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盐酸米诺环素软膏联合布洛芬对慢性牙周炎患者龈沟液 TNF- α 、IL-1 β 、IL-8 水平及生活质量的影响 *

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摘要 目的:探讨盐酸米诺环素软膏联合布洛芬对慢性牙周炎患者龈沟液肿瘤坏死因子- α (TNF- α)、白细胞介素-1 β (IL-1 β)、白细胞介素-8(IL-8)水平及生活质量的影响。**方法:**选取成都医学院第一附属医院于2016年3月至2018年3月期间收治的84例慢性牙周炎患者,按照数表法随机分为观察组(n=42)和对照组(n=42)。对照组患者予以盐酸米诺环素软膏治疗,观察组患者则在对照组的基础上联合布洛芬治疗,比较两组临床治疗总有效率,比较治疗前、后龈沟液 TNF- α 、IL-1 β 、IL-8 水平,治疗前后菌斑指数(PLI)、牙龈指数(GI)水平,采用健康检查简表(SF-36)评价两组患者生活质量。**结果:**观察组临床治疗总有效率明显高于对照组($P<0.05$)。治疗后观察组患者龈沟液 TNF- α 、IL-1 β 、IL-8 水平均明显低于对照组($P<0.05$)。治疗后观察组患者 PLI、GI 水平均明显低于对照组($P<0.05$)。治疗后观察组 SF-36 量表各维度评分均显著高于对照组($P<0.05$)。**结论:**盐酸米诺环素软膏联合布洛芬治疗慢性牙周炎的疗效确切,且有效降低患者龈沟液 TNF- α 、IL-1 β 、IL-8 水平,有利于牙周组织的重建和恢复,提高患者生活质量。

关键词:慢性牙周炎;盐酸米诺环素;布洛芬;肿瘤坏死因子- α ;白细胞介素-1 β ;白细胞介素-8;生活质量

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Effects of Minocycline Hydrochloride Ointment Combined with Ibuprofen on the Levels of TNF- α , IL-1 β and IL-8 in Gingival Crevicular Fluid and Quality of Life in Patients with Chronic Periodontitis*

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ABSTRACT Objective: To investigate the effects of minocycline hydrochloride ointment combined with ibuprofen on the levels of tumor necrosis factor- α (TNF- α), interleukin-1 β (IL-1 β), interleukin-8 (IL-8) in gingival crevicular fluid and quality of life in patients with chronic periodontitis. **Methods:** 84 patients with chronic periodontitis admitted to First Affiliated Hospital of Chengdu Medical College from March 2016 to March 2018 were randomly divided into observation group (n=42) and control group (n=42) according to the number table method. Patients in the control group were treated with minocycline hydrochloride ointment, while patients in the observation group were treated with ibuprofen on the basis of the control group. The total effective rate of clinical treatment was compared between the two groups. The levels of TNF- α , IL-1 β and IL-8 in gingival crevicular fluid, plaque index (PLI) and gingival index (GI) before and after treatment were compared, and the quality of life of the two groups was evaluated by health checklist (SF-36). **Results:** The total effective rate of the observation group was significantly higher than that of the control group ($P<0.05$). After treatment, the levels of TNF- α , IL-1 β and IL-8 in gingival crevicular fluid in the observation group were significantly lower than those in the control group ($P<0.05$). After treatment, PLI and GI levels in the observation group were significantly lower than those in the control group ($P<0.05$). After treatment, the SF-36 scale scores in the observation group were significantly higher than those in the control group ($P<0.05$). **Conclusion:** Minocycline hydrochloride ointment combined with ibuprofen is effective in the treatment of chronic periodontitis, and can effectively reduce the levels of TNF- α , IL-1 β and IL-8 in gingival crevicular fluid, which is conducive to the reconstruction and recovery of periodontal tissue and improve the quality of life of patients.

