

转氨酶在儿童阻塞性睡眠呼吸暂停低通气综合征中的变化及意义*

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[摘要] 目的:探讨阻塞性睡眠呼吸暂停低通气综合征(OSAHS)是否是引起儿童肝损伤的又一独立危险因素。方法:207例患儿分为 OSAHS 组(130 例)和对照组(77 例),均行 PSG、BMI、肝功能、血脂、空腹血糖和空腹胰岛素检查。结果:OSAHS 组转氨酶升高者 17 例,对照组 2 例,2 组比较差异有统计学意义($\chi^2=5.18, OR=5.64, CI 1.27-24.97$);肥胖组转氨酶升高者 15 例,非肥胖组 4 例,2 组比较差异有统计学意义($\chi^2=4.58; OR=1.97, CI 1.06-3.67$);转氨酶升高的脂肪肝组中同时患 OSAHS 者 14 例(93.3%),而转氨酶正常的非脂肪肝组中患 OSAHS 者 37 例(67.3%)。结论:OSAHS 为独立于肥胖之外的又一引起肝损伤的危险因素。肥胖儿童,尤其是伴有 OSAHS 的肥胖儿童转氨酶升高更为明显。

[关键词] 儿童;睡眠呼吸暂停低通气综合征;阻塞性;肥胖;转氨酶

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Changes of serum aminotransferase in children with obstructive sleep apnea hypopnea syndrome

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Abstract Objective: Obstructive sleep apnea hypopnea syndrome (OSAHS) and non-alcoholic fatty liver disease (NAFLD) are both strongly associated with obesity. Whether OSAHS is an independent risk factor for liver injury or not is uncertain. To assess the hypothesis that OSAHS is associated with liver injury independent of obesity. **Method:** One hundred and thirty children with OSAHS and 77 children with primary snoring (PS) were enrolled. Polysomnography was performed. Body mass index (BMI), liver function tests, serum lipids, fasting plasma glucose (FPG), and insulin (INS) were measured. **Result:** Seventeen children of OSAHS had elevated serum aminotransferase levels, while only 2 children of non-OAHS had elevated serum aminotransferase in healthy control group ($\chi^2=5.18, P<0.05; OR=5.64, CI 1.27-24.97$). Fifteen children of obese had elevated serum aminotransferase levels, while only 4 children had elevated serum aminotransferase in non-obese group ($\chi^2=4.58, P<0.05; OR=1.97, CI 1.06-3.67$). Seventy cases of obese children, 15 cases of elevated aminotransferase levels (21.4%), namely fatty liver patients, of these children, 14 had OSAHS (93.3%). In contrast, OSAHS was present in only 67.3% of obese children without elevated aminotransferase. **Conclusion:** OSAHS may be a risk factor for liver injury independent of obesity; Increased liver enzyme levels are frequently found in obese snoring children, particularly among those with OSAHS.

Key words children; sleep apnea hypopnea syndrome; obstructive; obesity; aminotransferase

阻塞性睡眠呼吸暂停低通气综合征(OSAHS)是儿童人群中发病率较高的睡眠呼吸性疾病,它以反复的呼吸暂停、白天嗜睡为特征,在学龄儿童中的发病率可达 2%^[1],且肥胖是其重要的危险因素^[2-3],肥胖儿童 OSAHS 的发病率可达 50%^[4]。另外,肥胖也与包括单纯性脂肪肝、脂肪性肝炎及

其相关肝硬化的非酒精性脂肪性肝病(non-alcoholic fatty liver disease, NAFLD)紧密关联。肥胖、高血压、高血脂和胰岛素抵抗被认为是 NAFLD 患者出现肝损害的基础。OSAHS 是引起脂肪肝或导致肝功能异常的危险因素^[5-6]。目前,关于 OSAHS 对儿童 NAFLD 的影响报道尚少^[7],本研究通过测定 OSAHS 患儿血清丙氨酸氨基转换酶(ALT)的变化,探讨 OSAHS 对儿童肝脏的影响及意义。

