Brazilian Journal of

OTORHINOLARYNGOLOGY

ORIGINAL ARTICLE

Follow-up of obstructive sleep apnea in children ☆

Emília Leite de Barros [a,*], **Marcia Pradella-Hallinan** [b,c], **Gustavo Antonio Moreira** [b,c], **Daniele de Oliveira Soares Stefanini** [a], **Sergio Tufik** [d], **Reginaldo Raimundo Fujita** [a]

[a] *Department of Otorhinolaryngology and Head and Neck Surgery, Universidade Federal de São Paulo (UNIFESP-EPM), São Paulo, SP, Brazil*
[b] *Universidade Federal de São Paulo (UNIFESP-EPM), São Paulo, SP, Brazil*
[c] *Instituto do Sono, São Paulo, SP, Brazil*
[d] *Department of Psychobiology, Universidade Federal de São Paulo (UNIFESP-EPM), São Paulo, SP, Brazil*

Abstract
Introduction: the evolution of snoring and OSAS in children is not well established since few studies of patients without surgical treatment have been published.
Objective: to evaluate the evolution of sleep disordered breathing in children who had not been submitted to upper airway surgery.
Method: twenty-six children with snoring who had not undergone upper airway surgery were evaluated prospectively. Patients were evaluated by full physical examination and nocturnal polysomnography, after which they were divided into 2 groups: apnea (16 children) and snoring (10 children). After 6 months following the initial evaluation, patients were submitted to a new nocturnal polysomnography, and all data were compared to those of the first examination.
Results: the groups did not show any differences regarding age, weight, height and airway physical examination. After 6 months of follow-up, the apnea index did not change, but the respiratory disturbance index increased in the snoring group and the number of hypopneas decreased in the group apnea.
Conclusion: there was an increase in the percentage of N1 sleep stage and the respiratory disturbance index in the patients with primary snore. The AHI did not show significant alteration in both groups, but the number of hypopneas decreased in patients with SAOS.
© 2014 Associação Brasileira de Otorrinolaringologia e Cirurgia Cérvico-Facial. Published by Elsevier Editora Ltda. All rights reserved.

☆ Please cite this article as: de Barros EL, Pradella-Hallinan M, Moreira GA, Stefanini DO, Tufik S, Fujita RR. Follow-up of obstructive sleep apnea in children. Braz J Otorhinolaryngol. 2014;80:277–84.
 * Corresponding author.
 E-mail: emilialdebarros@yahoo.com.br (E.L. de Barros).

PALAVRAS-CHAVE
Apneia do sono tipo;
obstrutiva;
Polissonografia;
Evolução clínica;
Criança

Acompanhamento clínico de crianças com distúrbios respiratórios do sono

Resumo

Introdução: a evolução do ronco e da síndrome da apneia/hipoapneia obstrutiva do sono (SAOS) na infância ainda não está bem estabelecida e poucos estudos desses pacientes sem o tratamento cirúrgico foram publicados.

Objetivo: avaliar a evolução da apneia e do ronco primário em crianças que não foram submetidas a cirurgia das vias aéreas superiores.

Métodos: foram avaliadas prospectivamente 26 crianças com ronco que não haviam sido submetidas a tratamento cirúrgico. Todas foram submetidas a exame físico, nasofibroscopia e polissonografia, a partir dos quais foram divididos em dois grupos: SAOS (16 crianças) e ronco (10 crianças). Após 6 meses da avaliação inicial, os exames foram repetidos, e os dados encontrados foram comparados.

Resultados: os grupos não apresentaram diferença entre si comparando idade, peso, altura e exame físico. Quando comparamos os resultados das duas polissonografias, houve um aumento da porcentagem do estágio do sono N1 no grupo ronco. O índice de apneia/hipoapnéeia (IAH) não apresentou alteração em ambos os grupos, o índice de distúrbios respiratórios (IDR) aumentou no grupo ronco, e o número de hipopneias diminuiu no grupo SAOS.

Conclusão: houve aumento da porcentagem do estágio 1 do sono não-REM e do IDR nos pacientes com ronco primário; o IAH não apresentou alteração significativa; o número de hipoapneias diminuiu nos pacientes com SAOS.

