

Oropharyngeal exercises to reduce symptoms of OSA after AT

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Abstract

Purpose This study evaluated the efficacy of oropharyngeal exercises in children with symptoms of obstructive sleep apnea syndrome (OSA) after adenotonsillectomy.

Methods Polysomnographic recordings were performed before adenotonsillectomy and 6 months after surgery. Patients with residual OSA (apnea-Hypopnea Index, AHI > 1 and persistence of respiratory symptoms) after adenotonsillectomy were randomized either to a group treated with oropharyngeal exercises (group 1) or to a control group (group 2). A morphofunctional evaluation with Glatzel and Rosenthal tests was performed before and after 2 months of exercises. All the subjects were re-evaluated after exercise through polysomnography and clinical evaluation. The improvement in OSA was defined by Δ AHI: (AHI at T1 - AHI at T2)/AHI at T1 \times 100.

Results Group 1 was composed of 14 subjects (mean age, 6.01 ± 1.55) while group 2 was composed of 13 subjects (mean age, 5.76 ± 0.82). The AHI was 16.79 ± 9.34 before adenotonsillectomy and 4.72 ± 3.04 after surgery ($p < 0.001$). The Δ AHI was significantly higher in group 1 (58.01 %; range from 40.51 to 75.51 %) than in group 2 (6.96 %; range from -23.04 to 36.96 %). Morphofunctional evaluation demonstrated a reduction in oral breathing ($p = 0.002$), positive Glatzel test ($p < 0.05$), positive Rosenthal test ($p < 0.05$), and increased labial seal ($p < 0.001$), and lip tone ($p < 0.05$).

Conclusions Oropharyngeal exercises may be considered as complementary therapy to adenotonsillectomy to effectively treat pediatric OSA.

Keywords Children · Oropharyngeal exercises · Residual OSA · Adenotonsillectomy

Introduction

Obstructive sleep apnea (OSA) in children is a sleep breathing disorder characterized by prolonged partial upper airway obstruction and/or intermittent complete obstruction that disrupts ventilation during sleep and sleep patterns [1]. Untreated pediatric OSA may result in various problems, such as cognitive impairment, attention and hyperactivity disorder, poor academic achievement, and cardiovascular and metabolic complications [2–5].

Various etiological factors may underlie pediatric OSA, including craniofacial dysmorphism, obesity, and hypotonic neuromuscular disease, though the most common cause is adenotonsillar hypertrophy [5, 6].

Adenotonsillectomy (AT) remains the first-line treatment in children with adenotonsillar hypertrophy, even if recent evidence suggests that the outcome of this surgical procedure may not be as favorable as expected and that residual OSA persists in some cases [7]. Recently, Bhattacharjee confirmed that AT cured OSA in only 27.2 % of obese and non-obese children [8].

Alternative treatments for OSA include orthodontic treatment, mandibular advancement, and weight loss; these treatments have variable results [9]. These treatments correct the oropharyngeal structure but may have no effect on either functionality or neuromuscular disorders. Oral breathing and lip hypotonia, which are typical of children with OSA, seldom change after surgical and/or medical treatment and may be the cause of residual OSA. They may actually alter the pharyngeal nasal tone (tongue and cartilage hypotonia), which leads to a collapse during inspiration and consequently increases nasal

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resistance. Therefore, it is necessary to test the efficacy of other modalities of treatment for OSA [10].

On the basis of these observations, we hypothesize that oropharyngeal hypotonia may also be implicated in the pathogenesis of OSA, and that oropharyngeal exercises may improve stomatognathic function and reduce neuromuscular impairment.

One study in adult patients showed that didgeridoo playing significantly ameliorated OSA severity and associated symptoms [11]. This might be due to training of the muscles of the upper airways, which control airway dilation and wall stiffening secondary to didgeridoo playing.

It may therefore be possible to supplement medical and surgical treatment with oropharyngeal exercises in order to re-establish nasal breathing, normal lip posture, and restore the correct swallowing pattern. The literature contains few studies designed specifically to investigate the effectiveness of orofacial re-education in OSA.

A study conducted on adult patients with moderate OSA confirmed the ability of oropharyngeal exercises, administered over a 3-month period, to reduce nocturnal respiratory symptoms and improve sleep efficiency and OSA severity [10]. Oropharyngeal rehabilitation consisted of isometric and isotonic exercises involving the tongue, soft palate, and lateral pharyngeal wall in order to ameliorate functions of suction, swallowing, chewing, breathing, and speech.

The aim of our study was to evaluate the efficacy of oropharyngeal exercises as a means of reducing residual OSA in children after AT.

Materials and methods

Subjects

This prospective, case-control study was based on 42 children who were referred to our Pediatric Sleep Center (S. Andrea Hospital, Rome, Italy) for habitual snoring, apnea, or restless sleep as reported by their parents.

