

Obesity as a Risk Factor for Pediatric Obstructive Sleep Apnea: A Review

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Abstract

In recent years, obesity has increasingly become a common disorder among children. Obese children can have a higher prevalence of obstructive sleep apnea syndrome (OSAS). The objective of this review is to assess the risk factors of obese children with OSAS and discuss the updated information for diagnosis and treatment. A review of the literature demonstrates that there is an under-diagnosis of pediatric OSAS. An optimal treatment strategy should target OSAS and obesity simultaneously. Treatment options include behavior modifications, positive airway pressure (PAP) devices and surgery. The success of surgery is highly variable and there is a risk of a post-operative weight gain. For children who have failed surgeries, sleep endoscopy can be used to further assess the areas of obstruction and thus target subsequent surgeries. Weight loss may also be an alternative as first-line treatment option and would require family-based behavioral interventions. Pediatricians should be aware of its increased prevalence in obese children and screen for it.

Keywords

Children, Obesity, Sleep Apnea, Diagnosis, Therapies

肥胖儿童阻塞性睡眠呼吸暂停综合征的诊治进展

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摘要

近年来, 肥胖已经成为儿童中的常见病。肥胖儿童阻塞性睡眠呼吸暂停综合征(OSAS)的发病率较高。本综述的目的是评估OSAS肥胖儿童的危险因素, 并讨论诊断和治疗的最新进展。对文献的回顾表明儿科OSAS的诊断存在不足。最佳治疗策略应同时针对OSAS和肥胖。治疗方案包括行为改变、气道正压(PAP)装置和手术。手术的成功率存在个体差异, 并且有手术后体重增加的风险。对于有手术失败的儿童, 可以使用睡眠内窥镜检查进一步评估阻塞的区域, 从而确定手术方案。减肥可作为一线治疗选择的替代方案, 这需要基于家庭的行为干预。儿科医生应该意识到其在肥胖儿童中的流行率增加, 并对肥胖患儿进行OSAS的筛查。

关键词

儿童, 肥胖, 睡眠呼吸暂停, 诊断, 治疗

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1. 引言

儿童肥胖的发病率一直在增加。肥胖是阻塞性睡眠呼吸暂停综合征(OSAS)的主要危险因素。OSAS的特征是复发的部分或完全上呼吸道阻塞, 导致呼吸暂停, 低通气和脑电图(EEG)觉醒。阻塞性睡眠呼吸暂停的临床症状包括复发性低氧血症, 高碳酸血症和扰乱的睡眠结构, 导致白天过度睡眠和生活质量下降。呼吸事件的两个主要类别是呼吸暂停和低通气, 其通过多导睡眠图记录。阻塞性呼吸暂停定义为持续呼吸努力 ≥ 10 秒而口鼻气流不存在, 其通过胸腹部传感器测量[1] [2]。阻塞性低通气为口鼻流量 $\leq 50\%$ 、持续 ≥ 10 秒、持续呼吸努力伴有 $\geq 3\%$ 的血氧下降或 EEG 觉醒[1] [2]。中枢性呼吸暂停为没有呼吸努力的情况下没有口鼻气流 ≥ 10 秒。混合性呼吸暂停定义为具有中枢和阻塞两者的特点[1] [2]。呼吸暂停低通气指数(AHI)为呼吸暂停和低通气的总和[1] [2]。由于 OSAS 的潜在严重后果以及肥胖儿童的高发病率, 本综述的目的是评估 OSAS 肥胖儿童的危险因素, 并讨论其诊断和治疗的最新进展。

2. 肥胖作为儿童 OSAS 的危险因素

大样本研究表明, 与正常体重的儿童相比, 肥胖儿童患 OSAS 的风险高 4~5 倍[3]。另一项研究表明, OSAS 在肥胖儿童中的患病率高达 46% [3]。新加坡的流行病学调查也表明, OSAS 在体重超过标准体重

180%的儿童患病率为13.3%，而OSAS在正常体重儿童中的患病率为0.7% [4]。意大利2000多名青少年的问卷调查发现，身重指数(BMI)在第90百分位数或更大的儿童中打鼾的发生率更高[5]。此外，BMI超过第95百分位数的受试者比BMI低于第75百分位的儿童打鼾的可能性高2.6倍[5]。一项德国研究发现了类似的结果：肥胖儿童与BMI在75%或更低的同龄人相比，打鼾的风险是其4倍以上[6]。Sánchez-Armengol使用问卷来评估打鼾的青少年，发现肥胖患者体重更高，腰臀比更高[7]。在医院应用夜间多导睡眠监测，以估计OSAS的患病率[8]。