Introduction

The obstructive sleep apnea syndrome (OSAS), characterized by repeated episodes of upper airway obstruction, associated with intermittent hypoxia and hypercapnia,[1] is a respiratory sleep disorder that affects both adults and children. The sleep-disordered breathing (SDB) is very common in childhood, and it is estimated that 3–26% of young children have habitual snoring and 1–3% have OSAS.[1,2] The SDB includes primary snoring, increased airway resistance syndrome and OSAS as more relevant conditions.[3]

The main risk factors for childhood OSAS are adenotonsillar hypertrophy, obesity, neuromuscular disorders, craniofacial abnormalities and genetic diseases.[1,4–7] Among all these factors, tonsillar and adenoid hypertrophy predominates as the main etiology.[8–10]

The most common symptom is habitual snoring and the occurrence of OSAS in the absence of snoring is considered unlikely.[11] Snoring, alone or associated with other symptoms cannot differentiate OSAS from primary snoring and the increased upper airway resistance syndrome.[12]

SDB and especially childhood OSAS are comorbidities that can affect the central nervous system by causing hyperactivity, daytime sleepiness, cognitive impairment and poor school performance,[13–17] as well as the cardiovascular system by altering blood pressure, causing ventricular hypertrophy and endothelial dysfunction,[18–20] and the metabolic system, contributing to insulin resistance, increased leptin and altering serum lipids,[21,22] growth and development.[23,24]

The diagnosis of OSAS in children remains problematic. The attempted use of a combination of signs and symptoms to distinguish between primary snoring and obstructive sleep apnea proved to be ineffective and the gold standard test for the diagnosis is the polysomnography.[3,12,25,26]

Despite its importance, currently the natural history of snoring and OSAS in children is not well established and few studies have been published that evaluated the outcome of these patients without surgical treatment. Snoring is a common symptom and one does not know which children will improve spontaneously and which ones will progress to OSAS.

Ali, in 1993, carried out a research study through a questionnaire applied to 782 children to assess the prevalence of snoring and related symptoms.[27] After two years, 507 of these children were reassessed and, although the prevalence of habitual snoring showed no difference, more than half of the children who reported snoring in the first assessment no longer reported that complaint.[2]

Marcus, in 1998, evaluated a cohort of 20 children with primary snoring,[1–3] who were submitted to repeated polysomnographic assessment years after the first examination and found no significant changes in the apnea-hypopnea index (AHI) and ventilatory parameters, whereas two children (10%) had OSAS in the second examination.[18] However, it is not well established whether the children who underwent surgical treatment before the second examination were included in the comparative analysis.

Topol, in 2001, also carried out a study in a cohort of 13 children with primary snoring using polysomnography and found no differences in the re-examination after three years.[28]

Anuntaseree, in 2001, carried out an epidemiological study through a questionnaire applied to 1088 children aged seven years, and a new study three years later (2005) on those children without treatment showed that there had been a reduction of snoring in 65% of cases, whereas 4.5% of

children without snoring started to snore, and 9% of children developed OSAS.[29,30] However, the polysomnography was only performed in six children who already had a diagnosis of OSAS in the first study and seven more children who had sleep-related symptoms, which may have underestimated the number of new cases of OSAS.

Li, in 2010, also carried out a study recruiting patients from a previous epidemiological study and re-evaluated 45 children that had OSAS after two years. Worsening of OSAS was observed in 29% of the children, and, in this group of patients, there was an increase in waist circumference, higher prevalence of hypertrophic tonsils and habitual snoring.[31]

No prospective study was performed to evaluate the evolution of OSAS and primary snoring in patients who did not undergo surgical treatment. All previous studies were performed by reassessing the patients years after the first evaluation.

The aim of this study was to evaluate the variation of sleep disordered breathing (OSAS and primary snoring) in children who were not submitted to upper airway surgery.

Materials and methods

A total of 26 patients, aged 2–12 years of both genders, who complained of snoring or difficulty breathing during sleep and who had not undergone surgery for removal of tonsils and/or adenoids, or nasal cavity surgeries, were prospectively assessed at the Pediatric Otorhinolaryngology Outpatient Clinic from November 2009 to November 2011.

Procedure

At baseline, the children were evaluated by the otorhinolaryngologist (the author of this study), who performed the medical history, general physical examination, otorhinolaryngology assessment and nasal endoscopy. All children with a history of habitual snoring were selected (more than 5 times a week for a period longer than 6 months), associated with tonsillar and adenoid hypertrophy and who had not undergone any surgical procedure of the upper airways.

