sleep apnea syndrome in children. Rev Bras Otorrinolaringol. 2005;71:74-80.
2. Grupo Español de Sueño (GES). Consenso Nacional sobre el síndrome de apneas-hipopneas del sueño. Arch Bronconeumol. 2005;41 Supl 4:1-110.
3. Lim J, Mckean M. Adenoamigdalectomía para la apnea del sueño en niños (Revisión Cochrane traducida). In: the Cochrane Plus Library, number 2, 2006. Oxford, Update Software Ltd.
4. Nieminen P, Tolonen U. Snoring and obstructive sleep apnea in children. A 6-month follow-up study. Arch Otolaryngol Head Neck Surg. 2000;126:481-6.
5. Marcus C. Sleep–disordered breathing in children. State of the art. Am J Respir Crit Care Med. 2001;164:16-30.
6. Villa Asensi JR, de Miguel Díez J. Síndrome de apnea obstructiva del sueño en la infancia. An Esp Pediatr. 2001;54:58-64.
7. Guilleminault C, Lee JH. Does benign primary snoring ever exist in children? Chest. 2004;126:1467-72.
8. Primhak R, O'Brien C. Sleep apnoea. Arch Dis Child Educ Pract Ed. 2005;90:87-91.
9. Guilleminault C, Lee JH, Chan A. Pediatric obstructive sleep apnea syndrome. Arch Pediatr Adolesc Med. 2005;159:775-85.
10. Martins Carvalho C, Vazel L, Potard G, Fortun C, Marianowski R. Syndrome d'apnée obstructive du sommeil de l'enfant. EMC, Oto-Rhino-Laryngologie. 2006;20:622-A-10.
11. Llorente Arenas EM, Adiego Leza I, Marín Garrido C, Carmen Sampériz L, Hernández Montero E, Vicente Gonzalez E. Algunas consideraciones diferenciales del SAOS en adultos y niños. Anales ORL Iber-Amer. 2002;XXIX:213-20.
12. Uliel S, Tauman R, Greenfeld M, Sivan Y. Normal polysomnographic respiratory values in children and adolescents. Chest. 2004; 125:872-8.
13. Tal A, Bar A, Leiberman A. Sleep characteristics following adenotonsillectomy in children with obstructive sleep apnea syndrome. Chest. 2003;124:948-53.
14. Jain A, Sahni JK. Polysomnographic studies in children undergoing edenoidectomy and/or tonsillectomy. J Laryngol Otol. 2002;116:711-5.
15. Schechter MS, Section on Pediatric Pulmonology, Subcommittee on obstructive sleep apnea syndrome. Technical Report: Diagnosis and management of childhood obstructive sleep apnea syndrome. Pediatrics. 2002;109:e69.
16. Nieminen P, Lopponen T, Tolonen U, Lanning P, Knip M, Lopponen H. Growth and biochemical markers of growth in children with snoring and obstructive sleep apnea. Pediatrics. 2002;109:e55.
17. Section on Pediatric Pulmonology, Subcommittee on Obstructive Sleep Apnea Syndrome. American Academy of Pediatrics. Clinical practice guideline: diagnosis and management of childhood obstructive sleep apnea syndrome. Pediatrics. 2002;109:704-12.
18. Erler T, Paditz E. Obstructive sleep apnea syndrome in children: a state-of- the-art review. Treat Respir Med. 2004;3:107-22.
19. Nixon GM, Kermack AS, Davis GM, Manoukian JJ. Planning adenotonsillectomy in children with obstructive sleep apnea: The role of overnight oximetry. Pediatrics. 2004;113:19-25.
20. Kotagal S. Childhood obstructive sleep apnea. BMJ. 2005; 330:978-9.
21. Brietzke SE, Gallagher D. The effectiveness of tonsillectomy and adenoidectomy in the treatment of pediatric obstructive sleep apnea/hypopnea syndrome: a meta-analysis. Otolaryngol Head Neck Surg. 2006;134:976-84.
22. Mora R, Salami A, Passali FM, Mora F, Cordone MP, Ottoboni S, et al. OSAS in children. Int J Pediatr Otorhinolaryngol. 2003; 67:S229-31.
23. Messner AH. Treating pediatric patients with obstructive sleep disorders: an update. Otolaryngol Clin North Am. 2003;36:519-30.
24. Goldstein NA, Pugazhendhi V, Rao SM, Weedon J. Clinical assessment of pediatric obstructive sleep apnea. Pediatrics. 2004;114:33-43.
25. Bar A, Tarasiuk A, Segev Y, Phillip M, Tal A. The effect of adenotonsillectomy on serum insulin-like growth factor-I and growth in children with obstructive sleep apnea syndrome. J Pediatr. 1999;135:76-80.
26. Nieminen P, Lopponen T, Tolonen U, Lanning P, Knip M, Lopponen H. Growth and biochemical markers of growth in children with snoring and obstructive sleep apnea. Pediatrics. 2002;109:e55.
