

Metabolic profile and quality of life in obese children with sleep-disordered breathing

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Abstract

Introduction: Sleep Disordered Breathing (SDB) in adults have been associated to an increase in cardiovascular risks for inducing changes in the metabolism. Current literature has scarce and conflicting data concerning the changes in the metabolic profile found in children with SDB.

Objective: The objectives were to evaluate the metabolic profile in obese children with SDB and to analyze repercussions on their quality of life.

Methods: A total of 73 children were included and grouped according to their body mass index and the presence or absence of respiratory symptoms. Each child answered an OSA-18 questionnaire for quality-of-life evaluation, and fasting serum levels of metabolic profile markers were analyzed. The results were compared between Group I - obese children with SDB, Group II - obese children without SDB and Group III (Control) - non-obese children without SDB.

Results: In the analysis (Group I vs. Group II vs. Group III), the amount of insulin, the glucose/insulin ratio and the HOMA showed significant metabolic changes in both obese groups (Group I and Group II) when compared to those of the control group (Group III), without showing the influence of SDB. The obese group without SDB (Group II) presented higher TGL values. The OSA-18 questionnaire showed that SDB jeopardizes the quality of life of children with respect to sleep disturbances, physical suffering and parents' concern.

Conclusion: SDB jeopardizes the quality of life of children without changing their metabolic profile. Obesity seems to be the most significant risk factor in developing insulin resistance in the studied population.

Introduction

Sleep-Disordered Breathing (SDB) represent a group of breathing disorders characterized by an increase in resistance, or even an alteration, in the airflow through the upper respiratory tract during sleep [1]. The clinical presentation varies from primary snoring to complete and intermittent obstructions of the upper respiratory tract, of which Obstructive Sleep Apnea Syndrome (OSAS) is the most severe form. High blood pressure is observed in children with OSAS [2], but this diagnostic criterion is different from that observed in adults [1].

The prevalence of SDB in children reaches 3% [3,4], and is more common among boys than girls [5], with most children presenting between 3 and eight years of age, when there is a larger disproportion between the growth of the pharyngeal lymphatic tissue (palatine tonsils and adenoids) and that of the face [6,7], thus, the hypertrophy of the tonsils narrows the still small upper airway. However, just as in the adult population, obese children have an increased risk of presenting with SDB. The prevalence of OSAS in obese children is 36 to 60% [8,9].

SDB is associated with several systemic repercussions. Among children, the correlation between OSAS and metabolic alterations has been the target of recent but controversial studies. There is currently increasing interest in establishing if OSAS could cause metabolic alterations in children that would also affect their health as adults.

The distribution of body fat, as measured by the area of visceral adipose tissue at L4 (vertebra used as reference), is a strong predictor

of obstructive sleep apnea and possibly contributes to the relationship between obesity and OSAS in children [10].

In depth investigations about childhood obesity should be performed because it has been considered a global epidemic, reaching 7 to 22% of the child population in occidental countries [11,12]. Increasing obesity indexes in the child population has been associated with an increase in the risk of apnea, which puts SDB in a prominent position as a relevant public health issue [11-13].

Increased insulin and adiposity values in childhood are predictors of obesity, hypertension and dyslipidemia in adulthood and contribute to a later increase in cardiovascular risk [14].

There are few studies that analyze the metabolic profile of children with sleep-related breathing disorders. We have suggested the hypothesis that children exposed to two metabolic dysfunction risk factors, SDB and obesity, suffer exacerbated changes in their metabolic profile. Thus, considering the known systemic repercussions of SDB,

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Key words: *metabolism, obesity, child, sleep disordered breathing*

Received: September 28, 2018; **Accepted:** October 16, 2018; **Published:** October 23, 2018

we investigated the metabolic profile of obese children to study any positive correlation between the alterations.

Objective

The objective of this study was to evaluate the repercussions of SDB on the metabolic profile and quality of life by applying the OSA-18 questionnaire to obese children with and without SDB.

Methods

This study was approved by the Ethics Committee (record number 3589/2010). The parents or legal guardians of all the children were instructed about participation in and the objectives of the study and signed an informed consent form.

Participants

The children included in the study were of both sexes, obese, and aged between 3 and 11.

We considered children with SDB to be children who presented with snoring three or more days in the week and with breathing pauses with or without associated frequent awakening or restless sleep. We considered children without SDB to be children who did not present snoring or breathing pauses, mouth breathing or restless sleep on any day of the week.

