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Impact of weight-loss management on children and adolescents with obesity and obstructive sleep apnea☆

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ABSTRACT

Objectives: To evaluate the impact of weight-loss management on obstructive sleep apnea (OSA) in children and adolescents with obesity. We hypothesized that a reduction in the degree of obesity was associated with a reduction in the apnea-hypopnea index (AHI).

Methods: OSA (AHI ≥2) was investigated using a type 3 portable sleep device (Nox T3) in children and adolescents aged 7–18 years with overweight or obesity (body mass index standard deviation score (BMI SDS) > 1.28) at enrollment in a chronic care multidisciplinary overweight- and obesity treatment clinic. Individuals with OSA were included prospectively and longitudinally. A follow-up sleep examination was performed after 6 and 12 months from baseline accompanied by anthropometric measurements.

Results: At baseline, 62 children with OSA were included (median age = 13.4 years, median BMI SDS = 3.16). A total of 55 out of 62 children (89%) attended the first follow-up, and 29 out of 34 children (85%) with residual OSA attended the second follow-up. By the end of the study, the AHI was normalized in 27 out of 62 children (44%). In a multiple linear regression analysis, the decrease in BMI SDS was associated with the decrease in AHI upon the first follow-up ($p = 0.02$) independently of sex; age; baseline puberty stage; baseline tonsillar hypertrophy; baseline AHI; baseline BMI SDS; and time to follow-up. There was no association between change in BMI SDS and change in AHI from the first to the second follow-up ($p = 0.81$).

Conclusions: OSA improved during obesity treatment, and the reduction in BMI SDS was significantly associated with the reduction in AHI after approximately six months of treatment. This indicates that obesity treatment should be considered among the first-line treatments of OSA in children and adolescents affected by overweight or obesity.

1. Introduction

In recent years, the link between obesity and pediatric obstructive sleep apnea (OSA) has received increasing attention. OSA results from prolonged partial upper airway obstruction and/or intermittent complete obstruction that disrupts normal breathing during sleep [1], and children with overweight or obesity are at greater risk of having OSA compared with their normal-weight counterparts [2–5]. The prevalence rates are as high as 24–61% in children with overweight/obesity [6–9].

The recommended first-line treatment for pediatric OSA is adenotonsillectomy (AT) [1]. However, several studies have reported that obesity increases the risk of persistent OSA after AT [10,11]. Moreover, a high recurrence rate of OSA one year after AT is reported in children with overweight/obesity [12]. Continuous positive airway pressure is a last resort treatment for persistent OSA, but poor compliance is a strong limitation to this therapy [13,14].

Weight-loss management could be key in the treatment of obesity-related OSA in children and adolescents. This idea is supported by studies reporting an association between body mass index standard deviation score (BMI SDS) and the apnea-hypopnea index (AHI) [4,15]. In adults, several studies have reported that OSA improves during weight-loss management [16,17]. In contrast, only few studies have investigated the impact of obesity treatment on OSA in children and adolescents [6–8], and it has yet to be clarified whether a reduction in

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the degree of obesity could result in a reduction in AHI.

The aim of this study was to investigate whether OSA improves during a chronic care multidisciplinary overweight- and obesity treatment. We hypothesized that a reduction in the BMI SDS was associated with a reduction in the AHI. Moreover, we investigated if sex, age, pubertal development stage, tonsillar hypertrophy, and previous severity of OSA affected the AHI upon follow-up.

2. Material and methods

2.1. Design and study population

Children and adolescents with overweight/obesity were recruited while entering the chronic care multidisciplinary treatment program at the Children's Obesity Clinic, Department of Pediatrics, Holbæk University Hospital, Denmark, from June 2015 to July 2016. The two inclusion criteria were age 7–18 years; and a BMI SDS > 1.28, corresponding to the 90th percentile according to a Danish age- and sex-adjusted reference [18]. The exclusion criteria were as follows: neuromuscular disease; craniofacial syndromes/abnormalities; laryngeal and/or tracheal malformations. All individuals underwent a baseline sleep examination using a portable type 3 device (Nox T3). The baseline study is described in detail previously [19].

Children and adolescents were included in this longitudinal study if OSA (AHI ≥2) was present at baseline. Sleep examinations were repeated after 6 and 12 months from baseline. At each visit anthropometrics were measured and the absolute change in BMI SDS was calculated. The follow-up period ended in June 2017. Fig. 1 illustrates the study design including the procedures performed at different times.

2.2. The obesity treatment program

The treatment program was based on the Children's Obesity Clinic's treatment protocol [20]. The protocol builds on the understanding of obesity as a complex and chronic disease [21], and on the understanding that active neuroendocrine regulation of fat mass interacts with treatment [22]. The approach is family-centered. Through a questionnaire-based interview, knowledge about the families' intake at all meals, physical activities, psychosocial wellbeing, sedentary behaviors, sleep times, and school attendance was reported as amounts, qualities, and frequencies. An individualized treatment plan consisting of 10–20 interventions regarding lifestyle changes was then produced, and the families were guided in the implementation of the plan in everyday life. The treatment team consisted of pediatricians, nurses, dieticians, a psychologist, and a social worker. The frequency of consultations was tailored to the individual and depended on the child's needs, the degree of treatment success, and practical limitations such as the place of residence.

