

· 临床研究 ·

乳果糖与莫沙必利治疗老年患者慢性功能性便秘及伴随症状的前瞻性随机对照研究

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【摘要】 **目的** 评价乳果糖与莫沙必利对老年患者慢性功能性便秘及其伴随症状的临床疗效。**方法** 选取2019年2月至6月复旦大学附属华东医院就诊的老年慢性功能性便秘患者80例,根据随机数表法随机分为乳果糖组和莫沙必利组,每组患者40例。乳果糖组予每天口服乳果糖1次,每次15 ml,疗程为4周。莫沙必利组予以每天口服枸橼酸莫沙必利片3次,每次5 mg,疗程为4周。分别在干预前后记录2组的Wexner便秘评分、焦虑自测量表(SAS)评分及抑郁自测量表(SDS)评分。对比分析2组患者治疗便秘的疗效及临床症状等改善情况。采用SPSS 23.0软件进行数据分析。根据数据类型,组间比较分别采用 t 检验、秩和检验及 χ^2 检验。**结果** 乳果糖组治疗便秘总有效率为75% (30/40),高于莫沙必利组35% (14/40),差异有统计学意义($P < 0.05$)。乳果糖组在改善排便频率评分[0(0,1)和1(0,1)分]、排便困难评分[1(1,2)和2(1.25,3)分]、腹痛评分[1(0,2)和2(1,2)分]、排便时间评分[1(1,2)和2(1,2)分]方面优于莫沙必利组(均 $P < 0.05$)。乳果糖组中焦虑和(或)抑郁状态占比较干预前降低[52.50% (21/40)和25.00% (10/40), $P < 0.05$];莫沙必利组与干预前比较,差异无统计学意义[70.00% (28/40)和52.50% (21/40)]。**结论** 乳果糖可改善老年慢性功能性便秘患者的临床症状,降低便秘相关的焦虑、抑郁评分。

【关键词】 老年人;慢性功能性便秘;乳果糖;莫沙必利;临床疗效

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Lactulose and mosapride in treatment of chronic functional constipation and its concomitant symptoms in the elderly: a prospective randomized controlled trial

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【Abstract】 **Objective** To evaluate the clinical efficacy of lactulose and mosapride in treatment of senile chronic functional constipation and its concomitant symptoms. **Methods** A total of 80 elderly patients with chronic functional constipation admitted in our hospital from February to June 2019 were prospectively recruited and randomly divided into lactulose group ($n = 40$) and mosapride group ($n = 40$). The patients in the lactulose group took lactulose orally once a day, 15 ml each time for 4 weeks, and those in the mosapride group took Moxapride citratetablet orally 3 times a day, 5 mg each time for 4 weeks. Wexner constipation score, and scores of self-rating anxiety scale (SAS) and self-rating depression scale (SDS) were recorded in the 2 groups before and after intervention, and the efficiency and changes in clinical signs and symptoms were compared between them. SPSS statistics 23.0 was used for statistical analysis. Intergroup comparison was performed using student's t test, rank sum test or Chi-square test depending on data types. **Results** The total effective rate for constipation was 75% (30/40) in the lactulose group, which was significantly higher than that of the mosapride group [35% (14/40), $P < 0.05$]. Lactulose treatment resulted in better scores in defecation frequency [0 (0, 1) vs 1 (0, 1) points], defecation difficulty [1 (1, 2) vs 2 (1.25, 3) points], abdominal pain [1 (0, 2) vs 2 (1, 2) points], and defecation time [1 (1, 2) vs 2 (1, 2) points] when compared with mosapride treatment (all $P < 0.05$). What's more, the proportions of the patients having anxiety and/or depression were decreased from 52.50% (21/40) before treatment to 25.00% (10/40) after lactulose treatment ($P < 0.05$), but there was no such change in the mosapride group [70.00% (28/40) vs 52.50% (21/40), $P > 0.05$]. **Conclusion** To the elderly patients with chronic functional constipation, lactulose significantly alleviates their clinical symptoms and reduces their SAS and SDS scores simultaneously.

