·临床研究·

中老年餐后不适综合征患者的临床症状和脑肠肽水平分析

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【摘 要】 目的 探讨中老年与青年餐后不适综合征(PDS)患者在中医证候、临床症状和脑肠肽方面的差异。**方法** 选取2018年3月至2018年10月在北京中医药大学东方医院针灸科就诊的PDS患者65例,将患者分为中老年组(>45岁)和青年组(≤45岁),对2组患者进行中医辨证分型,并分别采用消化不良症状指数(SID)、尼平消化不良指数(NDI)及医院焦虑抑郁量表(HADS)依次评估其消化不良严重程度、生活质量受影响严重程度及焦虑抑郁状态。采用酶联免疫吸附法检测患者血浆中降钙素基因相关肽(CGRP)、血管活性肠肽(VIP)、胃饥饿激素(ghrelin)和P物质(SP)的浓度。采用SPSS 20.0统计软件对数据进行分析。根据数据类型,组间比较采用独立样本 t 检验、Mann-Whitney U 检验或卡方检验。**结果** 2组患者肝胃不和证、脾胃气滞证、脾胃湿热证构成比比较差异无统计学意义($\chi^2=4.787$, $P=0.091$)。与青年组比较,中老年组患者上腹烧灼感症状评分[1(0,1)]显著高于青年组[0(0,1)],差异有统计学意义($P<0.05$),但其他症状及量表评分在2组患者间比较差异无统计学意义($P>0.05$)。中老年组血浆中CGRP浓度[(1.06±0.24)ng/ml]显著高于青年组[(0.93±0.25)ng/ml],差异有统计学意义($P<0.05$),但VIP、SP及ghrelin浓度在2组患者间比较差异均无统计学意义($P>0.05$)。**结论** 中老年PDS患者存在较严重的上腹烧心感症状,且血浆中CGRP水平明显升高,这可能与年老导致的胃肠道运动降低及胃肠排空延迟有关。

【关键词】 餐后不适综合征;中老年;功能性消化不良;脑肠肽
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Clinical symptoms and brain-gut peptide level in middle-aged and elderly patients with postprandial distress syndrome

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【Abstract】 Objective To explore the differences of traditional Chinese medicine (TCM) syndromes, clinical symptoms and brain-gut peptide level between middle-aged and elderly patients with young patients with postprandial distress syndrome (PDS). **Methods** A total of 65 PDS patients admitted to our Acupuncture Department from March to October 2018 were enrolled in this study, and divided into the middle-aged and elderly group (>45 years old) and the young group (≤45 years old). The 2 groups of patients were classified according to TCM syndrome differentiation. The severities of dyspepsia, quality of life, anxiety and depression were evaluated by symptom index of dyspepsia (SID), Nepean dyspepsia index (NDI) and hospital anxiety and depression scale (HADS), respectively. The plasma levels of calcitonin gene-related peptide (CGRP), vasoactive intestinal peptide (VIP), ghrelin and substance P (SP) were measured by enzyme-linked immunosorbent assay (ELISA). The data was analyzed using SPSS statistics 20.0. Depending on the types of data, independent sample t test, Mann-Whitney U test, or Chi-square test was used for comparison between 2 groups. **Results** There was no significant differences in the compositions of liver-stomach disharmony syndrome, spleen-stomach weakness syndrome and spleen-stomach dampness-heat syndrome between the 2 groups (Chi-square=4.787, $P=0.091$). The score of epigatric burning symptom was significantly higher in the middle-aged and elderly group than the young group [1(0,1) *vs* 0(0,1), $P<0.05$], but no such differences were seen in the other symptoms, and scores of NDI and HADS between them ($P>0.05$). The plasma level of CGRP was significantly higher in the middle-aged and elderly group than the young group [(1.06±0.24) *vs* (0.93±0.25)ng/ml, $P<0.05$], but there was no significant differences in the levels of VIP, SP and ghrelin between the 2 groups ($P>0.05$). **Conclusion** The middle-aged and elderly PDS patients experience severe epigastric burning symptom, and have significantly increased

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plasma CGRP level, which may be associated with ageing-related decreased gastrointestinal motility and delayed gastrointestinal emptying.