肥胖儿童患OSAS的风险更大。然而，研究中观察到的流行率差异很大，从13%到59%不等[9]。观察到的流行率差异是由于许多因素，包括研究对象的种族、年龄和青春期状态的差异，以及使用不同的诊断标准有关[9]。这些因素使得对肥胖儿童的OSAS患病率的统计计算非常困难。不是所有的研究都发现BMI和呼吸暂停低通气指数之间有相关性，而呼吸暂停-低通气指数可能与身体脂肪的分布相关性更大。虽然几项研究已经证明了肥胖和儿童OSAS的关系，但是大多数医生没有对这部分患者进一步筛选[10]。

3. 睡眠呼吸暂停在肥胖儿童中的发病机制

由肥胖引起的OSAS的普遍认可的机制包括：1) 上气道和解剖异常，2) 肺功能降低，和3) 中枢和神经肌肉调节异常。

1) 上气道解剖异常：

入睡后，人体肌肉张力减弱，咽部肌肉松弛，导致上气道变窄或阻塞，特别是在肥胖儿童中。研究表明，OSAS肥胖患者睡眠呼吸障碍的严重程度与其上呼吸道周围脂肪组织体积呈正相关。正常儿童OSAS的典型危险因素是腺样体和/或扁桃体肥大[11]。在肥胖儿童中，淋巴肥大和肥胖可以损害上呼吸道。例如，OSAS肥胖儿童患扁桃体增大的可能性增加7倍，腺样体增大的可能性增加4倍[3]，而没有腺样体肥大的受试者只有轻度的呼吸异常[12]。在正常体重和超重受试者的混合组中，Brooks等证明肥胖程度是呼吸暂停-低通气指数的唯一预测因子，而淋巴样增生也会影响阻塞性呼吸暂停的持续时间和血氧下降的严重性[13]。

2) 肥胖儿童肺功能下降：

上气道通畅程度受肺体积的影响。过度的脂肪沉积存在于肥胖儿童的胸部和腹部，这限制了胸部运动并且可能导致功能残留能力降低[14]。成人的许多研究表明，腰围或内脏脂肪含量与OSAS的严重程度密切相关，通常比BMI更相关[14]。然而，脂肪分布作为肥胖儿童和青少年睡眠呼吸暂停的危险因素的重要性目前了解甚少。一项调查问卷的研究发现，腰围较大的儿童与睡眠呼吸障碍(SDB)有更高的相关性[15]。在对101名青少年进行的研究中，打鼾与较高的腰臀比相关[7]。腹部肥胖也与呼吸干扰指数(RDI)的增加值相关[15]。

3) 中枢和神经肌肉调节：

肥胖患者可能存在咽部松弛和异常神经调节，使得上呼吸道比正常受试者更容易塌陷。Carotenuto等假设在呼吸暂停事件期间，身体可以采取异常姿势作为放松或减轻由呼吸暂停引起的肌肉压力[16]。可以开发特定的物理治疗以改善这种运动肌肉链的张力[16]。

4. OSAS的并发症

睡眠期间重复呼吸暂停和低通气的主要后果是间歇性缺氧，这触发了氧化应激和炎症反应[17]。几项研究已经证明OSAS肥胖儿童的氧化应激和炎症标志物增加[18]。OSAS交感神经活动增加[19]，并与血清皮质醇水平增高[20]和其他由次级睡眠负债引起的激素变化相关[21] [22] [23]。SDB在儿童中的神经认

知和行为后果已有充分研究。常见的体征和症状包括睡不安稳，早晨头痛，白天疲劳，嗜睡和夜间遗尿[24] [25] [26]。此外，睡眠呼吸暂停的儿童在集中注意力、学习障碍、学校表现缺陷、行为问题包括多动、抑郁症状和执行功能障碍的风险较高[27] [28] [29]。在肥胖儿童中，睡眠呼吸暂停可增加代谢和心血管发病率。横断面研究表明，肥胖儿童和青少年 SDB 的严重程度增加与代谢综合征的风险增加相关[30] [31] [32]，舒张压的增加，血压的夜间下降钝化[33] [34]，左心室肥厚，功能下降[35] [36]。此外，儿童睡眠呼吸暂停和胰岛素抵抗和血脂异常之间存在正相关性[37]。