27. Williams EF 3rd, Woo P, Miller R, Kellman RM. The effects of adenotonsillectomy on growth in young children. Otolaryngol Head Neck Surg. 1991;104:509-16.
28. Mitchell RB, Kelly J. Child behavior after adenotonsillectomy for obstructive sleep apnea syndrome. Laryngoscope. 2005; 115:2051-5.
29. de Serres L, Derkay C, Sie K, Biavati M, Jones J, Tunkel D. Impact of adenotonsillectomy on quality of life in children with obstructive sleep disorders. Arch Otolaryngol Head Neck Surg. 2002;128:489-96.
30. Mitchell RB, Kelly J, Call E, Yao N. Quality of life after adenotonsillectomy for obstructive sleep apnea in children. Arch Otolaryngol Head Neck Surg. 2004;130:190-4.
31. Tran KD, Nguyen CD, Weedon J, Goldstein NA. Child behavior and quality of life in pediatric obstructive sleep apnea. Arch Otolaryngol Head Neck Surg. 2005;131:52-7.
32. Mitchell RB, Kelly J. Behavioral changes in children with mild sleep-disordered breathing or obstructive sleep apnea after adenotonsillectomy. Laryngoscope. 2007;117:1685-8.
33. Mitchell RB. Adenotonsillectomy for obstructive sleep apnea in children: outcome evaluated by pre- and post-operative polysomnography. Laryngoscope. 2007;117:1844-54.
34. Shine NP, Lannigan FJ, Coates HL, Wilson A. Adenotonsillectomy for obstructive sleep apnea in obese children: effects on respiratory parameters and clinical outcome. Arch Otolaryngol Head Neck Surg. 2006;132:1123-7.
35. Mitchell RB, Kelly J. Outcome of adenotonsillectomy for obstructive sleep apnea in obese and normal-weight children. Otolaryngol Head Neck Surg. 2007;137:43-8.
36. Guilleminault C, Huang YS, Glamann C, Li K, Chan A. Adenotonsillectomy and obstructive sleep apnea in children: a prospective survey. Otolaryngol Head Neck Surg. 2007;136: 169-75.
37. Kerschner JE, Lynch JB, Kleiner H, Flanary VA, Rice TB. Uvulopalatopharyngoplasty with tonsillectomy and adenoidectomy as a treatment for obstructive sleep apnea in neurologically impaired children. Int J Pediatr Otorhinolaryngol. 2002;62:229-35.
38. Koslo JR, Derkay CS. Uvulopalatopharyngoplasty: treatment of obstructive sleep apnea in neurologically impaired pediatric patients. Int J Pediatr Otorhinolaryngol. 1995;32:241-6.
39. Magardino TM, Tom LW. Surgical management of obstructive sleep apnea in children with cerebral palsy. Laryngoscope. 1999;109:1611-5.
40. Rose E, Schessl J. Orthodontic procedures in the treatment of obstructive sleep apnea in children. J Orofac Orthop. 2006;67:58-67.
41. Carvalho FR, Lentini-Oliveira DA, Machado MAC, Saconato H, Prado LBF, Prado GF. Oral appliances and functional orthopaedic appliances for obstructive sleep apnea in children. Cochrane Database of Systematic Reviews 2007, Issue 2. Art. N.º: CD005520. DOI: 10.1002/14651858.CD005520.pub2.
42. Cohen SR, Simms C, Burstein FD, Thomsen J. Alternatives to tracheostomy in infants and children with obstructive sleep apnea. J Pediatr Surg. 1999;34:182-6.
43. Cohen SR, Holmes RE, Machado L, Magit A. Surgical strategies in the treatment of complex obstructive sleep apnoea in children. Paediatr Respir Rev. 2002;3:25-35.

44. Guilleminault, Christian MD, Li K. Maxillomandibular expansion for the treatment of sleep-disordered breathing: Preliminary result. Laryngoscope. 2004;114:893-6.
45. Bell RB, Turvey TA. Skeletal advancement for the treatment of obstructive sleep apnea in children. Cleft Palate Craniofac J. 2001;38:147-54.
46. Lin S Y, Halbower C, Tunkel DE. Relief of upper airway obstruction with mandibular distraction surgery. Arch Otolaryngol Head Neck Surg. 2006;132:437-41.
47. Monasterio FO, Drucker M, Molina F, Ysunza A. Distraction osteogenesis in Pierre Robin sequence and related respiratory problems in children. J Craniofac Surg. 2002;13:79-83.
48. Steinbacher DM, Kaban LB, Troulis MJ. Mandibular advancement by distraction osteogenesis for tracheostomy-dependent with severe micrognathia. J Oral Maxillofac Surg. 2005;63:1072-9.
49. Cohen SR, Simms C, Burstein FD. Mandibular distraction osteogenesis in the treatment of upper airway obstruction in children with craniofacial deformities. Plast Reconstr Surg. 1998;101:312-8.