【Key words】 postprandial distress syndrome; middle-aged and elderly; functional dyspepsia; brain-gut peptide

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功能性消化不良(functional dyspepsia,FD)是指患者存在上腹部疼痛、烧灼感、胀闷、早饱感或餐后饱胀等症状,但内镜及相关检查未见器质性异常。根据罗马Ⅳ诊断标准,FD 按症状分为餐后不适综合征(postprandial distress syndrome,PDS)和上腹痛综合征(epigastric pain syndrome,EPS),其中 PDS 发病率明显高于 EPS(5.6% ~ 13.9% *vs* 0.9% ~ 9.5%)[1]。PDS 属于中医痞满范畴[2]。近年来,我国人口老龄化加剧,老年人口比例不断增加,老年人上消化道结构和功能存在生理性退化[3],消化不良症状发生率随年龄的增加而升高[4]。本研究基于中医对 PDS 的独特认识,拟观察中老年与青壮年 PDS 患者的发病表现差异,从患者临床症状严重程度、焦虑抑郁状态、生活质量及脑肠肽水平等方面进行分析探讨,以期为临床工作者对 PDS 的认识提供科学参考。

1 对象与方法

1.1 研究对象

选取 2018 年 3 月至 2018 年 10 月在北京中医药大学东方医院针灸科就诊的 PDS 患者 65 例。纳入标准:(1)年龄 18~65 岁;(2)PDS 诊断标准为餐后饱胀不适感或早饱感,且 1 周内至少发作 3 d,症状出现至少 6 个月,症状最近 3 个月持续存在[5];(3)近 1 年胃镜检查无异常;(4)自愿签署知情同意书。排除标准:(1)存在慢性疾病(可引起消化不良症状的疾病);(2)腹部手术史;(3)胃镜检查有器质性病变。根据既往文献[6],青年和中老年的年龄分界点是 45 岁,据此将 PDS 患者分为中老年组(>45 岁,$n=31$)和青年组(≤45 岁,$n=34$)。中老年组男性 9 例,女性 22 例,年龄(56.7±6.3)岁,BMI 值 23.65 kg/m^2,病程为 60(24,120)个月;青年组男性 11 例,女性 23 例,年龄(29.9±6.7)岁,BMI 值 22.20 kg/m^2,病程为 18(7,60)个月。2 组患者性别($P=0.772$)和 BMI 值($P=0.057$)比较差异无统计学意义,年龄($P<0.001$)及病程($P=0.004$)比较差异有统计学意义。

1.2 方法

1.2.1 记录中医辨证分型 按照《消化不良中医诊疗共识意见(2009)》中的中医证型辨证诊断[7]对患者进行分型。脾胃虚弱证。主要症状为:(1)脘腹痞闷或胀痛;(2)食少纳呆。次要症状为:(1)面色萎黄;(2)嗳气;(3)疲乏无力;(4)大便稀溏,舌脉为舌质淡,苔薄白,脉细弦。肝胃不和证。主要症状为:(1)胃脘痞满;(2)两胁窜痛,情志不遂易诱发或加重。次要症状为:(1)嗳气;(2)口干口苦;(3)烧心泛酸;(4)急躁易怒,舌质红,苔白,脉弦或弦细。脾胃湿热证。主要症状为:(1)脘腹痞满或疼痛;(2)食少纳呆。次要症状为:(1)头身困重;(2)口苦口黏;(3)大便不爽而滞;(4)小便短黄,舌质红,苔黄厚腻,脉滑。证型的确定为主要症状 2 项加次要症状 1 项,或主要症状的第 1 项加次要症状 2 项。

1.2.2 消化不良症状严重程度评估 根据消化不良症状指数(symptom index of dyspepsia,SID)量表评价餐后饱胀、早饱感、上腹胀、上腹痛、上腹烧灼感、恶心、呕吐及嗳气 8 个症状。每项为 0~3 分,总计 24 分。

