

## · 临床研究 ·

# 不同程度老年阻塞性睡眠呼吸暂停低通气综合征患者髓过氧化物酶和胰淀素水平分析

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**【摘要】目的** 研究不同程度老年阻塞性睡眠呼吸暂停低通气综合征(OSAHS)患者血清髓过氧化物酶(MPO)和胰淀素水平变化及意义。**方法** 回顾性分析2012年2月至2016年10月成都市第六人民医院耳鼻咽喉科收治的老年OSAHS患者134例,根据呼吸暂停低通气指数(AHI)分为重度组55例、中度组41例和轻度组38例。比较3组患者多导睡眠监测(PSG)指标及MPO和胰淀素水平,Spearman相关法分析胰淀素及MPO的影响因素。应用SPSS 13.0统计软件对数据进行分析。依据数据类型采用方差分析或 $\chi^2$ 检验进行组间比较。**结果** 相比重度组患者,轻度组和中度组患者AHI、氧减指数(ODI)、呼吸暂停和低通气次数显著降低,夜间最低血氧饱和度(LSaO<sub>2</sub>)和平均动脉血氧饱和度(MSaO<sub>2</sub>)水平显著升高,差异均具有统计学意义( $P<0.05$ )。重度组持续气道正压通气治疗前相比轻度组和中度组患者血清胰淀素[(47.85±6.41)和(20.29±3.06)ng/ml;(47.85±6.41)和(31.57±5.27)ng/ml]和MPO[(37.92±9.88)和(7.61±2.04)ng/mg;(37.92±9.88)和(23.33±4.56)ng/mg]水平高,差异均具有统计学意义( $P<0.05$ )。重度组患者持续气道正压通气治疗6个月及1年后相比治疗前血清胰淀素[(34.17±4.96)和(47.85±6.41)ng/ml;(27.14±3.86)和(47.85±6.41)ng/ml]和MPO[(21.06±8.39)和(37.92±9.88)ng/mg;(12.17±7.53)和(37.92±9.88)ng/mg]水平显著降低,差异均具有统计学意义( $P<0.05$ )。Spearman相关分析结果表明MPO和胰淀素水平与LSaO<sub>2</sub>、MSaO<sub>2</sub>负相关,与AHI、呼吸暂停次数正相关。**结论** 血胰淀素和MPO水平测定对老年OSAHS患者并发胰岛素抵抗危险及持续气道正压通气治疗效果评估具有参考价值。

**【关键词】** 过氧化物酶;睡眠呼吸暂停,阻塞性;呼吸

**【中图分类号】** R563.9;R592

**【文献标志码】** A

**【DOI】** 10.11915/j.issn.1671-5403.2019.12.188

## Analysis of myeloperoxidase and amylin in elderly obstructive sleep apnea hypopnea syndrome patients with different severities

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**【Abstract】 Objective** To study the changes of serum myeloperoxidase (MPO) and amylin levels in elderly obstructive sleep apnea hypopnea syndrome (OSAHS) patients with different severities and its significances. **Methods** A total of 134 elderly OSAHS patients admitted to our hospital from February 2012 to October 2016 were retrospectively recruited in this study. According to their apnea hypopnea index (AHI), they were divided into severe group ( $n=55$ ), moderate group ( $n=41$ ) and mild group ( $n=38$ ). Polysomnography (PSG) indicators, MPO and amylin levels were compared among the 3 groups. Spearman correlation analysis was used to analyze the influencing factors of amylin and MPO levels. SPSS statistics 13.0 was employed to analyze the data. Analysis of variance or Chi-square test was applied to make intergroup comparison according to different data types. **Results** Compared with the severe group, AHI, oxygen desaturation index (ODI), apnea and hypopnea frequency were decreased significantly, and the lowest oxygen saturation (LSaO<sub>2</sub>) and mean arterial oxygen saturation (MSaO<sub>2</sub>) at night were increased obviously in the mild group and the moderate group ( $P<0.05$ ). Before continuous positive airway pressure (CPAP) ventilation treatment, the severe group had notably higher serum levels of amylin [(47.85±6.41) vs (20.29±3.06) and (31.57±5.27)ng/ml] and MPO [(37.92±9.88) vs (7.61±2.04) and (23.33±4.56)ng/mg] than the mild and moderate groups ( $P<0.05$ ). In 6 months and 1 year after the treatment, the serum levels of amylin [(34.17±4.96) and (27.14±3.86) vs (47.85±6.41)ng/ml] and MPO [(21.06±8.39) and (12.17±7.53) vs