【Key words】 aged; chronic functional constipation; lactulose; moxapride; curative effect

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慢性便秘是指病程超过半年,以排便频数减少、排便费力及排便不尽等为主要表现的一种疾病。慢性便秘在人群中非常常见,老年人和女性尤其突出^[1]。流行病学调查显示,60岁以上老年人的慢性便秘患病率为15%~20%,而80岁以上高龄老人则高达20.0%~37.3%^[2]。老年人便秘可导致患者生理不适,还可导致患者焦虑及抑郁等精神心理障碍风险增加等众多危害^[3]。

1 对象与方法

1.1 研究对象

选择2019年2月至6月于复旦大学附属华东医院就诊的老年患者80例,根据随机数表法随机分为乳果糖组和莫沙必利组,每组患者40例。本研究通过了上海市复旦大学附属华东医院的伦理委员会审核,ISRCTN注册号(伦理委员会方案编号)为2019K080。

纳入标准:(1)年龄≥60岁。(2)符合罗马IV慢性功能性便秘诊断标准^[4]。功能性便秘至少符合以下6条中2条:≥25%的排便费力感,≥25%的排便为块状便或硬便,≥25%的排便有不尽感,≥25%的排便有肛门、直肠梗阻感/阻塞感,≥25%的排便需要手法辅助,每周自发排便少于3次。(3)能签署知情同意书,并保证完成疗程。

排除标准:(1)合并心脑血管、消化、泌尿及造血系统等严重原发性疾病;(2)过敏性体质;(3)近1个月服用阿片类镇痛药、三环类抗抑郁药及抗胆碱能等致便秘药物;(4)近1个月服用其他通便药;(5)合并消化道、腹腔及盆腔器质性疾病;(6)患者合并意识障碍或认知功能障碍等影响问卷真实性;(7)既往有胃肠道手术。

1.2 方法

(1)乳果糖组:予口服乳果糖(北京韩美药品有限公司,国药准字H20065730,规格:100 ml/瓶)每天1次,每次15 ml,疗程为4周。(2)莫沙必利组:予口服莫沙必利(新络纳,成都康弘药业公司,国药准字:H20031110,规格5 mg×20片/盒)每天3次,每次5 mg,疗程为4周。

1.3 评分方法

分别在干预前后记录乳果糖组和莫沙必利组

Wexner便秘评分、焦虑自测量表(self-rating anxiety scale, SAS)评分及抑郁自测量表(self-rating depression scale, SDS)评分。Wexner便秘评分是对便秘、排便频率、排便困难及腹痛等症状的综合评估。SAS是用来评估患者焦虑主观症状的量表,≥50分为焦虑,<50分为正常。SDS是用来评估患者抑郁主观症状的量表,≥53分为抑郁,<53分为正常。

1.4 疗效评价

疗效指数=(治疗前Wexner评分-治疗后Wexner评分)/治疗前Wexner评分×100%。根据疗效指数分为以下4型:(1)若疗效指数≥95%,则为临床痊愈;(2)若70%≤疗效指数<95%,则为显效;(3)若30%≤疗效指数<70%,则为有效;(4)若疗效指数<30%,则为无效。总有效率=(痊愈例数+显效例数+有效例数)/总例数×100%。

1.5 统计学处理

采用SPSS 23.0统计软件进行数据分析。符合正态分布的计量资料用均数±标准差($\bar{x} \pm s$)表示,采用t检验;非正态分布的计量资料,用中位数(四分位数间距)[$M(Q_1, Q_3)$]表示,采用秩和检验。计数资料用例数(百分率)表示,采用 χ^2 检验。 $P < 0.05$ 为差异有统计学意义。

2 结果

2.1 2组患者一般资料比较

2组在年龄、身高、体质量、性别构成及便秘的病程方面比较,差异均无统计学意义(均 $P > 0.05$;表1)。

2.2 2组患者临床疗效比较

乳果糖组治疗老年慢性功能性便秘的有效率高于莫沙必利组,差异有统计学意义($P < 0.05$;表2)。

2.3 2组患者Wexner便秘评分比较

干预前,乳果糖组和莫沙必利组在Wexner量表各项评分差异均无统计学意义($P > 0.05$)。干预后,除便秘病程评分外,乳果糖组的Wexner余各项评分均较干预前有所下降($P < 0.05$),而莫沙必利组除腹痛评分、便秘病程评分外,余各项评分均较前下降($P < 0.05$)。乳果糖组在改善排便频率、排便困难、腹痛、排便时间评分方面优于莫沙必利组($P < 0.05$;表3)。

