·临床研究·

高龄高血压患者血压变异性与认知功能损害

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【摘 要】 **目的** 探讨高龄高血压患者血压变异性与认知功能损害的关系。**方法** 入选2017年3月至2017年12月北京积水潭医院干部保健科高龄高血压住院患者177例,根据认知功能评估结果分为轻度认知障碍(MCI)组114例和认知正常组63例,比较2组患者的一般情况、实验室检查、平均血压、血压变异系数、昼夜节律和晨峰血压。采用SPSS 17.0统计软件对数据进行处理。组间比较采用t检验或χ^2检验。**结果** 2组患者一般情况差异无统计学意义($P>0.05$)。与MCI组患者相比,认知正常组患者收缩压变异系数[(0.11±0.02)% *vs* (0.08±0.03)%]、舒张压变异系数[(0.12±0.02)% *vs* (0.11±0.03)%]水平明显增高,差异具有统计学意义($P<0.05$)。2组患者收缩压下降率、舒张压下降率和舒张压晨峰差异无统计学意义($P>0.05$)。MCI组患者收缩压晨峰明显高于认知正常组患者[(17.37±5.36) *vs* (13.60±3.57)mmHg],差异有统计学意义($P<0.05$)。2组患者非杓型、杓型、反杓型和超杓型血压比例差异无统计学意义($P>0.05$)。**结论** 控制血压变异性及收缩压晨峰有利于改善高龄高血压患者的认知功能。

【关键词】 认知障碍;昼夜节律;血压;老年人
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Blood pressure variability and cognitive impairment in very elderly hypertensive patients

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【**Abstract**】 **Objective** To explore the relationship of blood pressure variability and cognitive impairment in the very elderly patients with hypertension. **Methods** A total of 177 hypertensive patients (80 – 91 years old) admitted in our department from March to December 2017 were recruited in this study. According to the results of Montreal cognitive assessment (MoCA), the patients were divided into mild cognitive impairment group (MCI group, $n=114$) and normal cognitive group (control group, $n=63$). The general conditions, laboratory examination results, mean blood pressure, variable coefficient and circadian rhythms of blood pressure, and morning surge in blood pressure were compared between the 2 groups. SPSS statistics 17.0 was used to perform the statistical analysis. Student's test or Chi-square was employed for comparison between two groups. **Results** There were no significant differences in general conditions between the 2 groups ($P>0.05$). The patients from MCI group had obviously higher variable coefficient of systolic blood pressure [(0.11±0.02)% *vs* (0.08±0.03)%, $P<0.05$] and diastolic blood pressure [(0.12±0.02)% *vs* (0.11±0.03)%, $P<0.05$] than those in the control group. No significant differences were seen in declined rate of systolic blood pressure and diastolic blood pressure and morning diastolic blood pressure surge between the 2 groups ($P>0.05$). The morning systolic blood pressure surge was also significantly higher in the MCI group than the control group [(17.37±5.36) *vs* (13.60±3.57) mmHg, $P<0.05$]. No significant differences were seen in the ratios of patients presenting non-dipper type, dipper type, reverse dipper type and over dipper type of blood pressure between the 2 groups($P>0.05$). **Conclusion** Controlling blood pressure variability and morning systolic blood pressure surge is helpful to the improvement of cognitive function in very elderly hypertensive patients.

【**Key words**】 cognitive impairment; circadian rhythm; blood pressure; aged
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高血压是导致血管性痴呆和阿尔茨海默病发生和进展的重要因素[1]。但血压水平和认知功能损害的关系比较复杂,血压升高或过低均可导致高龄患者认知功能损害[2,3]。近年血压波动和昼夜节律与认知功能障碍的关系越来越受关注。血压变异性是指血压随机体内部和外部环境的变化而在一定时间及范围内波动的程度,是反映全天血压动态变化的可靠指标。本研究通过对高龄高血压患者24 h动态血压监测并计算晨峰血压、血压变异及昼夜节律的参数,通过蒙特利尔认知评估(Montreal Cognitive Assessment,MoCA)量表评估认知功能,从而探讨血压变异性对高龄高血压患者认知功能的影响。