( $37.92 \pm 9.88$ ) ng/mg] were significantly lower in the patients of the severe group when compared with the levels before treatment ( $P < 0.05$ ). Spearman correlation analysis showed that MPO and amylin levels were negatively correlated with  $\text{LSaO}_2$  and  $\text{MSaO}_2$ , and positively correlated with AHI and apnea frequency. **Conclusion** Serum amylin and MPO levels show reference values in evaluation of the risk for insulin resistance and of the therapeutic effect of CPAP in elderly OSAHS patients.

**[Key words]** myeloperoxidase; sleep apnea, obstructive; breathing

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老年阻塞性睡眠呼吸暂停低通气综合征( obstructive sleep apneahypopnea syndrome, OSAHS)患者可合并多系统损害,其对胰岛的损害早期常表现为胰岛素抵抗,具体机制尚不清楚<sup>[1,2]</sup>。有报道称OSAHS患者睡眠中出现的呼吸紊乱、间断缺氧是合并糖代谢紊乱的重要因素<sup>[3]</sup>。另有研究表明OSAHS合并糖代谢紊乱患者体内氧化应激水平增高,可经活性氧( reactive oxygen species, ROS)介导激活多种细胞内相关信号通路,参与胰岛细胞的损伤<sup>[4]</sup>。胰淀素和髓过氧化物酶( myeloperoxidase, MPO)是分别评估血糖平衡和氧化应激水平的重要指标。胰淀素是一种淀粉样多肽,主要由胰岛B细胞生成和分泌,可拮抗胰岛素的作用而调节血糖平衡<sup>[5]</sup>;MPO是评估机体氧化应激水平的良好指标<sup>[6,7]</sup>。为此笔者分析了不同程度老年OSAHS患者MPO和胰淀素水平变化及意义。

## 1 对象与方法

### 1.1 研究对象

回顾性分析2012年2月至2016年10月成都市第六人民医院耳鼻咽喉科收治的老年OSAHS患者134例,均行多导睡眠监测( polysomnography, PSG)确诊为OSAHS。根据呼吸暂停低通气指数( apnea hypopnea index, AHI)分为重度组( AHI > 30次/h)55例、中度组41例(AHI 16~30次/h)和轻度组38例(AHI 5~15次/h)<sup>[8]</sup>。AHI正常<5次/h。其中重度组患者均住院佩戴呼吸机治疗,并于出院后自行购买呼吸机坚持家庭治疗>1年。纳入标准:(1)无高血压或糖尿病;(2)颅脑核磁共振成像( magnetic resonance imaging, MRI)检查无异常;(3)未服用镇静及阿司匹林抑制剂等药物。排除标准:(1)甲状腺疾病患者;(2)近期手术、创伤及饮酒者。

### 1.2 PSG 监测

采用多导睡眠监测仪Alice 6(飞利浦伟康,中国)进行PSG,检查时间≥8 h,从夜间22:00时到早晨7:00时。检查前2 d禁酒、浓茶、镇静药物、咖啡等。患者拆除仪器后收集和分析数据,包括夜间最低血氧饱和度( lowest oxygen saturation,  $\text{LSaO}_2$ )、

AHI、平均动脉血氧饱和度( mean arterial oxygen saturation,  $\text{MSaO}_2$ )、氧减指数( oxygen desaturation index, ODI)、呼吸暂停和低通气次数。