In all cases, the diagnosis of OSA was confirmed by means of a laboratory polysomnography (PSG) yielding an obstructive apnea/hypopnea index (AHI) >1 ev/h, according to the standard criteria of the American Academy of Sleep Medicine (AASM) [12]. We adopted a clinical cutoff value of AHI >5 for moderate-severe OSA [13, 14], while residual OSA was defined as an AHI index >1 ev/h after AT and persistence of respiratory symptoms (snoring, oral breathing, and sleep apnea).

Exclusion criteria were positive history for recurrent laryngospasm, allergy, asthma, acute or chronic cardiorespiratory or neuromuscular diseases, chronic inflammatory diseases, major craniofacial abnormalities, chromosomal syndromes, or epilepsy.

Inclusion criteria were children >4 years old, to ensure better compliance in the execution of the exercises, a PSG recording with a diagnosis of moderate-severe OSAS, and residual OSA after AT. Informed consent was obtained from parents, and the study was approved by the Ethics Committee of the Sant'Andrea Hospital.

Study design

The clinical history was obtained for all the patients. All the children underwent an ear, nose, and throat (ENT) and orthodontic assessment to evaluate the presence of adenotonsillar hypertrophy, malocclusion, and/or ogival palate.

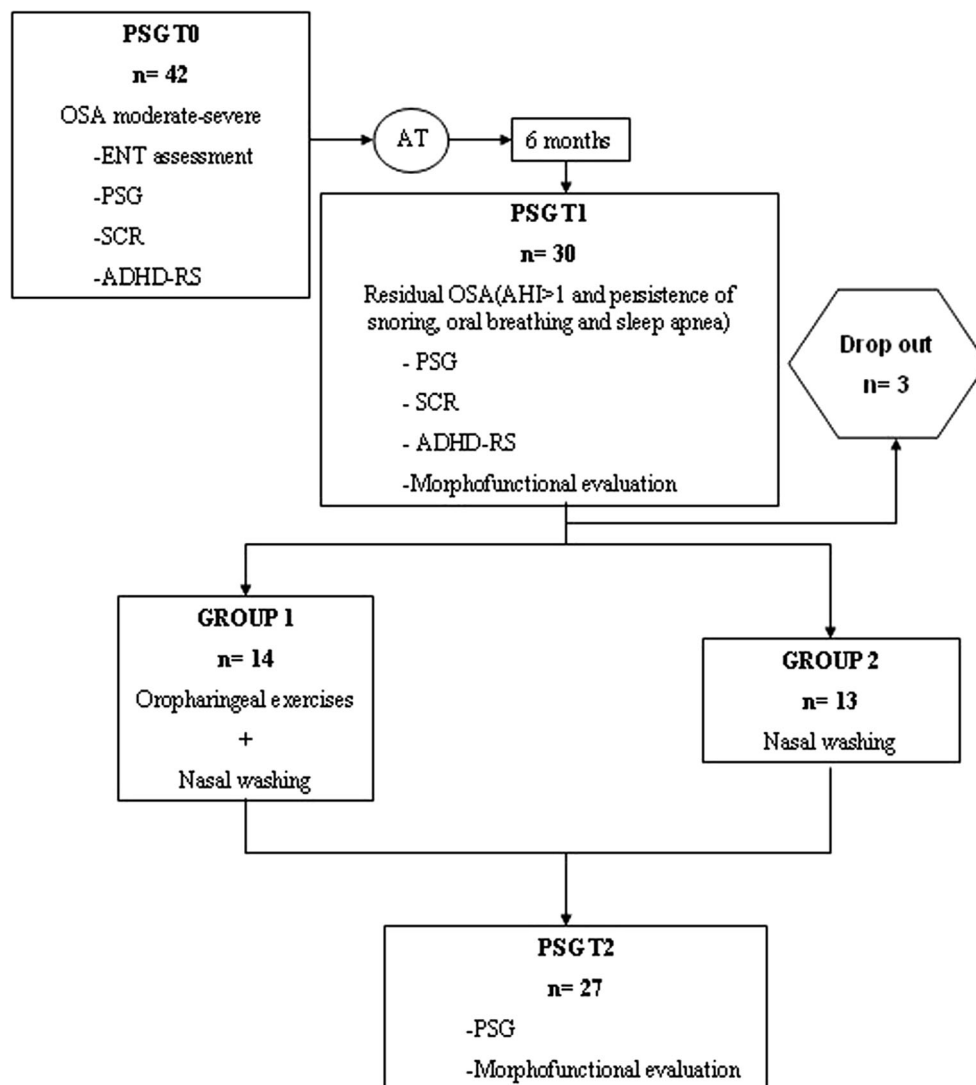
Polysomnographic recordings were performed, and the Sleep Clinical and Rating Scale was administered before AT (T0) and 6 months after (T1). Thereafter, patients with residual OSA were randomized in two groups—a case group treated with oropharyngeal exercises plus nasal washing consisting of the application of saline in each nostril three times a day (group 1) and a control group treated with nasal washing alone (group 2). All the subjects were re-evaluated by means of a PSG and clinical evaluation (Fig. 1, study design graph) 2 months later (T2), in order to avoid possible influences from seasonal changes.