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1 资料与方法

1.1 临床资料

选取 2010-01—2012-06 因打鼾及睡眠呼吸异常在济宁医学院附属金乡医院门诊就诊及住院患儿 207 例,男 109 例,女 98 例;年龄 7~15 岁。经询问病史、体检及辅助检查,排除了心血管系统、呼吸系统、泌尿系统、内分泌、代谢性疾病以及神经肌肉疾病。将全部患儿分为 OSAHS 组和单纯鼾症(对照组)。OSAHS 组 130 例,男 74 例,女 56 例;年龄(10.8±3.9)岁;对照组 77 例,男 35 例,女 42 例,年龄(10.4±2.5)岁。本研究已获得家长知情同意。

1.2 诊断标准

儿童 OSAHS 诊断标准:依据《儿童 OSAHS 诊疗指南草案(乌鲁木齐)》,并参考国外其他文献^[8]即:睡眠过程中口鼻气流量较基础水平降低 50%以上,持续时间≥6 s,伴 SaO₂ 下降≥4%为低通气;口鼻气流停止≥6 s 为呼吸暂停;以 AHI≥5 次/h,伴 LSaO₂≤92%作为儿童 OSAHS 的诊断标准。

单纯鼾症诊断标准:①睡眠时打鼾;②无打鼾引起的白天症状或睡眠紊乱;③PSG 监测:经常在睡眠中有长时间的打鼾;睡眠期间无觉醒、睡眠不受干扰及 CO₂ 分压在正常范围;表现为该年龄正常的睡眠形式;表现为该年龄正常的睡眠中的呼吸形式;不符合其他睡眠障碍性疾病的诊断标准。

1.3 方法

睡眠研究采用美国 Respironics 公司生产的 Night-owl polywin 多导睡眠仪进行睡眠监测,包括脑电图、眼电图、心电图、颏舌肌电图、胸式呼吸、腹式呼吸、口鼻气流、LSaO₂、鼾声、体位、肢体活动等,连续记录并自动储存在计算机中,监测时间每晚不少于 8 h,次日进行详细分析。所有受试者监测当日禁浓茶、咖啡及具有镇静作用或影响睡眠的药物。受检者禁食 12 h 后,次日早晨做肝功能、空腹血糖、胰岛素和血脂检查。计算入选者的 BMI,参照肥胖的诊断标准^[9],将其分为肥胖组与非肥胖组,再依据转氨酶值,把肥胖组分为 NAFLD 与非 NAFLD 两亚组。NAFLD 诊断标准参照成人 NAFLD 诊断标准^[10],肥胖儿童肝脏 B 超表现符合弥漫性脂肪肝诊断标准而又排除常见肝炎病毒感染、药物性肝病、全胃肠外营养和自身免疫性肝病及常见可能引起肝脂肪变性的代谢性疾病者,可伴有乏力、消化不良、肝区隐痛、肝脾肿大、肝酶升高等症状和体征。以转氨酶>40 U/L 示患有脂肪肝。

1.4 统计学方法

应用 SPSS13.0 进行统计学分析。计量资料以 $\bar{x} \pm s$ 表示,采用 *t* 检验,计数资料以 χ^2 检验。

以 $P < 0.05$ 为差异有统计学意义。

2 结果

2.1 OSAHS 组与对照组相关参数比较

OSAHS 患儿中转氨酶升高者 17 例,PS 组仅 2 例。2 组一般资料见表 1。

表 1 OSAHS 组与对照组的相关参数比较 $\bar{x} \pm s$

变量	OSAHS 组	对照组
年龄	10.80±2.90	10.40±2.50
BMI	22.70±3.10	23.20±3.40
呼吸暂停低通气指数	9.70±1.20	3.50±2.80
指脉氧饱和度	82.40±6.50	94.10±2.20
血糖/(mmol·L ⁻¹)	3.80±0.70	3.00±0.50
胰岛素/U/L	13.00±0.80	8.70±1.10
三酰甘油/(mmol·L ⁻¹)	1.21±0.29	1.00±0.34
胆固醇/(mmol·L ⁻¹)	4.06±0.61	3.48±0.53
HDL/U/(mmol·L ⁻¹)	1.04±0.27	1.26±0.35
LDL/(mmol·L ⁻¹)	2.33±0.49	2.13±0.52
ALT/U/L	20.18±2.50	19.90±3.60