The children's parents or guardians received information on the study and signed the free and informed consent form approved by the Ethics Committee, protocol number 0237/10. Then, the children were evaluated with a nocturnal polysomnography. Patients who complained of rhinitis started treatment with nasal corticosteroids prior to the first polysomnography and remained on treatment while the complaint persisted.

All children who had surgical indication for adenotonsillectomy were referred to pre-operative and pre-anesthetic evaluation. Due to the large number of patients in the service, the surgery can be delayed for 6–8 months. During the follow-up period, a new polysomnography was requested to be performed six months after the first examination. All children were re-evaluated before the second polysomnography and none showed any significant alteration in BMI (e.g., overweight to obesity) or otorhinolaryngological examination.

None of the patients had the surgery date changed due to the research protocol. All patients who had the surgery date prior to the polysomnography were automatically excluded.

Inclusion criteria

Habitual snoring.
Hypertrophic palatine tonsils.
Hypertrophic adenoids.
Children who underwent the assessment at pre-scheduled times according to this study protocol (initial and after 6 months).

Exclusion criteria

Children or parents/guardians who refused to participate in the study.
Those who did not understand the initial instructions.
Orofacial abnormality syndrome already established and/or undergoing investigation.
Lung disease, heart disease and obesity.
Diseases of metabolic or myopathic origin already established and/or undergoing investigation.
Children who did not undergo assessments at pre-scheduled times according to this study protocol (initial and after 6 months).
Children who had surgery scheduled before the completion of the second polysomnography.
Presence of infection or decompensation of allergic symptoms at the time of the examinations (nasofibroscopy or polysomnography).

Physical examination

The overall physical examination included height and weight measurements. The upper airway physical examination evaluated the palatine tonsils and adenoids, as well as the modified Mallampati index.

The palatine tonsils were divided into 4 grades, according to the classification of Brodsky[32]: Grade I – tonsils are situated slightly out of the tonsillar fossa, occupying less than 25% of the area between the oropharynx; Grade II – tonsils are readily visible, occupying 25% to 50% of the oropharynx; Grade III – tonsils occupy 50–75% of the oropharynx; and Grade IV – tonsils occupy more than 75% of the oropharynx.

The adenoids were classified based on the nasal endoscopy assessment regarding the percentage of obstruction of the paranasal sinuses, with 0 being absence of adenoid tissue, and 100% complete obstruction.

The modified Mallampati index used was the one proposed by Friedmann,[33] being divided into 4 classes; in class I, the entire oropharynx can visualized, including the inferior pole of the palatine tonsils, and, in class IV, only part of the hard palate and the soft palate are visualized, being impossible to visualize the posterior oropharynx wall and the insertion of the uvula.

Nasal endoscopy

Nasal endoscopy was performed using a flexible fiber optic cable (Machida), a xenon light source (Styker, Othobean II), a video camera (Toshiba CCD IK M30AK), and a video monitor (Sony KV – CR). All tests were performed after prior treatment of allergic rhinitis, if necessary. The examination

Table 1 Comparison between apnea and snoring groups regarding age, weight and height.

Group	Mean	Median	SD	Min	Max	*n*	CI	*p* value
Age								
Apnea	5.5	4.5	3.44	2	12	16	1.69	0.932
Snoring	5.4	5.5	1.58	3	8	10	0.98	
Weight								
Apnea	24.1	18	14.3	12.5	59	16	7	0.982
Snoring	24.2	23.4	11.2	10	44	10	6.9	
Height								
Apnea	1.16	1.09	0.23	0.92	1.62	16	0.11	0.786
Snoring	1.18	1.17	0.14	1.01	1.39	10	0.08	

SD, standard deviation; Apnea group, patients that had obstructive sleep apnea syndrome; Snoring group, patients that had primary snoring; *n*, number of children; *p*, descriptive level, ANOVA statistical test.

was performed with the child sitting on the lap of a parent or guardian and a 2% lidocaine spray was applied to both nostrils. The fiber was inserted into the right nasal cavity through the inferior meatus until the choana was visualized. The same procedure was performed on the left side, but with visualization of the laryngeal tonsils and adenoids.