Sleep analysis

All the subjects were evaluated in our Pediatric Sleep Center by means of a full-night PSG after a night of adaptation in the hospital. Children were studied in a quiet, darkened room with an ambient temperature of 24 °C in the company of one of their parents. All the recordings started at the patients' usual bedtime and continued until spontaneous awakening. Standard overnight PSG recordings were obtained by means of a Grass Heritage polygraph. The variables recorded included an electroencephalogram with at least eight channels (frontal, central, temporal and occipital, referred to the contralateral mastoid), an electro-oculogram (electrodes placed 1 cm above the right outer cantus and 1 cm below the left outer cantus and referred to the mastoid electrode), a submental electromyogram, and an electrocardiogram (one derivation). Chest and abdomen movements were measured by strain gauges. Oronasal airflow was recorded with a thermocouple and nasal pressure cannula and tracheal sound with a microphone sensor. Arterial oxygen saturation was monitored using a pulse oximeter. A digital time-synchronized video recording was performed.

Sleep stages were scored according to the AASM standard criteria [12]. All the following sleep architecture parameters were evaluated: total sleep time (TST = time from sleep onset to the end of the final sleep epoch minus time awake); sleep efficiency (defined as the percentage ratio between TST and time in bed); and percentage of stages 1, 2, and 3 nonrapid eye

Fig. 1 Study design graph. The graph shows the enrolled patients follow-up. *AHI* Apnea-Hypopnea Index; *AT* adenotonsillectomy, *ENT* ear, nose, and throat; *OSA* obstructive sleep apnea syndrome; *PSG* polysomnography; *ADHD-RS* Attention Deficit Hyperactive Disorder Rating Scale, *SCR* sleep clinical record



movement (NREM) sleep and rapid eye movement (REM) sleep. Central, obstructive, and mixed apnea events were counted according to the criteria established by the AASM [12].

Re-education

Oropharyngeal exercises were divided into three categories, i.e., (1) nasal breathing rehabilitation, (2) labial seal and lip tone exercises, and (3) tongue posture exercises. Examples of exercises are described in Fig. 2.

Children were required to perform the exercises every day at home, at least three times a day, doing 10–20 repetitions each time. Group 1 underwent three monthly meetings with a therapist. In the first meeting (T1), the therapist carried out a morphofunctional evaluation and taught the patients and their parents nasal breathing rehabilitation exercises and exercises designed to restore competence and tone lip, which children were required to perform daily at home for 2 months. All the

patients were also required to fill in a diary in which their compliance to exercises was recorded. The aim of the second meeting was to ensure that the home exercises were being executed correctly. In the third meeting (T2), group 1 underwent the second morphofunctional evaluation.

In order to reduce a possible observer bias, the therapist who performed all the morphofunctional evaluations in both groups at T1 and T2 was always the same and he was blinded to the group because another therapist had taught the exercises.

Nasal washing was performed using the Neti Pot filled with 2.5 % saline hypertonic solution. All the patients performed nasal washing two times, in the morning and evening, for 2 months.

Sleep questionnaire data

We proposed the Sleep Clinical Record (SCR), which combines the patient's history and clinical items, for each child [15]. The first part considers the nose, oropharynx, dental, and









Breathe in through the nose and breathe out through the mouth strongly enough to displace a balloon	A 
Breathe in through the nose and breathe out through the mouth using a straw placed in a glass of water and making bubbles for as long as possible	A 
Breathe in through one nostril and breathe out through the other, using the thumb to close the other nostril	A 
Lower the upper lip over the incisors in such a way as to hamper the contemporary relaxation of the chin muscle	B 
Place a button tied to 15-20 cm of thread inside the mouth vestibule and pull it perpendicularly forward	B 
Press one lip against the other keeping the teeth closed	B 
Vibrate the lips blowing out noisily	B 
Place the tongue on the incisor taste bud and move from right to left using a movement resembling that of a windscreen wiper	C 

Fig. 2 Examples of some oropharyngeal exercises. **a** Nasal breathing rehabilitation, **b** labial seal and lip tone exercises, and **c** tongue posture exercises

skeletal occlusion. Tonsillar hypertrophy was graded according to a standardized scale ranging from 0 to 4. Tonsillar size was graded as: 1+=medial borders of tonsils lateral to or extending to the pillars, 2+=medial borders of tonsils lateral to or extending to the lateral uvular margins, 3+=medial borders of tonsils medial to the lateral uvular margins, and 4+=includes “kissing” tonsils, which meet at the midline [16]. Grades 3 and 4 were considered as positive. The palate position was graded according to the Friedman classes, considering classes 3 and 4 as positive [17]. The second part is based on the Brouillette questionnaire [18], while the last part examines the presence of symptoms of inattention and hyperactivity using the Attention Deficit Hyperactive Disorder Rating Scale (ADHD-RS) [19], which had previously been filled out by the parents of all the participants. We have previously validated and explained elsewhere [15] how to obtain the

overall score from these evaluations. However, an overall score ≥ 6.5 is considered highly predictive of OSA.

