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通窍鼻炎片联合克拉霉素对慢性鼻窦炎患者嗅觉功能、鼻黏液纤毛传输速度及血清炎性因子的影响*

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摘要 目的:探讨通窍鼻炎片联合克拉霉素对慢性鼻窦炎患者嗅觉功能、鼻黏液纤毛传输速度及血清炎性因子的影响。**方法:**于2017年11月~2020年6月期间,选取我院门诊收治的慢性鼻窦炎患者86例。根据入院序号奇偶性将患者分为对照组和观察组,各43例。对照组采用克拉霉素治疗,观察组采用通窍鼻炎片联合克拉霉素治疗,均治疗4周。对比两组疗效、临床症状评分、嗅觉功能、鼻黏液纤毛传输速度及血清炎性因子,记录两组不良反应发生情况。**结果:**观察组的临床总有效率高于对照组($P<0.05$)。两组治疗4周后T&T主观嗅觉测试法分级均较治疗前改善,且观察组的改善效果优于对照组($P<0.05$)。两组不良反应发生率对比无明显差异($P>0.05$)。治疗4周后,两组鼻黏膜纤毛输送率(MTR)和鼻黏膜纤毛清除率(MCC)均较治疗前升高,且观察组高于对照组($P<0.05$)。治疗4周后,两组血清白介素-5(IL-5)、白介素-6(IL-6)和肿瘤坏死因子- α (TNF- α)水平均较治疗前降低,且观察组低于对照组($P<0.05$)。治疗4周后,观察组鼻塞、头晕头痛、鼻漏、嗅觉下降、流涕、喷嚏症状评分低于对照组($P<0.05$)。**结论:**通窍鼻炎片联合克拉霉素治疗慢性鼻窦炎患者疗效显著,可有效改善患者嗅觉功能及鼻黏液纤毛传输速度,缓解临床症状并降低机体炎性因子水平,且安全性较好。

关键词:通窍鼻炎片;克拉霉素;慢性鼻窦炎;嗅觉功能;鼻黏液纤毛传输速度;炎性因子

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Effect of Tongqiao Biyan Tablet Combined with Clarithromycin on Olfactory Function, Nasal Mucociliary Transport Velocity and Serum Inflammatory Factors in Patients with Chronic Sinusitis*

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ABSTRACT Objective: To investigate the effect of Tongqiao Biyan tablet combined with clarithromycin on olfactory function, nasal mucociliary transport velocity and serum inflammatory factors in patients with chronic sinusitis. **Methods:** 86 patients with chronic sinusitis in our outpatient department from November 2017 to June 2020 were selected. The patients were divided into the control group and the observation group according to the parity of admission serial number, 43 cases in each group. The control group was treated with clarithromycin, and the observation group was treated with Tongqiao Biyan tablets combined with clarithromycin, all patients were treated for 4 weeks. The curative effect, clinical symptom score, olfactory function, nasal mucociliary transport velocity and serum inflammatory factors were compared between the two groups, and the incidence of adverse reactions between the two groups was recorded. **Results:** The total effective rate of the observation group was higher than that of the control group ($P<0.05$). 4 weeks after treatment, T & T subjective olfactory test scores of the two groups were improved compared with before treatment, and the improvement effect of the observation group was better than that of the control group ($P<0.05$). There was no significant difference in the incidence of adverse reactions between the two groups ($P>0.05$). 4 weeks after treatment, the nasal mucociliary transport rate (MTR) and nasal mucociliary clearance rate (MCC) of the two groups were higher compared with before treatment, and the observation group was higher than the control group ($P<0.05$). 4 weeks after treatment, the levels of interleukin-5 (IL-5), interleukin-6 (IL-6) and tumor necrosis factor- α (TNF- α) of the two groups were lower than those before treatment, and the observation group was lower than the control group ($P<0.05$). 4 weeks after treatment, The symptom scores of nasal congestion, dizziness, headache, rhinorrhea, olfactory decline, runny nose and sneezing in the observation group were lower than those in the control group ($P<0.05$). **Conclusion:** Tongqiao Biyan tablet combined with clarithromycin

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has significant efficacy in the treatment of patients with chronic sinusitis, which can effectively improve the olfactory function and nasal mucociliary ciliary transport speed, alleviate clinical symptoms and reduce the level of inflammatory factors, with good safety.