Polysomnography

The polysomnography was performed at night in a dark and quiet room with ambient air, and in the presence of the child's parent/guardian. No sleep deprivation or sedation methods were used. Electrophysiological and cardiorespiratory parameters were recorded in a computerized system, using data from the electroencephalogram (F4/M1, F3/M2, C4/M1, C3/M2, O2/M1, O1/M2), submental and bilateral tibial electromyogram, right and left electrooculogram, nasal airflow through oronasal pressure cannula and thermistor, thoracic and abdominal respiratory effort by uncalibrated inductance plethysmography, oxyhemoglobin saturation (SpO2) by pulse oximetry, snoring sensor (microphone) and sleeping position. The data were evaluated according to the criteria of the American Academy of Sleep Medicine 2007 manual.[34]

OSAS was considered: obstructive apnea index (AI) > 1 event per hour or apnea and hypopnea index (AHI) > 1.5 events per hour, minimum oxygen saturation (SpO2 peak) $\leq$ 92%. Patients with AI < 1 event per hour or AHI < 1.5 events per hour, SpO2 peak > 92% with snoring were classified as having primary snoring.[35]

Patients were reassessed according to the same treatment protocol and underwent a new polysomnography 6

months after the first evaluation, while waiting to undergo surgical treatment.

Statistical analysis

Data obtained were compared between the two groups. Statistical analysis was performed using a significance level of 5% (0.05) and identified with an * when significant. The equality of two proportions test was used to compare the qualitative variables.

The ANOVA test was used to compare groups for quantitative variables such as age, weight, height and adenoid size.

Finally, an intragroup analysis was performed for the values of polysomnography, i.e., comparing the results of the initial examination and after 6 months using the paired Student's *t* test (when the same individual is study subject and his own control).

Statistical analysis was performed using SPSS V16, Minitab 15 and Microsoft Office Excel 2007 software.

Results

A total of 26 patients were included in the study, of whom 16 had obstructive sleep apnea (apnea group) and 10 primary snoring (snoring group).

Overall group assessment

The groups did not show any difference regarding age, weight and height as shown in Table 1. When compared regarding the otorhinolaryngological physical examination,

Table 2 Comparison between apnea and snoring groups regarding tonsil size.

	Grade I	Grade II	Grade III	Grade IV
Apnea *n* (%)	1 (6.3)	4 (25)	6 (37.5)	5 (31.3)
Snoring *n* (%)	1 (10)	3 (30)	3 (30)	3 (30)
p value	0.727	0.78	0.696	0.946

Apnea group, patients that had obstructive sleep apnea syndrome; Snoring group, patients that had primary snoring; tonsil size according to the classification of Brodsky; *n*, number of children, %, percentage of children; *p*, descriptive level, statistical test for equality of two proportions.

Table 3 Comparison between apnea and snoring groups according to modified Mallampati classification.

	Class I	Class II	Class III	Class IV
Apnea *n* (%)	3 (18.8)	6 (37.5)	4 (25)	3 (18.8)
Snoring *n* (%)	1 (10)	5 (50)	3 (30)	1 (10)
p value	0.547	0.53	0.78	0.547

Apnea group, patients that had obstructive sleep apnea syndrome; Snoring group, patients that had primary snoring; *n*, number of children, %, percentage of children; *p*, descriptive level, statistical test for equality of two proportions.

Table 4 Comparison between apnea and snoring groups regarding the size of the adenoids (%).

	n	Mean	Median	SD	CI	*p* value
Apnea	16	72	82.5	23.8	11.7	0.12
Snoring	10	56	65	26.3	16.3	

SD, standard deviation; Apnea group, patients that had obstructive sleep apnea syndrome; Snoring group, patients that had primary snoring; *n*, number of children; *p*, descriptive level, ANOVA statistical test.

there were no significant differences between the groups either, as shown in Tables 2–4.

Polysomnographic assessment

The comparison of the initial polysomnography and after 6 months in both groups is shown in Table 5 for the snoring group, and in Table 6 for the apnea group.

There was no statistical difference regarding sleep efficiency. There was an increase in the percentage of sleep stage N1 in the snoring-group assessment after 6 months when compared to the initial test, with a statistically significant difference, but this percentage remained within the normality range. The distribution of other sleep stages showed no statistical difference when comparing the initial examination and after 6 months in either group.