Morphofunctional schedule

The therapist completed a morphofunctional evaluation form that assessed respiratory pattern (nasal or oral), labial seal (competent or not), and lip tone (normal or not) [20, 21]. All the participants also underwent the Glatzel and Rosenthal tests, which assess nasal patency (Fig. 3).

Statistical analysis

Data are expressed as means \pm standard deviation (SD). The normality of the data distribution was assessed by the Kolmogorov-Smirnov test. *T* test was used for parametric

MORPHOFUNCTIONAL SCHEDULE

Date/...../.....

Name.....

		T1	T2
Respiratory pattern	Oral	<input type="checkbox"/>	<input type="checkbox"/>
	Nasal	<input type="checkbox"/>	<input type="checkbox"/>
Labial seal	Competent	<input type="checkbox"/>	<input type="checkbox"/>
	Not Competent	<input type="checkbox"/>	<input type="checkbox"/>
Lip tone	Normal	<input type="checkbox"/>	<input type="checkbox"/>
	Hypotonic	<input type="checkbox"/>	<input type="checkbox"/>
Glatzel test	Negative	<input type="checkbox"/>	<input type="checkbox"/>
	Positive	<input type="checkbox"/>	<input type="checkbox"/>
Rosenthal test	Negative	<input type="checkbox"/>	<input type="checkbox"/>
	Positive	<input type="checkbox"/>	<input type="checkbox"/>

Fig. 3 Schedule for morphofunctional evaluation during monthly meeting. T1 6 months after adenotonsillectomy, T2 2 months after T1

data. Contingency tables (the χ^2 test) were used to compare the frequencies of categorical variables.

The improvement in OSA was defined by Δ AHI (AHI at T1 - AHI at T2)/AHI at T1 \times 100. A *p* value <0.05 was considered statistically significant. The statistical analysis was performed using a commercial software package (SPSS, version 11; SPSS; Chicago, IL, USA).

Results

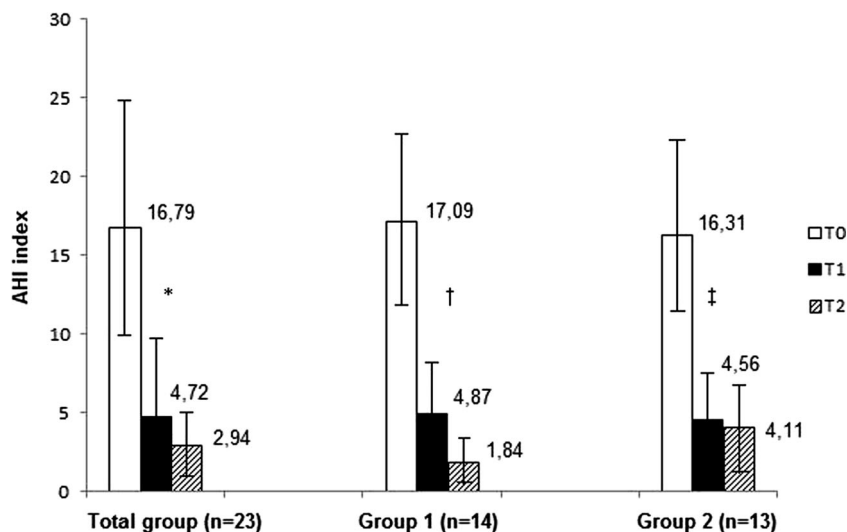
We enrolled 42 children, but 12 children (5.04 %) who did not display residual OSA at T1 were excluded, another two from

group 1 who did not comply with the exercises they were required to perform, and one from group 2 who not only did nasal washes but also nasal steroids for 3 months. The mean age of the remaining 27 patients included in the final analysis, 24 of whom were male (88.8 %), was 4.82 \pm 1.36 years.

The AHI index decreased significantly from baseline (T0) to T1 (16.79 \pm 9.34 versus 4.72 \pm 3.04, *p*<0.0001) (Fig. 4), as well as SCR score (9.42 \pm 1.60 versus 4.20 \pm 1.95, *p*<0.0001) in all the children. By contrast, the ADHD-RS score did not decrease significantly (Table 1).