### 1.3 持续气道正压通气治疗

重度组患者使用Auto持续气道正压通气( continuous positive airway pressure, CPAP)呼吸机(飞利浦伟康,型号BIPAPAP407,中国)进行治疗,治疗压力设定为4~16 cmH<sub>2</sub>O(1 cmH<sub>2</sub>O=0.098 kPa),每晚治疗6~8 h,治疗1年,严格按照说明书使用和操作。

### 1.4 MPO 和胰淀素检测

晨起空腹采外周血10 ml,2500转/min离心15 min,将上清液取出分为两份,-70℃冰箱保存备用,酶联免疫吸附法检测MPO和胰淀素。试剂盒购自长沙维尔生物科技有限公司,严格按照试剂盒说明书进行操作。

### 1.5 随访

采取门诊复查方式对重度组患者跟踪随访。患者出院时于出院记录中告知佩戴呼吸机治疗详细方案及注意事项,注明下一次复诊时间,并提前1周由责任护士电话通知。门诊复诊时间为CPAP治疗6个月及1年后。

### 1.6 统计学处理

应用SPSS 13.0统计软件对数据进行分析。计量资料用均数±标准差( $\bar{x} \pm s$ )表示,组间比较采用方差分析。计数资料用例数(百分率)表示,组间比较采用 $\chi^2$ 检验。Spearman相关法分析指标间的相关性。 $P < 0.05$ 为差异有统计学意义。

## 2 结 果

### 2.1 3组患者基线资料比较

3组患者年龄、性别、体质量指数( body mass index, BMI)、身高、颈围及吸烟比例等差异无统计学意义( $P > 0.05$ ;表1)。

### 2.2 3组患者PSG监测指标比较

相比重度组患者,轻度组和中度组患者AHI、ODI、呼吸暂停和低通气次数显著降低, $\text{LSaO}_2$ 和 $\text{MSaO}_2$ 水平显著升高,差异均具有统计学意义( $P < 0.05$ ;表2)。

## 2.3 3组患者MPO和胰淀素水平比较

重度组CPAP治疗前相比轻度组和中度组患者血清胰淀素和MPO水平高,差异具有统计学意义( $P<0.05$ )。重度组患者CPAP治疗6个月及1年后相比治疗前血清胰淀素和MPO水平显著降低,差异均具有统计学意义( $P<0.05$ ;表3)。

## 2.4 Spearman相关分析胰淀素及MPO的影响因素

Spearman相关分析结果表明MPO和胰淀素水平与 $LSaO_2$ 、 $MSaO_2$ 负相关,与AHI、呼吸暂停正相关( $P<0.05$ )。其他指标相关性详见表4。

## 3 讨论

本研究PSG监测结果表明重度组患者AHI、ODI、呼吸暂停及低通气次数水平显著高于轻度及中度组,与Sato等<sup>[9]</sup>的研究结果一致。重度组患者 $LSaO_2$ 及 $MSaO_2$ 显著降低,ODI显著升高的原因主要是卧位时横隔上移,肺通气量减少;呼吸暂停可导

致氧气吸入减少,二氧化碳潴留,而重度患者的呼吸暂停及低通气次数均显著高于中低度患者,因此肺通气量减少及二氧化碳潴留程度更严重, $LSaO_2$ 及 $MSaO_2$ 显著降低。

本研究表明重度组CPAP治疗前相比轻度组和中度组患者血清胰淀素和MPO水平显著高,说明病情越重,血清胰淀素和MPO水平越高。胰淀素为胰岛细胞分泌的一种多肽,可与胰岛素通过蛋白质交联形成的二聚体结构对胰岛素产生拮抗作用,是反映胰岛素抵抗程度的因子。MPO主要由活化的中性粒细胞产生,是评估氧化应激反应的重要指标。张红霞等<sup>[10]</sup>研究显示重度OSAHS患者血清MPO水平显著高于轻度患者。秦冉冉等<sup>[11]</sup>研究显示重度OSAHS患者胰淀素水平显著高于轻度组患者,本研究结果与其一致,分析原因是OSAHS患者多存在肥胖,肥胖使得胰岛功能相对不足,且低氧血症可引起胰岛素分泌减少,因此OSAHS患者胰岛功能损

