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首荟通便胶囊联合莫沙必利对功能性便秘患者血清 SP、MTL、NO 水平及生活质量的影响 *

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摘要 目的:探讨首荟通便胶囊联合莫沙必利对功能性便秘患者血清 P 物质(SP)、胃动素(MTL)、一氧化氮(NO)水平及生活质量的影响。**方法:**选取 2018 年 3 月~2020 年 2 月期间我院接收的功能性便秘患者 127 例,随机分为对照组(n=63,莫沙必利治疗)和研究组(n=64,首荟通便胶囊联合莫沙必利治疗),对比两组疗效、症状评分、生活质量及血清 SP、MTL、NO 水平,记录两组治疗期间不良反应情况。**结果:**对照组治疗 4 周后的总有效率为 77.78%(49/63),低于研究组治疗 4 周后的 90.63%(58/64)($P<0.05$)。两组治疗 4 周后排便困难、粪便性状、排便间隔、排便不尽感评分均较治疗前下降,且研究组低于对照组($P<0.05$)。两组治疗 4 周后心理功能、躯体功能、社会功能、物质生活状态评分均较治疗前升高,且研究组高于对照组($P<0.05$)。两组治疗 4 周后血清 SP、MTL 高于治疗前,且研究组较对照组更高($P<0.05$),血清 NO 比治疗前更低,且研究组较对照组更低($P<0.05$)。两组均未见明显不良反应发生。**结论:**在莫沙必利基础上,联合首荟通便胶囊治疗功能性便秘患者,能较好的减轻临床症状,缓和不良体征,促进生活质量改善,疗效确切,其作用机制可能与调节血清 SP、MTL、NO 水平有关。

关键词:首荟通便胶囊;莫沙必利;功能性便秘;P 物质;胃动素;一氧化氮;生活质量

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Effect of Shouhui Tongbian Capsule Combined with Mosapride on Serum SP, MTL, NO Levels and Quality of Life in Patients with Functional Constipation*

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ABSTRACT Objective: To investigate the effect of Shouhui Tongbian capsule combined with mosapride on serum substance P (SP), motilin (MTL), nitric oxide (NO) and quality of life in patients with functional constipation. **Methods:** 127 patients with functional constipation in our hospital from March 2018 to February 2020 were selected, and randomly divided into control group (n=63, mosapride treatment) and study group (n=64, Shouhui Tongbian capsule combined with Mosapride treatment). The efficacy, symptom score, quality of life, serum SP, MTL, NO levels of the two groups were compared, and the adverse reactions of the two groups during treatment were recorded. **Results:** The total effective rate of the control group after 4 weeks of treatment was 77.78%(49/63), which was lower than 90.63%(58/64) of the study group after 4 weeks of treatment. 4 weeks after treatment, the defecation difficulty, stool characteristics, defecation interval and incomplete defecation scores of the two groups decreased compared with those before treatment, and the study group was lower than the control group($P<0.05$). 4 weeks after treatment, the scores of psychological function, physical function, social function and material life state of the two groups were higher than those before treatment, and the study group was higher than the control group ($P<0.05$). 4 weeks after treatment, serum SP and MTL of the two groups were higher than those before treatment, and the study group was higher than the control group ($P<0.05$), and serum NO was lower than that before treatment, and the study group was lower than the control group ($P<0.05$). No obvious adverse reactions occurred in both groups. **Conclusion:** On the basis of Mosapride, combined with Shouhui Tongbian capsule in the treatment of functional constipation patients, can better alleviate clinical symptoms, alleviate adverse

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signs, promote the improvement of quality of life, which has definite curative effect, the mechanism may be related to the regulation of serum SP, MTL, NO levels.

Key words: Shouhui Tongbian capsule; Mosapride; Functional constipation; Substance P; Motilin; Nitric oxide; Quality of life

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前言

便秘是一种常见病症,多数由消化疾病引起,主要表现为每周大便次数小于3次、粪便干结、持续排便不畅等^[1]。以往报道统计^[2],我国成年人便秘的发生率为6%,其中女性多于男性,且以老年群体较为常见,65岁以上老年人便秘的发生率约为30%。而功能性便秘属于无器质性病变的便秘,发病因素较多,包括精神低落、不良生活、饮食习惯和药物副作用等^[3]。功能性便秘除了引起排便障碍外,还可引起患者腹痛、食欲不振,导致情绪失常,给患者生活质量带来严重影响^[4,5]。现临床有关功能性便秘的治疗尚无特效方案,莫沙必利可促进胃肠动力改善,临床常用于治疗功能性便秘^[6]。然而应用西药治疗后,有很大一部分患者病情反复发作,甚至不断应用单一西药治疗会增加患者病情加重、癌变的风险^[7]。首荟通便胶囊是治疗功能性便秘的中成药,具有通便排毒、减肥降脂的功效^[8]。本研究通过联合首荟通便胶囊与莫沙必利,探索其在功能性便秘治疗上的疗效,以期临床诊治提供一定参考。