2.3. Sleep examinations

Sleep examinations were performed for one night using a portable type 3 device (Nox T3). Respiratory airflow was measured by nasal pressure cannula; respiratory effort via chest and abdominal belts; body position and activity via an integrated accelerometer; and pulse and oxygen saturation via an oximeter. All sleep examinations were manually analyzed by the same registered polysomnographic technologist (RPSGT) according to the pediatric respiratory rules defined by the American Academy of Sleep Medicine [23]. The RPSGT was blinded to previous results of any sleep examinations and to the BMI SDS of the children. Due to practical circumstances, baseline sleep examinations were performed during the initial stay at the obesity clinic while the follow-up sleep examinations were performed at home.

Apneas were identified if there was a ≥90% drop in airflow for the duration of at least two breaths. Apneas associated with respiratory effort throughout the entire period of the event were classified as obstructive, whereas apneas associated with absent respiratory effort in one portion of the event and the presence of respiratory effort in another portion were classified as mixed. Hypopneas were identified if there was a ≥30% drop in airflow for the duration of at least two breaths associated with a ≥3% drop in oxygen saturation. The AHI was calculated as the sum of apneas and hypopneas divided by the total recording time [24]. OSA was defined as AHI ≥2. Mild OSA was defined as 2 ≤ AHI < 5, moderate OSA as 5 ≤ AHI < 10, and severe OSA as AHI ≥10. The oxygen desaturation index (ODI) was defined as the average number of oxygen desaturations ≥4% per hour of sleep.

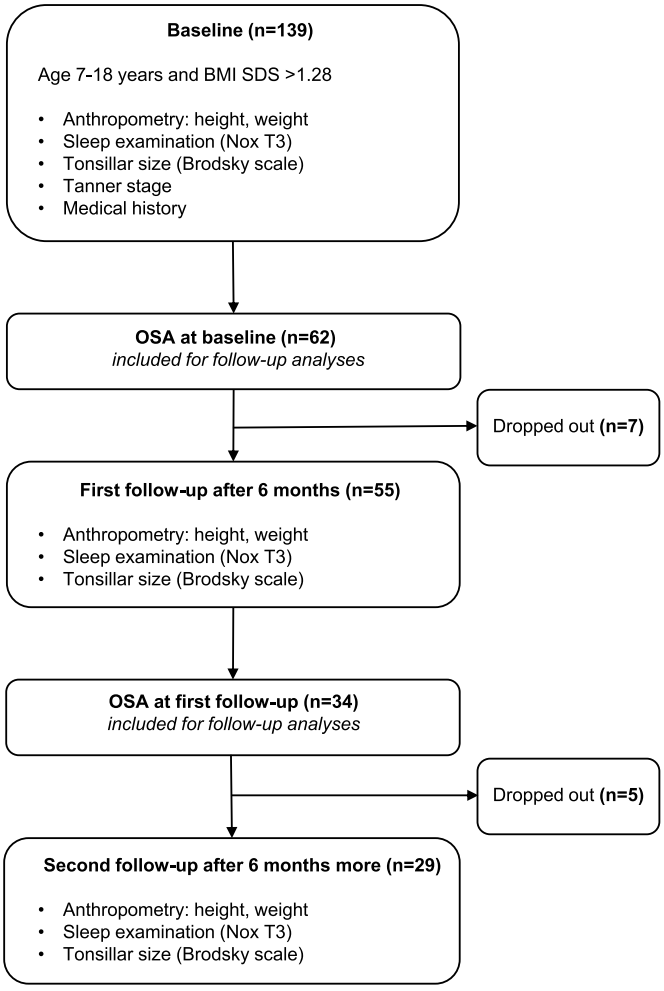

Fig. 1. Flow chart describing the study design and inclusion of children and adolescents.

2.4. Procedures

Height was measured to the nearest 0.1 cm using a stadiometer and weight was measured to the nearest 0.1 kg. The children wore light indoor clothing and no shoes during the measurements. BMI was calculated as weight in kilograms over height in meters squared and was further analyzed as BMI SDS using the LMS method (LMS refers to three smooth age specific curves called L (lambda), M (mu), and S (sigma) [25]) based on Danish references [18].

The tonsillar size was visually quantified and graded from 0 to 4 using the Brodsky scale [26]. Pubertal development was assessed according to Tanner stages after evaluation of pubic hair and breasts [27,28]. Testicular size was measured by Prader's orchidometer.

2.5. Informed consent and ethical approvals

Informed consent was obtained from all individual participants included in the study. The study was approved by the Regional Danish Ethics Committee (Protocol ID SJ-404) and by the Danish Data Protection Agency (ID no. REG-111-2014).

2.6. Statistical analyses

Statistics were performed in SAS Enterprise Guide version 7.1.