2.2 肥胖组与非肥胖组比较

207 例患儿中有 70 例肥胖儿童,其中 51 例(72.9%)符合 OSAHS 诊断标准,15 例儿童转氨酶升高,符合 NAFLD 的诊断标准。137 例非肥胖儿童中,79 例(57.7%)符合 OSAHS 诊断标准,见表 2。肥胖儿童患脂肪肝的危险性较非肥胖儿童明显升高($\chi^2 = 4.58, P < 0.05; OR = 1.97, CI 1.06-3.67$)。

表 2 肥胖组与非肥胖组相关参数比较 $\bar{x} \pm s$

变量	肥胖组	非肥胖组
年龄	9.80±2.10	9.40±2.00
BMI	24.60±2.10	20.20±2.50
呼吸暂停低通气指数	10.70±2.10	4.60±1.70
血糖/(mmol·L ⁻¹)	3.90±0.60	3.20±0.50
胰岛素/U/L	14.30±0.70	12.30±1.50
三酰甘油/(mmol·L ⁻¹)	1.46±0.26	1.20±0.32
胆固醇/(mmol·L ⁻¹)	3.82±0.58	3.43±0.60
HDL/(mmol·L ⁻¹)	0.90±0.28	1.10±0.22
LDL/(mmol·L ⁻¹)	3.33±0.53	2.32±0.58
ALT/U/L	29.18±2.50	19.90±3.60

2.3 脂肪肝组与非脂肪肝组情况

依据转氨酶的异常情况,把 70 例肥胖儿童分为脂肪肝组 15 例与非脂肪肝组 55 例。脂肪肝组有 OSAHS 患儿 14 例(93.3%),而非脂肪肝组有 37 例(67.3%),见表 3。与非脂肪肝组儿童相比,脂肪肝危险性在肥胖的 OSAHS 儿童中明显增高

($\chi^2 = 4.05, P < 0.05; OR = 6.81, CI 1.05 - 43.8$)。

表 3 脂肪肝组与非脂肪肝组相关参数比较 $\bar{x} \pm s$

变量	脂肪肝组	非脂肪肝组
年龄	11.10 ± 2.40	10.40 ± 3.80
BMI	24.70 ± 3.10	24.20 ± 2.40
呼吸暂停低通气指数	9.70 ± 1.20	3.50 ± 2.80
三酰甘油/(mmol · L ⁻¹)	1.37 ± 0.57	1.08 ± 0.74
胆固醇/(mmol · L ⁻¹)	4.72 ± 0.87	3.54 ± 0.70
HDL/(mmol · L ⁻¹)	0.92 ± 0.54	1.56 ± 0.48
LDL/(mmol · L ⁻¹)	3.11 ± 0.80	2.14 ± 0.66

3 讨论

OSAHS 是一种具有潜在危险的儿童常见性疾病,由于它可引起多器官及生理系统的严重危害^[11-12],因此受到广泛关注。本研究结果显示肥胖 OSAHS 儿童脂肪肝的发病率高于其他儿童,这与 Verhulst 等^[7]和 Kheirandish-Gozal 等^[13]研究结论一致。与单纯性肥胖患儿相比,脂肪肝在肥胖 OSAHS 患儿中的危险性增高近 7 倍(OR = 6.81),提示呼吸障碍可能是肥胖人群肝脂肪变性的危险因素。与非脂肪肝组患儿相比,脂肪肝组儿童的 OSAHS 发生率也更高,分别为 93.3% 及 67.3%。