表1 2组患者基本资料比较

Table 1 Comparison of clinical data between two groups

(n=40)

Group	Age (years, $\bar{x} \pm s$)	Height (m, $\bar{x} \pm s$)	Body mass (kg, $\bar{x} \pm s$)	Duration of constipation (years, $\bar{x} \pm s$)	Gender [n(%)]	
					Male	Female
Lactulose	66.18±3.08	1.63±0.06	61.58±6.55	2.65±1.19	17(42.50)	23(57.50)
Mosapride	66.70±2.74	1.64±0.06	62.83±8.98	2.92±1.20	19(47.50)	21(52.50)

表 2 2 组患者临床疗效比较

Table 2 Comparison of clinical efficacy between two groups [n=40, n(%)]

Group	Cured	Marked effective	Effective	Ineffective	Effective rate
Lactulose	0(0.00)	1(2.50)	29(72.50)	10(25.00)	30(75.00)
Mosapride	0(0.00)	0(0.00)	14(35.00)	26(65.00)	14(35.00)*

Compared with lactulose group, *P<0.05.

表 3 2 组患者 Wexner 便秘评分比较

Table 3 Comparison of Wexner constipation score between two groups [n=40, points, M(Q₁, Q₃)]

Variable	Lactulose group		Mosapride group	
	Before treatment	After treatment	Before treatment	After treatment
Frequency of bowel movements	1.0(1.0,2.0)	0.0(0.0,1.0)*	1.5(1.0,2.0)	1.0(0.0,1.0)*#
Difficulty; painful evacuation effort	3.0(2.0,3.0)	1.0(1.0,2.0)*	3.0(2.0,3.0)	2.0(1.2,3.0)*#
Completeness; feeling incomplete evacuation	3.0(2.0,3.0)	2.0(1.0,2.8)*	3.0(2.0,3.0)	2.0(2.0,3.0)*
Pain; abdominal pain	1.0(1.0,2.0)	1.0(0.0,2.0)*	2.0(1.0,2.0)	2.0(1.0,2.0)*#
Time; minutes in lavatory per attempt	2.0(2.0,3.0)	1.0(1.0,2.0)*	2.0(2.0,3.0)	2.0(1.0,2.0)*#
Assistance; type of assistance	1.0(1.0,2.0)	1.0(0.0,1.0)*	1.0(1.0,2.0)	1.0(0.0,1.0)*
Failure; unsuccessful attempts for evacuation per 24 h	1.0(1.0,2.0)	1.0(0.0,1.0)*	1.0(1.0,1.0)	1.0(0.0,1.0)*
History; duration of constipation	3.0(2.0,4.0)	3.0(2.0,4.0)	3.0(2.0,3.0)	3.0(2.0,3.0)
Overall score	16.0(14.0,17.0)	9.5(7.0,12.8)*	16.0(14.0,17.8)	13.0(11.0,14.0)*#

Compared with before treatment in the same group, *P<0.05; compared with lactulose group, #P<0.05.

2.4 2 组患者焦虑和抑郁状态比较

SAS 是用来评估患者焦虑主观症状的量表, ≥50 分为焦虑, <50 分为正常。SDS 是用来评估患者抑郁主观症状的量表, ≥53 分为抑郁, <53 分为正常。本研究将情绪简化为 2 种状态, 分别是焦虑和(或)抑郁状态和正常状态。干预前, 乳果糖组和莫沙必利组的焦虑和(或)抑郁状态分布, 差异无统计学意义, 具有可比性。干预后, 乳果糖组中焦虑和(或)抑郁状态占比均较干预前下降(P<0.05), 而莫沙必利组中焦虑和(或)抑郁状态占比与干预前比较, 差异无统计学意义(表 4)。

表 4 2 组患者焦虑和抑郁状态比较

Table 4 Comparison of anxiety and depression between two groups [n=40, n(%)]

Group	Anxiety/Depression	Normal
Lactulose		
Before treatment	21(52.50)	19(47.50)
After treatment	10(25.00)	30(75.00)*
Mosapride		
Before treatment	28(70.00)	12(30.00)
After treatment	21(52.50)	19(47.50)

Compared with before treatment in the same group, *P<0.05.