1 资料与方法

1.1 一般资料

选取2018年3月~2020年2月期间我院接收的127例功能性便秘患者,纳入标准:(1)西医诊断以《便秘诊治暂行标准》^[9]为准,排便次数每周少于3次,排便费力感,排便不尽感;(2)中医诊断标准参考《上海市中医病证诊疗常规(第2版)》^[10],辨证分型为气阴两虚型;(3)病程均在3个月以上;(4)患者及其家属知情并签好同意书;(5)患者没有交流障碍,意识清醒。排除标准:(1)患有严重心脑血管疾病或糖尿病患者;(2)存在心力衰竭、肝功能不足者;(3)对本次研究用药过敏者;(4)腹部及肠道存在既往肿瘤等器质性疾病或手术史;(5)合并精神疾患,无法配合研究者。127例患者随机分为对照组(63例)、研究组(64例),其中对照组男24例,女39例,年龄42~73岁,平均(59.82±4.48)岁;病程3~8月,平均(5.37±0.83)月;体质量指数21~27 kg/m²,平均(24.28±0.95)kg/m²。研究组男25例,女39例,年龄43~74岁,平均(60.13±3.92)岁;病程4~10月,平均(5.51±0.76)月;体质量指数20~27 kg/m²,平均(24.19±0.90)kg/m²。两组一般资料无差异($P>0.05$),具有可比性。我院医学伦理委员会已批注此研究。

1.2 方法

给予两组患者改正不良生活习惯、改善饮食结构及增加运动等措施。对照组在此基础上联合莫沙必利(成都康弘药业集团股份有限公司,国药准字H19990313,规格:5 mg 治疗,口服,5 mg/次,3次/d。研究组给予首荟通便胶囊(鲁南厚普制药有限公司,国药准字Z20150041,规格:每粒装0.35 g(相当于饮片0.79 g)联合莫沙必利治疗,首荟通便胶囊2粒/次,3次/d,口服;莫沙必利治疗方案同对照组。两组均治疗4周。

1.3 评价指标

(1)总有效率=显效率+有效率。显效:腹胀、排便困难等症状消失,每日排便1次,且排便通畅,大便成稀软形;有效:腹部胀气、排便费力等病症减轻,每周排便大于3次,大便变软;无效:治疗后症状未减轻甚至加重^[11]。(2)观察两组患者不良反应情况。(3)观察两组治疗前、治疗4周后的排便困难、粪便性状、排便间隔及排便不尽感评分,其中排便困难:无为0分,轻微为1分,中等为2分,明显为3分。粪便性状:根据 Bristol 分型评定,其中IV、V、VI为0分,III型为1分,II型为2分,I型为3分。排便间隔:>3次/周为0分,2次/周为1分,≤1次/周为3分。排便不尽感:无为0分,轻微为1分,中等为2分,明显为3分^[12]。(4)于两组治疗前、治疗4周后采用生活质量综合评定问卷(GQLI/74)评估患者生活质量。GQLI/74包括心理功能、躯体功能、社会功能、物质生活状态这4项,每个项目各为100分,分数越高,生活质量越好^[13]。(5)于两组治疗前、治疗4周后留取患者肘静脉血5 mL,需空腹状态下采集,血样本经4300 r/min 离心12 min,离心半径9 cm,分离得血清待测。借助放射免疫法检测血清P物质(SP)、胃动素(MTL),采用硝酸还原酶法检测一氧化氮(NO),所有试剂盒采购自深圳芬德生物技术有限公司,按试剂盒说明书严格操作。

1.4 统计学方法

统计分析用SPSS20.0统计,均采用双侧检验。计数资料以率的形式表示,行卡方检验,计量资料以($\bar{x} \pm s$)的形式表示,行t检验。 $P<0.05$ 为差别有统计学意义。

2 结果

2.1 总有效率比较

与对照组相比,研究组治疗4周后的总有效率更高($P<0.05$),见表1。

表1 总有效率比较[例(%)]