The children were divided into three groups:

- Group I: obese children with SDB
- Group II: obese children without SDB
- Group III (control): children eutrophic, without any respiratory complaints.

In total, 120 children were invited, through their parents or guardians, to participate in the study. After applying the inclusion and exclusion criteria, 73 children completed the study.

Inclusion and exclusion criteria

They came from the breathing disorders ambulatory of the discipline of otorhinolaryngology of the child obesity ambulatory of the pediatric department and from the pediatric surgery infirmary of the same institution.

Children with neurological disorders, known heart conditions, genetic syndromes with muscular tonus alterations or craniofacial growth alterations were excluded. Children taking medication that affected metabolic function were also excluded.

Measures and procedures

Evaluation for obesity: All the children underwent an evaluation of their weight and height. Their body mass index (BMI), calculated according to the mass/ (height × height) formula, was used to determine inclusion in the study. The following were defined as obese: children with BMI plus 3 standard deviation (SD) scores above average for the age for children up to 5 years old and BMI plus 2 standard deviations above average for children over 5 years old. We used the AnthroPlus, a freeware developed by the World Health Organization (WHO, <http://www.who.int/childgrowth/en>).

Metabolic markers of blood samples: Fasting blood samples of the patients were collected to analyze the metabolic profile

including glycemia, insulin, lipid profile (HDL, LDL, VLDL, TGL), Thyroid Stimulating Hormone (TSH), and Thyroxine (T4) levels. The Homeostatic Model Assessment (HOMA) was used to quantify insulin resistance and the glucose/insulin ratio was calculated to measure insulin sensitivity. The HOMA index was calculated according to the following formula:

$$\text{HOMA} = \frac{\text{Glucose} \times \text{insulin}}{22.5}$$

Quality of life and sleep: The parents or guardians answered the OSA-18 questionnaire adapted to the Portuguese of Brazil [15] to assess the quality of life of the patients through evaluation of respiratory complaints during sleep. The questionnaire is composed of a quality-of-life Visual Analog Scale (VAS) (from zero to ten) and of 18 questions grouped into five domains (sleep disturbances, physical suffering, emotional suffering, day problems and parent/guardian concerns) with a score from 1 to 7 attributed to each question. The minimum total score of the questionnaire is 18 and the maximum is 126, with the higher the score indicating the parents' negative perception of the sleep quality of their children.

Statistical analyses

The results were presented as the mean ± Standard Deviation (SD). The comparison between the groups was calculated through the analysis of variance (ANOVA), with a classification factor followed by Turkey's multiple comparison test for the quantitative variables. A 5% significance level was used for all the tests. The analyses were made using SAS for Windows. Version 9.12.

Results

In all, 73 children completed the study and were distributed as follows:

- Group I: 48 obese children with SDB
- Group II: 15 obese children without SDB
- Group III (control): 10 eutrophic children without SDB

The age of the children in Group I was similar to that of the other groups, but the age of Group II was higher than the age of the control group. There was no difference in BMI between the two groups of obese children. There were no differences among the groups in the glycemia analysis. Group I and Group II presented increased insulin and HOMA values compared to those of Group III but had no differences when compared to each other. Group I and Group II presented decreased glycemia and insulinemia values when compared to those of Group III but had no differences when compared to each other, as shown in Table 1.

No differences between total cholesterol, LDL, and VLDL were observed between the three groups. Group III presented higher HDL values and lower TGL values than those of Group II. The values of TSH and Free T4 did not show any differences between the three groups, as shown in Table 2.

The OSA-18 questionnaire showed differences between the groups in sleep disturbances, physical suffering, and parents' concern, with higher values in Group I than those in Group II. The VAS did not show any differences between Group I and Group II; however, the VAS of the former was lower than that of Group II, as shown in Table 3.

Table 1. Comparison of sex, age, BMI and metabolic profile among the three groups

	GI - OBESE W/ SDB	GII - OBESE W/O SDB	G III-CONTROL	p value		
	1	2	3	1 vs. 2	1 vs. 3	2 vs. 3
Sex (masc. / fem.)	17/2	5/10	10/0	----	----	----
Age (years)	7.9 ± 2.9	9.5 ± 2.2	6.5 ± 2.7	NS	NS	0.02
BMI (kg/m ²)	27.8 ± 6.1	26.6 ± 3.2	18.4 ± 1.4	NS	0.0003	0.005
Glycemia (mg/dL)	83.8 ± 17.8	85.69 ± 8.90	78.6 ± 7.4	NS	NS	NS
Insulin (μUI/mL)	14.5 ± 9.3	19.68 ± 10.56	5.9 ± 2.8	NS	0.03	0.002
GLUC/INSUL	7.8 ± 5.6	5.76 ± 3.24	22.4 ± 21.7	NS	0.004	0.03
HOMA	4.5 ± 3.1	4.3 ± 2.6	1.1 ± 0.6	NS	0.0003	0.0004

Results are expressed as the mean ± standard deviation; NS: Not Significant; OBESE W/ SDB: group of Obese patients with Sleep-Disordered Breathing; OBESE W/O SDB: group of Obese patients without Sleep-Disordered Breathing.