2.5 2 组患者不良反应

本试验过程中, 乳果糖组有 2 例患者服用乳果糖后有轻微腹胀, 可自行缓解; 莫沙必利组患者未发现明显严重不良反应。

3 讨论

随着年龄的增加, 人体器官逐渐出现生理性衰老, 肠道功能同样也会减退。因此, 老年功能性便秘较中青年更为常见^[5]。乳果糖被国内外多项指南推荐为老年人慢性便秘的常用药物^[6]既往乳果糖治疗老年便秘的相关临床研究多着重观察排便频率的改善, 本研究主要观察乳果糖对老年功能性便秘患者便秘相关的一系列症状及精神心理状况的综合改善情况, 并和莫沙比利进行对照分析。莫沙必利为 5-HT₄ 受体激动剂, 作用于肠肌间神经丛, 释放运动性神经递质, 促进肠道蠕动, 改善慢传输型便秘患者的临床症状^[2]。

本研究显示, 干预 4 周后, 乳果糖组总有效率显著高于莫沙必利组(P<0.05)。国内一项系统评价显示乳果糖治疗便秘的总有效率为 91.1%^[7], 高于本组结果, 推测可能是本研究对象均为老年患者, 基础情况差, 同时本研究未对功能性便秘的类型及便秘严重程度进一步细化分层研究。

Wexner 量表是对便秘症状的综合评估, 本研究运用 Wexner 量表对便秘相关各项症状进行干预前后对比, 结果显示乳果糖治疗 4 周后可总体改善老年便秘患者的各项临床症状, 与文献报道^[8]相仿。与莫沙必利组相比, 乳果糖组可更有效地增加老年便秘患者地排便次数、降低排便困难程度、减轻排便时腹痛、缩短排便时间(P<0.05)。分析其原因, 乳果糖作为常见的渗透性泻药, 对肠道黏膜刺激较小,

能够有效保留大便中水分,增加大便体积,促进肠道蠕动,加速排便;另外,乳果糖作为一种益生元,有利于肠道益生菌的生长,更好地发挥肠道功能^[2]。

慢性便秘增加焦虑、抑郁的发生风险;同时,焦虑、抑郁亦会提高老年便秘的治疗难度,显著降低老年便秘患者的生存质量^[9]。一项国内的流行病学调查^[10]显示,52.70%慢性便秘患者合并有焦虑和(或)抑郁状态,与本研究便秘患者合并焦虑或抑郁状态占比相仿,说明便秘的治疗不仅要关注生理,伴随的心理障碍也不容忽视。随着便秘症状的改善,部分便秘患者的焦虑、抑郁症状也可以消除或减轻^[11]。本研究也显示,随着乳果糖改善便秘症状的同时,患者焦虑或抑郁评分较前下降,且比例下降率高于莫沙必利组($P < 0.05$)。

近年来,学界发现了肠道菌群紊乱和焦虑、抑郁有关,并推测肠道菌群可能是通过神经内分泌系统与大脑沟通参与了这些疾病的发生、发展^[12]。乳果糖,作为常见的益生元,有利于双歧杆菌、乳酸杆菌等肠道益生菌的生长,抑制肠杆菌、梭状芽孢杆菌等有害菌群的繁殖,调节肠道菌群紊乱^[13]。故推测,乳果糖可能是通过优化肠道菌群从而改善老年慢性功能性便秘患者的焦虑和抑郁症状。本研究结果与刘先秒等^[14]报道补充益生菌显著改善便秘患者焦虑和抑郁症状结果相似,具有一定的可信度。

综上,本研究结果提示乳果糖能有效改善老年慢性功能性便秘患者相关临床症状、降低便秘相关的SAS和SDS评分,综合疗效优于莫沙必利。慢性功能性便秘患者合并焦虑、抑郁状态不容小觑,今后我们应加大对其精神心理的关注和干预,在心理、生理两方面改善便秘患者的生活质量。同时,本组研究存在样本量小、单中心、未作长期疗效随访等诸多不足,未来还需加以完善。

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