

doi: 10.13241/j.cnki.pmb.2014.23.030

双歧四联活菌多药联合对根除幽门螺杆菌患者的临床疗效观察*

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摘要 目的:研究双歧四联活菌多药联合对根除幽门螺杆菌(*Helicobacter pylori*, Hp)患者的临床疗效。方法:从2012年3月到2013年3月,共计60例病患因腹部不适就诊。以数字法随机分成实验组及对照组。对照组以埃索美拉唑镁肠溶片(剂量为20 mg bid)和胶体酒石酸铋钠(剂量为165 mg qid)以及克拉霉素片(剂量为0.5 bid)和阿莫西林胶囊(剂量为1.0 bid)等药物治疗。实验组则在对照组基础之上另以双歧四联活菌(剂量为1.5 tid)药物治疗。对比两组疗效和治疗后不良反应,以及治疗依从性情况。结果:实验组的根除率为86.67%(26/30),显著高于对照组的63.33%(19/30);未根除率为13.33%(4/30),显著低于对照组的36.67%(11/30)。实验组有不良反应者8例,占比26.67%,显著少于对照组的17例,占比56.67%;实验组在治疗后的依从性为好者占比90.00%(27/30),显著高于对照组的66.67%(20/30),依从性为差者占比10.00%(3/30),显著低于对照组的33.33%(10/30),差异均有统计学意义(均 $P < 0.05$)。结论:双歧四联活菌采用多药联合方式可明显提升对于Hp的根除率,同时减少不良反应,增加病患依从性。效果显著,值得临床推荐。

关键词: 双歧四联活菌;多药联合;根除;幽门螺杆菌;疗效

中图分类号:R573 文献标识码:A 文章编号:1673-6273(2014)23-4510-03

Clinical Efficacy Observation of Bifidobacterium Tetravaccine Multi-drug Combination for the Patients with Eradication of *Helicobacter Pylori**

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ABSTRACT Objective: To study clinical efficacy observation of Bifidobacterium tetravaccine multi-drug combination for the patients with eradication of *Helicobacter pylori* (Hp). **Methods:** Between March 2012 and March 2013, a total of 60 cases of patients with abdominal discomfort got treatment. Number randomly divided them into the experimental group and the control group. The control group was treated with esomeprazole magnesium enteric-coated tablets (dose of 20mg bid) and colloidal bismuth sodium tartrate (dose of 165mg qid) and clarithromycin tablets (dose of 0.5 bids) and amoxicillin (dose of 1.0 bid) and other drugs. On the basis of the control group, the experimental group was added with Bifidobacterium tetravaccine (dose of 1.5 tid) drug for treatment. Compare the treatment efficacy and adverse reactions, and treatment compliance situation between the two groups. **Results:** The eradication rate of the experimental group was 86.67% (26/30), which was significantly higher than the control group of 63.33% (19/30). The not-eradicated rate of experimental group was 13.33% (4/30), which was significantly lower than the control group of 36.67% (11/30). The experimental group's adverse reactions was 8 cases, accounting for 26.67%, while in control group 17 cases had adverse reactions, accounting for 56.67%; 90.00% of patients (27/30) in the experimental group had good compliance after treatment, which was significantly higher than the control group of 66.67% (20/30). Only 10.00% of patients (3/30) in experimental group showed poor compliance which was significantly lower than the control group of 33.33% (10/30). The differences were statistically significant (both $P < 0.05$). **Conclusion:** Bifidobacterium tetravaccine multi-drug combination can significantly improve Hp eradication rate reduce adverse reactions, and increase patients' compliance. Its effect is significant and it is worthy of recommendation.

Key words: Bifidobacterium tetravaccine; Multi-drug combination; Eradication; *Helicobacter pylori*; Efficacy

Chinese Library Classification(CLC): R573 **Document code:** A

Article ID: 1673-6273(2014)23-4510-03

前言

在临床上,有流行病学的资料表明, Hp 感染率已在全球人群中超过了 50%, 而我国成人 Hp 感染率在 40%至 60%间,大

约有 10%的人曾患有消化性溃疡^[1]。从上世纪初的“无酸无溃疡”等观点形成,至本世纪“无 Hp 无溃疡”等观点的确立,在一定程度上揭示了 Hp 感染对于消化性溃疡(Peptic ulcer, PU)而言,是主要病因。因此,根除 Hp 可有效治疗 PU,并防止疾病复