肥胖症和 OSAS 具有导致慢性炎症诱导的许多共同途径。促炎症信号通路的上调，特别是通过 NF- κ B，HIF-1 α 和代谢活性脂肪因子介导的那些通路，导致促动脉粥样硬化因子的表达增加，从而加速内皮功能障碍，促进涉及动脉粥样硬化的病变的斑块形成[17]。重合的途径促进了 OSAS 的发生，肥胖和心血管或代谢疾病之间的存在联系的假设，其早在儿童心血管系统正常代谢储备的情况下就已开始[17]。这些关联的确切机制仍有待进一步明确，可能是多因素的。

儿科医师对于确诊儿童 OSAS 非常重要。OSAS 与儿童肥胖相关，因为炎症的影响可以在成年时才表现出来。肥胖、OSAS、激活炎症通路的诱导和基因多态性的调节作用之间的相互作用比较复杂[17]。如果开发可靠的预测算法来确定 OSAS 肥胖儿童的短期和长期发病风险，所有这些都必须整合到单个多因素模型中[17]。

5. 治疗

文献综述表明，最佳治疗策略应同时针对 OSAS 和肥胖。三个主要的治疗选择包括：1) 手术，2) 减肥，3) 其它：如气道正压通气装置，口腔器具和位置治疗，抗炎治疗等。

首先，手术(腺样体切除术)通常是患有腺样体肥大的儿童睡眠呼吸暂停的一线治疗。最近已经证明，在一些情况下，舌扁桃体切除也可以有助于 OSAS 的缓解。接受睡眠手术的肥胖儿童可能有残留的 OSAS [38] [39]。最近的分析发现，腺样体切除术可逆转不到一半的肥胖儿童的 OSAS [40]。此外，一些研究表明，肥胖儿童可在腺样体切除术后增加体重[41] [42]。术后体重增加可导致治疗失败，并可增加手术后的胰岛素抵抗[41] [42]。除了腺样体切除之外，还有其他睡眠手术治疗 OSAS，例如舌状扁桃体切除术，悬雍垂-腭-咽成型术(UPPP)，超声造影术和扩张咽成形术，这需要根据患者的不同情况而定。

成功率不高并不意味着手术应该完全放弃。然而，需要进行更多的研究来确定那些最有可能从手术中受益的儿童。近年来，药物诱导的睡眠内窥镜检查已成为气道阻塞定位的稳定可靠的工具[43]。睡眠磁共振成像(MRI)已被用于研究 OSAS 患者在自然睡眠期间的上气道塌陷情况[44]。这些方法可以帮助定位阻塞的区域，并且手术可以针对阻塞并且潜在的改善手术结果。由于肥胖儿童的手术失败率较高，通常建议进行术后行多导睡眠监测。

第二、减轻体重可作为一线治疗选择的替代方案，并需要基于家庭的干预。因为肥胖儿童 OSAS 的患病率较高，并且 OSAS 可以加重肥胖的并发症，所以最佳治疗策略应该同时针对 OSAS 和肥胖。多学科治疗方法至关重要。一个综合的多学科团队可由儿科睡眠医师，儿科耳鼻喉科医生和儿科内分泌专家组成。综合中心的其它资源将包括体重管理计划，由医生和营养学家、运动生理学家和提供心理支持的辅导员组成，治疗应该个性化。OSAS 的长期缓解与体重减轻相关[45] [46]。减肥是肥胖儿童任何治疗方案的重要组成部分[45] [46]，是无腺样体肥大的 OSAS 肥胖儿童的一线治疗。研究表明，肥胖的严重程度与睡眠呼吸障碍的严重程度成正比[45] [46]。减少体重指数，在一定程度上也显著降低 OSAS 的严重性[46]。因此，肥胖儿童 OSAS 治疗中的一个重要组成部分是减肥，然后保持较低的体重。系统评价减肥对儿童 SDB 严重程度的影响很少。Kalra 等研究了 34 例接受肥胖手术的病态肥胖青少年[47]。在手术前，55%的受试者被诊断患有 OSAS，并且在手术减重后，只有一个受试者患有睡眠呼吸暂停[47]。初步证据