1.2.3 生活质量评估 根据尼平消化不良指数[8](Nepean dyspepsia index,NDI)量表评价患者生活质量,问卷有 25 个问题,涵盖 5 个领域,包括干扰、认识/控制、食物/饮料、睡眠打扰和工作/学习。每项 0~4 分,总计 100 分,评分越高说明患者生活质量受到的影响越严重。

1.2.4 抑郁和焦虑评估 医院焦虑及抑郁量表(hospital anxiety and depression scale,HADS)[9]包括测定焦虑和抑郁的 2 个亚量表,各有 7 个问题,每个问题 0~3 分,总计 21 分。每个量表 0~7 分为无症状;8~10 分为可疑阳性;11~21 分为明显阳性。

1.2.5 脑肠肽检测 患者在测评后第 2 天早晨采集空腹静脉血,采血管为 5 ml 规格(含抗凝剂 EDTA-K2),采集后立即 3000 转/min 离心 10 min,收集上清液。酶联免疫吸附法检测 PDS 患者血浆中降钙素基因相关蛋白(calcitonin gene related protein,CGRP)、血管活性肠肽(vasoactive intestinal peptide,VIP)、胃饥饿激素(ghrelin)和 P 物质(substance P,SP)。CGRP、VIP 和 ghrelin 试剂盒购自德国 Phonix Pharmaceuticals 公司,SP 试剂盒购自美国 Enzo 公司。

1.3 统计学处理

采用SPSS 20.0统计软件对数据进行分析。计量资料呈正态分布者以均数±标准差($\bar{x}\pm s$)表示,组间比较采用独立样本 t 检验,不符合正态分布者以中位数(M)和四分位数间距(Q)表示,组间比较采用Mann-Whitney U 检验。计数资料以例数(百分率)表示,组间比较采用卡方检验。$P<0.05$ 为差异有统计学意义。

2 结 果

2.1 2组患者中医辨证分型比较

中老年组肝胃不和证、脾胃虚弱证、脾胃湿热证占比分别为48.4%(15例)、38.7%(12例)、12.9%(4例),青年组上述比例依次为23.5%(8例)、50.0%(17例)、26.5%(9例)。2组患者3个证型构成比比较差异无统计学意义($\chi^2=4.787$,$P=0.091$)。

2.2 2组患者相关量表评分比较

中老年组上腹烧灼感评分显著高于青年组($P<0.05$),其他指标评分比较差异无统计学意义($P>0.05$;表1)。

表1 2组患者消化不良症状、生活质量及焦虑抑郁评分比较

Table 1 Comparison of dyspepsia symptoms, quality of life, anxiety and depression scores between two groups (score)

Item	Middle-aged and elderly group ($n=31$)	Young group ($n=34$)
SID[$M(Q_1,Q_3)$]		
Postprandial fullness	2(1,2)	2(1,2)
Early satiation	1(0,2)	1(1,2)
Upper abdominal bloating	2(1,2)	1(1,2)
Epigastric pain	1(0,2)	0(0,1)
Epigastric burning	1(0,1)*	0(0,1)
Nausea	0(0,1)	1(0,1)
Vomit	0(0,0)	0(0,0)
Belching	1(1,2)	1(1,2)
NDI[$M(Q_1,Q_3)$]	50(42,64)	51(38,54)
HAS($\bar{x}\pm s$)	5.55±3.94	4.62±2.90
HDS[$M(Q_1,Q_3)$]	6(3,9)	3(2,8)

SID: symptom index of dyspepsia scale; NDI: Nepean dyspepsia index; HAS: hospital anxiety scale; HDS: hospital depression scale. Compared with young group, *$P<0.05$.