There was no statistical difference when the apnea-hypopnea index (AHI) was compared in both groups. There was no difference when comparing separately the number of central, obstructive or mixed apneas, and the number of episodes of respiratory effort-related arousals (RERAs) in both groups. The number of obstructive apnea episodes in the snoring group showed a significant alteration in the standard deviation due to the considerable increase in the number of these events in one patient.

When assessing patients individually, we observed that 4 patients in the snoring group (40%) developed OSAS according to the criteria used in the test performed after 6 months. In the apnea group, 6 patients (37.5%) ceased to have OSAS according to the criteria used and 4 patients (25%) showed an increase in AHI. Of the patients who showed OSAS improvement, 2 had moderate, and 4 mild OSAS at the initial assessment.

Table 5 Results of the initial polysomnography and after 6 months for the snoring group.

	Initial	After 6 months	*p* value
SE (%)	83.5 ± 6.2	85.9 ± 8.2	0.21
N1 (%)	1.96 ± 1.75	5.65 ± 3.53	0.015[a]
N2 (%)	40 ± 7.6	40.2 ± 8.4	0.958
N3 (%)	34.1 ± 14.6	32.9 ± 10.7	0.868
REM (%)	22.0 ± 5.4	21.3 ± 5.6	0.778
IA	11.0 ± 3.8	12.1 ± 5.7	0.569
AHI	0.25 ± 0.24	1.22 ± 1.82	0.12
RDI	0.25 ± 0.24	1.50 ± 1.71	0.044[a]
CA	0.50 ± 1.90	0.60 ± 1.90	0.876
MA	0	0	×
OA	0.40 ± 0.97	4.40 ± 10.28	0.259
RERAs	0	0	×
Hypopnea	0.80 ± 0.79	3.70 ± 6.46	0.186
Peak SPO2	94.0 ± 2.7	92.3 ± 5.9	0.42

Snoring group, patients that had primary snoring; *p*, descriptive level; Statistical Student's paired *t*-test; SE, sleep efficiency; IA, index of arousal; AHI, apnea-hypopnea index; RDI, respiratory disturbance index; CA, central apnea; MA, mixed apnea; OA, obstructive apnea; RERAs, respiratory effort-related arousals.

[a] significant p value.

Table 6 Results of the initial polysomnography and after 6 months for the apnea group.

	Initial	After 6 months	p value
SE (%)	82.7 ± 8.9	84.3 ± 8.9	0.437
N1 (%)	3.88 ± 3.33	5.92 ± 4.80	0.222
N2 (%)	44.0 ± 9.1	47.5 ± 9.9	0.237
N3 (%)	30.4 ± 6.9	27.5 ± 9.4	0.313
REM (%)	21.8 ± 7.7	19.0 ± 6.6	0.187
IA	13.6 ± 5.2	13.4 ± 6.2	0.927
AHI	8.61 ± 9.76	6.99 ± 14.12	0.358
RDI	8.64 ± 9.74	7.65 ± 14.09	0.554
CA	11.38 ± 28.76	21.69 ± 82.77	0.509
MA	12.25 ± 31.34	1.25 ± 2.79	0.17
OA	6.06 ± 5.32	12.44 ± 20.51	0.219
RERAs	0.63 ± 1.75	2.38 ± 5.37	0.137
Hypopnea	26.06 ± 18.34	13.31	0.005[a]
Peak SPO2	87.8 ± 5.3	87.9 ± 8.0	0.94

Apnea group, patients that had the obstructive sleep apnea syndrome; p, descriptive level; Statistical student's paired t-test; SE, sleep efficiency; IA, index of arousal; AHI, apnea-hypopnea index; RDI, respiratory disturbance index; CA, central apnea; MA, mixed apnea; OA, obstructive apnea; RERAs, respiratory effort-related arousals.

[a] significant p value.

The number of hypopnea events showed a statistically significant decrease in the apnea group at the test after 6 months compared with the initial assessment, although the AHI showed no statistically significant change.

As for the respiratory disturbance index (RDI), there was a statistically significant increase in the snoring group and there was no statistical difference in the apnea group. Regarding the peak oxygen saturation, there was no statistical difference between the moments evaluated for both groups.