Comparison of descriptive characteristics between groups was performed using chi-square test or Fisher's exact test for categorical variables and Mann-Whitney test for continuous variables. The Wilcoxon signed-rank test was used to compare data before and after treatment.

A multiple regression analysis was used to estimate the effect of change in BMI SDS (from baseline to the first follow-up) on AHI upon the first follow-up. The analysis was adjusted for the following variables: sex, baseline age, baseline puberty stage, baseline tonsillar hypertrophy, baseline AHI, baseline BMI SDS, and time from baseline to the first follow-up.

A similar multiple regression analysis was used to estimate the effect of change in BMI SDS (from the first to the second follow-up) on AHI upon the second follow-up. The analysis was adjusted for the same variables, but with values deriving from the first follow-up and the time between the first and the second follow-up.

To test for interaction between change in BMI SDS and tonsillar hypertrophy, an interaction term between these factors was included in the adjusted analyses.

In all analyses tonsillar size and puberty stage were dichotomized: Tonsillar hypertrophy was defined as a Brodsky score > 2. Tanner stage 1 was defined as pre-pubertal and Tanner stages 2–5 were defined as pubertal/post-pubertal.

Two tailed p-values less than 0.05 were considered statistically significant.

3. Results

3.1. Baseline characteristics

The study included 62 children with OSA at baseline (Table 1) of which 71% had mild OSA, 18% had moderate OSA, and 11% had severe OSA. Table 1 compares the baseline characteristics between the group with and without OSA. Children with OSA were older (p = 0.002) and had higher BMI SDS (p = 0.02) compared with children without OSA.

3.2. First follow-up study

A total of 55 out of 62 children (89%) attended the first follow-up after a median of 6.5 months (range: 5.1–10.5). Residual OSA was present in 34 out of 55 children (62%) at the first follow-up. Children with residual OSA (n = 34) had higher AHI at baseline (p = 0.006); higher BMI SDS at follow-up (p = 0.02); achieved a smaller reduction in BMI SDS from baseline to first follow-up (p = 0.03); and reported more frequently a history of tonsillectomy (p = 0.01) and adenoidectomy (p = 0.03) compared with children who normalized their AHI (n = 21) (Table 2).

3.3. Second follow-up study

Of the 34 children with residual OSA at the first follow-up, 29 attended the second follow-up (85%). The median interval between the first and the second follow-up was 6.6 months (range: 4.4–10.8), and the median interval between baseline and the second follow-up was 13 months (range: 11.7–19.4). Residual OSA continued to persist in 23 out of 29 children (79%) after the second follow-up.

Overall the AHI was normalized in 27 out of 62 children (44%) by

Table 1
Characteristics of children and adolescents with and without obstructive sleep apnea (OSA) at the baseline visit.

	OSA (AHI ≥ 2) (n = 62)	Non-OSA (AHI < 2) (n = 77)	*p*-value
Demographics/anthropometrics			
Boys, n (%)	27/62 (43.6)	32/77 (41.6)	0.81
Age, years	13.4 (11.4–15.1)	11.6 (9.3–13.5)	**0.002**
Tanner stage boys			
Pre-pubertal, n (%)	8/27 (29.6)	13/32 (40.6)	0.40
Tanner stage girls			
Pre-pubertal, n (%)	8/35 (22.9)	16/45 (35.6)	0.22
Tonsillar hypertrophy, n (%)	12/62 (19.4)	9/77 (11.7)	0.21
Tonsillectomy, n (%)	9/62 (14.5)	5/76[a] (6.6)	0.12
Adenoidectomy, n (%)	12/62 (19.4)	6/75[b] (8.0)	0.050
Asthma, n (%)	5/62 (8.1)	11/77 (14.3)	0.25
BMI SDS	3.16 (2.64–3.31)	2.83 (2.43–3.24)	**0.02**
BMI SDS > 2.33*, n (%)	56/62 (90.3)	60/77 (77.9)	0.051
Sleep characteristics			
AHI, events/hour	3.3 (2.7–5.7)	0.8 (0.3–1.3)	< **0.0001**
Sleep time, hours	7.7 (5.9–8.4)	7.6 (6.3–8.5)	0.74
Oxygen saturation	95.0 (94.0–95.8)	95.8 (95.0–96.4)	**0.0013**
ODI, events/hour	2.3 (1.7–3.9)	1.1 (0.7–1.7)	< **0.0001**

For continuous variables, data are presented with medians and interquartile ranges.
Bold values indicate p < 0.05.
History of tonsillectomy, adenoidectomy, and asthma was self-reported.
[a]one did not know the answer, [b]two did not know the answer.
*BMI SDS > 2.33 was defined as obesity [18].
BMI SDS: body mass index standard deviation score, AHI: apnea-hypopnea index, ODI: oxygen desaturation index.

Table 2
Characteristics of children and adolescents with and without residual obstructive sleep apnea (OSA) at the first follow-up visit.