1 对象与方法

1.1 研究对象

入选2017年3月至2017年12月北京积水潭医院干部保健科高血压住院患者177例,其中男性122例,女性55例,年龄80~91岁。根据认知功能评估结果分为轻度认知障碍(mild cognitive impairment,MCI)组114例,认知正常组63例。纳入标准:年龄≥80岁;符合中国高血压防治指南(2010年修订版)中原发性高血压的诊断标准[4];性别不限;能配合MoCA评估及抽血化验;自愿参加本研究,并签署知情同意书。排除标准:明确诊断为痴呆;存在可引起认知功能障碍的脑部疾病(如额颞叶变性、多系统萎缩、帕金森病等);6个月内发生过急性脑血管疾病(包括脑梗死、脑出血);重症感染、重度心力衰竭、严重肝肾功能不全或恶性肿瘤终末期;焦虑症、抑郁症或正在服用抗焦虑、抗抑郁类药物;严重听力障碍、视力障碍等不能完成MoCA评估。MCI诊断根据2011中国痴呆与认知障碍诊治指南[5]。

1.2 方法

1.2.1 记录患者的一般情况 记录患者性别、年龄、既往病史(冠心病、糖尿病、脑血管病)、是否服用降压药物。入院第2天空腹抽血化验生化指标,包括空腹血糖(fasting blood glucose,FBG)、糖化血红蛋白(glycosylated hemoglobin A1c,HbA1c)、总胆固醇(total cholesterol,TC)、高密度脂蛋白胆固醇(high-density lipoprotein cholesterol,HDL-C)、低密度脂蛋白胆固醇(low-density lipoprotein cholesterol,LDL-C)、甘油三酯(triglycerides,TG)、同型半胱氨酸(homocysteine,Hcy)等。

1.2.2 评估认知功能 住院期间由两名经过培训的医师对患者进行神经系统查体及MoCA评估。评估在患者情绪较佳状态及安静环境下进行,患者注意力要集中。MoCA评估包括注意与集中、执行功能、记忆、语言、视结构技能、抽象思维、计算和定向力等8个领域的11个检查项目,总分30分。≥26分为认知功能正常,<26分为MCI。

1.2.3 24 h动态血压监测 患者入院第2~3天进行24 h动态血压监测,每天清晨8:00~8:30开始记录,夜间60 min测1次,白天30 min测1次,总记录时间不少于24 h,数据有效率>85%。测量指标包括平均血压和血压变异指标。平均血压指标:24 h平均收缩压(24-hour systolic blood pressure,24hSBP)、24 h平均舒张压(24-hour diastolic blood pressure,24hDBP)、白天平均收缩压(day systolic blood pressure,dSBP)、白天平均舒张压(day diastolic blood pressure,dDBP)、夜间平均收缩压(night systolic blood pressure,nSBP)、夜间平均舒张压(night diastolic blood pressure,nDBP)。血压变异指标:收缩压变异系数、舒张压变异系数。变异系数为动态血压标准差除以血压平均值乘以100%。血压昼夜节律用夜间平均压下降率来表示,计算公式:(白天平均压-夜间平均压)/白天平均压×100%,下降率<10%为非杓型血压,10%~20%者为杓型血压,>20%者为超杓型血压,<0%为反杓型血压。晨峰血压(morning surge in blood pressure,MSBP)为清晨觉醒后血压迅速升高的峰值,即醒后2 h(6:00~8:00)内收缩压平均值减去夜间睡眠时(22:00~次日6:00)最低收缩压值(包括最低值在内前后2个收缩压的均值)[6]。

1.3 统计学处理

采用SPSS 17.0统计软件对数据进行处理。计量资料用均数±标准差($\bar{x}\pm s$)表示,组间比较采用t检验。计数资料用百分率表示,组间比较用χ^2检验。$P<0.05$为差异有统计学意义。

2 结 果

2.1 2组患者基线资料比较

2组患者年龄、性别、冠心病、糖尿病、脑血管病发生率及服用降压药物比例差异无统计学意义($P>0.05$);2组患者FBG、HbA1c、TC、HDL-C、LDL-C、TG、Hcy指标差异无统计学意义($P>0.05$)。MCI组患者MoCA评分明显低于对照组,差异有统计学意义($P<0.05$;表1)。

2.2 2组患者平均血压指标比较

2组患者24hSBP、24hDBP、dSBP、dDBP、nSBP、nDBP差异无统计学意义($P>0.05$;表2)。

2.3 2组患者血压变异系数比较

MCI组患者和认知正常组收缩压变异系数分别

为(0.11±0.02)%,和(0.08±0.03)%,舒张压变异系数分别为(0.12±0.02)%和(0.11±0.03)%,MCI组患者水平明显高于认知正常组患者,差异具有统计学意义($P<0.05$)。

2.4 2组患者血压昼夜节律和晨峰血压比较

2组患者收缩压下降率、舒张压下降率和舒张压晨峰差异无统计学意义($P>0.05$);MCI组患者收缩压晨峰明显高于认知正常组患者,差异有统计学意义($P<0.05$;表3)。2组患者非杓型、杓型、反杓型和超杓型血压比例差异无统计学意义($P>0.05$;表4)。