Discussion

This study evaluated patients continuously aiming to identify variations in the clinical and polysomnographic profile of children with OSAS and primary snoring, which limits the sample size and study period. Furthermore, all patients with an indication for adenotonsillectomy were referred for surgery (all patients with OSAS and patients with snoring and adenotonsillar hypertrophy without improvement with clinical treatment). Throughout the evaluation period, no significant changes in BMI and otorhinolaryngological assessment of patients were observed.

As for otorhinolaryngological alterations (size of the tonsils and adenoids and modified Mallampati classification) the groups showed no statistical difference. Consistent with the literature, none of these data without the polysomnography assessment was able to differentiate patients with OSAS from primary snoring.[3,12,25,26]

The criteria for OSAS diagnosis in childhood according to the AHI are not standardized in different scientific publications,[18,31,36] and further studies are still being performed to establish the normality criteria.[37-39] To evaluate the natural history of the disease is essential for the consolidation of these criteria and, especially, to define which patients need a more detailed follow-up.

Sleep architecture is considered preserved in most children with OSAS when comparing REM and non-REM sleep.[10,11] However, late evaluations after adenotonsillectomy showed a significant increase in slow-wave sleep in children.[23,40,41] Roemmich et al. showed significant reduction in the stage 1 of the sleep accompanied by the improvement in AHI one year after adenotonsillectomy in children.[42] In this study, we observed a significant increase in stage 1 of the non-REM sleep in patients with primary snoring, and, although the mechanism is unclear, sleep fragmentation can result in behavioral changes and poor academic performance.[13-16]

As for the AHI, there was no statistically significant difference in either group. During the 6-month evaluation period, it is apparent that the patients had no alteration in the natural history of the disease in either group. However, when assessing individual patients, we observed that 4 patients with primary snoring at the first examination (40%) had apnea at the examination performed after 6 months, even with no significant changes in BMI and physical examination, a higher value than the one found in the literature.[18,28,30]

Of the patients with OSAS, 4 (25%) had worsening of AHI, of which 3 had moderate to severe OSAS at the first examination (AHI ≥ 5 events per hour). Anuntaseree et al. observed that children with OSAS had the worse indices at the second evaluation, and Li et al. also observed worsening in 29% of patients with OSAS.[30,31] It is noteworthy that there was a statistically significant decrease in the number of hypopnea events in patients with OSAS, even if they did not interfere with the AHI.

In the group of patients with primary snoring, RDI showed a statistically significant increase, even if there was no difference in AHI and RERA when compared separately. More recently introduced in the polysomnographic evaluation, the RDI has no normality criteria yet.

It is unlikely that the differences found are due to the variability between the nights when the examination was performed. One factor that could affect this variation is nasal obstruction caused by allergic rhinitis, but all patients with complaints of rhinitis were treated with nasal corticosteroids before the examinations. Moreover, it is well established that one night of recording, provided that there are no technical complications, is sufficient to identify SDB. Katz et al. evaluated the results of polysomnographies performed on two nights with an interval of 7–27 days and observed no statistical difference in AHI or respiratory variables of patients, concluding that the examination of a single night is suitable for measurement of childhood OSAS.[43] Li et al. compared the polysomnography of children in 2 consecutive nights and concluded that the examination of a single night is sufficient to identify 84.6% of cases of SDB.[44]

No differences were observed in AHI in patients when analyzed in group, but when assessed individually, this variation can be decisive for the choice of treatment. As the findings of this study did not show an evolution of children with primary snoring to OSAS within 6 months, although individual variations were found, it reinforces the need to maintain the clinical follow-up of children with SDB and be watchful of any change in the clinical picture.

Conclusion

After 6 months of follow-up of patients with SDB without surgical treatment, there were no variations in SDB.

1. There was an increase in the percentage of stage 1 of non-REM sleep and RDI in patients with primary snoring.
2. The AHI showed no significant change in either group.
3. The number of hypopneas decreased in OSAS patients.

Conflicts of interest

The authors declare no conflicts of interest.

