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复合凝乳酶对功能性消化不良儿童营养状态和摄食行为的影响*

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摘要 目的:观察复合凝乳酶胶囊对不同亚型功能性消化不良儿童临床表现、营养状态和摄食行为的影响及安全性。**方法:**以 2017 年 8 月至 2018 年 9 月在湖北省妇幼保健院儿童消化内科就诊的功能性消化不良(Functional dyspepsia, FD)儿童为研究对象进行问卷调查,观察治疗前和复合凝乳酶治疗 2 w 后患儿临床症状变化及药物相关不良反应的发生情况,监测患儿身高和体重,进行膳食情况的调查。**结果:**共 163 例儿童纳入研究,发生餐后不适综合征(Postprandial distress syndrome, PDS)66 例,上腹痛综合征(Epigastric pain syndrome, EPS)97 例。治疗前,PDS 组儿童症状总分明显高于 EPS 儿童(6.9 ± 2.7 vs 3.6 ± 1.7 , $t=5.90$, $P=0.00$)。PDS 组儿童 WAZ、WHZ、HAZ、身高别体质量 Z 值(weight for height Z score, WHZ)、年龄别身高 Z 值(height for age Z score, HAZ)、年龄别体质量 Z 值(weight for age Z score, WAZ)、体质量指数(body mass index, BMI)、膳食多样化分数(Dietary diversity score, DDS)均明显低于 EPS 组(P 均 <0.05)。治疗 2 w 后,PDS 儿童症状总分明显降低($P=0.00$),改善程度依次为:厌食 $>$ 早饱 $>$ 腹痛 $>$ 嗝气 $>$ 恶心 $>$ 腹胀。EPS 儿童症状总分无明显变化($P=0.11$)。PDS 儿童 WAZ、WHZ、DDS 均有明显升高(P 均 <0.05)。EPS 儿童 DDS 无明显变化($t=0.22$, $P=0.30$)。研究期间未见明显药物相关不良反应。**结论:**复合凝乳酶胶囊可改善 PDS 患儿的临床症状、营养状态和膳食多样性,且安全性高。

关键词:功能性消化不良;餐后不适综合征;上腹痛综合征;营养调查;复合凝乳酶;食物多样化

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Impact of Gastropylor Complex Capsules on the Nutritional and Dietary Diversity of Children with Functional Dyspepsia*

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ABSTRACT Objective: To evaluate the efficacy of Gastropylor Complex Capsules on the symptom, nutritional and dietary diversity of children with functional dyspepsia and its safety. **Methods:** Medical histories were collected in the Department of Digestive and Nutritional, Women and Children's Hospital of Hubei Province from August 2017 to September 2018. The questionnaire investigation was performed. The changes of symptom and drug-related adverse reactions were evaluated after two weeks therapy of Gastropylor Complex Capsules. The height and weight of children were measured. The diet investigation was also included. **Results:** A total of 163 children were enrolled into the study, including 66 cases with postprandial distress syndrome (PDS) and 97 cases with epigastric pain syndrome (EPS). Compared to those in children with EPS, total symptom score increased (6.9 ± 2.7 vs 3.6 ± 1.7 , $t=5.90$, $P=0.00$), while WAZ, WHZ, HAZ and dietary diversity score (DDS) decreased in PDS children before treatment (all $P<0.05$). The Gastropylor Complex Capsules were treated for 2 weeks, symptom improved in PDS, which from high to low is: anorexia $>$ early satiety $>$ abdominal pain $>$ belch $>$ nausea $>$ abdominal distension. WAZ, WHZ and DDS increased in PDS children (all $P<0.05$). No significant drug-related adverse reaction was found during the study. **Conclusions:** Gastropylor Complex Capsules can improve the functional dyspepsia symptoms significantly, such as anorexia, early satiety, abdominal pain, abdominal distension, etc. The same efficacy was also in nutritional and dietary diversity in PDS children. No obvious drug-related adverse reaction is observed.

Key words: Functional dyspepsia (FD); Postprandial distress syndrome (PDS); Epigastric pain syndrome (EPS); Nutrition investigation; Gastropylor Complex Capsules; Dietary diversity score (DDS)

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前言

FD 是儿童期最常见的功能性胃肠疾病之一,我国儿童 FD

发生占儿科门诊的 8%~30%。由于儿童学习压力的增加,尤其饮食习惯的不规律等原因,儿童 FD 的发病率呈现逐年上升的趋势^[1,2]。临床工作中,FD 儿童常同时存在挑食厌食,且症状反