3 讨 论

MCI是介于正常衰老和痴呆的中间状态,是痴呆高危人群,其发展为痴呆的危险性明显高于正常老人。积极控制危险因素可改善MCI向痴呆的进

表1 2组患者基线资料比较

Table1 Comparison of baseline data between two groups

Item	MCI group ($n=114$)	Control group ($n=63$)	t/χ^2	P value
Age(years, $\bar{x}\pm s$)	84.5±3.4	83.9±2.1	0.550	0.585
Male[n(%)]	80(70.2)	42(66.7)	0.233	0.629
CHD[n(%)]	36(31.6)	13(20.6)	2.428	0.119
DM[n(%)]	37(32.5)	17(27.0)	0.573	0.449
CVD[n(%)]	43(37.7)	17(27.0)	2.087	0.149
Antihypertensive drug[n(%)]	96(84.2)	59(93.7)	3.322	0.068
FBG(mmol/L, $\bar{x}\pm s$)	5.68±1.97	5.08±0.94	1.144	0.258
HbA1c(mmol/L, $\bar{x}\pm s$)	5.87±0.73	5.74±0.77	0.559	0.579
TC(mmol/L, $\bar{x}\pm s$)	4.12±0.93	3.93±0.98	0.655	0.516
HDL-C(mmol/L, $\bar{x}\pm s$)	1.38±0.31	1.42±0.26	−0.393	0.696
LDL-C(mmol/L, $\bar{x}\pm s$)	2.19±0.69	2.02±0.78	0.804	0.425
TG(mmol/L, $\bar{x}\pm s$)	1.17±0.49	1.27±0.75	0.541	0.591
Hcy(mmol/L, $\bar{x}\pm s$)	15.47±4.75	14.74±5.23	0.489	0.627
MoCA(score, $\bar{x}\pm s$)	20.05±3.99	26.80±0.56	−6.496	0.000

MCI: mild cognitive impairment; CHD: coronary heart disease; DM: diabetes mellitus; CVD: cerebrovascular disease; FBG: fasting blood glucose; HbA1c: glycosylated hemoglobin A1c; TC: total cholesterol; HDL-C: high-density lipoprotein cholesterol; LDL-C: low-density lipoprotein cholesterol; TG: triglycerides; Hcy: homocysteine; MoCA: Montreal Cognitive Assessment

表2 2组患者平均血压指标比较

Table 2 Comparison of mean blood pressure indices between two groups (mmHg, $\bar{x}\pm s$)

Item	MCI group ($n=114$)	Control group ($n=63$)	t	P value
24hSBP	138.37±13.06	136.30±9.99	0.456	0.651
24hDBP	72.60±9.54	71.10±5.74	0.467	0.643
dSBP	139.10±13.54	137.71±10.21	0.299	0.767
dDBP	73.57±10.44	72.00±6.39	0.445	0.659
nSBP	136.07±15.02	131.60±10.70	0.867	0.392
nDBP	70.73±10.46	68.23±6.16	0.929	0.361

MCI: mild cognitive impairment; 24hSBP: 24-hour systolic blood pressure; 24hDBP: 24-hour diastolic blood pressure; dSBP: day systolic blood pressure; dDBP: day diastolic blood pressure; nSBP: night systolic blood pressure; nDBP: night diastolic blood pressure. 1 mmHg=0.133 kPa

表3 2组患者血压昼夜节律和晨峰血压比较

Table 3 Comparison of circadian rhythm of blood pressure and morning surge in blood pressure between two groups ($\bar{x}\pm s$)

Item	MCI group ($n=114$)	Control group ($n=63$)	t	P value
Declined rate of SBP(%)	3.81±2.14	4.66±3.84	0.425	0.631
Declined rate of DBP(%)	5.84±3.68	6.89±4.24	0.354	0.723
MSBPS(mmHg)	17.37±5.36	13.60±3.57	2.517	0.015
MDBPS(mmHg)	11.11±8.75	11.75±6.59	−0.210	0.835

MCI: mild cognitive impairment; SBP: systolic blood pressure; DBP: diastolic blood pressure; MSBPS: morning systolic blood pressure surge; MDBPS: morning diastolic blood pressure surge. 1 mmHg=0.133 kPa

表4 2组患者血压波动类型比较

Table 4 Comparison of blood pressure variability between two groups [n(%)]

Item	MCI group (n=114)	Control group (n=63)	χ^2	P value
Non-dipper	68(59.6)	42(66.7)	0.849	0.357
Dipper	19(16.7)	12(19.0)	0.159	0.690
Over-dipper	1(0.9)	0(0.0)	0.556	0.456
Reverse-dipper	26(22.8)	9(14.3)	1.857	0.173