There were no differences in the children’s anthropometric, clinical, or respiratory parameters between group 1 (14; mean age, 6.01 \pm 1.55 years) and group 2 (13; mean age, 5.76 \pm

Fig. 4 Apnea-hypopnea index (AHI) before (T0) and after (T1) adenotonsillectomy in total group, group 1, and group 2. T0 before adenotonsillectomy, T1 6 months after adenotonsillectomy; *, †, ‡ differences between AHI at T0 and T1 $p < 0.001$



0.82 years), nor did any significant difference emerge between the two groups in the AHI at T1 (Table 2).

The efficacy of oropharyngeal exercises expressed by Δ -AHI was higher in children in group 1 (58.01 %; range from 40.51 to 75.51 %) than in those in group 2 (6.96 %; range from -23.04 to 36.96 %) as showed in Fig. 5.

After 2 months of oropharyngeal exercises, the morphofunctional evaluation revealed a significant reduction in oral breathing, a positive Glatzel test, a positive Rosenthal test, as well as increased labial seal and lip tone; by contrast, the morphofunctional evaluation in group 2 did not detect any significant difference after 2 months of nasal washing (Table 3).

Discussion

This prospective and randomized study shows, for the first time, that oropharyngeal exercises can be used to treat residual

Table 1 Anthropometric, clinical, and polysomnographic characteristics of total sample at T0 and T1. Data are expressed in mean \pm SD (standard deviation)

	Total group (n=27)		p
	T0 (baseline)	T1 (after AT)	
Age (years)	4.82 \pm 1.36	5.59 \pm 1.35	ns
Weight (kg)	19.93 \pm 7.15	23.47 \pm 7.79	ns
Height (cm)	107.19 \pm 10.39	109.22 \pm 23.54	ns
BMI centile	58.70 \pm 36.71	67.52 \pm 29.58	ns
AHI (ev/h)	16.79 \pm 9.34	4.72 \pm 3.04	<0.0001
SaO2 average (%)	96.69 \pm 1.80	97.8 \pm 1.09	ns
SCR	9.42 \pm 1.60	4.20 \pm 1.95	<0.0001
ADHD-RS	4.33 \pm 5.64	3.72 \pm 4.50	ns

AHI Apnea-Hypopnea Index, BMI body mass index, ADHD-RS Attention Deficit Hyperactive Disorder Rating Scale, SCR sleep clinical record, T0 before adenotonsillectomy, T1 6 months after adenotonsillectomy

OSA. In 2010, both Bhattacharjee [8] and Ye [22] confirmed that AT resolves OSA in only 27.2 and 30 % of children, respectively. Orthodontic treatment and medical treatment (intranasal and topical corticosteroids) may also have a short-term beneficial effect on AHI, but do not definitively cure this disorder [9, 23]. Furthermore, the optimal dosage and duration of therapy have yet to be clearly understood, as well as the groups of patients (e.g., younger versus older or normal weight versus obese) who can respond better to such therapies [24]. In addition, it is still unclear whether the addition of other anti-inflammatory agents, such as leukotriene receptor antagonists, has additive or synergistic effects [25, 26].

However, AT remains the first-line treatment for pediatric OSA, particularly in patients who have a moderate to severe condition combined with adenotonsillar hypertrophy [27]. In our study, we had observed a significant reduction in respiratory symptoms and in the AHI index after AT, though the disease resolved completely (AHI <1 ev/h) in approximately

Table 2 Anthropometric, clinical, and polysomnographic characteristics of each group at T1 (after AT). Data are expressed in mean \pm SD (standard deviation)

	Group 1 (n=14)	Group 2 (n=13)	p
Age (years)	6.01 \pm 1.55	5.76 \pm 0.82	ns
Weight (kg)	25.62 \pm 9.18	20.13 \pm 3.10	ns
Height (cm)	108.94 \pm 30.08	109.67 \pm 7.33	ns
BMI centile	81.85 \pm 29.94	68.22 \pm 28.68	ns
AHI (ev/h)	4.87 \pm 2.96	4.56 \pm 3.22	ns
SaO2 average (%)	97.80 \pm 1.22	97.74 \pm 0.97	ns
SCR	4.07 \pm 2.22	4.50 \pm 1.12	ns
ADHD-RS	2.69 \pm 3.61	4.40 \pm 5.86	ns

AHI Apnea-Hypopnea Index, BMI body mass index, ADHD-RS Attention Deficit Hyperactive Disorder Rating Scale, SCR sleep clinical record