表明, 延长随访的时间有利于儿童长期的体重控制[48] [49]。

第三、其它的治疗措施。PAP 装置对治疗 OSAS 有效。PAP 装置是不能降低 BMI 和/或具有对手术禁忌的患者的良好选择[50] [51]。可以在睡眠实验室中进行 PAP 滴定。使用 PAP 装置的儿童应频繁随访以帮助改善 PAP 的依从性。口腔器具适合不能手术或不能耐受 PAP 治疗的儿童[52]。口腔器具由治疗睡眠呼吸暂停患者的牙医定制安装和管理。近年来, 研究人员提出, 在 OSAS 的发生发展中, 存在慢性和/或全身性炎症。研究人员使用白三烯受体拮抗剂, 鼻类固醇和其他抗炎药物治疗轻度至中度 OSAS 术后残留或复发 OSAS 患者, 有明显改善[53] [54]。过敏性鼻炎, 鼻窦炎和鼻病的 OSAS 患者应该对这些问题进行治疗。定位治疗可用于成人和儿童的 OSAS。但结果差异性很大, 通常不能治愈 OSAS [55]。

6. 结论

儿童肥胖与 OSAS 的患病率增加有关。肥胖儿童 OSAS 的严重程度受 BMI、脂肪沉积位置、腺样体肥大和/或舌扁桃体肥大的影响。用于定位阻塞区域的其他工具包括药物诱导的睡眠内窥镜检查和睡眠 MRI。腺样体切除术成功率是高度可变的, 并且存在术后体重增加的风险。减肥可作为一线治疗的替代方案, 但需要基于家庭的行为干预。一些儿童可以选择气道正压通气设备和口腔器具治疗。对儿科医生来说, 重要的是识别和筛查肥胖儿童中的 OSAS 患者。并于个体化的综合干预措施。多学科的协作诊治将对这部分患者进行有效管理, 提高这部分患儿的生活质量。

参考文献 (References)

- [1] Katz, E.S. and Marcus, C.L. (2005) Diagnosis of Obstructive Sleep Apnea Syndrome in Infants and Children. In: Sheldon, S.H., Ferber, R. and Kryger, M.H., Eds., *Principles and Practices of Pediatric Sleep Medicine*, Elsevier Saunders, United States of America, 197-210.
- [2] Chervin, R.D., Ruzicka, D.L., Giordani, B.J., Weatherly, R.A., Dillon, J.E., Hodges, E.K., Marcus, C.L. and Guire, K.E. (2006) Sleep-Disordered Breathing, Behavior and Cognition in Children before and after Adenotonsillectomy. *Pediatrics*, **117**, e769-e778. <https://doi.org/10.1542/peds.2005-1837>
- [3] Marcus, C.L., Brooks, L.J., Draper, K.A., Gozal, D., Halbower, A.C., Jones, J., Schechter, M.S., Ward, S.D., Sheldon, S.H., Shiffman, R.N., Lehmann, C. and Spruyt, K. (2012) Diagnosis and Management of Childhood Obstructive Sleep Apnea Syndrome. *American Academy of Pediatrics*, **130**, e714-e755. <https://doi.org/10.1542/peds.2012-1672>
- [4] Chay, O.M., Goh, A., Abisheganaden, J., Tang, J., Lim, W.H., Chan, Y.H., Wee, M.K., Johan, A., John, A.B., Cheng, H.K., Lin, M., Chee, T., Rajan, U., Wang, S. and Machin, D. (2000) Obstructive Sleep Apnea Syndrome in Obese Singapore Children. *Pediatric Pulmonology*, **29**, 284-290. [https://doi.org/10.1002/\(SICI\)1099-0496\(200004\)29:4<284::AID-PPUL8>3.0.CO;2-D](https://doi.org/10.1002/(SICI)1099-0496(200004)29:4<284::AID-PPUL8>3.0.CO;2-D)
- [5] Corbo, G.M., Forastiere, F., Agabiti, N., Pistelli, R., Dell'Orco, V., Perucci, C.A. and Valente, S. (2001) Snoring in 9- to 15-Year-Old Children: Risk Factors and Clinical Relevance. *Pediatrics*, **108**, 1149-1154. <https://doi.org/10.1542/peds.108.5.1149>
- [6] Urschitz, M.S., Guenther, A., Eitner, S., Urschitz-Duprat, P.M., Schlaud, M., Ipsiroglu, O.S. and Poets, C.F. (2004) Risk Factors and Natural History of Habitual Snoring. *Chest*, **126**, 790-800. <https://doi.org/10.1378/chest.126.3.790>
- [7] Sanchez-Armengol, A., Fuentes-Pradera, M.A., Capote-Gil, F., Garcia-Diaz, E., Cano-Gomez, S., Carmona-Bernal, C. and Castillo-Gomez, J. (2001) Sleep-Related Breathing Disorders in Adolescents Aged 12 - 16 Years: Clinical and Polysomnographic Findings. *Chest*, **119**, 1393-1400. <https://doi.org/10.1378/chest.119.5.1393>
- [8] Gwynne, D. and Church, M.D. (2012) The Role of Polysomnography in Diagnosing and Treating Obstructive Sleep Apnea in Pediatric Patients. *Current Problem in Pediatric and Adolescent Health Care*, **42**, 2-25. <https://doi.org/10.1016/j.cppeds.2011.10.001>
- [9] Verhulst, S.L., Schrauwen, N., Haentjens, D., Suys, B., Rooman, R.P., Van Gaal, L., De Backer, W. and Desager, K.N. (2007) Sleep-Disordered Breathing in Overweight and Obese Children and Adolescents: Prevalence, Characteristics and the Role of Fat Distribution. *Archives of Disease in Childhood*, **92**, 205-208. <https://doi.org/10.1136/adc.2006.101089>
- [10] Tamay, Z., Akcay, A., Kilic, G., Suleyman, A., Ones, U. and Guler, N. (2006) Are Physicians Aware of Obstructive Sleep Apnea in Children? *Sleep Medicine*, **7**, 580-584. <https://doi.org/10.1016/j.sleep.2006.04.004>