Key words: Tongqiao Biyan tablet; Clarithromycin; Chronic sinusitis; Olfactory function; Nasal mucociliary transport velocity; Inflammatory factors

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前言

慢性鼻窦炎是鼻科领域的常见多发病,临床症状主要有鼻塞,并伴有脓性、黏性鼻涕,常累及鼻腔和鼻窦黏膜,病情严重者可引发鼻源性眶内并发症,降低患者生活质量^[1,2]。该病的主要发病机制为鼻炎、病原菌感染、鼻腔机械性堵塞引发的鼻窦黏膜非特异性炎症反应^[3]。现临床针对此类疾病的治疗尚无统一方案,克拉霉素属于大环内酯类抗生素,主要用于敏感细菌所致的上、下呼吸道感染,也是临床用于治疗慢性鼻窦炎的常用药物^[4,5]。然而慢性鼻窦炎是一种易反复发作的疾病,单用克拉霉素效果有限。通窍鼻炎片是近年来慢性鼻窦炎重要的辅助用药,具有散风消炎、宣通鼻窍之功效^[6]。现临床有关通窍鼻炎片联合克拉霉素治疗慢性鼻窦炎患者的相关报道尚不多见,本文就此展开分析,旨在为临床治疗提供指导。

1 资料与方法

1.1 一般资料

于2017年11月~2020年6月期间,选取我院门诊收治的慢性鼻窦炎患者86例。根据入院序号奇偶性将患者分为对照组和观察组。对照组43例,女性、男性分别为21例、22例,病程4个月~2年(1.08 ± 0.27)年;年龄25~60(42.75 ± 5.81)岁;双侧慢性鼻窦炎13例,单侧慢性鼻窦炎30例;体质指数 $19 \sim 26 \text{ kg/m}^2$ (23.43 ± 0.67) kg/m^2 。观察组43例,女性、男性分别为19例、24例,病程4个月~3(1.23 ± 0.47)年;年龄27~57岁(42.61 ± 6.42)岁;双侧慢性鼻窦炎11例,单侧慢性鼻窦炎32例;体质指数 $20 \sim 26 \text{ kg/m}^2$ (23.55 ± 0.53) kg/m^2 。两组一般资料对比无明显差异($P > 0.05$),具有可比性。

1.2 纳入排除标准

纳入标准:(1)参考《慢性鼻-鼻窦炎诊断和治疗指南》^[7],并经鼻内镜或CT等影像学手段确诊;(2)患者及其家属知情本研究且签署同意书;(3)近1周内未接受任何相关治疗者。排除标准:(1)因其他细菌、病毒引起的慢性鼻窦炎患者;(2)妊娠或哺乳期妇女;(3)合并鼻中隔偏曲、鼻腔结构异常者;(4)合并哮喘、呼吸道感染、支气管炎等呼吸道疾病者。(5)合并心肝肾等脏器功能不全者。

1.3 方法

所有患者入院后均嘱其卧床休息、清淡饮食、适量运动,在此基础上,对照组给予克拉霉素[国药准字H20057573,沈阳东星医药科技有限公司,规格:0.25 g(按 $\text{C}_{38}\text{H}_{69}\text{NO}_{13}$ 计)]治疗,0.25 g/次,2次/d。观察组在克拉霉素的基础上(克拉霉素的治疗方案同对照组)联合通窍鼻炎片(国药准字Z20093013,山东齐都药业有限公司,规格:每片重0.37 g)治疗,5~7片/次,3次/d。两组均治疗4周。

1.4 疗效判定标准^[7]