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复,给患儿生长发育和家庭生活质量造成不同程度的影响^[3,4]。目前,儿童FD缺乏确实有效的药物治疗方法^[5,6]。临床上主要采取阿莫西林+克拉霉素+奥美拉唑(三联疗法)治疗FD,但是长期的治疗效果不显著,而且耐药性持续升高^[7,8]。有研究显示,采用复合凝乳酶能够有效治疗儿童FD,改善患儿的身体状况,保障患儿的身体健^[9]。复合凝乳酶胶囊含有多种生物活性成分,由凝乳酶、蛋白水解酶等多种生物活性酶组成,促进胃肠道腺体分泌,增加消化吸收,代偿胃肠消化功能,同时也可保护胃肠道黏膜,且具有抗酸作用,未发现不良反应^[10-12]。本研究应用复合凝乳酶配合营养干预治疗FD取得了较好效果,可明显改善部分FD儿童的临床表现、营养状态和膳食摄入行为,现报道如下,以期临床用药提供依据。

1 对象与方法

1.1 研究对象

选择2010年6月至2018年5月在湖北省妇幼保健院儿内科门诊就诊儿童(3~14岁)223例,均符合功能性胃肠疾病罗马IV标准中功能性消化不良(FD)的标准^[13]:①餐后饱胀;②早饱;③上腹疼痛或烧灼感,与排便无关;④经过适当评估,症状不能用其他疾病来完全解释。在诊断前2个月,至少符合以上1个,且每个月这种症状出现至少4 d。

排除标准:系统性器质性疾病者;内镜或消化道X线钡剂检查异常者;腹部手术史;精神疾病不合作者;入组前1周内服用影响或可能影响胃肠动力和胃感觉功能的药物。

根据症状将FD分为2个亚型^[14]:①餐后不适综合征(Postprandial distress syndrome, PDS):餐后饱胀不适或早饱感,影响正常进食。支持诊断的标准:上腹胀气、餐后恶心或过度打嗝。②上腹痛综合征(Epigastria pain syndrome, EPS):必须包括以下所有条件:a.严重上腹疼痛或烧灼感,影响日常生活;b.疼痛非全腹,局限于腹部其他部位或胸部区域;c.排便或排气后不能缓解。支持诊断的标准:a.疼痛可能为烧灼样但不包括胸骨后疼痛;b.疼痛通常由进食诱发或缓解,但也可在空腹时发生。凡符合PDS者均归入PDS亚型。

1.2 方法

1.2.1 治疗方法 所有患儿均注意避免引起症状加重的食物(如含咖啡因、辛辣、高脂食物)。适当运动。对可加重症状的心理因素加以疏导。复合凝乳酶胶囊[葵花药业集团(唐山)生物制药有限公司(国药准字H13024290)]服用方法:3~7岁,每次1粒(不会吞服胶囊者,只服内容物),每日3次;7~14岁,每次2粒,每日三次;均于饭后温水送服。治疗2 w。

1.2.2 症状变化 试验期间,患儿/和其监护人每日记录症状的严重程度。采用问卷调查法,评估所有患儿治疗前及治疗2 w后症状改善程度。根据患儿出现(腹痛、早饱、腹胀、嗝气、恶心、呕吐、反酸)七个症状分为:无、轻、中、重四级,分别计0、1、2、3分^[15]。同时记录用药过程中出现的任何不良事件,包括腹泻、皮疹、发热、头晕、头痛等。

1.2.3 人体学测量 由研究者测量。身高测量精确到0.1 cm;体质量测量使用电子称,精确到0.1 kg。均测量2次取平均值。采用WHO Anthro及Anthro Plus 3.2.2版本软件计算身高别体质量Z值(Weight for height Z score, WHZ)、年龄别身高Z值

(Height for age Z score, HAZ)、年龄别体质量Z值(Weight for age Z score, WAZ)、体质量指数(Body mass index, BMI)的Z值(BMI-Z)。WAZ<-2为低体质量,HAZ<-2为生长迟缓,WHZ<-2为消瘦^[16]。

1.2.4 膳食分类及多样化评分方法 10类食物包括:①富含维生素A的蔬果;②豆及豆制品、坚果、种子;③蛋类;④禽畜肉类;⑤动物内脏类;⑥其他蔬果类;⑦深绿色叶菜;⑧乳及乳制品;⑨谷薯类;⑩鱼虾类。根据询问发,判断近一周这些食物的摄入情况。膳食多样化分数(dietary diversity score, DDS)的计算^[17]:DDS即患儿在调查前一月内所食用某种食物频次,每周≥4次,记2分;每周1~3次,记1分;每月≤1次,记0分;每类食物得分相加即为DDS,分值0~20分^[18-20]。

