·临床报告·

阻塞性睡眠呼吸暂停低通气综合征对视网膜神经纤维层厚度的影响

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Evaluation of retinal nerve fiber layer thickness in patients with obstructive sleep apnea-hypopnea syndrome

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Abstract

• AIM: To compare the retinal nerve fiber layer (RNFL) thickness in patients with different severities of obstructive sleep apnea-hypopnea syndrome (OSAHS) versus normal controls.

• METHODS: This was an observational case-control study. Totally 79 patients presenting with snoring and daytime sleepiness who underwent overnight polysomnography (PSG) to determine OSAHS severity were recruited, and subsequently referred for ophthalmologic evaluation. The data including intraocular pressure (IOP), RNFL thickness etc was collected.

• RESULTS: A total of 73 subjects were recruited, including 53 patients with OSAHS and 20 normal control subjects. IOP was significantly higher for the moderate and severe OSAHS group than for the control group (both $P<0.05$). The RNFL in the average and superior quadrants were significantly thinner for the moderate and severe OSAHS group than for the control group (both $P<0.05$). AHI was negatively correlated with RNFL thickness in the superior quadrants, and with average RNFL thickness ($r=-0.316$, -0.205; both $P<0.01$). Negative correlations were also identified between RNFL thickness in the superior quadrants and the ODI ($r=-0.24$, $P=0.005$). Positive correlations were identified between SaO_2 on PSG and RNFL thickness in the superior quadrants ($r=0.277$, $P=0.001$).

• CONCLUSION: RNFL of the patients with OSAHS is thinned. Furthermore, it is observed that the greater severity of OSAHS, the greater the loss of RNFL. Among the four quadrants observed, the most affected quadrant was the superior quadrant.

• KEYWORDS: obstructive sleep apnea - hypopnea syndrome; retinal nerve fiber layer; intraocular pressure

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摘要

目的:比较不同程度阻塞性睡眠呼吸暂停低通气综合征(obstructive sleep apnea hypopnea syndrome,OSAHS)患者与正常对照组的视神经纤维层(retinal nerve fiber layer,RNFL)厚度的差异。

方法:病例对照研究。选取 2014-01/2015-12 期间表现为打鼾及白天嗜睡的可疑患者 79 例在上海中山医院青浦分院呼吸科接受多导睡眠监测(polysomnography,PSG),进行 OSAHS 的诊断和严重程度分级,然后转诊到眼科进行眼部检查。测量眼内压(intraocular pressure,IOP)、RNFL 厚度等。

结果:共有 73 例被纳入本研究,对照组(无 OSAHS)20 例,OSAHS 组 53 例。中度、重度 OSAHS 组的 IOP 比对照组高(均 $P<0.05$)。中度、重度 OSAHS 组的平均 RNFL 及上方 RNFL 较对照组薄(均 $P<0.05$)。AHI 与上方 RNFL 及平均 RNFL 呈负相关($r=-0.316$、-0.205,均 $P<0.01$)。上方 RNFL 与氧饱和度指数(oxygen desaturation index, ODI)呈负相关($r=-0.24$, $P=0.005$),与平均血氧分压(SaO_2)呈正相关($r=0.277$,$P=0.001$)。

结论:OSAHS 患者的 RNFL 变薄,OSAHS 病情越严重 RNFL 丢失越多。上方 RNFL 受 OSAHS 影响较大。

关键词:阻塞性睡眠呼吸暂停低通气综合征;视神经纤维层;眼内压
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0 引言

阻塞性睡眠呼吸暂停低通气综合征(obstructive sleep apnea hypopnea syndrome, OSAHS)是一种常见但却经常被忽视的疾病,表现为睡眠过程中反复发作上气道狭窄或阻塞,出现鼾声呼吸暂停或通气不足,引起中度缺氧、夜间惊醒和白天嗜睡等[1]。人们逐渐认识到该疾病引起的低氧血症会提高许多疾病的发病率,包括卒中、认知力下降、抑郁、头痛、周围神经病变和非动脉炎性缺血性视神经病变和眼睑松弛综合征等[2-9]。OSAHS 与青光眼是否有关一直有争议。一些研究证明 OSAHS 与正常眼压性青光眼或原发性开角型青光眼有关[10-17]。然而,也有一些研究认为没有关系[18-22]。RNFL 厚度反映了视网膜神经节细胞轴突的数量。近年来,有不少关于 OSAHS 与视神经纤维层(retinal nerve fiber layer, RNFL)厚度的研究,可是结果不太一致[23]。国内的报道不多[24],且未按照严重程度将 OSAHS 分组,因此本研究拟通过测量不同程度 OSAHS 患者的 RNFL 厚度证实 OSAHS 对眼部的影响。