治疗4周后,由专人统计两组患者的临床疗效。疗效具体的判定标准如下:鼻内镜检查窦口开放良好,窦腔黏膜上皮化,流涕、鼻塞、鼻甲肿胀等症状消失,无脓性分泌物为治愈。鼻内镜检查见窦腔黏膜部分区域水肿、肥厚或肉芽组织形成,上述临床症状明显改善,有少量脓性分泌物为好转。鼻内镜检查见窦口狭窄或闭锁,症状无改善,息肉形成,有脓性分泌物为无效。总有效率=治愈率+好转率。

1.5 观察指标

(1)于治疗前、治疗4周后,将糖精颗粒置于患者下鼻甲上表面,嘱其每隔15 s吞咽1次,运用糖精试验测量鼻黏膜纤毛输送率(MTR)和鼻黏膜纤毛清除率(MCC)。(2)于治疗前、治疗4周后,采集患者5 mL清晨空腹肘静脉血,采用酶联免疫吸附试验法(试剂盒购自北京佳科生物技术公司)检测血清白介素-5(IL-5)、白介素-6(IL-6)和肿瘤坏死因子- α (TNF- α)水平。(3)于治疗前、治疗4周后,采用T&T主观嗅觉测试法测试两组嗅觉功能,分为3个等级:I级为嗅觉正常,II级为嗅觉轻度损害,III级为嗅觉中重度损害。(4)于治疗前、治疗4周后,采用视觉模拟评分法(VAS)^[8]对患者鼻塞、流涕、喷嚏、头晕头痛、嗅觉下降症状进行评分,评分范围0~10分,分数越高,症状越严重。(5)记录两组不良反应情况。

1.6 统计学方法

采用SPSS26.0进行数据分析。计数资料用例数及率描述,采用 χ^2 检验。等级资料用例数及率描述,采用秩和检验。计量资料以均值 $\pm$ 标准差的形式表示,行t检验。检验水准 $\alpha=0.05$ 。

2 结果

2.1 两组疗效比较

治疗4周后,对照组治愈8例、好转23例、无效12例,总有效率72.09%(31/43)。观察组的治愈12例、好转28例、无效3例,总有效率93.02%(40/43)。观察组的临床总有效率高于对照组($\chi^2=6.541$, $P=0.011$)。

2.2 两组嗅觉功能对比

两组治疗4周后T&T主观嗅觉测试法分级均显著改善($P < 0.05$),观察组的改善效果优于对照组($P < 0.05$),详见表1。

2.3 两组鼻黏膜纤毛传输速度对比

治疗前,两组MTR、MCC对比无统计学差异($P > 0.05$),治疗4周后,两组MTR、MCC均较治疗前升高,且观察组高于对照组($P < 0.05$),详见表2。

2.4 两组血清炎症因子水平对比

治疗前,两组血清IL-5、IL-6、TNF- α 水平对比无明显差异($P > 0.05$),治疗4周后,两组血清IL-5、IL-6、TNF- α 水平均降低,且观察组低于对照组($P < 0.05$),详见表3。

表 1 两组嗅觉功能对比 例(%)

Table 1 Comparison of olfactory function between the two groups [n(%)]

Groups	Before treatment grade			4 weeks after treatment grade		
	I grade	II grade	III grade	I grade	II grade	III grade
Control group(n=43)	4(9.30)	12(27.91)	27(62.79)	21(48.84)	13(30.23)	9(20.93)
Observation group(n=43)	5(11.63)	10(23.26)	28(65.12)	28(65.12)	12(27.91)	3(6.98)
U		0.459			5.369	
P		0.136			0.018	

表 2 两组鼻黏膜纤毛传输速度对比($\bar{x} \pm s$)Table 2 Comparison of nasal mucociliary transport velocity between the two groups($\bar{x} \pm s$)