展。一项对广州市社区5276例≥55岁人群认知功能损害的调查发现,认知障碍患病率为17.4%[7]。本研究纳入177例高龄患者,有114例存在MCI,患病率为64.4%,明显高于上述研究,考虑与研究患者年龄较高有关。在评估认知功能的量表中,MoCA识别MCI的敏感性高于简易精神状态检查(mini-mental state examination,MMSE)量表[8],但国内外此类研究选择MMSE量表较多,本研究最终选用MoCA作为评估量表来探讨动态血压参数与MCI的关系,结果更准确,这也是本研究MCI发病率高于国内其他研究的原因之一。

目前关于血压水平与认知功能相关性的研究仍有争议[9,10]。本研究表明2组患者24hSBP、24hDBP、dSBP、dDBP、nSBP、nDBP无明显差异,提示平均血压水平与高龄高血压患者MCI无关,而血压变异性则与认知障碍有明显关系。Sakakura等[11]通过比较80岁以上和61~79岁患者发现,高龄老年患者血压变异性明显大于年轻老年患者,且血压变异性增加和高龄老年认知功能障碍相关。Yamaguchi等[12]研究发现收缩压变异性增高是颅内微血管病变进展和认知功能减退的有效预测因子。但国内也有研究表明血压变异性对高龄高血压患者的认知功能无明显影响[13]。本研究表明MCI组患者收缩压变异系数和舒张压变异系数明显高于认知正常组患者,提示血压变异性可能与高龄高血压患者认知功能障碍相关,机制可能是:(1)血压波动大时,脑血管因氧化应激作用可发生重塑和纤维化,从而导致其反应性和自主调节能力减弱;当血压较低时,脑组织因灌注不足缺血、缺氧,颅内小血管损害最严重,长期反复发作可引起脑白质缺血性损伤、无症状脑梗死等,最终导致认知功能障碍甚至痴呆[14]。(2)血压变异性增大时血管内压力或剪切力变化较大,可直接造成血管内皮细胞损伤。损伤的血管内皮会导致动脉硬化狭窄和原位血栓形成概率增加,同时可引起血管平滑肌细胞增殖而影响微循环系统,减少脑灌注,导致颅内葡萄糖和氧气运输障碍,进一步引起神经元生物合成及突触传递代谢异常,引发大脑退行性病变,影响神经元突触神经递质的正常活动,从而导致认知功能早期轻度损害,最终出现脑萎缩、持久或进行性加重的认知功能障碍[15]。(3)血压变异性增加可激活体液调节系统,特别是肾上腺素-血管紧张素-醛固酮系统,促进细胞凋亡和炎症反应,进而损害血管正常结构,导致脑血管通透性增高,局部脑组织水肿及炎症性改变,同时引起脑胶质细胞增殖[15],最终导致神经元变异,累及大脑记忆功能区而发生认知障碍。因此,血压变异指标可用于预测高龄高血压患者认知功能是否减退。

此外,本研究表明高龄高血压患者的MSBP水平与认知功能损害有关。清晨血压迅速升高的现象为血压晨峰现象,研究表明患者MSBP升高可增加心脑血管事件发生率及全因死亡率[16]。Rothwell等[17]发现MSBP升高是脑梗死患者认知功能损害的独立危险因素。本研究2组患者dMSBP无明显差异,但MCI组患者SMSBP明显高于认知正常组,提示SMSBP升高与高龄高血压患者认知障碍有关。因此,对于平均血压控制理想的患者,仍要注意MSBP水平,合理控制SMSBP对减少认知障碍发生具有积极意义。但SMSBP目前还没有合理的控制标准,还需大规模临床研究进一步发现。

老年患者的血压昼夜节律异常与认知功能损害的关系尚无统一定论。Nagai等[18]研究显示夜间收缩压下降率是认知功能障碍的强大预测指标。常霞[19]研究发现血压昼夜节律异常可引起血管性认知功能障碍,主要影响执行、延迟回忆和注意,非杓型血压最常见。本研究表明2组患者收缩压下降率及舒张压下降率无明显差异,非杓型、杓型、反杓型和超杓型血压比例也无明显差异,但非杓型血压的比例高于杓型和反杓型,而超杓型比例最低,这与目前国内相关研究结果不同[20]。考虑原因为本研究对象为年龄≥80岁的高龄患者,其血压昼夜节律及曲线类型与其他人群有所差别。

综上所述,高龄高血压患者平均血压水平及血压昼夜节律与认知功能障碍无明显关系,控制血压变异性及MSBP,有利于改善高龄高血压患者的认知功能。

【参考文献】

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