1 对象和方法

1.1 对象 2014-01/2015-12 在上海中山医院青浦分院呼吸科接受多导睡眠监测(PSG)的患者 79 例被转诊到眼科接受眼科检查。其中 20 例为正常对照组(无 OSAHS),59 例被诊断为 OSAHS。我们排除了 6 例,其中 3 例有糖尿病、2 例有高度近视,还有 1 例接受过眼部手术。最后,一共有 53 例 OSAHS 患者和 20 例正常对照入组。上海中山医院青浦分院伦理委员会同意了本次研究。所有参与本研究的患者签署了知情同意书。

1.2 方法

1.2.1 PSG 方法 患者采用可携带的睡眠监测设备进行睡眠监测(SW-SM2000CB)。由同一呼吸科医生在患者接受 PSG 的当天教授仪器的使用方法和注意事项。PSG 的结果也由同一个医生进行评分。睡眠呼吸紊乱指数(AHI)根据美国睡眠医学会(AASM)的标准进行评分。根据 AHI 对患者进行分组,AHI<5 为正常对照组,5≤AHI<15 为轻度组,15≤AHI<30 为中度组,AHI≥30 为重度组。并收集氧饱和度指数(oxygen desaturation index, ODI)(反映 1h 内动脉氧饱和度下降超过 4% 的频率)和平均血氧分压(SaO_2)的数据。

1.2.2 眼部检查方法 所有患者在接受 PSG 后 1d 的上午接受全面的眼科检查,包括:视力、电脑验光、非接触眼压、裂隙灯检查、眼底检查、OCT(OSE-2000)。所有的检查由同一个不知晓患者 PSG 结果的眼科技师完成。

统计学分析:所有的数据采用 SPSS 20.0 统计软件处理。计量资料用 $\bar{x}\pm s$ 描述,采用单因素方差分析,随后的两两比较采用 LSD-t 检验。计数资料的比较采用 χ^2 检验。采用 Pearson 相关分析分析 RNFL 与 PSG 指数(AHI, SaO_2, ODI)的关系。$P<0.05$ 为差异有统计学意义。

2 结果

2.1 患者基本情况及与 OSAHS 相关的指标 共有 73 例被纳入本研究,按照 AHI 进行分组:对照组 20 例 40 眼,轻度 OSAHS 组 15 例 30 眼,中度组 16 例 32 眼,重度组 22 例 44 眼。患者基本情况及 OSAHS 相关的指标见表 1。患者的双眼数据均被纳入进行统计分析,因为 OSAHS 对眼部的影响可以是不对称的[25-26]。两组年龄、性别比、高血压率、等效球镜度(SE)差异无统计学意义($P>0.05$)。然而 BMI 指数各组间差异有统计学意义($P=0.002$)。重度 OSAHS 组的 BMI 比对照组及中度 OSAHS 组高,差异有统计学意义($P<0.01$、0.027)。不同组别间 IOP 差异也有统计学意义($P<0.001$)。中度、重度 OSAHS 组的 IOP 均比对照组高,重度 OSAHS 组的 IOP 比轻度 OSAHS 组高,差异有统计学意义(均 $P<0.05$)。且 IOP 与 AHI、ODI 及 SaO_2 都相关($r=0.329$、0.243、-0.22, 均 $P<0.01$),但与 BMI 无相关性($r=0.087$, $P=0.297$)。

2.2 OCT 检查的结果 各组的 RNFL 厚度见表 2。上方及平均 RNFL 各组间差异有统计学意义($F=7.45$、6.244,均 $P<0.01$)。中度、重度 OSAHS 组的上方 RNFL 较对照组(均 $P<0.01$)及轻度 OSAHS 组薄($P=0.038$、0.031),差异有统计学意义。中度、重度 OSAHS 组的平均 RNFL 较对照组薄,差异有统计学意义(均 $P<0.05$);中度 OSAHS 组的平均 RNFL 较轻度组薄,差异有统计学意义($P=0.001$)。

2.3 AHI 与各指标的相关性分析 AHI 与上方 RNFL 及平均 RNFL 呈负相关($r=-0.316$、-0.205, 均 $P<0.01$),但与下方、鼻侧、颞侧 RNFL 不相关($r=-0.032$、0.073、0.046, $P=0.702$、0.384、0.580)。上方 RNFL 与 ODI 呈负相关($r=-0.24$, $P=0.005$),与 SaO_2 呈正相关($r=0.277$, $P=0.001$)。