1.3 统计学方法

采用SPSS 17.0软件进行数据分析,计量资料采用平均值±标准差表示,采用配对t检验,计数资料采用 χ^2 检验,以 $P<0.05$ 有统计学意义。

2 结果

2.1 两组临床症状的变化比较

本研究共纳入患儿163例,其中PDS66例(PDS组),EPS97例(EPS组),两组儿童性别构成(36/30 vs. 55/42, $\chi^2=0.07$, $P=0.80$)、年龄(5.8 ± 2.2 vs. 6.2 ± 2.4 , $t=0.67$, $P=0.20$)、病程(6.8 ± 3.2 vs. 7.4 ± 4.0 , $t=0.62$, $P=0.90$)差异均无统计学意义。入组时(T0),PDS儿童症状总分明显高于EPS儿童(6.9 ± 2.7 vs. 3.6 ± 1.7 , $t=5.90$, $P=0.00$),除早饱外,PDS儿童厌食、恶心、嗝气发生率明显高于EPS儿童,腹痛/不适少于EPS儿童(均 $P<0.05$)。治疗2 w(T1),PDS儿童症状总分明显降低(6.9 ± 2.7 vs. 1.5 ± 1.0 , $t=15.24$, $P=0.00$),其各症状均有明显改善(均 $P<0.05$),改善程度依次为:厌食>早饱>腹痛>嗝气>恶心>腹胀。EPS儿童症状总分无明显变化(3.6 ± 1.7 vs. 3.3 ± 1.5 , $t=1.30$, $P=0.11$);以腹痛、厌食、腹胀改善明显(均 $P<0.05$)。两组儿童症状总分差异仍有统计学意义(1.5 ± 1.0 vs. 3.3 ± 1.5 , $t=5.26$, $P=0.00$),PDS儿童早饱、腹痛改善较EPS儿童明显(均 $P<0.05$)。见表1。

2.2 两组营养状态的变化比较

治疗前(T0),EPS儿童低体重发生率为10.3%($n=10$),消瘦发生率为12.4%($n=12$),生长迟缓发生率为2.1%($n=2$);PDS儿童发生率分别为28.8%($n=19$)、31.8%($n=21$)和10.6%($n=7$),均明显高于EPS儿童($\chi^2=9.17, 9.20, 5.49$, P 均 <0.05),EPS儿童中有4例超重。PDS儿童WAZ、WHZ、HAZ均明显低于EPS儿童($t=6.38, 6.97, 7.72$, P 均 <0.05)。治疗2 w(T1)后,PDS儿童WAZ、WHZ均有明显升高($t=4.58, 4.39$, P 均 <0.05),仍低于EPS儿童($t=5.25, 4.48$, P 均 <0.05)。EPS儿童仅WAZ明显升高($t=5.25$, $P=0.00$),见表2。

2.3 两组膳食多样化的变化比较

入组时,PDS儿童DDS评分为 10.7 ± 4.2 ,EPS儿童为 15.9 ± 3.7 ,两组比较差异有统计学意义($t=5.14$, $P=0.00$)。两组患儿每日均会摄入谷薯类,其次是新鲜肉类;摄入频率最低为动物内脏类。经治疗2 w后,PDS儿童DDS明显升高,为 13.8 ± 3.5 ($t=4.61$, $P=0.00$);EPS儿童DDS无明显变化,为 16.0 ± 2.6 ($t=0.22$, $P=0.30$),EPS儿童DDS明显高于PDS儿童($t=2.83$, $P=0.00$)。

表 1 两组儿童症状的比较[例(%)]

Table 1 Comparison of the symptoms between the two groups of children [n (%)]

	PDS(n=66)		EPS(n=97)	
	T0	T1	T0	T1
Abdominal pain/discomfort	37(56.1) [#]	13(19.7) ^{*#}	97(100.0)	76(78.4) [*]
Early satiety	60(90.9) [#]	7(10.6) ^{*#}	0(0)	0(0)
Anorexia	66(100.0) [#]	10(15.2) [*]	45(46.4)	22(22.7) [*]
Bloating	18(27.3)	6(9.1) [*]	24(24.7)	15(15.5) [*]
nausea	34(51.5) [#]	12(18.2) [*]	19(19.6)	14(14.4)
Helium	18(27.3) [#]	4(6.1) [*]	5(5.2)	4(4.1)

Note: Compared with the group before treatment (T0), * $P<0.05$; compared with the same period EPS group, [#] $P<0.05$.

表 2 两组患儿营养和体格发育的比较

Table 2 Comparison of the nutrition and physical development between the two groups

	PDS		EPS	
	T0	T1	T0	T1
WAZ	-1.8± 0.8 [#]	-1.2± 0.7 ^{*#}	-0.5± 0.6	-0.2± 0.3 [*]
WHZ	-1.9± 1.4 [#]	-1.0± 0.9 ^{*#}	-0.2± 0.4	-0.2± 0.5
HAZ	-0.9± 0.5 [#]	-0.9± 0.5 [#]	0.1± 0.5	0.2± 0.3

WAZ: age Z body mass Z value; HAZ: age height height Z value; WHZ height body body mass Z value.