- [11] Kohler, M., Lushington, K., Couper, R., Martin, J., van den Heuvel, C., Pamula, Y. and Kennedy, D. (2008) Obesity and Risk of Sleep Related Upper Airway Obstruction in Caucasian Children. *Journal of Clinical Sleep Medicine*, **4**, 129-136.
- [12] Silvestri, J.M., Weese-Mayer, D.E., Bass, M.T., Kenny, A.S., Hauptman, S.A. and Pearsall, S.M. (1993) Polysomnography in Obese Children with a History of Sleep-Associated Breathing Disorders. *Pediatric Pulmonology*, **16**, 124-129. <https://doi.org/10.1002/ppul.1950160208>
- [13] Brooks, L.J., Stephens, B.M. and Bacevice, A.M. (1998) Adenoid Size Is Related to Severity but Not the Number of Episodes of Obstructive Apnea in Children. *The Journal of Pediatrics*, **132**, 682-686. [https://doi.org/10.1016/S0022-3476\(98\)70360-9](https://doi.org/10.1016/S0022-3476(98)70360-9)
- [14] Schafer, H., Pauleit, D., Sudhop, T., Gouni-Berthold, I., Ewig, S. and Berthold, H.K. (2002) Body Fat Distribution, Serum Leptin, and Cardiovascular Risk Factors in Men with Obstructive Sleep Apnea. *Chest*, **122**, 829-839. <https://doi.org/10.1378/chest.122.3.829>
- [15] Carotenuto, M., Bruni, O., Santoro, N., Del Giudice, E.M., Perrone, L. and Pascotto, A. (2006) Waist Circumference Predicts the Occurrence of Sleep-Disordered Breathing in Obese Children and Adolescents: A Questionnaire-Based Study. *Sleep Medicine*, **7**, 357-361. <https://doi.org/10.1016/j.sleep.2006.01.005>
- [16] Carotenuto, M., Gimigliano, F., Fiordelisi, G., Ruberto, M. and Esposito, M. (2013) Positional Abnormalities during Sleep in Children Affected by Obstructive Sleep Apnea Syndrome: The Putative Role of Kinetic Muscular Chains. *Medical Hypotheses*, **81**, 306-308. <https://doi.org/10.1016/j.mehy.2013.04.023>
- [17] Rakesh Bhattacharjee, M.D., Jinkwan Kim, M.P.H., Leila Kheirandish-Gozal, M.D., et al. (2011) Obesity and Obstructive Sleep Apnea Syndrome in Children: A Tale of Inflammatory Cascades. *Pediatric Pulmonology*, **46**, 313-323. <https://doi.org/10.1002/ppul.21370>
- [18] Tauman, R., O'Brien, L.M. and Gozal, D. (2007) Hypoxemia and Obesity Modulate Plasma C-Reactive Protein and Interleukin-6 Levels in Sleep-Disordered Breathing. *Sleep Breath*, **11**, 77-84. <https://doi.org/10.1007/s11325-006-0085-7>
- [19] Villa, M.P., Ianniello, F., Tocci, G., Evangelisti, M., Miano, S., Ferrucci, A., Ciavarella, G.M. and Volpe, M. (2012) Early Cardiac Abnormalities and Increased C-Reactive Protein Levels in a Cohort of Children with Sleep Disordered Breathing. *Sleep Breath*, **16**, 101-110. <https://doi.org/10.1007/s11325-010-0462-0>
- [20] Bratel, T., Wennlund, A. and Carlstrom, K. (1999) Pituitary Reactivity, Androgens and Catecholamines in Obstructive Sleep Apnoea. Effects of Continuous Positive Airway Pressure Treatment (CPAP). *Respiratory Medicine*, **93**, 1-7. [https://doi.org/10.1016/S0954-6111\(99\)90068-9](https://doi.org/10.1016/S0954-6111(99)90068-9)
- [21] Spiegel, K., Knutson, K., Leproult, R., Tasali, E. and Van Cauter, C.E. (2005) Sleep Loss: A Novel Risk Factor for Insulin Resistance and Type 2 Diabetes. *Journal of Applied Physiology*, **99**, 2008-2019. <https://doi.org/10.1152/jappphysiol.00660.2005>
- [22] Verhulst, S.L., Schrauwen, N., Haentjens, D., Rooman, R.P., Van, G.L., De Backer, W.A. and Desager, K.N. (2008) Sleep Duration and Metabolic Dysregulation in Overweight Children and Adolescents. *Archives of Disease in Childhood*, **93**, 89-90. <https://doi.org/10.1136/adc.2007.124768>
- [23] Leproult, R. and Van Cauter, E. (2010) Role of Sleep and Sleep Loss in Hormonal Release and Metabolism. *Endocrine Development*, **17**, 11-21. <https://doi.org/10.1159/000262524>
- [24] Esposito, M., Gallai, B., Parisi, L., Roccella, M., Marotta, R., Lavano, S.M., Mazzotta, G., Patriciello, G., Precenzano, F. and Carotenuto, M. (2013) Visuomotor Competencies and Primary Monosymptomatic Nocturnal Enuresis in Prepubertal Aged Children. *Neuropsychiatric Disease and Treatment*, **9**, 921-926.
- [25] Esposito, M., Carotenuto, M. and Roccella, M. (2011) Primary Nocturnal Enuresis and Learning Disability. *Minerva Pediatrica*, **63**, 99-104.
- [26] Carotenuto, M., Esposito, M. and Pascotto, A. (2011) Facial Patterns and Primary Nocturnal Enuresis in Children. *Sleep Breath*, **15**, 221-227. <https://doi.org/10.1007/s11325-010-0388-6>
- [27] Landau, Y.E., Bar-Yishay, O., Greenberg-Dotan, S., Goldbart, A.D., Tarasiuk, A. and Tal, A. (2012) Impaired Behavioral and Neurocognitive Function in Preschool Children with Obstructive Sleep Apnea. *Pediatric Pulmonology*, **47**, 180-188. <https://doi.org/10.1002/ppul.21534>
- [28] Carotenuto, M., Esposito, M., Parisi, L., Gallai, B., Marotta, R., Pascotto, A. and Roccella, M. (2012) Depressive Symptoms and Childhood Sleep Apnea Syndrome. *Neuropsychiatric Disease and Treatment*, **8**, 369-373. <https://doi.org/10.2147/NDT.S35974>
- [29] Esposito, M., Antinolfi, L., Gallai, B., Parisi, L., Roccella, M., Marotta, R., Lavano, S.M., Mazzotta, G., Precenzano, F. and Carotenuto, M. (2013) Executive Dysfunction in Children Affected by Obstructive Sleep Apnea Syndrome: An Observational Study. *Neuropsychiatric Disease and Treatment*, **9**, 1087-1094. <https://doi.org/10.2147/NDT.S47287>
- [30] Gozal, D., Capdevilla, O.S. and Kheirandish-Gozal, L. (2008) Metabolic Alterations in Obstructive Sleep Apnea