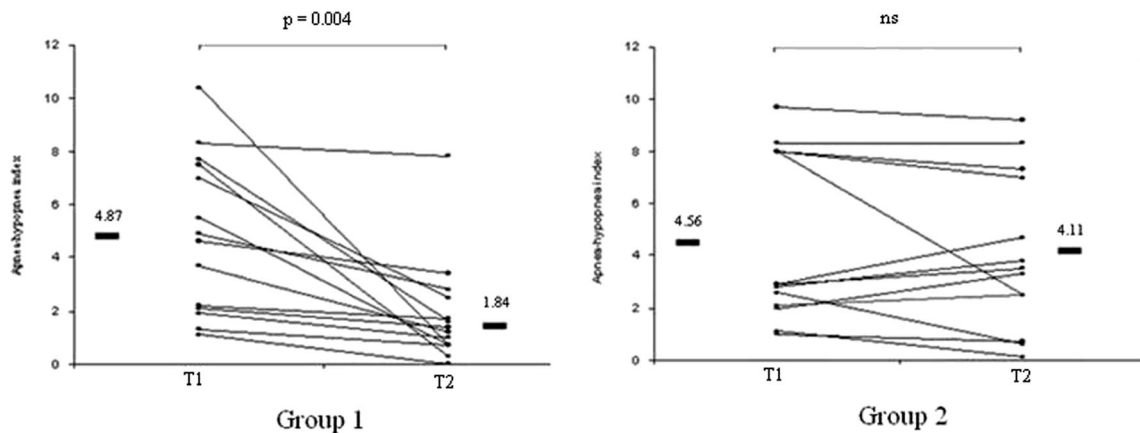


Fig. 5 Individual values for Apnea-Hypopnea Index (AHI). In group 1, AHI from T1 to T2 decreased significantly. In contrast, in group 2, AHI from T1 to T2 was similar. T1 6 months after adenotonsillectomy, T2 2 months after T1

30 % of children, a finding that is in keeping with the data in the literature [7, 8].

Although there have been numerous reports of residual OSA following orthodontic, medical, and surgical treatment, the causes and mechanisms underlying the incomplete resolution of OSA are still unknown. In 2010, when Bhattacharjee et al. quantified the effect of demographic and clinical confounders known to affect the success of AT, they found that age, BMI, presence of asthma, and severity of pre-AT AHI emerged as the main factors contributing to post-AT AHI [8].

It should be borne in mind that although surgical (removal of tonsils and adenoids), orthodontic (enlarging the maxilla through rapid maxillary expansion), and medical (reducing lymphadenoid tissue size) treatments correct the oropharyngeal structure they have no effect on either functionality or neuromuscular disorders.

For example, oral breathing and lip hypotonia, which are typical of children with OSA, do not usually change after surgical, orthodontic, and/or medical treatment and may cause residual OSA.

In their study published in 2012, Gallerano et al. focused on the effect of oropharyngeal exercises following surgical-orthodontic treatment as a means of achieving long-term success in dentoskeletal dysmorphisms [28]. They observed that such treatment promotes the recovery of neuromuscular

function and re-educates all the functions that do not comply with structural surgical changes.

Assuming that this is true, what role does neuromuscular dysfunction play in the etiopathogenesis of residual OSA? Is neuromuscular dysfunction a cause or a consequence of residual OSA?

We hypothesize that some signs, such as oral breathing, hypotonic lips, and an incorrect swallowing pattern, may predispose subjects to OSA and they may contribute to residual disease. An alternative approach to pediatric OSA aimed at rehabilitating neuromuscular function is therefore warranted. In this regard, oropharyngeal exercises may help to resolve the stomatognathic dysfunction that persists following other types of standard therapy.

In our study, oropharyngeal exercises led to a significant decrease in nasal obstruction, which in turn reduced the proportion of positive Glatzel and Rosenthal tests and improved nasal patency, thereby allowing patients to regain nasal breathing; moreover, seal lip exercises designed to strengthen the lips also allowed children to regain correct labial seal.

The data published by Guimarães suggest that the role of oropharyngeal exercises in adult patients with OSA is limited, which, as Guilleminault points out, highlights the importance of identifying and promptly intervening in children with OSA in order to optimize the normal growth of the airways and to

Table 3 Morphofunctional evaluation in each group

	Group 1 (n=14)			Group 2 (n=13)		
	T1 (%)	T2 (%)	p	T1 (%)	T2 (%)	p
Oral breathing	13/14 (92.9)	4/14 (28.5)	0.002	12/13 (92.3)	11/13 (84.6)	ns
Labial seal	2/14 (14.3)	12/14 (85.7)	<0.001	1/13 (7.7)	1/13 (7.7)	ns
Lip tone	3/14 (21.4)	10/14 (78.6)	<0.05	2/13 (15.4)	2/13 (15.4)	ns
Positive Glatzel test	10/14 (71.4)	3/14 (21.4)	<0.05	7/13 (53.8)	6/13 (46.2)	ns
Positive Rosenthal test	10/14 (71.4)	3/14 (21.4)	<0.05	7/9 (53.8)	6/9 (46.2)	ns

T1 6 months after adenotonsillectomy, T2 2 months after T1

ensure a lasting impact in the treatment of sleep disorder breathing [10, 29].