Table 1 Comparison of total effective rate [n(%)]

Groups	Remarkable effect	Effective	Invalid	Total effective rate
Control group(n=63)	18(28.57)	31(49.21)	14(22.22)	49(77.78)
Study group(n=64)	23(35.94)	35(54.69)	6(9.38)	58(90.63)
χ^2				3.949
P				0.047

2.2 症状评分比较

两组治疗前排便困难、粪便性状、排便间隔、排便不尽感评分对比无差异($P>0.05$),治疗 4 周后两组粪便性状、排便困难、

排便间隔、排便不尽感评分比治疗前更低,且研究组较对照组更低($P<0.05$),见表 2。

表 2 两组症状评分比较($\bar{x} \pm s$,分)

Table 2 Comparison of symptom scores between the two groups($\bar{x} \pm s$, scores)

Groups	Time points	Defecation difficulty	Stool characteristics	Defecation interval	Incomplete defecation
Control group(n=63)	Before treatment	2.36± 0.31	2.26± 0.27	2.18± 0.21	1.93± 0.16
	4 weeks after treatment	1.78± 0.28 ^a	1.69± 0.22 ^a	1.57± 0.19 ^a	1.51± 0.22 ^a
Study group(n=64)	Before treatment	2.31± 0.29	2.29± 0.25	2.14± 0.25	1.89± 0.17
	4 weeks after treatment	1.21± 0.26 ^{ab}	1.21± 0.14 ^{ab}	1.18± 0.19 ^{ab}	1.14± 0.19 ^{ab}

Note: compared with before treatment, ^a $P<0.05$; compared with control group, ^b $P<0.05$.

2.3 生活质量评分比较

两组治疗前心理功能、躯体功能、社会功能、物质生活状态评分对比无差异($P>0.05$),治疗 4 周后两组躯体功能、心理功

能、社会功能、物质生活状态评分比治疗前更高,且研究组较对照组更高($P<0.05$),见表 3。

表 3 生活质量评分比较($\bar{x} \pm s$,分)

Table 3 Comparison of quality of life scores($\bar{x} \pm s$, scores)

Groups	Time points	Psychological function	Physical functi	Social function	Material life state
Control group(n=63)	Before treatment	56.24± 6.27	53.72± 7.81	55.91± 6.08	58.65± 7.52
	4 weeks after treatment	66.17± 5.14 ^a	71.39± 6.92 ^a	68.93± 7.91 ^a	72.03± 6.54 ^a
Study group(n=64)	Before treatment	56.12± 9.32	53.28± 6.34	56.03± 5.18	58.94± 6.87
	4 weeks after treatment	82.86± 6.79 ^{ab}	84.54± 5.87 ^{ab}	82.71± 6.05 ^{ab}	82.64± 5.64 ^{ab}

Note: compared with before treatment, ^a $P<0.05$; compared with control group, ^b $P<0.05$.

2.4 血清 SP、MTL、NO 水平比较

治疗前两组血清 SP、MTL、NO 水平对比无差异($P>0.05$),治疗 4 周后两组血清 SP、MTL 均较治疗前更高,且研究组较对

照组更高($P<0.05$),血清 NO 比治疗前更低,且研究组较对照组更低($P<0.05$),见表 4。

表 4 两组血清 SP、MTL、NO 水平比较($\bar{x} \pm s$)

Table 4 Comparison of serum SP, MTL and NO levels between the two groups($\bar{x} \pm s$)

Groups	Time points	SP(pg/ml)	MTL(ng/ml)	NO(mmol/L)
Control group(n=63)	Before treatment	32.68± 5.09	223.38± 31.86	128.16± 21.74
	4 weeks after treatment	41.65± 4.98 ^a	286.47± 29.45 ^a	95.83± 11.59 ^a
Study group(n=64)	Before treatment	32.34± 5.97	225.97± 29.34	127.43± 20.81
	4 weeks after treatment	49.72± 5.63 ^{ab}	325.96± 36.23 ^{ab}	72.45± 9.47 ^{ab}

Note: compared with before treatment, ^a $P<0.05$; compared with control group, ^b $P<0.05$.