50. Wittenborn W, Panchal J, Marsh JL, Sekar KC, Gurley J. Neonatal distraction surgery for micrognathia reduces obstructive apnea and the need for tracheotomy. J Craniofac Surg. 2004;15: 623-30.
51. Statham MM, Elluru RG, Buncher R, Kalra M. Adenotonsillectomy for obstructive sleep apnea syndrome in young children. Prevalence of pulmonary complications. Arch Otolaryngol Head Neck Surg. 2006;132:476-80.
52. Brown KA, Morin I, Hickey C, Manoukian JJ, Nixon GM, Brouillette RT. Urgent adenotonsillectomy: an analysis of risk factors associated with postoperative morbidity. Anesthesiology. 2003;99:586-95.
53. Sanders JC, King MA, Mitchell RB, Kelly JP. Perioperative complications of adenotonsillectomy in children with obstructive sleep apnea syndrome. Anesth Analg. 2006;103: 1115-21.
54. Walker P, Whitehead B, Rowley M. Criteria for elective admission to the paediatric intensive care unit following adenotonsillectomy for severe obstructive sleep apnoea. Anaesthesia and Intensive Care. 2004;32:43-6.
55. Marcus CL, Rosen G, Ward SL, Halbower AC, Sterni L. Adherence to and effectiveness of positive airway pressure therapy in children with obstructive sleep apnea. Pediatrics. 2006;117:442-51.
56. Massa F, Gonsalez S, Laverty A, Wallis C, Lane R. The use of nasal continuous positive airway pressure to treat obstructive sleep apnoea. Arch Dis Child. 2002;87:438-43.
57. Palombini L, Pelayo R, Guilleminault C. Efficacy of automated continuous positive airway pressure in children with sleep-related breathing disorders in an attended setting. Pediatrics. 2004;113:412-7.
58. Waters KA, Everett FM, Bruderer JW, Sullivan CE. Obstructive sleep apnea: the use of nasal CPAP in 80 children. Am J Respir Crit Care Med. 1995;152:780-5.
59. McNamara F, Sullivan CE. Obstructive sleep apnea in infants and its management with nasal CPAP. Chest. 1999;116:10-6.
60. Downey R, Perkin RM, MacQuarrie J. Nasal continuous positive airway pressure use in children with obstructive sleep apnea younger than 2 years of age. Chest. 2000;117:1608-12.
61. Nixon GM, Brouillette RT. Obstructive sleep apnea in children: do intranasal corticosteroids help? Am J Respir Med. 2002;1:159-66.
62. Broullette RT, Manoukian JJ, Ducharme FM, Oudjhane K, Earle LG, Ladan S. Efficacy of fluticasone nasal spray for pediatric obstructive sleep apnea. J Pediatr. 2001;138:838-44.
63. Arens R. Is it time to consider a new treatment for children with sleep- disordered breathing? Am J Respir Crit Care Med. 2005;172:264-5.
64. Goldbart AD, Goldman JL, Li RC, Brittian KR, Tauman R, Gozal D. Differential expression of cysteinyl leukotriene receptors 1 and 2 in tonsils of children with obstructive sleep apnea syndrome or recurrent infection. Chest. 2004;126:13-8.
65. Goldbart AD, Golman JL, Veling MC, Gozal D. Leukotriene modifier therapy for mild sleep-disordered breathing in children. Am J Respir Crit Care Med. 2005;172:364-70.
66. Goldbart AD, Krishna J, Li RC, Serpero LD, Gozal D. Inflammatory mediators in exhaled breath condensate of children with obstructive sleep apnea syndrome. Chest. 2006;130:143-8.
67. Gozal D, Serpero LD, Sans Capdevila O, Kheirandish-Gozal L. Systematic inflammation in non-obese children with obstructive sleep apnea. Sleep Med. 2007;5 [Epub ahead of print].
68. Li AM, Chan MH, Yin J, So HK, Ng SK, Chan IH, et al. C-reactive protein in children with obstructive sleep apnea and the effects of treatment. Pediatr Pulmonol. 2008;43:34-40.
69. Kheirandish L, Goldbart AD, Gozal D. Intranasal steroids and oral leukotriene modifier therapy in residual sleep-disordered breathing after tonsillectomy and adenoidectomy in children. Pediatrics. 2006;117:61-6.
70. Kaditis AG, Alexopoulos EL, Syrogiannopoulos GA. Assessing the role of antiinflammatory medications in children with mild sleep-disordered breathing. Am J Respir Crit Care Med. 2006;173:358.
71. Don DM, Goldsteins NA, Crockett DM, Ward SD. Antimicrobial therapy for children with adenotonsillar hypertrophy and obstructive sleep apnea: a prospective randomised trial comparing azithromycin vs placebo. Otolaryngol Head Neck Surg. 2005;133:562-8.