Table 2. Comparison of metabolic profile among the three groups

	GI - OBESE W/ SDB	GII - OBESE W/O SDB	G III-CONTROL	p value		
	1	2	3	1 vs. 2	1 vs. 3	2 vs. 3
TC (mg/dL)	165.6 ± 30.2	161.3 ± 35.1	151.7 ± 31.3	NS	NS	NS
HDL (mg/dL)	44.6 ± 12.0	41.0 ± 8.2	54.5 ± 11.6	NS	NS	0.03
LDL (mg/dL)	102.0 ± 25.5	107.4 ± 28.6	85.9 ± 24.3	NS	NS	NS
TGL (mg/dL)	103.8 ± 47.4	114.9 ± 47.8	68.8 ± 19.4	NS	NS	0.04
TSH (μUI/mL)	3.1 ± 1.5	3.7 ± 2.1	2.3 ± 1.2	NS	NS	NS
Free T4 (mg/dL)	1.3 ± 0.2	1.3 ± 0.1	1.3 ± 0.2	NS	NS	NS

Results are expressed as the mean ± standard deviations; NS: Not Significant; OBESE W/SDB: group of Obese patients with Sleep-Disordered Breathing; OBESE W/O SDB: group of Obese patients without Sleep-Disordered Breathing

Table 3. Comparison of OSA-18 Questionnaire among the three groups

	GI - OBESE W/ SDB	GII - OBESE W/O SDB	G III-CONTROL	p value		
	1	2	3	1 vs. 2	1 vs. 3	2 vs. 3
Sleep disorders	16.2 ± 7.7	7.2 ± 2.4	6.2 ± 2.3	< 0.001	0.002	NS
Physical suffering	13.3 ± 5.0	8.5 ± 4.1	8.2 ± 3.8	0.03	0.01	NS
Emotional suffering	7.5 ± 4.2	7.6 ± 5.4	5.2 ± 3.9	NS	NS	NS
Daytime problems	7.0 ± 4.3	7.2 ± 3.6	5.2 ± 3.1	NS	NS	NS
Parent/guardian concerns	13.2 ± 6.9	8.8 ± 3.8	7.2 ± 2.8	0.04	0.02	NS
Total score	57.0 ± 19.9	39.3 ± 10.5	32.1 ± 10.3	NS	NS	NS
Visual analog scale	7.1 ± 2.2	8.3 ± 1.0	9.3 ± 1.0	NS	0.01	NS

Results are expressed as the mean ± standard deviations; NS: Not Significant; OBESE W/SDB: group of Obese patients with Sleep-Disordered Breathing. OBESE W/O SDB: group of Obese patients without Sleep-Disordered Breathing

Discussion

The study investigated if the co-existence of obesity and sleep disordered breathing would upregulate metabolic disturbances, as each disorder is considered an independent risk factor for these [12,13,16]. Obese children are considered to be at higher risk for SDB as they have diminished pharyngeal lumen due to fat deposits in the parapharyngeal spaces, but also have smaller lung volume, greater collapsibility of the airways and alterations in gas exchange [13,16].

In our analysis, including obese children with and without SDB, the values of insulin, the glycemia/insulin ratio and the HOMA showed insulin resistance in both obese populations when compared to the control group. The influence of SDB did not up-regulate the system insulin-glycemia showing mostly the effect of obesity in insulin resistance (Table 1). These findings are similar to those from a previous study which assessed 135 children and found that obesity was the most determinant factor in insulin resistance among children with SDB [17]. Relying more strongly on this possible correlation, a recent study verified improvement of the metabolic profile after adenotonsillectomy, which eliminated the obstructive factor of respiratory disturbance, but still noted a residual metabolic dysfunction related to underlying adiposity [18,19].