3 讨论

关于 OSAHS 眼部并发症的发病机制主要有两种学说:血管学说和机械学说。血管学说认为 OSAHS 患者中眼动脉和中央视网膜动脉的血供不足以营养 RNFL 和视神经造成损伤[27]。反复的窒息会直接对视神经造成低氧损伤或间接地影响视乳头的血流,从而造成 RNFL 的丢失。后者可能继发于:(1)交感神经兴奋引起的动脉高血压和高血压性动脉硬化;(2)由于 NO(血管扩张剂)与内皮素(血管收缩剂)失衡造成的血管调节障碍;(3)异常的血小板聚集和活化造成视神经的微梗塞;(4)周期性的颅内压升高[28-33]。此外,低氧血症及继发的再灌注会导致氧化应激和炎症,表现为炎性标记物及反应性的氧化产物升高[34]。最终,低氧血症间接增加了睡眠期间的颅内压,脑部灌注压的降低会影响视神经的血供。虽然 RNFL 厚度与 OSAHS 的关系仍有争议,大部分研究支持 OSAHS 患者存在 RNFL 的丢失[23],与我们的结果一致。但是把 RNFL 分成四个区域进行分析时,各研究结果有些差异。本研究结果显示各组间 RNFL 厚度的差异主要集中在上方的区域。Casas 等[35]报道的差异集中在鼻侧。Sagiv 等[36]认为主要改变在上方及下方。Zengin 等[37]则报道差异在上方、下方和鼻侧。我们发现 AHI 与上方 RNFL 及平均 RNFL 呈负相关,与 Zengin 等[37]、Huseyinoglu 等[38]和 Lin 等[39]的结果类似。机械学说强调眼压的作用,认为高眼压会引起筛板各层变形移位产生剪切力,使筛板区视神经轴浆阻滞,轴突蛋白的生成和转运减少,从而导致细胞代谢受损,持续高眼压状态及 24h 内眼压的非节律性波动均会导致神经纤维层缺氧、水肿、梗死,从而导致视神经不可逆的损伤。在这个研究

表 1 患者基本情况及 OSAHS 相关的指标

指标	对照组	轻度 OSAHS	中度 OSAHS	重度 OSAHS	F/χ^2	P
眼数	40	30	32	44		
年龄($\bar{x}\pm s$,岁)	46.2±8.0	46.9±9.2	48.4±9.1	51.0±9.4	2.356	0.074
男(%)	80	66.7	75	77.3	0.859	0.835
HBP(%)	30	40	31.2	31.8	0.441	0.932
SE($\bar{x}\pm s$,D)	−0.30±1.18	−0.04±1.75	−0.81±1.96	−0.49±1.55	1.283	0.283
BMI($\bar{x}\pm s$)	25.47±3.05	26.93±3.35	26.55±2.89	28.29±3.87	5.06	0.002
AHI($\bar{x}\pm s$)	1.42±1.12	10.06±3.1	25.81±3.28	50.09±9.8	554.983	<0.001
ODI($\bar{x}\pm s$)	2.12±1.21	13.45±11.47	28.26±12.97	58.93±12.49	222.948	<0.001
SaO_2($\bar{x}\pm s$,%)	97.9±0.6	95.6±1.2	95.5±2.5	93.6±1.6	51.278	<0.001
IOP($\bar{x}\pm s$,mmHg)	14.6±2.6	15.6±2.1	16.5±2.2	17.0±2.3	7.958	<0.001

表 2 各组的 RNFL 厚度 ($\bar{x}\pm s$,μm)

RNFL	对照组	轻度 OSAHS 组	中度 OSAHS 组	重度 OSAHS 组	F	P
上方	121.8±12.5	115.9±16.8	107.5±13.8	107.8±18.5	7.45	<0.001
下方	138.3±16.9	139.5±15.7	130.3±12.3	137.8±17.9	2.172	0.094
鼻侧	93.9±11.7	95.0±11.6	86.6±10.0	91.9±17.4	2.526	0.060
颞侧	84.5±15.8	86.0±24.1	81.8±16.1	83.7±13.2	0.322	0.809
平均	109.6±8.2	109.1±8.2	101.5±6.5	105.3±10.8	6.244	0.001

中我们发现中度、重度 OSAHS 组的 IOP 均比对照组高,重度 OSAHS 组的 IOP 比轻度 OSAHS 组高,且 IOP 与 AHI、ODI 及 SaO_2 都相关,与 Mojon 等[14]、Moghimi 等[15]、Lin 等[39]、Sergi 等[10]、Karakucuk 等[27]的研究结果相似,但 Xin 等[16]未发现 AHI 与 IOP 相关。

本研究的主要不足之处是样本量较小。此外,由于试验对象都是由呼吸科的睡眠监测中心转诊而来,会造成选择性偏倚,无法代表所有的 OSAHS 患者。所有组别中,男性比例都多过女性,可能是因为 OSAHS 在男性更常见。另一个局限之处是我们没有对患者进行长期的随访以观察 RNFL 是否会随着病程增长进一步变薄,在接受治疗后,RNFL 的损害是否可以恢复。未来还需要进一步的前瞻性、长期、大样本的研究来明确 RNFL 厚度与 OSAHS 的关系。

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