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奥美拉唑联合多潘立酮治疗小儿胃食管反流病的疗效观察

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摘要 目的：探究奥美拉唑联合多潘立酮治疗小儿胃食管反流病的临床疗效。**方法：**选择 2012 年 10 月～2015 年 12 月期间内因胃食管反流病入院接受治疗的患儿 80 例，所有患儿均采用奥美拉唑和多潘立酮联合治疗。在治疗前和治疗后 8 周内，观察患者的临床治疗效果、24 h 食管下段 pH 值监测、电子胃镜检查和内镜下黏膜活检。**结果：**研究对象用药前后呕吐、恶心、反酸、上腹痛、烧心、胸骨后痛、咳嗽、气喘等八项临床症状得到了明显的改善，甚至消失，差异具有统计学意义(P<0.05)；患儿治疗后的反流次数、反流时间≥ 5 min 的次数、最长反流时间、总 PH<4 时间占总时间的百分比以及综合评分均较治疗前明显降低，差异具有统计学意义(t=33.385、40.862、47.710、21.806、53.508，P<0.05)；与治疗前对比，研究对象治疗后有 1 例存在重度反流性食管炎未能恢复，28 例存在不同程度改善，43 例完全恢复，差异有统计学意义(Z=37.775，P<0.05)；不良反应出现 5 例（3 例轻微腹泻、2 例轻微腹痛），发生率为 6.25%。**结论：**奥美拉唑联合多潘立酮治疗小儿胃食管反流病的临床效果较为显著，能够明显改善小儿胃食管反流症状，安全性较高，值得在临床上进一步推广使用。

关键词：奥美拉唑；多潘立酮；小儿胃食管反流病

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The Observation of the Clinical Efficacy of Omeprazole and Domperidone for Gastroesophageal Reflux Disease in Children

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ABSTRACT Objective: To evaluate the clinical efficacy of omeprazole combined with domperidone in the treatment of gastroesophageal reflux disease in children. **Methods:** From October 2012 to December 2015, 80 cases of children with gastroesophageal reflux disease admitted into hospital for treatment were included into the study, which omeprazole combined with domperidone in treating. Before treatment and after treatment of 8 weeks, the clinical therapeutic effect of patients, 24 h lower esophageal pH monitoring, electronic gastroscopy and endoscopic mucosal biopsy were observed. **Results:** there was a certain degree of improvement after treatment for vomiting, nausea, acid regurgitation, upper abdominal pain, heartburn, retrosternal pain, cough, asthma and so on eight clinical symptoms, the data were statistically significant (P<0.05). Cases with indicator including reflux times, times with reflux time≥ 5 times, the longest reflux time, the total PH<4 percentage of time and comprehensive score index after the treatment were significantly lower than before treatment, the data difference was statistically significant (t=33.385, 40.862, 47.710, 21.806, 53.508, P<0.05). By endoscopic biopsy, only 1 patient had severe anti reflux esophagitis failed to restore, and 28 cases had different degrees of improvement, 43 cases recovered completely, the difference was statistically significant (Z=37.775, P<0.05). Adverse reactions occurred in 5 cases (3 cases of mild diarrhea, 2 cases of mild abdominal pain, the incidence was 6.25%. **Conclusion:** The treatment of cases with gastroesophageal reflux disease combined with omeprazole and domperidone, clinical effect was significant.Children with gastroesophageal reflux symptoms can be significantly improved, higher safety of clinical treatment. Therefore, it is worthy of clinical further promotion to use.

Key words: Omeprazole; Domperidone; Gastroesophageal reflux disease

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胃食管反流病（gastroesophageal reflux disease, GERD）是指机体内食管对胃液过度接触，导致患者出现烧心、反酸以及胸骨后灼烧样疼痛等临床表现的一种综合性疾病，若患者经常出现胃食管反流，则会损伤食管黏膜。有研究调查结果显示[1]，GERD 的发病率在 25%～35%左右，而在我国因 GERD 导致的反流性食管炎患病率超过 5%。相关研究结果表明[2]，小儿 GER 发病率处在较高水平，2 月龄健康婴儿有 50%以上存在 GERD 相关症状，而 1/300～1/1000 的儿童因存在 GER 症状。在临床上，小儿 GERD 不具有特异性，其临床特征为腹痛、反复呕吐和呼吸道感染以及哮喘，而且由于儿童发育尚未完善，胃食管黏膜较为脆弱，容易遭受损伤，出现其他并发症，如反流性食管炎(RE)、非糜烂性反流病(NERD)以及 Barrett 食管炎(BD)等[3]。临床上对小儿胃食管反流病的治疗方法尚未得到金标准，本次研究采用奥美拉唑和多潘立酮进行联合治疗，观察其临床治疗效果，现报道如下。