表1 3组患者基线资料比较

Table 1 Comparison of baseline data among three groups

Group	n	Age (years, $\bar{x}\pm s$ )	Gender (male/female, n)	BMI (kg/m <sup>2</sup> , $\bar{x}\pm s$ )	Height (cm, $\bar{x}\pm s$ )	Neck circumference (cm, $\bar{x}\pm s$ )	Smoking [n (%)]
Mild	38	69.4±4.9	30/8	25.39±2.96	167.82±10.35	39.45±3.87	19(50.00)
Moderate	41	67.5±5.1	33/8	24.88±3.02	168.33±12.41	39.81±4.02	21(51.22)
Severe	55	68.9±6.0	44/11	26.01±3.82	168.97±11.27	40.16±4.07	28(50.91)
F/ $\chi^2$		0.662	0.532	0.586	0.691	0.936	0.844
P value		0.628	0.714	0.678	0.609	0.469	0.518

BMI: body mass index.

表2 3组患者PSG监测指标水平比较

Table 2 Comparison of PSG monitoring indicators among three groups

( $\bar{x}\pm s$ )

Group	n	AHI(times/h)	$LSaO_2$ (%)	$MSaO_2$ (%)	ODI(times/h)	Apnea(times/7h)	Hypopnea(times/7h)
Mild	38	11.14±4.15*	87.25±7.74*	91.56±6.05*	32.09±2.33*	72.54±10.98*	40.25±5.71*
Moderate	41	26.94±3.82*	80.62±8.66*	84.68±4.27*	40.54±4.28*	142.17±19.57*	65.81±9.24*
Severe	55	57.65±10.33	68.39±10.11	80.12±2.41	52.12±6.25	216.05±32.82	106.84±16.37

PSG: polysomnography; AHI: apnea hypopnea index;  $LSaO_2$ : lowest oxygen saturation;  $MSaO_2$ : mean arterial oxygen saturation; ODI: oxygen desaturation index. Compared with severe group, \* $P<0.05$ .

表3 3组患者MPO和胰淀素水平比较

Table 3 Comparison of level of MPO and amylin among three groups

( $\bar{x}\pm s$ )

Group	n	MPO(ng/mg)			Amylin(ng/ml)		
		Before treatment	6 months after treatment	1 year after treatment	Before treatment	6 months after treatment	1 year after treatment
Mild	38	7.61±2.04*	-	-	20.29±3.06*	-	-
Moderate	41	23.33±4.56*	-	-	31.57±5.27*	-	-
Severe	55	37.92±9.88	21.06±8.39#	12.17±7.53#	47.85±6.41	34.17±4.96#	27.14±3.86#

MPO: myeloperoxidase; -: no data. Compared with severe group, \* $P<0.05$ ; compared with before treatment, # $P<0.05$ .

**表4 Spearman 相关分析胰淀素及 MPO 的影响因素**

Table 4 Spearman correlation analysis of influencing factors of amylin and MPO

Factor	Amylin		MPO	
	r	P value	r	P value
Age	0.079	0.184	0.126	0.136
BMI	0.170	0.104	0.092	0.129
LSaO <sub>2</sub>	-0.488	<0.001	-0.531	<0.001
AHI	0.635	<0.001	0.679	<0.001
MSaO <sub>2</sub>	-0.654	0.040	-0.751	0.013
ODI	0.312	0.027	0.296	0.369
Apnea	0.422	0.023	0.279	0.049
Hypopnea	0.305	0.313	0.367	0.008

MPO: myeloperoxidase; BMI: body mass index; LSaO<sub>2</sub>: lowest oxygen saturation; AHI: apnea hypopnea index; MSaO<sub>2</sub>: mean arterial oxygen saturation; ODI: oxygen desaturation index.