2.4 两组不良反应的发生情况比较

两组研究期间未见明显药物相关不良反应。

3 讨论

根据功能性消化不良(FD)发病机制的不同,功能性胃肠病罗马 IV 标准将 FD 分为餐后不适综合征(PDS)和上腹痛综合征(EPS)两个亚型^[5,21]。PDS 以餐后饱胀感为主要症状,提示其发病机制主要为消化不良、胃排空障碍;而 EPS 以腹痛为主,提示可能与胃酸分泌过多有关。因此,PDS 多采用促动力药,而 EPS 常采用质子泵抑制剂进行治疗^[22]。但目前儿童 FD 药物治疗效果并不满意^[7],需要寻找有效治疗方案。

3.1 FD 儿童临床症状、营养、膳食多样性的变化

本组 FD 儿童中,以 EPS 为主。本组 FD 儿童主诉多为反复腹痛、厌食,可能与腹痛/不适、厌食、早饱等症状更易被家长关注有关。EPS 儿童症状以腹痛为主,部分患儿仅有腹痛,故症状总分明显低于 PDS 儿童。PDS 儿童症状以早饱为主,厌食、恶心、嗝气发生率明显高于 EPS 儿童,这与文献报道一致^[5]。PDS 儿童症状总分高,伴随膳食多样性低,营养不良发生率亦较高,PDS 儿童低体重发生率为 28.8%,消瘦发生率为 31.8%,生长迟缓发生率为 10.6%,均明显高于 EPS 儿童;PDS 组儿童 WAZ、WHZ、HAZ 亦明显低于 EPS 儿童。FD 儿童尤其 PDS 儿童如未得到及时、有效的治疗,可能引起营养问题而最终导致生长发育迟缓。

3.2 复合凝乳酶对 FD 儿童临床症状的影响

复合凝乳酶是羔羊第四胃胃粘膜总提取物,主要成分为凝乳酶、蛋白水解酶、粘蛋白、双歧因子、维生素 B12 等生物活性成分制成的胶囊剂^[23]。粘蛋白可保护胃肠道粘膜,蛋白水解

酶、胃蛋白酶、凝乳酶,均可促进蛋白质分解吸收,也有助于食物消化后胃排空。蛋白水解酶又称胃动素,可促胃肠动力。双歧因子可促进双歧杆菌的生长,使双歧杆菌产生的短链脂肪酸如乙酸、丙酸、丁酸等增加,使肠道内 pH 值降低,抑制大肠杆菌等机会致病菌的生长繁殖,并促进肠道蠕动,防止便秘^[7]。采用复合凝乳酶治疗 2 w,PDS 儿童的症状积分明显降低,其各症状均有明显改善,改善程度依次为:厌食>早饱>腹痛>嗝气>恶心>腹胀,提示复合凝乳酶可有效改善 PDS 儿童临床症状。EPS 儿童症状总分无明显下降;但腹痛、厌食、腹胀改善明显。

3.3 复合凝乳酶对 FD 儿童营养状态的影响

治疗 2 w 后,PDS 儿童 WAZ、WHZ 均有明显升高,提示 PDS 儿童体重有明显追赶,但 PDS 儿童 WAZ、WHZ 仍低于 EPS 儿童,提示复合凝乳酶在改善 PDS 儿童症状的基础上,伴随营养状态的改善;可能在于复合凝乳酶通过改善患儿消化功能,从而改善患儿营养状态^[24]。

3.4 复合凝乳酶对 FD 儿童膳食多样化的影响

膳食指南建议人们膳食多样化的食物来提高身体所需的营养^[25,26]。膳食多样化与营养素摄入量及其充足状态呈正相关^[27];膳食多样化与儿童生长发育、成人体质指数以及某些慢性疾病均有关^[28]。膳食多样化分数(Dietary diversity score, DDS)调查作为评估膳食营养质量的一种工具,具有简单、易行等优点^[29,30]。本研究选择食物频率问卷,调查 FD 儿童的膳食情况,结果显示,是否进行食物定量对 DDS 并无影响^[10],但未进行每类膳食的定量。经复合凝乳酶治疗 2 w 后,PDS 儿童 DDS 明显升高($P=0.00$),EPS 儿童 DDS 改善不明显($P=0.30$)。因复合凝乳酶改善 PDS 儿童饭后不适、厌食等症状,促进患儿膳食多样化。

综上,复合凝乳酶可以明显改善 PDS 儿童早饱、厌食等症

状,可促进 PDS 儿童的膳食多样化,伴随营养状态的改善;对 EPS 儿童症状、膳食多样化及营养状态影响不大。因此,复合凝乳酶可用于 PDS 儿童的治疗。本研究尚有以下不足之处:(1)未能进一步随访治疗的远期效果;(2)纳入样本两少,结果可能存在一定的偏移,因此后续还需要进一步深入研究。

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