Several authors suggest that suggesting a pathogenic role for SDB in lipid homeostasis and in systemic inflammation, regardless of the

level of obesity [20,21]. In this study, we observed significant higher triglyceride levels in obese children, independently of the presence of SDB, as well as higher cholesterol levels, LDL levels and lower HDL levels. HDL is a known protector of the cardiovascular system, showing the negative effect of obesity on the lipid profile, independent from SDB (Table 2). Again, we could not show an increase of dysregulation when children were exposed to both risk factors, SDB and obesity. In concordance to our data, in a study enrolling obese and non-obese children, Alexoupoulos et al showed that OSA severity had a negative association to HDL serum levels, the more severe OSA, the lower the HDL levels. However, that association was not observed in obese children, possibly due to the effect of adiposity on lipid serum levels [22].

SDB is associated to a negative impact on quality of life which is investigated by OSA-18 [15]. In our population, the OSA-18 questionnaire showed a higher negative impact on sleep disorders, physical suffering and parent's concern on children with SDB (Table 3) when compared to the results for the groups without SDB. This finding is in agreement with the results of previous studies [23-25], enhancing the importance sleep for the perception of good quality of life and well-being. Curiously, although obesity has a strong negative impact on health, neither the parents nor the children considered it as a negative factor.

As already proposed by the pioneer study by Vella & de la Eva [26], our study also shows the impact of SDB and obesity on metabolic profile and on quality of life. Knowing that SDB, from primary snoring up to obstructive sleep apnea, influences many physiological aspects, long-term follow-up of these children should be observed to strengthen this evidence. Pediatric SDB and OSA is related mostly to hypertrophy of the tonsils which has its peak at pre-school age. Possibly some systemic repercussions as metabolic ones depend on exposition time which in children is shorter in contrast to the longer exposure of the adult population. Nevertheless, there are emerging studies showing that SDB may be a substantial threat to cardiovascular health and stress and needs to be recognized in order to manage the comorbidities of obesity and their importance of understanding the pediatric origins of adult diseases.

Our study could not classify the severity of SDB as we had no access to perform a full-night polysomnography, a complementary exam which confirms the diagnosis of Obstructive Sleep Apnea (OSA), the most severe form of SDB. However, the cardinal symptoms of SDB are snoring for more than three nights per week during the last month, observed apneas and restless sleep. Although this might be considered a bias of our study, we believe that the clinical investigation of any respiratory complaint made sure the presence or absence of SDB. Nevertheless, the lack of the polysomnographic classification of OSA severity and the small number of children enrolled did not allow a subgroup analysis for the repercussion of severe OSA and obesity.

It is also important to observe that this study was performed in just one center, so our sample was limited. We suggest that the sample size should be expanded in future studies, considering the possibility of multicentric studies to confirm these dates.

Conclusions

This study observed that SDB had no direct influence on the metabolic profile of carbohydrates and lipids in children, even though they had a negative impact on the quality of life. An increase in insulin resistance was noted in the groups of obese children with and without SDB, which should alert pediatricians and otorhinolaryngologists to the possible repercussions in adulthood.