- among Non-Obese and Obese Prepubertal Children. *American Journal of Respiratory and Critical Care Medicine*, **177**, 1142-1149. <https://doi.org/10.1164/rccm.200711-1670OC>
- [31] Verhulst, S.L., Schrauwen, N., Haentjens, D., Rooman, R., Van Gaal, L., De Backer, W. and Desager, K. (2007) Sleep-Disordered Breathing and the Metabolic Syndrome in Overweight and Obese Children and Adolescents. *The Journal of Pediatrics*, **150**, 612-616. <https://doi.org/10.1016/j.jpeds.2007.01.051>
- [32] Redline, S., Storfer-Isser, A., Rosen, C.L., Johnson, N.L., Kirchner, H.L., Emancipator, J. and Kibler, A.M. (2007) Association between Metabolic Syndrome and Sleep Disordered Breathing in Adolescents. *American Journal of Respiratory and Critical Care Medicine*, **176**, 401-408. <https://doi.org/10.1164/rccm.200703-375OC>
- [33] Amin, R.S., Carroll, J.L., Jeffries, J.L., Grone, C., Bean, J.A., Chini, B., Bokulic, R. and Daniels, S.R. (2004) Twenty-Four-Hour Ambulatory Blood Pressure in Children with Sleep-Disordered Breathing. *American Journal of Respiratory and Critical Care Medicine*, **169**, 950-956. <https://doi.org/10.1164/rccm.200309-1305OC>
- [34] Marcus, C.L., Greene, M.G. and Carroll, J.L. (1998) Blood Pressure in Children with Obstructive Sleep Apnea. *American Journal of Respiratory and Critical Care Medicine*, **157**, 1098-1103. <https://doi.org/10.1164/ajrccm.157.4.9704080>
- [35] Amin, R.S., Kimball, T.R., Bean, J.A., Jeffries, J.L., Willging, J.P., Cotton, R.T., Witt, S.A., Glascock, B.J. and Daniels, S.R. (2002) Left Ventricular Hypertrophy and Abnormal Ventricular Geometry in Children and Adolescents with Obstructive Sleep Apnea. *American Journal of Respiratory and Critical Care Medicine*, **165**, 1395-1399. <https://doi.org/10.1164/rccm.2105118>
- [36] Amin, R.S., Kimball, T.R., Kalra, M., Jeffries, J.L., Carroll, J.L., Bean, J.A., Witt, S.A., Glascock, B.J. and Daniels, S.R. (2005) Left Ventricular Function in Children with Sleep-Disordered Breathing. *American Journal of Cardiology*, **95**, 801-804. <https://doi.org/10.1016/j.amjcard.2004.11.044>
- [37] Carotenuto, M., Santoro, N., Grandone, A., Santoro, E., Pascotto, C., Pascotto, A., Perrone, L. and del Giudice, E.M. (2009) The Insulin Gene Variable Number of Tandemrepeats Genotype and Sleep Disordered Breathing in Childhood Obesity. *Journal of Endocrinological Investigation*, **32**, 752-755. <https://doi.org/10.1007/BF03346531>
- [38] Chan, D.K., Jan, T.A. and Koltai, P.J. (2012) Effect of Obesity and Medical Comorbidities on Outcomes after Adjunct Surgery for Obstructive Sleep Apnea in Cases of Adenotonsillectomy Failure. *Archives of Otolaryngology-Head and Neck Surgery*, **138**, 891-896. <https://doi.org/10.1001/2013.jamaoto.197>