* 基金项目:广东省江门市科技计划项目(江科[2013]82 号第 35 项)

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(收稿日期:2013-12-15 接受日期:2014-01-13)

发,最终减少胃癌的发病风险。本文即通过对双歧四联活菌以多药联合方案根除 *Hp*,得到了一些结论,现报道如下。

1 资料和方法

1.1 临床资料

从 2012 年 3 月到 2013 年 3 月,共计 60 例病患因腹部不适就诊。年龄在 16 至 69 岁间,平均年龄为 45.3 ± 3.5 岁。含男 32 例,女 28 例。根据 2012 年 4 月 26 日 -28 日第四届全国幽门螺杆菌(*Hp*)共识会议^[2]所推荐的根除 *Hp* 适应证及推荐强度,选择入选病例。入选标准:全部病患均经胃镜和 13C 呼气试验,确诊消化性溃疡。排除标准^[3]为:既往有幽门螺杆菌根除治疗史者。本次治疗前 2 周内曾服用质子泵抑制剂或 H₂ 受体拮抗剂者,本次治疗前 4 周内曾服用抗生素或铋剂者。有严重心肝肾疾病、恶性肿瘤、消化道息肉者。妊娠期或哺乳期妇女。既往曾行胃肠道手术者。对本次研究药物过敏者。嗜酒、有药物成瘾、有精神障碍或依从性差者。经我院成立的伦理委员会审议批准,再由病患知情同意并签字后,以数字法随机分成实验组及对照组。每组各 30 例。其中实验组中含男 17 例,女 13 例。年龄在 16 至 67 岁间,平均年龄为 44.9 ± 3.2 岁。对照组中含男 15 例,女 15 例。年龄在 17 至 69 岁间,平均年龄为 45.6 ± 3.8 岁。两组在性别和年龄等方面对比,差异无统计学意义 ($P > 0.05$),具有可比性。

1.2 研究方法

对照组以埃索美拉唑镁肠溶片(剂量为 20mg bid)和胶体酒石酸铋钠(剂量为 165mg qid)以及克拉霉素片(剂量为 0.5 bid)和阿莫西林胶囊(剂量为 1.0 bid)等药物治疗。实验组则在对照组基础之上另以双歧四联活菌(剂量为 1.5 tid)药物治疗。一共用药 10d,在治疗结束之后依照病情需要继续用抑酸剂和其他药物,期间禁用抗生素和益生菌。在疗程结束之后 4 周,对 13C 呼气试验进行复查。

1.3 观察指标

对两组在治疗后的不良反应情况实施观察对比,其中不良反应主要包含恶心呕吐及味觉异常和腹泻,以及皮疹、头痛及失眠等。*Hp* 根治率判定标准是全部病患在治疗方案结束的四周之后以 13C 呼气试验实施复查,若结果显示为阴性,则判定为根除。

1.4 统计学方法

以 SPSS13.0 软件分析。数据比较以 χ^2 检验, $P < 0.05$ 为差异有统计学意义。

2 结果

2.1 两组 *Hp* 根除情况对比

实验组的根除率为 86.67%(26/30),显著高于对照组的 63.33%(19/30);未根除率为 13.33%(4/30),显著低于对照组的 36.67%(11/30)。差异均有统计学意义(均 $P < 0.05$)。提示实验组治疗方案可发挥更好的疗效。见下表 1。

表 1 两组 *Hp* 根除情况对比(例,%)

Table 1 Comparison of eradication condition of two groups (n,%)

组名 Group name	例数(n)	根除 Eradication	未根除 Not Eradication
实验组 Experimental group	30	26(86.67)	4(13.33)
对照组 Control group	30	19(63.33)	11(36.67)
χ^2 值 χ^2 Value	-	4.356	4.356
P 值 P Value	-	0.037	0.037

注:与对照组相比,* $P < 0.05$ 。

Note: Compared with the control group, * $P < 0.05$.

2.2 两组治疗后不良反应情况对比

实验组有不良反应者 8 例,占比 26.67%,显著少于对照组

的 17 例,占比 56.67%,差异有统计学意义($\chi^2=5.554$, $P=0.018$)。提示实验组治疗方案副作用较低。见下表 2。

表 2 两组治疗后不良反应情况对比(例,%)

Table 2 Comparison of the adverse reactions of two groups after treatment (n,%)

组别 Groups	例数(n) Cases(n)	恶心呕吐 Nausea and vomiting	味觉异常 Allotriogeusia	腹泻 Diarrhoea	皮疹 Erythra	头痛 Headache	失眠 Wakefulness
实验组 Experimental group	30	6(20.00)	6(20.00)	3(10.00)	1(3.33)	1(3.33)	4(13.33)
对照组 Control group	30	10(33.33)	8(26.67)	7(23.33)	2(6.67)	3(10.00)	5(16.67)

注:部分病患含多种不良反应。

Note: Some patients had several kinds of adverse reactions.