Groups	MTR(mm/min)		MCC(%)	
	Before treatment	4 weeks after treatment	Before treatment	4 weeks after treatment
Control group(n=43)	3.31± 0.48	5.95± 1.21 ^a	49.26± 5.37	63.69± 6.33 ^a
Observation group(n=43)	3.28± 0.32	8.66± 1.38 ^a	49.33± 4.29	78.27± 5.26 ^a
t	0.341	9.682	0.066	11.617
P	0.743	0.000	0.947	0.000

Note: Compared with before treatment, ^aP<0.05.表 3 两组血清炎症因子水平对比($\bar{x} \pm s$)Table 3 Comparison of levels of inflammatory factors between the two groups($\bar{x} \pm s$)

Groups	IL-5(ng/L)		IL-6(ng/L)		TNF-α(ng/L)	
	Before treatment	4 weeks after treatment	Before treatment	4 weeks after treatment	Before treatment	4 weeks after treatment
Control group(n=43)	42.76± 4.13	31.61± 5.14 ^a	67.81± 5.24	44.23± 6.12 ^a	41.31± 5.23	29.66± 4.39 ^a
Observation group(n=43)	42.83± 5.26	20.35± 4.47 ^a	67.24± 6.31	28.69± 4.28 ^a	41.35± 4.39	21.98± 4.67 ^a
t	0.069	10.840	0.456	13.645	0.038	7.857
P	0.945	0.000	0.650	0.000	0.969	0.000

Note: Compared with before treatment, ^aP<0.05.

2.5 两组临床症状评分对比

症状评分对比无明显差异(P>0.05),治疗4周后,两组上述症

治疗前,两组鼻漏、鼻塞、流涕、喷嚏、头晕头痛、嗅觉下降

状评分均降低,且观察组较对照组低(P<0.05),详见表4。

表 4 两组临床症状评分对比($\bar{x} \pm s$,分)Table 4 Comparison of clinical symptom scores between the two groups($\bar{x} \pm s$, scores)

Groups	Rhinitis		Nasal obstruction		Runny nose		Sneezing		Dizziness and headache		Decreased olfactory sense	
	Before treatment	4 weeks after treatment	Before treatment	4 weeks after treatment	Before treatment	4 weeks after treatment	Before treatment	4 weeks after treatment	Before treatment	4 weeks after treatment	Before treatment	4 weeks after treatment
Control group(n=43)	7.87± 1.23	4.27± 1.05 ^a	8.39± 1.07	4.57± 1.02 ^a	8.28± 1.12	3.89± 1.01 ^a	7.92± 1.23	4.17± 1.03 ^a	7.76± 1.04	4.11± 0.99 ^a	6.89± 1.27	3.78± 1.03 ^a
Observation group(n=43)	7.85± 1.25	2.17± 1.03 ^a	8.41± 1.05	2.03± 1.00 ^a	8.26± 1.09	1.87± 0.98 ^a	7.94± 1.25	4.25± 0.89 ^a	7.78± 1.06	2.03± 0.97 ^a	6.90± 1.23	1.88± 0.93 ^a
t	0.075	9.362	0.087	11.660	0.084	9.412	0.075	14.066	0.088	9.841	0.037	8.978
P	0.941	0.000	0.930	0.000	0.933	0.000	0.941	0.000	0.930	0.000	0.971	0.000

Note: Compared with before treatment, ^aP<0.05.

2.6 两组不良反应发生率对比

治疗期间,观察组不良反应发生率为 11.63%(5/43),包括皮疹、胃肠道不适各 2 例,呕吐 1 例;对照组不良反应发生率为 9.30%(4/43),包括胃肠道不适 2 例、呕吐及皮疹各 1 例;均未做针对性处理,停药后自行缓解,两组不良反应发生率对比未见显著差异($\chi^2=0.124, P=0.725$)。