2.3 2组PDS患者脑肠肽比较

中老年组CGRP水平明显高于青年组($P<0.05$),而VIP、SP、ghrelin水平在2组间比较差异无统计学意义($P>0.05$;表2)。

3 讨 论

中老年人随着年龄增加,其消化道结构和功能逐渐虚弱,同时躯体长期受到多种内外界刺激,易产生情绪障碍,从而使PDS的发病率逐渐升高[2]。PDS具有病程长、反复发作的特点,本研究结果也显示与青年组比较,中老年组PDS患者的病程较长,差异有统计学意义($P<0.05$)。PDS属中医的"痞满"范畴,病位在胃,与肝脾胃三脏失调密切相关,主要发病机制为肝郁脾虚[10]。脾胃虚弱,升降失调,导致水谷运化失常,气机郁滞,故出现痞满、积滞等症状。气机郁滞进而影响肝主疏泄,导致肝气郁结,胃气下降,致使出现痞满和情志不遂的表现。研究报道PDS患者中肝胃不和型和脾胃虚弱型占77%[11],这与本研究结果相似。但中老年和青壮年组患者3个中医证型占比无差异,提示PDS患者的中医证型与年龄相关性不大。研究结果还显示,中老年组消化不良症状中上腹烧灼感评分显著高于青年组,我们认为上腹烧灼感可能与年龄增加有关,因为随着年龄的增长上消化道结构和功能会发生生理性退化,表现为胃蠕动减少和胃酸分泌异常,因而会出现上腹烧灼感的症状。这也与临床上老年患者多以"烧心"为主诉就诊的现象相吻合。

脑肠肽是分布在中枢神经系统和胃肠道中的多肽类物质,其在脑肠轴各个环节的交互作用中起到了连接和调控介质的功能,并直接参与调节胃肠道的运动、感觉和分泌。研究发现,多种脑肠肽参与了功能性胃肠病的发病[12],其中CGRP、SP、VIP和ghrelin等脑肠肽水平异常可导致内脏高敏感性[13]。CGRP主要具有延迟胃排空、抑制胃肠道运动和调节胃肠激素分泌作用[14]。而SP具有促进胃肠蠕动而加快胃排空[15]和胃肠黏膜保护作用,在功能性胃肠病患者血浆中SP显著降低[16,17]。VIP具有抑制胃肠蠕动和胃排空、减慢小肠运动、降低消化道括约

表2 2组患者脑肠肽水平比较

Table 2 Comparison of brain-gut peptide level between two groups

Group	n	VIP[ng/ml, $M(Q_1,Q_3)$]	CGRP(ng/ml, $\bar{x}\pm s$)	SP[pg/ml, $M(Q_1,Q_3)$]	Ghrelin[ng/ml, $M(Q_1,Q_3)$]
Middle-aged and elderly	31	0.48(0.24,0.66)	1.06±0.24*	823.59(703.40,886.23)	6.13±2.62
Young	34	0.42(0.24,0.72)	0.93±0.25	869.78(486.64,1158.77)	6.14±2.93

CGRP: calcitonin gene related protein; VIP: vasoactive intestinal peptide; SP: substance P. Compared with young group, *$P<0.05$.

肌紧张性、扩血管和减少胃酸等主要作用[18],在功能性胃肠病患者血浆中可见 VIP 升高[19]。ghrelin 具有促进食欲、胃酸分泌及胃排空的作用,可增强胃动力,增加食欲和食物摄入[20],但在功能性胃肠病患者血中可见 ghrelin 水平显著降低[21]。本研究结果显示,2 组患者 VIP、SP、ghrelin 等水平比较差异无统计学意义,但中老年组 CGRP 水平显著高于中青年组,考虑原因是中老年因机能衰退,神经系统对胃肠运动的抑制增加,分泌抑制胃肠道运动的脑肠肽增加,致使胃肠道运动降低和胃肠排空延迟[14]。

综上所述,与青壮年 PDS 患者相比,中老年 PDS 患者烧心症状明显,同时脑肠肽水平存在明显升高现象,这可能与年老导致的胃肠道运动降低及胃肠排空延迟有关。

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