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1 资料与方法

1.1 一般资料

选择 2012 年 10 月～2015 年 12 月期间因 GERD 入院接受治疗的 80 例患儿，其中男性 42 例，女性 38 例；年龄范围 5 月龄至 15 周岁，平均年龄(8.5± 1.39)岁，病程 1-5 月，平均病程(3.1± 1.13)月。所有患儿临床表现均为反复恶心呕吐、烧心、胸骨后疼痛等，经临床诊断和影像学检查结果均证实符合 GERD 的诊断标准[4]。排除标准：患儿在发病后短期内接受过胃酸抑制剂等药物治疗；患儿对奥美拉唑或多潘立酮药物过敏；患儿患有其他严重疾病无法进行本次研究等。本次研究所有患儿家属自愿参与，并签署知情同意书，经我院医学伦理委员会批准通过。

1.2 治疗方法

口服奥美拉唑(厂家：西安利君制药有限责任公司，批准文号：国药准字 H10940188，规格：20 mg/ 片)，晨起顿服，每日 1 次，1 次 1 片，同时服用多潘立酮片(商品名：吗丁啉，厂家：西安杨森制药有限公司，批准文号：国药准字 H10910003，规格:10 mg)进行治疗，每日 3 次，每次 1 片，餐前 15 min 服用，疗程持续 2 个月。

1.3 观察指标

治疗前及治疗 8 周后，进行临床症状观察、24 h 食管下段 pH 值监测、电子胃镜检查。(1)临床症状观察：包括恶心、呕吐及反酸、上腹痛、烧心和胸骨后痛、咳嗽和气喘等，并对其症状严重程度进行评价[5]，无：患儿无临床症状；轻：患儿临床症状较轻；中：患儿临床症状较为显著，需服药进行缓解；重：患儿临床症状显著，并对个人生活产生影响，长期服药才能缓解，甚至服药无效。(2)24 h 食管 pH 值监测：包括：① 24 h 总 pH 值是指患儿取卧位和立位时检测食管 pH 值 <4 的时间占总监测时间的比值；② 反流时间；③ 连续酸暴露时间 >5 min 的次数；④ 反流持续最长时间；⑤ Boix-ochoa 综合评分，是指对上述② -④ 指标的总评分，公式为(测定值 - 均数)/ 标准差 +1[6]。(3)胃镜检查：取 2 块黏膜作病理检测，反流性食管炎严重程度进行分级，采用 Olympus-xp260 电子胃镜检查患儿胃部、食管黏膜活检反流性胃食管症的临床诊断标准[7]主要分为 4 级：① 0 级是指机体正常，无组织学改变；② I 级是指黏膜出现点状或是条索状红肿、糜烂，无融合现象；③ II 级是指食管黏膜出现条索状红肿、糜烂，伴有融合，但无全周性溃疡；④ III 级是指病变具有广泛性，黏膜表面发红，糜烂融合，并有全周性溃疡。

1.4 统计学方法

采用 SPSS20.0 统计学软件处理数据。计量资料采用 t 检验；计数资料采用多个样本比较的秩和检验，等级资料采用秩和检验，P<0.05 为数据有统计学意义。

2 结果

2.1 治疗前后临床症状比较

治疗前及治疗 2 周，4 周，6 周，8 周后所有临床症状均存在一定程度改善，甚至消失，差异有统计学意义(P<0.05)，见表1。

表 1 治疗前后临床症状比较

Table 1 Comparison of clinical symptoms before and after treatment

Time	Nausea, vomiting, regurgitation				Upper abdominal pain				Heartburn, back chest Pain				Cough, asthma			
	No	Slight	Medium	Sever	No	Slight	Medium	Sever	No	Slight	Medium	Sever	No	Slight	Medium	Sever
Before treatment	9	16	42	13	3	24	31	12	33	29	13	5	19	34	23	4
After 2 week treatment	16	35	20	9	14	36	22	8	38	21	11	2	26	41	11	2
After 4 week treatment	21	40	15	4	19	42	16	3	63	13	4	0	40	35	5	0
After 6 week treatment	36	35	8	1	27	31	11	1	71	9	0	0	47	31	2	0
After 8 week treatment	48	30	2	0	43	30	7	0	74	6	0	0	55	25	0	0
H	80.309				62.217				31.376							
P	0.000				0.000				0.000							

2.2 治疗前后酸反流情况比较

治疗后，患儿反流次数、反流时间≥ 5 min 的次数、最长反流时间、总 pH<4 时间占总时间的百分比以及 Boix-ochoa 综合评分较治疗前均明显降低，差异有统计学意义(P<0.05)，见表 2。

表 2 治疗前后酸反流情况比较

Table 2 Comparison of acid reflux before and after treatment

Time	Number of reflux	The number of reflux ≥ 5 min	Longest reflux time (min)	Total PH<4 time percentage(%)	Boix-ochoa Comprehensive score
Before treatment	74.3± 16.32	8.1± 1.23	17.2± 2.37	10.2± 2.65	28.5± 3.86
After treatment	11.2± 4.41	0.8± 1.02	3.6± 0.94	3.4± 0.87	4.3± 1.21
t	33.385	40.862	47.710	21.806	53.508
P	0.000	0.000	0.000	0.000	0.000