3 讨论

慢性鼻窦炎多指由于纤毛破坏、真菌或细菌感染、窦口阻塞、变应性炎症、环境、遗传等致病因素导致窦腔内上皮通透性异常,引起的感染变应性炎症^[9-11]。此类患者通常伴有鼻黏膜纤毛功能障碍,可影响患者嗅觉功能^[12-14]。此外,以往的研究也证实^[15,16],鼻黏膜纤毛传输功能与鼻黏膜炎症密切相关。IL-5、IL-6、TNF- α 均是反映机体炎症反应的敏感性指标,其中 TNF- α 是由内皮细胞和单核巨噬细胞分泌的细胞因子,其含量过高能致使机体免疫网络平衡失调,还能够通过炎性损伤介导嗅神经胶质细胞变性坏死,造成嗅觉功能显著降低^[17]。IL-5、IL-6 参与活化 T 细胞增殖、分化,在机体出现炎症或损伤时会大幅度增加,可导致鼻黏膜毛细血管通透性增加,充血水肿,诱导鼻息肉形成^[18,19]。因此,如何阻断此类炎性细胞因子合成,对于缓解慢性鼻窦炎患者临床症状,促进嗅觉功能、鼻黏液纤毛传输功能恢复具有十分重要的意义。克拉霉素抗菌谱广,其可透过细菌细胞膜,在接近供体("P"位)与细菌核糖体的 50S 亚基成可逆性结合,有效阻断转移核糖核酸结合至 "P" 位上,因而细菌蛋白质合成受到抑制,发挥良好的抗菌效果^[20-22]。

然而单纯的西医药治疗慢性鼻窦炎患者疗效不甚理想,近年来,中成药逐渐应用于慢性鼻窦炎的治疗中,并取得了较好的效果。通窍鼻炎片的主要成分为苍耳子、辛夷、薄荷、防风、白术、白芷、黄芪等^[23],其中苍耳子、辛夷具有通利鼻窍、辛散风寒的功效,黄芪、白术健脾可益气固表,白芷、防风有祛风解表的效果,而薄荷辛凉入肺、疏散风热,以上药物共同发挥散风消炎、宣通鼻窍的功效^[24]。既往的研究证实^[25,26],通窍鼻炎片具有抗病毒、抗菌、消炎、镇痛等多种作用,可发挥扶正祛邪、标本兼治的功效;其对嗅觉障碍、鼻塞、鼻涕多、鼻黏膜充血等为主要表现的急、慢性鼻炎、鼻窦炎有良好的效果。本次研究结果显示,相较于单用克拉霉素治疗,联合通窍鼻炎片治疗的患者,其临床症状、嗅觉功能及鼻黏液纤毛传输速度改善效果均更佳。这可能是因为通窍鼻炎片主管散风固表,宣肺通窍,能够补益患者肺、脾气虚,可有效缓解鼻漏、鼻塞、流涕、喷嚏、头晕头痛、嗅觉下降等临床症状。同时,通窍鼻炎片能够有效巩固克拉霉素的抗炎、抗菌效果。现代药理研究表明,辛夷可有效改善局部血液循环,减少鼻部分泌物;而白芷联合苍耳子能够调节机体免疫,进而减少流涕,缓解鼻黏膜水肿,防止鼻部组织缺氧,起到间接的抑菌杀菌作用;薄荷具有清热解毒、收敛止血、镇痛消肿的效果,可促进鼻黏膜病变恢复;黄芪能够抑制葡萄球菌、链球菌对鼻黏膜的破坏^[27]。因此,检测两组的血清炎性因子水平可发现:观察组治疗 4 周后的血清 IL-5、IL-6、TNF- α 水平低于对照组,可见观察组患者的炎性反应缓解效果更好,这也可能是观察组患者症状改善、疗效优于对照组的原因之一。而两组不良反应发生率对比未见显著差异,提示方案安全可靠,易被

患者所接受。

综上所述,通窍鼻炎片联合克拉霉素治疗慢性鼻窦炎患者疗效显著,可有效改善患者嗅觉功能及鼻黏液纤毛传输速度,缓解临床症状并降低机体炎性因子水平,且安全性较好。

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