- [39] Mitchell, R.B. and Kelly, J. (2007) Outcome of Adenotonsillectomy for Obstructive Sleep Apnea in Obese and Normal-Weight Children. *Otolaryngology-Head and Neck Surgery*, **137**, 43-48. <https://doi.org/10.1016/j.otohns.2007.03.028>
- [40] Costa, D.J. and Mitchell, R. (2009) Adenotonsillectomy for Obstructive Sleep Apnea in Obese Children: A Meta-Analysis. *Otolaryngology-Head and Neck Surgery*, **140**, 455-460. <https://doi.org/10.1016/j.otohns.2008.12.038>
- [41] Apostolidou, M.T., Alexopoulos, E.I., Damani, E., Liakos, N., Chaidas, K., Bouladakakis, E., Apostolidis, T., Gourgoulisanis, K. and Kaditis, A.G. (2008) Absence of Blood Pressure, Metabolic, and Inflammatory Marker Changes after Adenotonsillectomy for Sleep Apnea in Greek Children. *Pediatric Pulmonology*, **43**, 550-560. <https://doi.org/10.1002/ppul.20808>
- [42] Amin, R., Anthony, L., Somers, V., Fenchel, M., McConnell, K., Jefferies, J., Willging, P., Kalra, M. and Daniels, S. (2008) Growth Velocity Predicts Recurrence of Sleep Disordered Breathing 1 Year after Adenotonsillectomy. *American Journal of Respiratory and Critical Care Medicine*, **177**, 654-659. <https://doi.org/10.1164/rccm.200710-1610OC>
- [43] Truong, M.T., Woo, V.G. and Koltai, P.J. (2012) Sleep Endoscopy as a Diagnostic Tool in Pediatric Obstructive Sleep Apnea. *International Journal of Pediatric Otorhinolaryngology*, **78**, 722-727. <https://doi.org/10.1016/j.ijporl.2012.02.028>
- [44] Shin, L.K., Holbrook, A.B., Capasso, R., et al. (2013) Improved Sleep MRI at 3 Tesla in Patients with Obstructive Sleep Apnea. *Journal of Magnetic Resonance Imaging*, **38**, 1-6.
- [45] Verrotti, A., Agostinelli, S., D'Egidio, C., Di Fonzo, A., Carotenuto, M., Parisi, P., Esposito, M., Tozzi, E., Belcastro, V., Mohn, A. and Battistella, P.A. (2013) Impact of a Weight Loss Program on Migraine in Obese Adolescents. *European Journal of Neurology*, **20**, 394-397. <https://doi.org/10.1111/j.1468-1331.2012.03771.x>
- [46] Verhulst, S.L., Franckx, H., Van Gaal, L., De Backer, W. and Desager, K. (2009) The Effect of Weight Loss on Sleep-Disordered Breathing in Obese Teenagers. *Obesity*, **17**, 1178-1183.
- [47] Kalra, M., Inge, T., Garcia, V., Daniels, S., Lawson, L., Curti, R., Cohen, A. and Amin, R. (2005) Obstructive Sleep Apnea in Extremely Overweight Adolescents Undergoing Bariatric Surgery. *Obesity Research*, **13**, 1175-1179. <https://doi.org/10.1038/oby.2005.139>
- [48] Epstein, L.H., Myers, M.D., Raynor, H.A. and Saelens, B.E. (1998) Treatment of Pediatric Obesity. *Pediatrics*, **101**, S554-S570.
- [49] Epstein, L.H., Paluch, R., Roemmich, J.N. and Beecher, M.D. (2007) Family-Based Obesity Treatment: Then and Now.