	Residual OSA (AHI ≥ 2) (n = 34)	Normalized AHI (AHI < 2) (n = 21)	*p*-value
Boys, n (%)	15/34 (44.1)	10/21 (47.6)	0.80
Age, years	13.4 (11.8–16.6)	13.6 (12.6–15.1)	0.38
Tanner stage boys			
Pre-pubertal, n (%)	4/15 (26.7)	3/10 (30.0)	1.0
Tanner stage girls			
Pre-pubertal, n (%)	4/19 (21.5)	2/11 (18.2)	1.0
Tonsillar hypertrophy, n (%)	7/34 (20.6)	4/21 (19.1)	0.90
Tonsillectomy, n (%)	9/34 (26.5)	0/21 (0)	**0.01**
Adenoidectomy, n (%)	10/34 (29.4)	1/21 (4.8)	**0.03**
Asthma, n (%)	4/34 (11.8)	2/21 (9.5)	0.80
BMI SDS	2.97 (2.48–3.36)	2.42 (2.07–2.90)	**0.02**
AHI, events/hour	4.3 (2.8–8.7)	1.1 (0.6–1.6)	< **0.0001**
Baseline BMI SDS	3.21 (2.78–3.36)	2.78 (2.61–3.22)	0.20
Baseline AHI, events/hour	4.7 (2.9–8.9)	2.9 (2.7–3.4)	**0.006**
Change in BMI SDS from baseline to first follow-up	−0.16 (−0.31–0.00)	−0.32 (−0.78 to −0.09)	**0.03**
Change in AHI from baseline to first follow-up	0.2 (−1.6–1.1)	−1.9 (−2.4–1.4)	**0.001**

For continuous variables, data are presented with medians and interquartile ranges.
Bold values indicate p < 0.05.
Tanner stages are the baseline assessments because puberty stage was only rated at baseline.
History of tonsillectomy, adenoidectomy, and asthma was self-reported.
BMI SDS: body mass index standard deviation score, AHI: apnea-hypopnea index.

the end of the study.

3.4. Dropouts

A total of 7 out of 62 children (11%) dropped out of the study at the first follow-up, and 5 out of 34 (15%) dropped out at the second follow-up because they chose to withdraw from the study for various reasons. There was no difference in sex, age, baseline AHI, and baseline BMI SDS between the dropouts (n = 12) and the children and adolescents who continued in the study (n = 50).

3.5. Changes in AHI and BMI SDS after treatment

From baseline to the second follow-up (n = 55), the AHI was reduced by a median of 1.2 (interquartile range (IQR): −2.3–0.8, p = 0.02), and the BMI SDS was reduced by a median of 0.19 (IQR: −0.49–0.00, p < 0.0001) corresponding to a relative BMI SDS decrease of 6.0%. From the first to the second follow-up (n = 29), the AHI was further reduced by a median of 1.4 (IQR: −2.7–0.7, p = 0.0001) while the BMI SDS increased by a median of 0.12 (IQR: −0.01–0.20, p = 0.0009).

3.6. Association between change in BMI SDS and change in AHI

The association between change in BMI SDS and change in AHI upon each follow-up visit was estimated in multiple regression analyses (Table 3).

The first analysis included a total of 55 children who attended the first follow-up. The analysis was adjusted for sex; baseline age; baseline puberty; baseline tonsillar hypertrophy; baseline AHI; baseline BMI SDS; and time from baseline to the first follow-up. A decrease in BMI SDS of one unit equaled an average decrease in AHI upon the first follow-up of 55% (95% confidence interval (CI): 13%–77%, p = 0.02, Table 3a).

The second analysis included 29 children with residual OSA who attended the second follow-up. No association between change in BMI SDS and change AHI from the first to the second follow-up was found (p = 0.81, Table 3b).

There was no statistically significant interaction between tonsillar hypertrophy and change in BMI SDS in any of the analyses (first follow-up: p = 0.51, second follow-up: p = 0.77).

Repeating the analyses with ODI as the primary outcome, similar estimates to those presented in Table 3 were achieved. A one-unit decrease in BMI SDS equaled an average decrease in the ODI of 51% upon the first follow-up (95% CI: 11–73%, p = 0.02).

Table 3
Multiple regression analyses investigating the effect of different independent variables on the apnea-hypopnea index (AHI) upon each follow-up visit in children and adolescents referred for obesity treatment. **a**) Estimates are presented as ratios on AHI upon the first follow-up. **b**) Estimates are presented as ratios on AHI upon the second follow-up.