Byrne^[14]及 Norman 等^[15]报道 OSAHS 患儿发生脂肪肝的机制与低氧血症有关。本研究中,OSAHS 组患儿的 SaO₂ 明显低于对照组。低氧血症可能通过如下机制形成脂肪肝:首先,低氧血症产生了大量的活性氧,造成细胞大分子的氧化损伤;活性氧可使肝细胞膜理化性质发生改变,导致肝细胞被破坏和坏死;活性氧导致肝细胞炎症,肝细胞凋亡及坏死,从而出现肝纤维化等脂肪性肝炎的改变。

其次,低氧血症产生了胰岛素抵抗。Seyed 等^[16]认为在控制了肥胖等其他混杂因素后,氧饱和度和胰岛素抵抗指数有相关性。本研究中 OSAHS 组儿童的血糖及血脂均高于对照组。这是由于 OSAHS 儿童糖利用率降低,出现了胰岛素抵抗,同时此抵抗降低了肝脏氧化清除游离脂肪酸的能力,三酰甘油增多,最终肝脏内三酰甘油过渡聚集形成肝脂肪变性和脂肪肝^[17]。再次,炎症反应也参与了 NAFLD 的形成,加速了儿童的肝损伤。Ahmed 等^[18]研究表明, NF- κ B 是炎症反应过程中的主要调节因子,而 OSAHS 人群中 NF- κ B 因子不但增加还可以激活 TNF- α 、CRP、IL-1、IL-6、MCP-1、MIF 等因子的活性,从而引起肝细胞炎症及纤维化的产生^[18]。

综上所述,本研究结果显示 OSAHS 不但引起儿童脂肪肝的发生,还易造成肝损伤。它是独立于肥胖之外的,又一引起肝损伤的危险因素,此危险性在伴有 OSAHS 的肥胖儿童身上表现的更为明显。

参考文献

- [1] ROSEN C L, LARKIN E K, KIRCHNER H L, et al. Prevalence and risk factors for sleep-disordered breathing in 8-to 11-year-old children: association with race and prematurity[J]. J Pediatr, 2003, 142: 383-389.
- [2] UDOMITTIPONG K, CHIERAKUL N, RUTTAN-AUMPAWAN P, et al. Severe obesity is a risk factor for severe obstructive sleep apnea in obese children[J]. J Med Assoc Thai, 2011, 94: 1346-1351.
- [3] KOHLER M J, THORMAEHLEN S, KENNEDY J D, et al. Differences in the association between obesity and obstructive sleep apnea among children and adolescents[J]. J Clin Sleep Med, 2009, 15: 506-511.
- [4] CANAPARI C A, HOPPIN A G, KINANE T B, et al. Relationship between sleep apnea, fat distribution, and insulin resistance in obese children[J]. J Clin Sleep Med, 2011, 7: 268-273.
- [5] PIGUET A C, STROKA D, ZIMMERMANN A, et al. Hypoxia aggravates non-alcoholic steatohepatitis in mice lacking hepatocellular PTEN[J]. Clin Sci (Lond), 2009, 118: 401-410.
- [6] NORMAN D, BARDWELL W A, AROSEMENA F, et al. Serum aminotransferase levels are associated with markers of hypoxia in patients with obstructive sleep apnea[J]. Sleep, 2008, 31: 121-126.
- [7] VERHULST S L, JACOBS S, AERTS L, et al. Sleep-disordered breathing: a new risk factor of suspected fatty liver disease in overweight children and adolescents[J]? Sleep Breath, 2009, 13: 207-210.
- [8] MARCUS C L, BROOKS L J, DRAPER K A, et al. Diagnosis and management of childhood obstructive sleep apnea syndrome [J]. Pediatrics, 2012, 130: 576-584.
- [9] 李辉,季成叶,宗心南,等. 中国 0~18 岁儿童、青少年体块指数的生长曲线[J]. 中华儿科杂志, 2009, 47(7): 493-498.
- [10] 中华医学会肝病学会脂肪肝和酒精性肝病学组. 非酒精性脂肪性肝病诊疗指南[J]. 中华肝脏病杂志, 2010, 18(3): 275-278.
- [11] ALMEIDA L A, ANSELMO-LIMA W T, VALERA F C. OSAS in children: where are we [J]? Braz J Otorhinolaryngol, 2011, 77: 273-273.
- [12] SANS CAPDEVILA O, WIENBERG P, HAAG O, et al. Comorbidities of sleep-disordered breathing in children[J]. Acta Otorrinolaryngol Esp, 2010, 61: 26-32.