坏<sup>[12]</sup>,重度OSAHS患者胰岛功能损害更严重。而胰淀素是反映胰岛素抵抗程度的重要因子,所以重度OSAHS患者胰淀素水平显著升高。另外,OSAHS患者长期反复夜间的间歇性缺氧,可引起交感神经系统兴奋性异常增加,氧化应激系统明显失衡,炎症因子水平显著升高<sup>[13]</sup>。MPO是评估氧化应激水平的重要指标,OSAHS病情加重可使氧化应激系统严重失衡,因此重度OSAHS患者MPO水平显著升高。

重度组患者CPAP治疗6个月及1年后相比治疗前血清胰淀素和MPO水平显著降低,说明CPAP治疗可较明显地纠正患者睡眠结构,改善缺氧状况,降低体内氧化应激和炎症反应程度,与秦冉冉等<sup>[11]</sup>研究结果一致。可能因为间断缺氧是合并糖代谢紊乱的重要因素<sup>[3]</sup>,CPAP治疗能够改善OSAHS患者呼吸紊乱状况,增加氧气吸入量以及胰岛素受体敏感性和胰岛素的亲和性,抑制交感神经递质等拮抗胰岛素相关因子的释放,减轻胰岛素抵抗,从而降低胰淀素和MPO水平。

本研究表明MPO及胰淀素与LSaO<sub>2</sub>、MSaO<sub>2</sub>负相关,与AHI和呼吸暂停次数正相关,说明氧化应激及胰岛功能损伤和病情程度成正比,与Kelly等<sup>[14]</sup>研究结果相一致。MPO和胰淀素两者在胰岛素抵抗发病中关系密切,分析原因,可能与OSAHS患者氧化应激水平升高可对胰岛细胞造成损伤、从而使胰淀素分泌紊乱、进一步引起胰岛素抵抗发生有关<sup>[15]</sup>。本研究表明MPO和胰淀素水平均和BMI无关,和高燕燕等<sup>[16]</sup>的研究结果一致,排除了肥胖对胰淀素的干扰。MPO和胰淀素水平和年龄无关,组间性别差异也无统计学意义,排除了PSG指标外的干扰因素。

综上,血胰淀素和MPO水平测定对老年OSAHS患者并发胰岛素抵抗危险及CPAP治疗效果评估具有参考价值。

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(编辑: 王彩霞)

## · 消息 ·

### 《中华老年多器官疾病杂志》“临床病理讨论”栏目征稿

临床病理讨论(Clinicopathological Conference, CPC)是临床实践中的一个重要环节,是多个学科合作对患者进行个体化诊治的一种形式,尤其对于一些疑难和罕见病例更为重要。综合患者的临床表现、实验室检查、影像学检查和病理检查等各项结果,一方面可以明确疾病的诊断并制定治疗方案,使患者受益,另一方面亦有利于为临床医师提供更好的经验和更开阔的思路,提高医师的诊疗能力。一篇好的临床病理讨论,往往是教科书上找不到的活教材,也是其他文体难以取代的好形式。

“临床病理讨论”一直以来都是本刊的一个特色栏目,深受广大读者喜爱。所刊登的一般多为回顾性的病例讨论与总结,旨在总结经验、吸纳教训和传播知识。在工作实践中,我们根据广大读者和作者的建议,对临床病理讨论文章的格式进行了调整。(1)作者在文题下署名(而非仅在文末注明由何人整理),作者拥有本文的著作权。(2)文章正文为中文,正文前有言简意赅的中英文摘要。论文性质等同于本刊“论著”。(3)所选病例可以是疑难、罕见病例,也可以是诊断明确、但病情危重或有诸多并发症、治疗上甚为棘手的病例,亦可为其他对临床实践有指导或提示意义的病例。

本刊热忱欢迎广大专家学者为本刊撰写或推荐相关稿件。

具体格式请参考本刊近期发表的“临床病理讨论”文章。

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