References

- [No authors listed] (1996) Standards and indications for cardiopulmonary sleep studies in children. American Thoracic Society. *Am J Respir Crit Care Med* 153: 866-878. [Crossref]
- Weber SAT, Santos VJB, Semenzati GO, Martin LC (2012) Ambulatory blood pressure monitoring in children with obstructive sleep apnea and primary snoring. *Int J Pediatr Otorhinolaryngol* 76: 787-790. [Crossref]
- Brunetti L, Rana S, Lospalluti ML, Pietrafesa A, Francavilla R, et al. (2001) Prevalence of obstructive sleep apnea syndrome in a cohort of 1,207 children of southern Italy. *Chest* 120: 1930-1935. [Crossref]
- Young T, Peppard PE, Gottlieb DJ (2002) Epidemiology of obstructive sleep apnea: a population health perspective. *Am J Respir Crit Care Med* 165: 1217-1239. [Crossref]
- Lumeng JC, Chervin RD (2008) Epidemiology of pediatric obstructive sleep apnea. *Proc Am Thorac Soc* 5: 242-252. [Crossref]
- Arens R, McDonough JM, Corbin AM, Rubin NK, Carrol ME, et al. (2003) Upper airway size analysis by magnetic resonance imaging of children with obstructive sleep syndrome. *Am J Resp Crit Care Med* 167: 65-70. [Crossref]
- Wing YK, Hui SH, Pak WM, Ho CK, Cheung A, et al. (2003) A controlled study of sleep related disordered breathing in obese children. *Arch Dis Child* 88: 1043-1047. [Crossref]
- Marcus CL, Curtis S, Koerner CB, Joffe A, Serwint JR, et al. (1996) Evaluation of pulmonary function and polysomnography in obese children and adolescents. *Pediatr Pulmonol* 21: 176-183. [Crossref]
- Verhulst SL, van Gaal L, Backer W, Desager K (2008) The prevalence, anatomical correlates and treatment of sleep disordered breathing in obese children and adolescents. *Sleep Med Rev* 12: 339-346. [Crossref]
- Canapari CA, Hoppin AG, Kinane B, Thomas BJ, Torriani M, et al. (2011) Relationship between sleep apnea, fat distribution, and insulin resistance in obese children. *J Clin Sleep Med* 7: 268-273.
- Oliveira CL, Fisberg M (2003) Obesidade na infância e adolescência: uma verdadeira epidemia. *Arq Bras Endocrinol Metab* 47: 107-108.
- Wang Y, Lobstein T (2006) Worldwide trends in childhood overweight and obesity. *Int J Pediatr Obes* 1: 11-25. [Crossref]
- Costa DJ, Mitchell R (2009) Adenotonsillectomy for obstructive sleep apnea in obese children: a meta-analysis. *Otolaryngol Head Neck Surg* 140: 455-460. [Crossref]
- Srinivasan SR, Myers L, Berenson GS (2002) Predictability of childhood adiposity and insulin for developing insulin resistance syndrome (syndrome x) in young adulthood: the Bogalusa Heart Study. *Diabetes* 51: 204-209.
- Franco RA Jr, Rosenfeld RM, Rao M (2000) First place--resident clinical science award 1999. Quality of life for children with obstructive sleep apnea. *Otolaryngol Head Neck Surg* 123: 9-16. [Crossref]
- Arens R, Muzumdar H (2010) Childhood obesity and obstructive sleep apnea syndrome. *J Appl Physiol (1985)* 108: 436-444. [Crossref]
- Tauman R, O'Brien LM, Ivanenko A, Gozal D (2005) Obesity rather than severity of sleep-disordered breathing as the major determinant of insulin resistance and altered lipidemia in snoring children. *Pediatrics* 116: e66-73. [Crossref]
- Koren D, Gozal D, Bhattacharjee R, Philby MF, Kheirandish-Gozal L (2016) Impact of Adenotonsillectomy on Insulin Resistance and Lipoprotein Profile in Nonobese and Obese Children. *Chest* 149: 999-1010. [Crossref]
- Waters KA, Sitha S, O'Brien LM, Bibby S, de Torres C, et al. (2006) Follow-up on metabolic markers in children treated for obstructive sleep apnea. *Am J Respir Crit Care Med* 174: 455-460. [Crossref]
- Kelly A, Dougherty S, Cucchiara A, Marcus CL, Brooks LJ (2010) Catecholamines, adiponectin, and insulin resistance as measured by HOMA in children with obstructive sleep apnea. *Sleep* 33: 1185-1191. [Crossref]
- Gozal D, Kheirandish L (2006) Oxidant stress and inflammation in the snoring child: Confluent pathways to upper airway pathogenesis and end-organ morbidity. *Sleep Med Rev* 10: 83-96. [Crossref]
- Alexopoulos EI, Gletsou E, Kostadima E, Kaditis D, Zakyntinos E, et al. (2011) Effects of obstructive sleep apnea severity on serum lipid levels in Greek children with snoring. *Sleep Breath* 15: 625-631. [Crossref]
- Sohn H, Rosenfeld RM (2003) Evaluation of sleep-disordered breathing in children. *Otolaryngol Head Neck Surg* 128: 344-352. [Crossref]
- Gomes Ade M, Santos OM, Pimentel K, Marambaia PP, Gomes LM, et al. (2012) Quality of life in children with sleep-disordered breathing. *Braz J Otorhinolaryngol* 78: 12-21. [Crossref]
- Stefanini DOS, Barros EL, Stefanini R, Pradella-Hallinan, Pignatari SSN, et al. (2012) Comparing the clinical profile of nonobese children with apnea and snoring. *Braz J Otorhinolaryngol* 78: 22-26. [Crossref]
- Waters KA, Sitha S, O'Brien LM, Bibby S, de Torres C, et al. (2006) Follow-up on metabolic markers in children treated for obstructive sleep apnea. *Am J Respir Crit Care Med* 174: 455-460. [Crossref]

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