References

1. Marcus CL, Omlin KJ, Basinki DJ, Bailey SL, Rachal AB, Von Pechmann WS, et al. Normal polysomnographic values for children and adolescents. Am Rev Respir Dis. 1992;146:1235–9.
2. Ali NJ, Pitson D, Stradling JR. Natural history of snoring and related behaviour problems between the ages of 4 and 7 years. Arch Dis Child. 1994;71:74–6.
3. Au CT, Li AM. Obstructive sleep breathing disorders. Pediatr Clin North Am. 2009;56:243–59.
4. Trang TTH, Desquerre I, Goldman M. Sleep-disordered breathing in young children with neuromuscular disorders. Am Rev Respir Dis. 1993;147:A760.
5. Marcus CL, Curtis S, Koerner CB, Joffe A, Serwint JR, Loughlin GM. Evaluation of pulmonary function and polysomnography in obeses children and adolescent. Pediatr Pulmonol. 1996;21:176–83.
6. Brooks LJ, Stephens BM, Bacevice AM. Adenoid size is related to severity but not the number of episodes of obstructive apnea in children. J Pediatr. 1998;132:682–6.
7. Mogayzel PJ, Carroll JL, Loughlin GM, Hurko O, Francomano CA, Macus CL. Sleep-disordered breathing in children with achondroplasia. J Pediatr. 1998;131:667–71.
8. Marcus CL. Sleep-disordered breathing in children. Am J Respir Crit Care Med. 2001;164:16–30.
9. Magnus GL, Lundell BPW. Tonsillar hyperplasia in children. Arch Otolaryngol. 1982;108:650–4.
10. American Thoracic Society. Consensus conference on indications and standards for cardiopulmonary sleep studies. Am Rev Respir Dis. 1989;139:559–68.
11. American Academy of Pediatrics. Clinical Practice Guideline: diagnosis and management of childhood obstructive sleep apnea syndrome. Pediatrics. 2002;109:704–12.
12. Carroll JL, McColley SA, Marcus CL, Curtis S, Loughlin GM. Inability of clinical history to distinguish primary snoring from obstructive sleep apnea syndrome in children. Chest. 1995;108:610–8.
13. Urschitz MS, Guenther A, Eggebrecht E, Wolff J, Urschitz-Dupratt PM, Schlaud M, et al. Snoring, intermittent hypoxia and academic performance in primary school children. Am J Respir Crit Care Med. 2003;168:464–8.
14. Kaditis AG, Ioannou MG, Chaidas K, Alexopoulos EI, Apostolidou M, Apostolidis T, et al. Cysteinyl leukotriene receptors are expressed by tonsillar T cells of children with obstructive sleep apnea. Chest. 2008;134:324–31.
15. Gottlieb DJ, Chase C, Vezina RM, Heeren TC, Corwin MJ, Auerbach SH, et al. Sleep-disordered breathing symptoms are associated with poorer cognitive function in 5-year-old children. J Pediatr. 2004;145:458–64.
16. O'Brien LM, Mervis CB, Holbrook CR, Bruner JL, Klaus CJ, Rutherford J, et al. Neurobehavioral implications of habitual snoring in children. Pediatrics. 2004;114:44–9.
17. Uema SFH, Pignatari SSN, Fujita RR, Moreira GA, Pradella-Hallinan M, Weckx L. Avaliação da função cognitiva da aprendizagem em crianças com distúrbios obstrutivos do sono. Braz J Otorhinolaryngol. 2007;73:315–20.
18. Marcus CL, Hamer A, Loughlin GM. Natural history of primary snoring in children. Pediatr Pulmonol. 1998;26:6–11.
19. Amin RS, Kimball TR, Bean JA, Jeffries JL, Willging JP, Cotton RT, et al. Left ventricular hypertrophy and abnormal ventricular geometry in children and adolescents with obstructive sleep apnea. Am J Respir Crit Care Med. 2002;165:1395–9.
20. O'Brien LM, Serpero LD, Tauman R, Gozal D. Plasma adhesion molecules in children with sleep-disordered breathing. Chest. 2006;129:947–53.
21. Waters KA, Sitha S, O'Brien LM, Bibby S, de Torres C, Vella S, et al. Follow-up on metabolic markers in children treated for obstructive sleep apnea. Am J Respir Crit Care Med. 2006;174:455–60.
22. Tauman R, Serpero LD, Capdevila OS, O'Brien LM, Goldbart AD, Kheirandish-Gozal L, et al. Adipokines in children with sleep disordered breathing. Sleep. 2001;30:443–9.
23. Bar A, Tarasiuk A, Segev Y, Phillip M, Tal A. The effect of adeno-tonsilectomy on serum insulin-like growth factor-I and growth in children with obstructive sleep apnea syndrome. J Pediatr. 1999;135:76–80.
24. Nieminen P, Lopponen T, Tolonen U, Lanning P, Knip M, Lopponen H. Growth and biochemical markes of growth in children with snoring and obstructive apnea. Pediatrics. 2002;109(4):e55.
25. Hoban TFH. Polysomnografy should be required both before and after adenotonsillectomy for childhood sleep disordered breathing. J Clin Sleep Med. 2007;3:675–7.
26. Marcus CL. Obstructive sleep apnea syndrome unanswered questions. Chest. 2008;134:1114–5.
27. Ali JN, Pitson D, Stradling JR. Snoring, sleep disturbance, and behavior in 4–5 year olds. Arch Dis Child. 1993;68:360–6.
28. Topol HI, Brooks LJ. Follow-up of primary snoring in children. J Pediatr. 2001;138:291–3.
29. Anuntaseree W, Rookkapan K, Kuasirikul S, Thongsuksai P. Snoring and obstructive sleep apnea in Thai School-age children: prevalence and predisposing factors. Pediatr Pulmonol. 2001;32:222–7.
30. Anuntaseree W, Kuasirikul S, Suntornlohanakul S. Natural history of snoring and obstructive sleep apnea in Thai school-age children. Pediatr Pulmonol. 2005;39:415–20.
31. Li AM, Au CT, Ng SK, Abdullah VJ, Ho C, Fok TF, et al. Natural history and predictors for progression of mild childhood obstructive sleep apnea. Thorax. 2010;65:27–31.
32. Brodsky L. Modern assessment of tonsils and adenoid. Pediatr Clin North Am. 1989;36:1551–69.
33. Friedman M, Tanyeri H, La Rosa M, Landsberg R, Vaidyanathan K, Pieri S, et al. Clinical predictors of obstructive sleep apnea. Laryngoscope. 1999;109:1901–7.
34. Redline S, Budhiraja R, Kapur V, Marcus CL, Mateika JH, Mehra R, et al. The scoring of respiratory events on sleep: reliability and validity. J Clin Sleep Med. 2007;3:169–200.
35. Witmans MB, Keens TG, Davidson SL, Marcus C. Obstructive hypopneas in children and adolescents normal values. Am J Respir Crit Care Med. 2003;168:1540.
36. Carroll JL. Obstructive sleep-disordered breathing in children: new controversies, new directions. Clin Chest Med. 2003;24:261–82.
37. Li AM, So HK, Au CT, Ho C, Lau J, Ng SK, et al. Epidemiology of obstructive sleep apnoea syndrome in Chinese children: a two-phase community study. Thorax. 2010;65:991–7.
38. Scholle S, Beyer U, Bernhard M, Eichholz S, Erler T, Graness P, et al. Normative values of polysomnographic parameters