Our prospective study and Guilleminault's retrospective study are the first studies conducted on oropharyngeal exercises in children with OSA; for this reason, it is impossible to ascertain at what age children are most likely to comply with treatment and at the same time be spared irreversible neuromuscular damage.

Experimental data have documented the efficacy of oropharyngeal exercises in other disorders, such as Noonan syndrome (multiple malformation disorder with an autosomal dominant inheritance pattern) and in Beckwith-Wiedemann syndrome (congenital disorder that involves a somatic overgrowth during the patient's first years of life), both of which have yielded successful outcomes [30, 31]. This study does have several limitations, which include the small sample size and the varying degree of children compliance. Moreover, it is not known if a longer follow-up time can influence the effect of the exercises or if it is enduring. More research is needed.

Conclusion

OSA does not resolve following first-line treatment in a considerable number of children. Postoperative PSG could be useful to identify subjects who may require additional therapy when symptoms persist. Although the reasons underlying the incomplete recovery following such treatments are still unclear, we hypothesize that residual OSA may be due to incomplete recovery of neuromuscular function after surgical, orthodontic, and medical treatments. Indeed, a major limitation of such treatments is that they act exclusively on the structural pathway. However, the most appropriate age for oropharyngeal exercises remains a matter of debate.

Our results, which are supported by those of other studies, highlight the need for further research to investigate the persistence of neuromuscular deficits after first-line treatments. It is worth bearing in mind that nonpharmacological therapies have very few side effects and tend to be considerably less expensive than other therapies. Furthermore, the rehabilitative exercises that we propose are easily taught, but since the parents' cooperation is essential, it is important to consider the family's psycho-sociocultural level, as well as to educate and motivate the family. We believe that all children with OSA who have received any kind of treatment for OSA should undergo a oropharyngeal evaluation aimed at assessing the need for neuromuscular rehabilitation.

Ethical standards Informed consent was obtained from parents, and the study was approved by the Ethics Committee of the Sant' Andrea Hospital.

Conflict of interest The authors declare that they have no conflict of interest.

References

- Marcus CL, Brooks LJ, Draper KA, Gozal D, Halbower AC, Jones J, Schechter MS, Sheldon SH, Spruyt K, Ward SD, Lehmann C, Shiffman RN (2012) Clinical practice guideline. Diagnosis and Management of Childhood Obstructive Sleep Apnea Syndrome. *Pediatrics* 130(3):576–584
- Gozal D, Lipton AJ, Jones KL (2002) Circulating vascular endothelial growth factor levels in patients with obstructive sleep apnea. *Sleep* 25(1):59–65
- Amin RS, Kimball TR, Bean JA, Jeffries JL, Willging JP, Cotton RT, Witt SA, Glascock BJ, Daniels SR (2002) Left ventricular hypertrophy and abnormal ventricular geometry in children and adolescents with obstructive sleep apnea. *Am J Respir Crit Care Med* 165(10):1395–1399
- Kheirandish-Gozal L, Bhattacharjee R, Gozal D (2010) Autonomic alterations and endothelial dysfunction in pediatric obstructive sleep apnea. *Sleep Med* 11(7):714–720
- Chang SJ, Chae KY (2010) Obstructive sleep apnea syndrome in children: epidemiology, pathophysiology, diagnosis and sequelae. *Korean J Pediatr* 53(10):863–871
- Arens R, Marcus CL (2004) Pathophysiology of upper airway obstruction: a developmental perspective. *Sleep* 27(5):997–1019
- Tauman R, Gozal D (2011) Obstructive sleep apnea syndrome in children. *Expert Rev Respir Med* 5(3):425–440
- Bhattacharjee R, Kheirandish-Gozal L, Spruyt K, Mitchell RB, Promchiarak J, Simakajornboon N, Kaditis AG, Splaingard D, Splaingard M, Brooks LJ, Marcus CL, Sin S, Arens R, Verhulst SL, Gozal D (2010) Adenotonsillectomy outcomes in treatment of obstructive sleep apnea in children: a multicenter retrospective study. *Am J Respir Crit Care Med* 182(5):676–683
- Villa MP, Rizzoli A, Miano S, Malagola C (2011) Efficacy of rapid maxillary expansion in children with obstructive sleep apnea syndrome: 36 months of follow-up. *Sleep Breath* 15(2):179–184
- Guimarães KC, Drager LF, Genta PR, Marcondes BF, Lorenzi-Filho G (2009) Effects of oropharyngeal exercises on patients with moderate obstructive sleep apnea syndrome. *Am J Respir Crit Care Med* 179(10):962–966
- Puhan MA, Suarez A, Cascio CL, Zahn A, Heitz M, Braendli O (2005) Didgeridoo playing as alternative treatment for obstructive sleep apnoea syndrome: randomised controlled trial. *BMJ* 332(7536):266–270
- Iber C, Ancoli-Israel S, Chesson A et al (2007) The AASM manual for the scoring of sleep and associated event: rules, terminology and technical specifications. *Am Acad Sleep Med* 1st ed Westchester
- Marcus CL, Omlin KJ, Basinki DJ, Bailey SL, Rachal AB, Von Pechmann WS, Keens TG, Ward SL (1992) Normal polysomnographic values for children and adolescents. *Am Rev Respir Dis* 146(5 Pt1):1235–1239
- Uliel S, Tauman R, Greenfeld M, Sivan Y (2004) Normal polysomnographic respiratory values in children and adolescents. *Chest* 125(3):872–878
- Villa MP, Paolino MC, Castaldo R, Vanacore N, Rizzoli A, Miano S, Del Pozzo M, Montesano M (2013) Sleep clinical record: an aid to rapid and accurate diagnosis of pediatric sleep disordered breathing. *Eur Respir J* 41(6):1355–1361
- Liistro G, Rombaux P, Belge C, Dury M, Aubert G, Rodenstein DO (2003) High Mallampati score and nasal obstruction are associated risk factors for obstructive sleep apnoea. *Eur Respir J* 21(2):248–252
- Friedman M, Ibrahim H, Joseph NJ (2004) Staging of obstructive sleep apnea/hypopnea syndrome: a guide to appropriate treatment. *Laryngoscope* 114(3):454–459
- Brouillette R, Hanson D, David R, Klemka L, Szatkowski A, Fernbach S, Hunt C (1984) A diagnostic approach to suspected obstructive sleep apnea in children. *J Pediatr* 105(1):10–14