a. First follow-up (n = 55)			
	Estimate	95% CI	*p*-value
Change in BMI SDS from baseline to first follow-up, one-unit decrease	0.45	0.23–0.87	**0.02**
Sex, male vs. female	0.65	0.38–1.10	0.11
Age, one-year increase	1.07	0.94–1.22	0.28
Puberty stage, prepubertal vs. pubertal/post-pubertal	1.39	0.63–3.06	0.41
Tonsillar hypertrophy, tonsil grade > 2 vs. tonsil grade ≤2	2.03	1.01–4.08	**0.047**
AHI at baseline, 100% increase	1.77	1.37–2.27	< **0.0001**

b. Second follow-up (n = 29)			
	Estimate	95% CI	*p*-value
Change in BMI SDS from first to second follow-up, one-unit decrease	1.16	0.32–4.21	0.81
Sex, male vs. female	1.02	0.64–1.64	0.93
Age, one-year increase	1.03	0.92–1.16	0.56
Puberty stage, prepubertal vs. pubertal/post-pubertal	0.84	0.37–1.90	0.66
Tonsillar hypertrophy, tonsil grade > 2 vs. tonsil grade ≤2	0.72	0.40–1.30	0.26
AHI at first follow-up, 100% increase	1.58	1.25–1.99	**0.0005**

a) adjusted for BMI SDS at baseline and the time between baseline and first follow-up.
b) adjusted for BMI SDS at first follow-up and the time between first and second follow-up.
Bold values indicate p < 0.05.
BMI SDS: body mass index standard deviation score, CI: confidence interval.

3.7. The effect of other variables on the AHI upon follow-up

The severity of OSA (i.e., a higher AHI) was associated with a higher AHI upon the next follow-up (Table 3a: p < 0.0001, and Table 3b: p = 0.0005). Baseline tonsillar hypertrophy was marginally significantly associated with the AHI upon the first follow-up (p = 0.047). Sex, age, and puberty stage did not have statistically significant effects on the AHI upon any of the follow-up visits (Tables 3a and 3b).

4. Discussion

In this prospective longitudinal study of children and adolescents with overweight/obesity, the AHI was normalized in 38% of the children after approximately 6 months of obesity treatment and in 44% one year after treatment initiation.

The AHI was significantly reduced from baseline to the first follow-up, and the multiple regression analysis estimated that a decrease in the BMI SDS of one unit equaled an average decrease in the AHI upon follow-up of 55% independently of sex; baseline age; baseline puberty stage; baseline tonsillar hypertrophy; baseline AHI; baseline BMI SDS; and time to follow-up. A similar result was found when using the ODI as outcome variable.

We adjusted for the AHI at baseline because children with a high initial AHI would be expected to have higher AHI values at follow-up compared with children with a low initial AHI. This hypothesis was confirmed in our analyses. The effect of the change in BMI SDS on the AHI upon follow-up remained significant after adjusting for the baseline AHI, indicating that different degrees of OSA at baseline were not responsible for this effect. Moreover, we controlled for the baseline BMI SDS and the time to follow-up to set aside the possible variation in AHI caused by different degrees of obesity and different times of intervention. Sex, age, and puberty stage did not have statistically significant effects on the AHI upon follow-up in the analyses.

To investigate whether the effect of the change in BMI SDS depended on the tonsillar size, we included an interaction term between these factors in the adjusted analyses. The interaction was not statistically significant, implying that children with tonsillar hypertrophy achieved the same effect of the change in BMI SDS as children without tonsillar hypertrophy.

Few and relatively small studies have assessed the impact of behavioral weight-loss management on the severity of OSA in children and adolescents. Siegfried et al. [7] studied 38 adolescents (mean age = 18 years) with severe obesity of which 9 adolescents (24%) were diagnosed with OSA (AHI > 5). The average AHI decreased by 50% after an average of 5.9 months, and the AHI was normalized in 6 out of 9 adolescents (67%). Verhulst et al. [6] studied 61 children and adolescents (mean age 14.8 years) with overweight/obesity of which 37 (61%) were diagnosed with OSA (AHI ≥2). After a median of 5.2 months, 21 children repeated the sleep examination, and the AHI was normalized in 13 children (62%). The study concluded that the relative

decrease in BMI SDS was significantly correlated with the change in AHI ($r = -0.51$; $p = 0.03$). However, no estimate of the effect was given and possible confounders were not considered. In two studies by Van Hoorenbeeck et al. [8,29] the cure rate of OSA after 4–6 months of weight-loss intervention was 71% (29 out of 41 children normalized their AHI [8]) and 76% (38 out of 50 children normalized their AHI [29]) using ODI ≥2 as the definition of OSA. None of these studies [8,29] estimated the association between change in BMI SDS and change in AHI.

Our study is most comparable to the study by Verhulst et al. [6] because the definition of OSA and the median baseline AHI corresponded. However, Verhulst et al. reported a higher cure rate which is likely to be caused by a bigger decrease in BMI SDS. The median relative decrease in the BMI SDS described by Verhulst et al. was 34.8% [6] compared with 6.0% upon the first follow-up in our study.

The mentioned studies only performed one follow-up sleep examination [6–8,29]. Therefore, we could not compare the results of our second follow-up with any of the previous studies. Our analysis on the 29 children with residual OSA who participated in the second follow-up showed no association between change in BMI SDS and change in AHI or ODI. We have no exact explanation for this finding but the analysis was based on a small and selected group consisting of the most severe cases who achieved a smaller reduction in BMI SDS from baseline to the first follow-up, and who increased their BMI SDS from the first to the second follow-up. The impact of OSA on physical activity has been investigated in adults. Hargens et al. [30] reported that the presence of OSA led to less physical activity and more sedentary behavior. However, we do not have data to support this in our study. Children with residual OSA also had a higher baseline AHI compared with children who normalized their AHI, and they more frequently reported a history of adenotonsillectomy (Table 2). It has been suggested that a history of adenotonsillectomy may serve as a marker of other underlying risk factors for OSA [31]. For instance, OSA in children who have had a tonsillectomy has been associated with familial risk of OSA [32].

