·临床研究·

# 伴阻塞性睡眠呼吸暂停低通气综合征高血压患者的血压控制研究

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**【摘 要】 目的** 探讨伴阻塞性睡眠呼吸暂停低通气综合征(OSAHS)的高血压患者,同时服用降压药和接受持续气道正压通气(CPAP)是否能有效控制血压。**方法** 选取2014年1月至2015年6月南京医科大学第一附属医院睡眠中心就诊的伴有OSAHS高血压患者180例,根据服用降压药物后血压是否被有效控制,分为控制组($n=87$)和未控制组($n=93$),两组在服用降压药同时接受CPAP 6个月,比较服用不同降压药方案和CPAP治疗前后血压是否得到有效控制的关系。**结果** 所有患者共使用13种不同的降压药方案进行治疗。控制组与未控制组患者降压药方案差异无统计学意义($P>0.05$),多因素logistic回归分析表明降压药方案不是影响伴OSAHS高血压患者血压控制的独立预测因子(OR=1.897,$P=0.094$)。使用CPAP后控制组、非控制组夜间收缩压(SBP)和舒张压(DBP)均下降,差异有统计学意义($P<0.01$)。**结论** 伴OSAHS高血压病患者的降压治疗方案与血压控制无明显相关性,而CPAP治疗可使降压药有效组和无效组患者的夜间血压都降低。

**【关键词】** 阻塞性睡眠呼吸暂停低通气综合征;高血压;降压药物;持续气道正压通气

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# Blood pressure control in hypertensive patients with obstructive sleep apnea hypopnea syndrome

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**【Abstract】 Objective** To investigate whether antihypertensive medication and continuous positive airway pressure (CPAP) treatment can effectively control blood pressure (Bp) in the hypertensive patients with obstructive sleep apnea hypopnea syndrome (OSAHS). **Methods** A total of 180 hypertensive patients with OSAHS admitted in the First Affiliated Hospital of Nanjing Medical University from January 2014 to June 2016 were recruited in this study. According to the outcome of hypertensive medication, they were divided into Bp controlled group ($n=87$) and Bp uncontrolled group ($n=93$). Then they were given CPAP treatment and hypertensive medication simultaneously for 6 months. Bp control results were compared among the patients undergoing different regimens of antihypertensive medications, and the relationship of Bp well-control with CPAP treatment was analyzed. **Results** A total of 13 different antihypertensive regimens were used among the enrolled subjects. There was no statistical difference in the regimen distribution between the Bp controlled group and Bp uncontrolled group ($P>0.05$). Multivariate factor logistic regression analysis revealed that antihypertensive regimen was not an independent predictor of Bp control outcome in the hypertensive patients with OSAHS (OR=1.897, $P=0.094$). However, CPAP treatment obviously decreased nocturnal systolic blood pressure (SBP) and diastolic blood pressure (DBP) in both the Bp controlled and uncontrolled groups ($P<0.01$). **Conclusion** In hypertensive patients with OSAHS, there is no significant association between antihypertensive medication regimens and Bp control. Additional CPAP treatment could further reduce nocturnal Bp in both Bp controlled and uncontrolled patients after antihpertensive medication.

**【Key words】** obstructive sleep apnea hypopnea syndrome; hypertension; antihypertensive medication; continuous positive airway pressure

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阻塞性睡眠呼吸暂停低通气综合征(obstructive sleep apnea hypopnea syndrome,OSAHS)是一种非常普遍的睡眠相关呼吸障碍,基本特点是睡眠期间上呼吸道反复出现气流停止(呼吸暂停)或气流减少(低通气)。低氧刺激颈动脉体化学感受器和(或)窒息刺激交感神经系统兴奋是OSAHS与高血压相关联的潜在机制[1]。然而,针对伴有OSAHS高血压患者的最有效血压控制方案仍不明确。持续气道正压通气(continuous positive airway pressure,CPAP)被认为是伴有OSAHS高血压患者的最好治疗方法,但CPAP对血压的控制仍有争议,单独使用CPAP难以有效控制血压,因此,患者仍需服用降压药物,但药物治疗方案的治疗效果不同,是否有特定方案对伴OSAHS高血压患者有效,目前的研究报道有限[2]。本研究的目的是确定伴有OSAHS高血压患者使用CPAP同时服用降压药物和血压是否得到有效控制的关系。