Twenty-Five Years of Pediatric Obesity Treatment. *Health Psychology*, **26**, 381-391.

<https://doi.org/10.1037/0278-6133.26.4.381>

- [50] Marcus, C.L., Rosen, G., Ward, S.L., *et al.* (2006) Adherence to and Effectiveness of Positive Airway Pressure Therapy in Children with Obstructive Sleep Apnea. *Pediatrics*, **117**, 117. <https://doi.org/10.1542/peds.2005-1634>
- [51] Koontz, K.L., Slifer, K.J., Cataldo, M.D. and Marcus, C.L. (2003) Improving Pediatric Compliance with Positive Airway Pressure Therapy: The Impact of Behavioral Intervention. *Sleep*, **26**, 1010-1015. <https://doi.org/10.1093/sleep/26.8.1010>
- [52] Villa, M.P., Miano, S. and Rizzoli, A. (2012) Mandibular Advancement Devices Are an Alternative and Valid Treatment for Pediatric Obstructive Sleep Apnea Syndrome. *Sleep Breath*, **16**, 971-976. <https://doi.org/10.1007/s11325-011-0595-9>
- [53] Berlucchi, M., Salsi, D., Valetti, L., Parrinello, G. and Nicolai, P. (2007) The Role of Mometasone Furoate Aqueous Nasal Spray in the Treatment of Adenoidal Hypertrophy in the Pediatric Age Group: Preliminary Results of a Prospective, Randomized Study. *Pediatrics*, **119**, 1392-1397. <https://doi.org/10.1542/peds.2006-1769>
- [54] Kheirandish-Gozal, L. and Gozal, D. (2008) Intranasal Budesonide Treatment for Children with Mild Obstructive Sleep Apnea Syndrome. *Pediatrics*, **122**, 149-155. <https://doi.org/10.1542/peds.2007-3398>
- [55] Dayyat, E., Maarafeya, M.M., Capdevila, O.S., Kheirandish-Gozal, L., Montgomery-Downs, H.E. and Gozal, D. (2007) Nocturnal Body Position in Sleeping Children with and without Obstructive Sleep Apnea. *Pediatric Pulmonology*, **42**, 374-379. <https://doi.org/10.1002/ppul.20590>

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