Pediatric OSA is multifactorial [33] and the role of obesity in the pathogenesis of OSA is not completely clear. OSA often results from a combination of anatomical factors narrowing the upper airway and factors affecting the upper airway collapsibility [33,34]. Obesity may have an impact on both mechanisms [35]. We recognize that the treatment of OSA should be individual. However, in the light of our findings, which is supported by other studies [6–8,29], and in the light of the high risk of persistent OSA after AT in individuals with obesity [10,11], weight-loss management should be considered a first-line alternative or supplement for treating OSA in children affected by overweight/obesity. Moreover, there are several other beneficial effects of weight loss [36–38], which further emphasizes the importance of weight-loss management in the treatment of obesity-related OSA.

There are some factors that could possibly influence our results. The follow-up sleep examinations were performed at home, whereas the baseline sleep examinations were performed under admission. The so called first-night effect refers to a reduced sleep quality in individuals sleeping with polysomnography (PSG) for two or more consecutive nights. Scholle et al. [39] investigated the first-night effect in children and found no significant night-to-night variability in the respiratory parameters such as the AHI. However, more research is needed to determine the night-to-night variability when using portable type 3 devices such as the Nox T3. Another factor that could affect the AHI is the developmental change in the upper airway during the intervention time.

It was a limitation to our study that only children and adolescents with OSA at baseline and those with residual OSA were offered follow-up sleep examinations. Having followed the entire cohort would have provided us with valuable information about the change in AHI in all children with and without baseline OSA. Another limitation was that we used portable sleep monitoring with a type 3 device because a full PSG was not available in the obesity clinic. We chose a clinically pragmatic approach reflecting that portable sleep monitoring is the realistic first choice in many sleep clinics. The Nox T3 device has demonstrated good measurement agreement compared with PSG [40], and a recent meta-analysis by Certal et al. concluded that portable type 3 devices are valid tools for predicting both the presence and the severity of OSA in children (pooled area under the curve 0.88) [41]. Furthermore, it was a limitation that we did not assess the adenoid size of our study population. A total of 12 children dropped out of the study, which corresponded to a dropout rate of 11% after 6 months and 19% after 12 months. Of note, there was no difference with regard to baseline characteristics, including baseline AHI and baseline BMI SDS, between the children who withdrew from the study and those who continued. Therefore, we do not expect that these children would have had a strong influence on the results.

5. Conclusions

In conclusion, this study suggests that the AHI is reduced during a chronic care multidisciplinary overweight- and obesity treatment, and we report an association between reduction in BMI SDS and reduction in AHI after approximately six months of treatment in our study population. This indicates that obesity treatment should be considered among the first-line treatments of OSA in children and adolescents affected by overweight/obesity.

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Conflicts of interest

Author IGA received a study related grant from ResMed Maribo, Denmark. Author JCH declares he has no conflict of interest. Author PH declares he has no conflict of interest.

Author contributions

The study was designed by IGA, PH and JCH. IGA collected and analyzed the data and drafted the manuscript. PH and JCH critically revised and approved the manuscript.

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References

[1] C.L. Marcus, L.J. Brooks, K.A. Draper, D. Gozal, A.C. Halbower, J. Jones, et al., Diagnosis and management of childhood obstructive sleep apnea syndrome, Pediatrics 130 (2012) 576–584, https://doi.org/10.1542/peds.2012-1671.
[2] Y.K. Wing, S.H. Hui, W.M. Pak, C.K. Ho, A. Cheung, A.M. Li, et al., A controlled study of sleep related disordered breathing in obese children, Arch. Dis. Child. 88 (2003) 1043–1047.
[3] D.W. Beebe, D. Lewin, M. Zeller, M. McCabe, K. MacLeod, S.R. Daniels, et al., Sleep in overweight adolescents: shorter sleep, poorer sleep quality, sleepiness, and sleep-disordered breathing, J. Pediatr. Psychol. 32 (2007) 69–79, https://doi.org/10.1093/jpepsy/jsj104.
[4] Z. Xu, A. Jiaqing, L. Yuchuan, K. Shen, A case-control study of obstructive sleep apnea-hypopnea syndrome in obese and nonobese Chinese children, Chest 133 (2008) 684–689, https://doi.org/10.1378/chest.07-1611.
[5] M.-S. Su, H.-L. Zhang, X.-H. Cai, Y. Lin, P.-N. Liu, Y.-B. Zhang, et al., Obesity in