in childhood and adolescence: quantitative sleep parameters. Sleep Med. 2011;12:542–9.

39. Scholle S, Wiater A, Scholle HC. Normative values of polysomnographic parameters in childhood and adolescence: cardiorespiratory parameters. Sleep Med. 2011;12: 988–96.

40. Tal A, Bar A, Lieberman A, Tarastuk A. Sleep characteristics following adenotonsillectomy in children with obstructive sleep apnea syndrome. Chest. 2003;124:948–53.

41. Montgomery-Downs HE, Crabtree VM, Gozal D. Cognition, sleep and respiration in at-risk children treated for obstructive sleep apnea. Eur Respir J. 2005;25:336–42.

42. Roemmich JN, Barkey JE, D'Andrea L, Nikova M, Rogol AD, Carskadon MA, et al. Increases in overweight after adenotonsillectomy in overweight children with obstructive sleep-disordered breathing are associated with decreases in motor activity and hyperactivity. Pediatrics. 2006;117:e200–8.

43. Katz ES, Greene MG, Carson KA, Galster P, Loughlin GM, Carroll J, et al. Night-to-night variability of polissonography in children with suspected obstructive sleep apnea. J Pediatr. 2002;140:589–94.

44. Li AM, Wing KY, Cheung A, Chan D, Ho C, Hui S, et al. Is a 2-night polysomnographic study necessary in childhood sleep-related disordered breathing? Chest. 2004;126:1467–72.