## 1 对象与方法

### 1.1 研究对象

选取2014年1月至2015年6月南京医科大学第一附属医院睡眠中心就诊的伴有OSAHS高血压患者180例,根据服用降压药物后血压是否被有效控制,分为控制组和未控制组,控制组患者87例,男性49例,女性38例,年龄(62.5±9.7)岁;未控制组患者93例,男性55例,女性38例,年龄(57.8±10.5)岁。

根据24 h动态血压监测(ambulatory blood pressure monitoring,ABPM)结果确诊和判定高血压是否得到有效控制,整夜多导睡眠图结果诊断OSAHS,通过睡眠呼吸暂停低通气指数(apnea hypopnea index,AHI)判定病情,5≤AHI≤15为轻度,15<AHI≤30为中度,AHI>30为重度。血压是否得到有效控制标准参照欧洲心脏病学会(European Society of Cardiology, ESC)和欧洲高血压学会(European Society of Hypertension,ESH)标准[3]。

### 1.2 方法

采用无创动态血压监测仪监测血压,袖带为22 cm×12 cm,缚于患者左上臂;血压监测时间24 h,设定早晨6:00至夜间22:00为白昼时间,夜间22:00至次日早晨6:00为夜间时间;测量次数分别为1次/30 min(白昼)和1次/60 min(夜间)。所有患者平均每天使用CPAP≥4 h,压力滴定法自动调节CPAP参数,使用CPAP的依从性由设备计数器评估。同时口服降压药物≥6个月,期间不改变药物治疗方案,直到随访结束。

### 1.3 随访

患者每隔1个月门诊随访,如有特殊情况随时随访,专业人员每隔1个月定期电话联系或家访部分患者,通过这些方式获得随访数据,包括口服降压药物、使用CPAP以及血压控制情况等,每位患者随访时间≥6个月,截止至2015年12月。

### 1.4 统计学处理

采用SPSS19.0统计软件对数据进行分析。计量资料中呈正态分布者用均数±标准差($\bar{x}\pm s$)表示,两组比较采用$t$检验。呈偏态分布者用四分位数表示,两组比较采用Wilcoxon秩和检验。计数资料以频数和百分率表示,两组比较采用$\chi^2$检验,多因素logistic回归分析影响血压控制的因素。以$P<0.05$为差异有统计学意义。

## 2 结 果

### 2.1 两组患者基线资料

控制组与未控制组患者在性别、体质量指数(body mass index, BMI)、颈围、腰围、吸烟习惯、OSAHS病情、AHI方面无明显差异。控制组患者血压明显低于未控制组患者,年龄较未控制组患者高,差异有统计学意义($P<0.05$;表1)。

### 2.2 两组患者降压方案情况

所有患者共采用了13种药物降压方案,控制组与未控制组患者降压药物治疗方案差异无统计学意义($P>0.05$;表2)。

### 2.3 两组患者使用CPAP前后血压情况

表3结果表明,对所有患者使用CPAP前后测得的动态血压数据进行分析,控制组与未控制组患者24 h平均收缩压和舒张压、白天收缩压和舒张压在使用CPAP前后差异均无统计学意义($P>0.05$),而夜间收缩压和舒张压较使用CPAP前均明显下降,差异有统计学意义($P<0.01$)。

### 2.4 影响血压控制的多因素logistic回归分析

针对180例伴OSAHS高血压患者,以血压是否控制为因变量,以年龄、性别、BMI、颈围、腰围、吸烟习惯、OSAHS病情、降压药物方案为自变量,进行二分类logistic回归分析,结果显示以上均不是影响伴OSAHS高血压患者血压控制的独立预测因子($P>0.05$;表4)。