children with different risk factors for obstructive sleep apnea: a community-based study, Eur. J. Pediatr. 175 (2016) 211–220, https://doi.org/10.1007/s00431-015-2613-6.
[6] S.L. Verhulst, H. Franckx, L. Van Gaal, W. De Backer, K. Desager, The effect of weight loss on sleep-disordered breathing in obese teenagers, Obesity 17 (2009) 1178–1183, https://doi.org/10.1038/oby.2008.673.
[7] W. Siegfried, A. Siegfried, M. Rabenbauer, J. Hebebrand, Snoring and sleep apnea in obese adolescents: effect of long-term weight loss-rehabilitation, Sleep Breath. 3 (1999) 83–88, https://doi.org/10.1007/s11325-999-0083-7.
[8] K. Van Hoorenbeeck, H. Franckx, P. Debode, P. Aerts, K. Wouters, J. Ramet, et al., Weight loss and sleep-disordered breathing in childhood obesity: effects on inflammation and uric acid, Obesity 20 (2012) 172–177, https://doi.org/10.1038/oby.2011.282.
[9] I.G. Andersen, J.-C. Holm, P. Homøe, Obstructive sleep apnea in obese children and adolescents, treatment methods and outcome of treatment - a systematic review, Int. J. Pediatr. Otorhinolaryngol. 87 (2016) 190–197, https://doi.org/10.1016/j.ijporl.2016.06.017.
[10] L.M. O'Brien, S. Sitha, L.A. Baur, K.A. Waters, Obesity increases the risk for persisting obstructive sleep apnea after treatment in children, Int. J. Pediatr. Otorhinolaryngol. 70 (2006) 1555–1560, https://doi.org/10.1016/j.ijporl.2006.04.003.
[11] R.B. Mitchell, J. Kelly, Outcome of adenotonsillectomy for obstructive sleep apnea in obese and normal-weight children, Otolaryngol. Head Neck Surg. 137 (2007) 43–48, https://doi.org/10.1016/j.otohns.2007.03.028.
[12] R. Amin, L. Anthony, V. Somers, M. Fenchel, K. McConnell, J. Jefferies, et al., Growth velocity predicts recurrence of sleep-disordered breathing 1 year after adenotonsillectomy, Am. J. Respir. Crit. Care Med. 177 (2008) 654–659, https://doi.org/10.1164/rccm.200710-1610OC.
[13] C.L. Marcus, S.E. Beck, J. Traylor, M.A. Cornaglia, L.J. Meltzer, N. DiFeo, et al., Randomized, double-blind clinical trial of two different modes of positive airway pressure therapy on adherence and efficacy in children, J Clin Sleep Med 8 (2012) 37–42, https://doi.org/10.5664/jcsm.1656.
[14] C.L. Marcus, G. Rosen, S.L.D. Ward, A.C. Halbower, L. Sterni, J. Lutz, et al., Adherence to and effectiveness of positive airway pressure therapy in children with obstructive sleep apnea, Pediatrics 117 (2006) e442–e451, https://doi.org/10.1542/peds.2005-1634.
[15] M. Kohler, K. Lushington, R. Couper, J. Martin, C. Van Den Heuvel, Y. Pamula, et al., Obesity and risk of sleep related upper airway obstruction in caucasian children, J Clin Sleep Med 4 (2008) 129–136.
[16] C.E. Kline, E.P. Crowley, G.B. Ewing, J.B. Burch, S.N. Blair, J.L. Durstine, et al., The effect of exercise training on obstructive sleep apnea and sleep quality: a randomized controlled trial, Sleep 34 (2011) 1631–1640, https://doi.org/10.5665/sleep.1422.
[17] G.D. Foster, K.E. Borradaile, M.H. Sanders, R. Millman, G. Zammit, A.B. Newman, et al., A randomized study on the effect of weight loss on obstructive sleep apnea among obese patients with type 2 diabetes: the Sleep AHEAD study, Arch. Intern. Med. 169 (2009) 1619–1626, https://doi.org/10.1001/archinternmed.2009.266.
[18] K. Nysom, C. Mølgaard, B. Hutchings, K.F. Michaelsen, Body mass index of 0 to 45-y-old Danes: reference values and comparison with published European reference values, Int. J. Obes. Relat. Metab. Disord. 25 (2001) 177–184, https://doi.org/10.1038/sj.ijo.0801515.
[19] I.G. Andersen, J.-C. Holm, P. Homøe, Obstructive sleep apnea in children and adolescents with and without obesity, Eur. Arch. Oto-Rhino-Laryngol. 276 (2019) 871–878, https://doi.org/10.1007/s00405-019-05290-2.
[20] J.-C. Holm, M. Gamborg, D.S. Bille, H.N. Grønbæk, L.C. Ward, J. Faerk, Chronic care treatment of obese children and adolescents, Int. J. Pediatr. Obes. 6 (2011) 188–196, https://doi.org/10.3109/17477166.2011.575157.