2.3 两组病患的治疗依从性情况对比

实验组在治疗后的依从性为好者占比 90.00%(27/30),显著高于对照组的 66.67%(20/30),依从性为差者占比 10.00%

(3/30),显著低于对照组的 33.33%(10/30),差异均有统计学意义(均 $P < 0.05$)。提示实验组治疗方案可明显提升治疗依从性。见下表 3。

表 3 两组病患的治疗依从性情况对比(例,%)
Table 3 Comparison of treatment compliance situation (n,%)

组名 Groups	例数(n) Cases(n)	依从性 Compliance	
		好 Good*	差 Worse*
实验组 Experimental group	30	27(90.00)	3(10.00)
对照组 Control group	30	20(66.67)	10(33.33)
x ² 值 x ² Value	-	4.812	4.812
P 值 P Value	-	0.028	0.028

注:与对照组相比,*P<0.05。

Note:Compared with the control group,*P<0.05.

3 讨论

大量研究表明^[4],Hp感染和慢性胃炎及消化性溃疡、胃癌等病症有紧密联系。因此,针对Hp感染实施预防和治疗对人体健康意义重大。目前,在临床实践中,已摸索出各类经典抗Hp疗法,例如,质子泵抑制剂药物亦或是铋剂联合抗生素组成的三、四联疗法已在临床备受推崇,成为主要的Hp根治方案^[5]。然而,近年来,有报道指出,Hp耐药性已逐渐上升,从而导致此类治疗方案的疗效有所下降^[6]。医务人员亦转而寻找更为理想的治疗方案以期进一步提升疗效。

本文通过对双歧四联活菌以多药联合方案根除Hp,结果发现,实验组的根除率为86.67%(26/30),显著高于对照组的63.33%(19/30);实验组不良反应更小,副作用更小;实验组治疗依从性更好。与Smiley R,Bailey J等人^[7]报道一致,获得上述治疗结果的原因可能是因为双歧四联活菌作为一种微生物类制剂,主要成分是双歧杆菌和粪肠球菌,以及嗜酸乳酸菌和蜡状芽孢杆菌等^[8]。可以抑制Hp黏附和定植,以及繁殖。同时形成抑菌类物质,例如乳酸,从而对Hp生长产生抑制。此外,还可发挥对炎症因子的抑制作用,缓解胃粘膜的炎症反应。而益生菌还可明显减少因抗生素引发的各类不良反应,在机体与其他厌氧菌构成肠道的微生物屏障^[9]。对致病细菌毒素产生形成抑制,并加以分解,维持机体肠道的正常生理功能。国外Moretti E,Collodel G等人^[10]报道称,以克拉霉素及甲硝唑组成的三联疗法对于Hp根除率只有57%,本文实验组根除率达到86.67%,基本符合专家所提出的Hp根除方案所得根除率需在90%的目标。可见双歧四联活菌的增用可进一步提升疗效。Hsiang J,Selvaratnam S等人^[11]亦有类似报道对本研究加以证实。

在不良反应方面,对照组主要是恶心呕吐和味觉异常以及腹泻等,这是因为抗生素过度使用能够降低肠道对于致病菌抗定植作用,致使过路菌不断繁殖,从而引发上述不良反应^[12-14]。而由于实验组加用了益生菌制剂,使得疗效提升,从而间接减少了不良反应。而对照组病患因为无法耐受不良反应,亦或是心里恐惧,极易造成依从性下降,最终可能不规则或者终止服药,从而形成恶性循环,进一步降低依从性^[15-18]。这亦为本文研究中对照组依从性较低的主要原因。彭卫斌,容海鹰等人^[19,20]报道称,在临床有高达2/3的比例病患提前终止Hp治疗是因无法耐受不良反应,亦或是对于药物的恐慌情绪,从而直接减少了依从性。

综上所述,双歧四联活菌采用多药联合方式可明显提升对于Hp的根除率,同时减少不良反应,增加病患依从性。效果显著,值得临床推荐。

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(上接第 4512 页)

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