2.3 治疗前后胃镜检查结果比较

本研究所有患儿在接受治疗前以及治疗后 2 周内进行电子胃镜检查,治疗后,仅 1 例存在重度反流性食管炎未能恢复,28 例存在不同程度改善,43 例完全恢复,差异有统计学意义(P<0.05),见表 3。

表 3 治疗前后胃镜检查结果比较

Table 3 Comparison of the results of gastroscopy before and after treatment

Time	0 grade	I grade	IIgrade	IIIgrade
Before treatment	9	38	26	7
After treatment	43	28	8	1
z	37.775			
P	0.000			

2.4 依从性及不良反应情况对比

所有患儿均完成疗程治疗,未出现失访或是药物漏服等情况。疗程中出现 3 例轻微腹泻、2 例轻微腹痛,经及时有效治疗后迅速缓解,无其他严重不良反应。

3 讨论

在小儿消化道疾病中最为常见的是胃食管反流病,其主要的临床表现为咳嗽、反酸、反复吞咽困难和疼痛、胃部灼热等,已经成为过敏、感染等问题之后导致小儿出现反复咳嗽的另一主因,对小儿生活造成严重影响[8]。经过临床及病理学研究证实胃食管反流病发生机制包括机体内抗反流机制功能降低,导致胃内胃酸以及胃内容物损伤食管黏膜,尤其是胃酸内的 H^+ 严重损伤食管黏膜[9-11]。在小儿中,GERD 的临床特征不具有特异性,主要有患儿腹痛、反复呕吐和呼吸道感染,可并发哮喘,主要包括反流性食管炎(RE)、非糜烂性反流病(NERD)以及 Barrett 食管炎(BD)。近年来,病理生理学报道称 RE、NERD 以及 BD 各自独立,相互之间较少存在转换,NERD 在部分患者中无病理性反流症状,其临床特征仅为黏膜对酸敏感性增强,食管下端括约肌一过性松驰;RE 的发生机制为患儿食管下段括约肌(LES)张力降低。目前,有相关研究报道表明[12]GERD 患者食管下段的鳞状上皮细胞间隙扩大,通透性增加,导致酸或是蛋白酶进入胃黏膜,从而出现损伤,并刺激细胞间隙中的感觉神经末梢,从而表现出临床症状。

近年来,随着相关研究深入,胃食管反流病机制主要是食道下段括约肌松弛,机体内胃的排空能力降低,胃内压进一步增加,形成反流[13]。在临床上,胃食管反流病主要治疗药物为奥美拉唑。作为质子泵抑制剂,奥美拉唑作用在胃黏膜壁细胞,形成巯基对抑制胃酸分泌,降低 K^+-ATP 酶活性。药物进入机体内之后,胃液内酸水平降低,使得高浓度胃酸损伤胃食管黏膜的过程受到抑制,最终缓解胃内的灼烧疼痛感。有临床报道称[14]奥美拉唑与多潘立酮联合治疗,其临床治疗效果更显著。多潘立酮有效调节食道下段括约肌,括约肌张力增加,胃排空加速,胃内压下降,抗反流作用得到有效增强[15]。两种治疗药物相辅相成,发挥临床作用快,显著改善临床症状,不良反应发生率低,其症状较轻,较适合治疗小儿胃食管反流症。

本次研究对所有患儿采用奥美拉唑联合多潘立酮进行治疗,80 例患儿均显著效果,对患儿临床症状情况进行分析可知,疗效较为显著,症状改善差异存在统计学意义(P<0.05)。有研究报道称[16]少数胃食管反流患儿治疗时采用奥美拉唑抑酸效果并不理想,分析其原因可能是胃食管反流症不仅存在酸反流,还有胆汁反流,胃酸与胆盐、胃蛋白酶的混合物破坏胃粘膜,使得食管黏膜损伤加重[17]。研究报道表明等[18]轻度 RE 患儿中多为单纯性酸反流或是胆汁反流,而重度 RE 中 70%以上为混合性反流。因此,在治疗方法中选择抑酸的奥美拉唑与胃肠动力药多潘立酮联合治疗,能够有效加速胃排空,使得胃窦部、十二指肠部的消化蠕动增强,胆汁反流情况减少,从而治疗疾病,达到疗效[19]。在对患儿不良反应情况进行观察,在疗程前后进行患儿血常规、尿液及粪便的三项常规检查,并对心肺和肝肾功能进行检查,所有指标均为正常范围内,仅出现 3 例轻微腹泻、2 例轻微腹痛,因此对二者联合作用效果还需要进行长期观察进行验证[20]。

综上所述,奥美拉唑联合多潘立酮进行小儿胃食管反流病治疗,临床效果较显著,患儿在疗程结束后症状明显减轻或消除,不良反应发生率较低,值得在临床上进一步推广使用。

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