19. DuPaul GJ, McGoey KE, Eckert TL, VanBrakle J (2001) Preschool children with attention-deficit/hyperactivity disorder: impairments in behavioral, social, and school functioning. *J Am Acad Child Adolesc Psychiatry* 40(5):508–515
20. Chauvois A, Fournier M, Girardin F (1991) Rééducation des fonctions dans la thérapeutique orthodontique. Editions Sid, Vanves
21. Levrini A (1997) Terapia miofunzionale. Rieducazione neuromuscolare integrata. Masson S.p.A, Milan
22. Ye J, Liu H, Zhang GH, Li P, Yang QT, Liu X, Li Y (2010) Outcome of adenotonsillectomy for obstructive sleep apnea syndrome in children. *Ann Otol Rhinol Laryngol* 119(8):506–513
23. Kuhle S, Urschitz MS (2011) Anti-inflammatory medications for obstructive sleep apnea in children. *Cochrane Database Syst Rev* CD007074
24. Kheirandish-Gozal L, Serpero LD, Dayyat E, Kim J, Goldman JL, Snow A, Bhattacharjee R, Gozal D (2009) Corticosteroids suppress in vitro tonsillar proliferation in children with obstructive sleep apnoea. *Eur Respir J* 33(5):1077–1084
25. Goldbart AD, Goldman JL, Veling MC, Gozal D (2005) Leukotriene modifier therapy for adenotonsillar hypertrophy and sleep disordered breathing in children. *Am J Respir Crit Care Med* 172(3):364–370
26. Kheirandish L, Goldbart AD, Gozal D (2006) Intranasal steroids and oral leukotriene modifier therapy in residual sleep disordered breathing following tonsillectomy and adenoidectomy in children. *Pediatrics* 117:E61–E66
27. Gozal D, Kheirandish-Gozal L (2008) The multiple challenges of obstructive sleep apnea in children: morbidity and treatment. *Curr Opin Pediatr* 20(6):654–658
28. Gallerano G, Ruoppolo G, Silvestri A (2012) Myofunctional and speech rehabilitation after orthodontic-surgical treatment of dento-maxillofacial dysgnathia. *Prog Orthod* 13(1):57–68
29. Guilleminault C, Huang YS, Monteyrol PJ, Sato R, Quo S, Lin CH (2013) Critical role of myofascial reeducation in pediatric sleep-disordered breathing. *Sleep Med* 14(6):518–525
30. Fonteles CS, de Miranda Mota AC, Lima RA, Borges PC, da Silveira A (2013) Conservative management of severe open bite and feeding difficulties in patient with Noonan syndrome. *Cleft Palate Craniofac J* 50(2):242–248
31. Abeleira MT, Seoane-Romero JM, Outumuro M, Caamaño F, Suárez D, Carmona IT (2011) A multidisciplinary approach to the treatment of oral manifestations associated with Beckwith-Wiedemann syndrome: a long-term case report. *J Am Dent Assoc* 142(12):1357–1364