## 3 讨 论

OSAHS患者高血压的患病率约50%[4]。尽管有伴OSAHS高血压患者的大量研究[5],但只有少部分是研究不同降压药物的疗效,而且大多是研究

**表1 两组患者基线资料比较**

Table 1 Comparison of baseline data between two groups

| Item | BP controlled group ($n=87$) | BP uncontrolled group ($n=93$) | $P$ value |
|---|---|---|---|
| Age(years, $\bar{x}\pm s$) | 62.8±9.7 | 57.9±12.1 | 0.037 |
| Male[$n$(%)] | 49(56.3) | 55(59.1) | 0.702 |
| BMI($kg/m^2$, $\bar{x}\pm s$) | 28.1±6.5 | 28.6±5.2 | 0.189 |
| Neck circumference (cm, $\bar{x}\pm s$) | 39.8±4.5 | 40.9±4.1 | 0.832 |
| Waist circumference (cm, $\bar{x}\pm s$) | 105.3±13.5 | 106.5±13.1 | 0.582 |
| Smoking habits[$n$(%)] | | | 0.162 |
| Non-smoking | 44(50.6) | 41(44.1) | |
| Former smoking | 32(36.8) | 30(32.3) | |
| Current smoking | 11(12.6) | 22(23.6) | |
| AHI(times/h, $\bar{x}\pm s$) | 38.5±11.7 | 40.5±12.3 | 0.764 |
| Condition of OSAHS[$n$(%)] | | | 0.712 |
| Mild | 22(25.3) | 19(20.4) | |
| Moderate | 41(47.1) | 45(48.4) | |
| Severe | 24(27.6) | 29(31.2) | |
| Data of 24h ABPM[mmHg, M($Q_1$, $Q_3$)] | | | |
| Mean 24h SBP | 121.7(111.7, 126.9) | 139.5(133.8, 146.2) | <0.001 |
| Mean 24h DBP | 73.6(63.3, 78.2) | 85.1(82.0, 89.9) | <0.001 |
| Daytime SBP | 127.0(117.9, 133.2) | 143.9(138.1, 152.8) | <0.001 |
| Daytime DBP | 77.9(69.7, 85.0) | 93.3(86.6, 99.7) | <0.001 |
| Night SBP | 114.3(97.8, 118.1) | 129.4(124.9, 145.3) | <0.001 |
| Night DBP | 65.6(57.7, 68.4) | 83.6(74.8, 92.4) | <0.001 |

BP: blood pressure; BMI: body mass index; AHI: apnea hypopnea index; OSAHS: obstructive sleep apnea hypopnea syndrome; ABPM: ambulatory blood pressure monitoring; SBP: systolic blood pressure; DBP: diastolic blood pressure

**表2 两组患者降压方案比较**

Table 2 Comparison of antihypertensive regimen between two groups [$n$(%)]

| Item | BP controlled group($n=87$) | BP uncontrolled group($n=93$) |
|---|---|---|
| ARB + diuretics | 13(14.9) | 15(16.1) |
| CCB + ARB | 10(11.5) | 5(5.4) |
| CCB | 9(10.3) | 8(8.6) |
| CCB + ACEI | 10(11.5) | 12(12.9) |
| CCB + β-blocker | 7(8.0) | 9(9.7) |
| ARB | 8(9.2) | 7(7.5) |
| ACEI | 6(6.9) | 9(9.7) |
| ACEI + diuretics | 6(6.9) | 5(5.4) |
| CCB + ACEI + diuretics | 5(5.7) | 9(9.7) |
| β-blocker | 4(4.6) | 3(3.2) |
| CCB + diuretics | 3(3.4) | 4(4.3) |
| Diuretics | 4(4.6) | 3(3.2) |
| β-blocker + diuretics | 2(2.3) | 4(4.3) |

BP: blood pressure; ARB: angiotensin Ⅱ receptor blockers; CCB: calcium channel blockers; ACEI: angiotensin-converting enzyme inhibitors

单个药物的降压疗效。Diogo 等[2]发现血管紧张素转换酶抑制剂和血管紧张素 AT1 受体拮抗剂可阻断β1 肾上腺素受体和肾素－血管紧张素－醛固酮系统,对伴 OSAHS 高血压患者有帮助。螺内酯可阻断醛固酮水平,对顽固性高血压患者[6]、严重OSAHS患者[7]、醛固酮水平经常升高患者[8]有效。容量负荷过重可使 OSAHS 病情进展[9],噻嗪类利尿剂对没有液体潴留的伴 OSAHS 高血压患者治疗无效[8]。钙通道阻滞剂虽然可有效降低血压,但可能负面影响伴 OSAHS 高血压患者的睡眠,特别是睡眠时间和睡眠质量[10]。本研究患者服用的降压药物中血管紧张素Ⅱ受体拮抗剂和利尿剂居多,一共有 61 例仅服用一种降压药,105 例服用两种降压药,14 例服用三种降压药,93 例患者未得到有效控制,两组患者的差异无统计学意义。多因素 logistic 回归分析结果表明,伴 OSAHS 高血压患者降压治疗方案与血压控制没有相关性。