[21] N.J. Farpour-Lambert, J.L. Baker, M. Hassapidou, J.C. Holm, P. Nowicka, G.O. malley, et al., Childhood obesity is a chronic disease demanding specific Health care - a position statement from the childhood obesity task force (COTF) of the European association for the study of obesity (EASO), Obes Facts 8 (2015) 342–349, https://doi.org/10.1159/000441483.
[22] M. Rosenbaum, R.L. Leibel, 20 YEARS OF LEPTIN: role of leptin in energy homeostasis in humans, J. Endocrinol. 223 (2014) T83–T96, https://doi.org/10.1530/JOE-14-0358.
[23] R. Berry, R. Brooks, C. Gamaldo, S. Harding, R. Lloyd, C. Marcus, et al., The AASM Manual for the Scoring of Sleep and Associated Events: Rules, Terminology and Technical Specifications, Version 2.1, American Academy of Sleep Medicine, Darien, Illinois, 2014.
[24] American Academy of Sleep Medicine, International Classification of Sleep Disorders, third ed., American Academy of Sleep Medicine, Darien, Illinois, 2014.
[25] T. Cole, P. Green, Smoothing reference centile curves: the LMS method and penalized likelihood, Stat. Med. 11 (1992) 1305–1319.
[26] L. Brodsky, Modern assessment of tonsils and adenoids, Pediatr. Clin. 36 (1989) 1551–1569.
[27] W.A. Marshall, J.M. Tanner, Variations in pattern of pubertal changes in girls, Arch. Dis. Child. 44 (1969) 291–303.
[28] W.A. Marshall, J.M. Tanner, Variations in the pattern of pubertal changes in boys, Arch. Dis. Child. 45 (1970) 13–23.
[29] K. Van Hoorenbeeck, H. Franckx, P. Debode, P. Aerts, J. Ramet, L.F. Van Gaal, et al., Metabolic disregulation in obese adolescents with sleep-disordered breathing before and after weight loss, Obesity 21 (2013) 1446–1450, https://doi.org/10.1002/oby.20337.
[30] T.A. Hargens, R.A. Martin, C.L. Strosnider, G.E.W. Giersch, C.J. Womack, Obstructive sleep apnea negatively impacts objectively measured physical activity, Sleep Breath. (2018), https://doi.org/10.1007/s11325-018-1700-0.
[31] J.C. Spilsbury, A. Storfer-Isser, C.L. Rosen, S. Redline, Remission and incidence of obstructive sleep apnea from middle childhood to late adolescence, Sleep 38 (2015) 23–29, https://doi.org/10.5665/sleep.4318.
[32] S. Morton, C. Rosen, E. Larkin, P. Tishler, J. Aylor, S. Redline, Predictors of sleep-disordered breathing in children with a history of tonsillectomy and/or adenoidectomy, Sleep 24 (2001) 823–829.
[33] H.-L. Tan, D. Gozal, L. Kheirandish-Gozal, Chapter 9: Children, European Respiratory Society Publications, 2015, https://doi.org/10.1183/2312508X.10000915.
[34] C.L. Marcus, Pathophysiology of childhood obstructive sleep apnea: current concepts, Respir. Physiol. 119 (2000) 143–154, https://doi.org/10.1016/S0034-5687(99)00109-7.
[35] S.M. Koenig, Pulmonary complications of obesity, Am. J. Med. Sci. 321 (2001) 249–279.
[36] T.R.H. Nielsen, M. Gamborg, C.E. Fonvig, J. Kloppenborg, K.N. Hvidt, H. Ibsen, et al., Changes in lipidemia during chronic care treatment of childhood obesity, Child. Obes. 8 (2012) 533–541, https://doi.org/10.1089/chi.2011.0098.
[37] J.-C. Holm, M. Gamborg, M. Neland, L. Ward, S. Gammeltoft, B.L. Heitmann, et al., Longitudinal changes in blood pressure during weight loss and regain of weight in obese boys and girls, J. Hypertens. 30 (2012) 368–374, https://doi.org/10.1097/HJH.0b013e32834e4a87.
[38] P.M. Mollerup, T.R.H. Nielsen, C. Bøjsøe, J.T. Kloppenborg, J.L. Baker, J.C. Holm, Quality of life improves in children and adolescents during a community-based overweight and obesity treatment, Qual. Life Res. 26 (2017) 1597–1608, https://doi.org/10.1007/s11136-017-1504-x.
[39] S. Scholle, H.C. Scholle, A. Kemper, S. Glaser, B. Rieger, G. Kemper, et al., First night effect in children and adolescents undergoing polysomnography for sleep-disordered breathing, Clin. Neurophysiol. 114 (2003) 2138–2145, https://doi.org/10.1016/S1388-2457(03)00209-8.
[40] A. Cairns, E. Wickwire, E. Schaefer, D. Nyanjom, A pilot validation study for the NOX T3TM portable monitor for the detection of OSA, Sleep Breath. 18 (2014) 609–614, https://doi.org/10.1007/s11325-013-0924-2.
[41] V. Certal, M. Camacho, J.C. Winck, R. Capasso, I. Azevedo, A. Costa-Pereira, Unattended sleep studies in pediatric OSA: a systematic review and meta-Analysis, Laryngoscope 125 (2015) 255–262, https://doi.org/10.1002/lary.24662.