2.5 安全性评价

两组在治疗期间遵医嘱,按规律服药,未曾出现过敏反应。服药期间对照组有 1 例出现轻微腹痛,经观察都与服用药物无关,嘱患者注意休息后,症状缓解,未见不良反应。研究组未曾出现不良反应。

3 讨论

功能性便秘是一种难治性疾病,大多由消化疾病引起,在临床上很常见,该病具有反复发作特点,长期罹患该病的患者可导致结肠憩室、肛周疾病等的发生,甚至对于合并有心脑血管疾病的患者来说,可增加其发生心脑血管意外的危险程度;

另功能性便秘还会引发各种情绪问题,如焦躁不安、心情低落和暴怒等,严重影响患者生活质量^[14-16]。功能性便秘的发病机制较为复杂,其中分子生物学、不良排便习惯、不良饮食结构、不良生活习惯、年龄、负压情绪等都是引发该病的重要原因^[17,18]。结肠蠕动无力及不协调引起粪便逐渐变硬影响正常排便,这是分子生物学方面导致的;加上不良饮食生活习惯、不良排便习惯,会使食物对肠道刺激减弱导致便秘;同时情绪压力会刺激中枢神经系统,导致大脑对排便反射反应迟钝^[19,20],其中结肠蠕动无力或不协调是导致结肠排空延迟的主要原因。以往相关研究结果显示^[21],结肠蠕动无力或不协调可能与排空缓慢、胃肠激素紊乱、自主神经功能异常等息息相关。便秘可引起自主神经

功能异常,使得食物残渣长久的停留于肠腔内,产生大量的NO,使肠管膨胀,静脉回流不畅,引起食欲不振、腹痛等症状^[22]。

目前临床上治疗功能性便秘多以药物治疗、调整饮食为主,心理干预为辅^[23]。莫沙必利是临床治疗功能性便秘的常用药物,主要成分为5-羟色胺4受体激动剂,口服后可被人体迅速吸收,促进乙酰胆碱释放,并刺激胃肠道胆碱能中间神经元,进而增强胃及十二指肠运动能力,从而促进胃排空^[24]。此外,莫沙必利还可调节肛门括约肌活性,激发肛门内括约肌舒张与直肠收缩能力^[25]。但近年来不少临床研究表明莫沙必利药物依赖性重,长期服用可对机体胃肠功能造成严重影响^[26,27]。因此,积极寻找一种更为有效的治疗方案,以避免治疗后反复发作尤为重要。中医将功能性便秘归属于中医便秘的范畴,其病机在于热结、寒凝、气滞,导致气血阴阳亏损,脏腑功能失调,故应补气养血、滋阴润肠以通便^[28]。首荟通便胶囊的组方遵循上述理论,主治气阴两虚兼毒邪内蕴,该药物包含黄芩、党参、茯苓、白术、决明子、何首乌、当归、炙甘草等主要成分。其中何首乌、当归填精益血、润燥通便,决明子、黄芩滋阴润肠以通便,白术、茯苓、党参健脾运气、加强运化,炙甘草调和诸药,改善肠胃,发挥泻通便、养阴益气的功效^[29]。

本研究中首荟通便胶囊联合莫沙必利治疗功能性便秘,可有效缓解患者临床症状及体征,疗效明确,可见该联合治疗方案从不同作用机制出发,可治标本,标本兼治,维持较好的疗效。SP是人体重要的肠神经递质,功能性便秘患者由于神经系统突触功能异常,导致肠胃推动性运动被弱化,SP水平降低。MTL分布于小肠,可刺激患者的胃肠及胆道组织,并发挥促进胃肠蠕动的功能,从而提高胃肠道对水和电解质的运送能力。NO作为一种信使分子,参与许多病理生理活动,NO与胃肠生理功能及动力失调等病理状态及有关疾病密切相关。本研究结果中研究组血清SP、MTL高于对照组,NO低于对照组,提示首荟通便胶囊联合莫沙必利治疗可改善上述指标水平,究其原因在于黄芩可减少机体氧自由基损伤,进一步减少NO的产生。白术可纠正神经系统突触功能异常,提高SP水平,促进胃肠蠕动。当归可增强结肠的传输功能,何首乌可促进胃肠蠕动,均可使机体气血津液生化正常,全面改善胃肠功能,肠道润泽,肠道菌群逐渐恢复正常,继而提高MTL水平^[30]。另两组均未见明显不良反应发生,提示治疗方案安全性确切。

综上所述,在莫沙必利基础上,联合首荟通便胶囊治疗功能性便秘患者,能较好地减轻临床症状,缓和不良体征,促进生活质量改善,疗效确切,其作用机制可能与调节血清SP、MTL、NO水平有关。

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