已有报道,伴 OSAHS 高血压患者每天晚上使用 CPAP 时间应≥4 h,这个标准能降低发病率[11]。Börgel 等[12]报道降压药不是 CPAP 治疗高血压效果的独立预测因子。此外,Dernaika 等[13]报道患者使用 CPAP 同时服用降压药,血压控制效果并不明显。Pépin 等[14]对从未接受任何治疗的伴 OSAHS 高血压患者进行了研究,评估 CPAP 和缬沙坦的降压效果。他们推测,对于服用特定降压药仍未控制血压的患者,同时使用 CPAP 可能效果会叠加,可有效降低平均 24 h 血压,疗效是单独使用 CPAP 的 4 倍。本研究结果表明使用 CPAP 后虽然对伴 OSAHS 高血压患者 24 h 平均收缩压和舒张压、白天收缩压和舒张压没有明显降压效果,但对患者夜间收缩压和舒张压作用明显,提示 CPAP 对夜间血压的作用更明显,特别是夜间收缩压。

**表3 CPAP前后血压比较**

Table 3 Comparison of blood pressure before and after CPAP [mmHg, M($Q_1$, $Q_3$)]

| Item | Controlled group ($n=87$) | | Uncontrolled group ($n=93$) | |
|---|---|---|---|---|
| | Before CPAP | After CPAP | Before CPAP | After CPAP |
| Mean 24h SBP | 121.7(111.7, 126.9) | 118.7(109.8, 126.8) | 139.5(133.8, 146.2) | 138.9(134.1, 145.8) |
| Mean 24h DBP | 73.6(63.3, 78.2) | 72.7(65.5, 77.9) | 85.1(82.0, 89.9) | 84.8(83.5, 88.7) |
| Daytime SBP | 127.0(117.9, 133.2) | 126.6(116.5, 135.1) | 143.9(138.1, 152.8) | 143.7(137.8, 153.2) |
| Daytime DBP | 77.9(69.7, 85.0) | 76.7(68.2, 84.7) | 93.3(86.6, 99.7) | 93.0(87.2, 99.5) |
| Night SBP | 114.3(97.8, 118.1) | 102.9(97.5, 107.2)** | 129.4(124.9, 145.3) | 115.8(105.6, 123.7)** |
| Night DBP | 65.6(57.7, 68.4) | 62.0(59.7, 69.5)** | 83.6(74.8, 92.4) | 77.3(67.1, 82.5)** |

CPAP: continuous positive airway pressure; SBP: systolic blood pressure; DBP: diastolic blood pressure. Compared with before CPAP, ** $P<0.01$

**表4 影响血压控制的多因素logistic回归分析**

Table 4 Multivariate logistic regression analysis of influencing factors for blood pressure control

| Factor | B | Wald | OR | 95% CI | *P* value |
|---|---|---|---|---|---|
| Age | 1.830 | 0.765 | 1.213 | 1.075 – 1.413 | 0.089 |
| Gender | 1.742 | 1.659 | 1.086 | 0.378 – 3.352 | 0.482 |
| BMI | 2.005 | 3.075 | 1.412 | 1.098 – 1.753 | 0.209 |
| Neck circumference | 1.098 | 1.504 | 0.875 | 0.326 – 1.805 | 0.134 |
| Waist circumference | 1.354 | 1.756 | 1.143 | 0.675 – 1.948 | 0.106 |
| Smoking habits | 1.542 | 1.765 | 1.098 | 0.432 – 1.854 | 0.504 |
| Condition of OSAHS | 1.638 | 1.067 | 1.376 | 1.015 – 3.356 | 0.075 |
| Antihypertensive regimen | 1.860 | 2.065 | 1.897 | 1.175 – 5.352 | 0.094 |

BMI: body mass index; OSAHS: obstructive sleep apnea hypopnea syndrome

本研究结果提示,在伴OSAHS的高血压病患者中,降压治疗方案与血压控制无相关性,CPAP治疗无论在降压药有效组还是在降压药无效组均可使夜间血压进一步降低。同时本研究也存在一定的局限性,首先评估降压药疗效时我们无法确定是否存在影响高血压严重程度的其他因素;其次样本数量小,并且患者在单一中心进行治疗,还有待进一步开展多中心大样本研究加以验证。

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