儿童气管异物的诊疗要点

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[摘要] 目的:探讨儿童气管异物的诊断及鉴别诊断,治疗及急救要点。方法:回顾性分析行气管异物取出术的 164 例患儿的临床资料。结果:163 例患儿于气管镜下手术取出异物;余 1 例患儿异物为图钉,气管镜下取出困难,经气管切开术取出异物。植物性异物 158 例,塑料异物 5 例及图钉 1 例。除 1 例术后出现皮下纵隔气肿,治疗后痊愈外,其他均无明显并发症发生。132 例患者术后 3 d 复查胸透或电子气管镜均未见异物残留。结论:对于气管异物应根据病史及体格检查作出快速判断。拍击音对诊断气管异物有高度特异性。在诊断气管异物方面电子气管镜检查相对胸透有更高的准确性。

[关键词] 气管异物;儿童;诊断;电子气管镜

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Diagnosis and treatment of trachea foreign bodies in children

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Abstract Objective: To discuss the diagnosis, differential diagnosis, treatment and first aid treatment of trachea foreign bodies in children. **Method:** One hundred and sixty-four patients, who were operated with the diagnosis of trachea foreign bodies were retrospectively analyzed. **Result:** The foreign bodies were successfully removed through the rigid bronchoscope in 163 patients and through the incision of tracheotomy in 1 patient. No post-operation complication in 163 patients except 1 patient with subcutaneous and mediastinum emphysema. No foreign body remained by the examination of perspective X-ray or electronic bronchoscope three days post-operation. **Conclusion:** History of foreign body aspiration and physical examination were significant important in diagnosis of trachea foreign bodies. The diagnosis must be made quickly based on the history and physical examination. The clapping sound has high specially in diagnosis of trachea foreign bodies. The electronic bronchoscope has a better accuracy in diagnosis of trachea foreign bodies than radiographic examination.

Key words trachea foreign bodies; children; diagnosis; electronic bronchoscope

儿童气管、支气管异物是小儿耳鼻咽喉科常见急症,若不能及时有效诊断和治疗会导致严重并发

症发生甚至危及生命。由于患儿误呛异物的病史经常被遗漏,气管支气管异物的临床表现与支气管炎、支气管肺炎、肺炎、肺不张、肺气肿等相似,鉴别较困难^[1]。气管异物相比支气管异物危险性更高,异物阻塞气管,或异物位于气管隆突处阻塞双

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[13] KHEIRANDISH-GOZAL L, SANS CAPDEVILA O, KHEIRANDISH E, et al. Elevated serum aminotransferase levels in children at risk for obstructive sleep apnea[J]. Chest, 2008, 133: 92-99.

[14] BYRNE C D. Hypoxia and non-alcoholic fatty liver disease[J]. Clin Sci (Lond), 2009, 118: 397-400.

[15] NORMAN D, BARDWELL W A, AROSEMENA F, et al. Serum aminotransferase levels are associated with markers of hypoxia in patients with obstructive sleep apnea[J]. Sleep, 2008, 31: 121-126.

[16] SEYED HAMID MOOSAVY, HOSSEIN FROUTAN,

NADER FAIAZI, et al. Effects of obstructive sleep apnea syndrome on serum aminotransferase levels and insulin resistance[J]. Medical Journal of the Islamic Republic of Iran, 2011, 24: 232-237.

[17] TIAN J L, ZHANG Y, CHEN B Y. Sleep apnea hypopnea syndrome and liver injury[J]. Chin Med J (Engl), 2010, 123: 89-94.

[18] AHMED M H, BYRNE C D. Obstructive sleep apnea syndrome and fatty liver: Association or causal link [J]? World J Gastroenterol, 2010, 16: 4243-4252.

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