Key words: Chronic periodontitis; Minocycline hydrochloride; Ibuprofen; TNF- α ; IL-1 β ; IL-8; Quality of life

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前言

牙周炎是临床上常见的口腔疾病之一,我国患病率高达

35.2~55.3%^[1-3]。该病主要累及牙齿周围的支持组织,患者临床症状表现为牙周袋形成、牙龈出血、牙龈炎症以及牙槽骨吸收

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等,病情严重者甚至会出现牙齿脱落^[46]。特别是中老年患者,由于其抵抗能力下降以及机体免疫力减退,慢性牙周炎症状较重,病程较长,对组织破坏不可逆,在一定程度上增加了临床治疗的难度^[79]。既往临床上主要采用牙周刮治、拔除患牙等方式对牙周炎进行治疗,但上述机械除菌方式不但会加重患者的疼痛程度,同时会对患者的牙根造成严重损害,临床治疗效果并不理想。近年来相关研究表明^[10],炎症因子在牙周炎发生、发展中起重要作用。盐酸米诺环素是一种半合成的四环素类抗生素,可以有效的改善牙周炎症,是目前治疗牙周疾病的重要药物。而布洛芬是临床上常用的非甾体抗炎药物,联合盐酸米诺环素可以发挥更好的治疗效果^[11]。本文旨在探讨盐酸米诺环素软膏联合布洛芬对慢性牙周炎患者龈沟液细胞因子及生活质量的影响,现报道如下。

1 资料与方法

1.1 临床资料

选取成都医学院第一附属医院于2016年3月至2018年3月期间收治的84例慢性牙周炎患者。纳入标准:(1)所有患者均经临床检查、X线片检查以及实验室检查确诊为慢性牙周炎;(2)年龄 ≥ 45 岁;(3)入院前3个月内未接受非甾体类药物或抗生素治疗;(4)牙周袋探诊深度在5 mm~8 mm之间;(5)患者口腔内牙齿数量在21颗以上。排除标准:(1)入院前6个月内接受过牙周治疗者;(2)合并风湿免疫系统以及内分泌系统疾病者;(3)对本研究药物过敏者;(4)入院前30d内接受过手术治疗者。按照数表法随机分为观察组($n=42$)和对照组($n=42$)。其中观察组男性27例,女性15例,年龄66~83岁,平均年龄(53.52 ± 5.43)岁;病程2~17年,平均病程(8.35 ± 1.31)年。对照组男性25例,女性17例,年龄65~82岁,平均年龄(53.63 ± 5.45)岁;病程2~18年,平均病程(8.43 ± 1.32)年。两组临床资料比较无差异($P>0.05$),具有可比性。

1.2 研究方法

两组患者入院后均予以基础治疗,主要包括根面平整、牙龈上部的洁治以及牙龈下部刮治等。对照组患者在此基础上予以盐酸米诺环素软膏(Sunstar INC.,注册证号:H20150106,规格:0.5 g)治疗,采用注射器将其注入患者牙周袋底部,直至牙龈边缘可观察到药物为止。观察组患者则在对照组的基础上联合布洛芬缓释胶囊(中美天津史克制药有限公司,国药准字H10900089)治疗,具体方式如下:在每支盐酸米诺环素软膏内加入0.7 g的布洛芬,制作成缓释凝胶,随后采用注射器将其注入患者牙周袋底部,直至牙龈边缘可观察到药物为止。两组患者治疗频率为1次/周,连续治疗2周。

1.3 观察指标

(1)临床治疗总有效率:疗效判定标准如下^[13]:显效:治疗后牙龈恢复正常,牙周袋深度减少 ≥ 2 mm,牙龈指数减少 $\geq 1/2$,菌斑清除率 $\geq 60\%$;好转:治疗后牙龈趋于正常,牙周袋深度减少 ≥ 1 mm,菌斑清除率在20%~60%之间;无效:未达到上述标准者。治疗总有效率=(显效人数+好转人数)/总人数 $\times 100\%$ 。(2)治疗前后龈沟液细胞因子水平:分别于治疗前后采集患者龈沟液3 mL在离心机内离心(10 min,3000 r/min),取上清液,-70℃冰箱保存待检,采用酶联免疫吸附法测定肿瘤坏死因子- α (Tumor necrosis factor- α , TNF- α)、白细胞介素1 β (Interleukin-1 β , IL-1 β)、白细胞介素-8 (Interleukin-8, IL-8)水平,试剂盒购自上海酶联有限公司,具体操作严格按照试剂盒说明书进行。(3)治疗前后菌斑指数(Plaque index, PLI)、牙龈指数(Gingival index, GI):PLI根据菌斑量分4级:龈沟区无菌斑为0分;视诊无菌斑,探诊时可观察到薄层菌斑为1分;牙周周围可见中等堆积量的软性沉淀物为2分;牙周周围有大量软性沉淀物为3分。GI根据病变程度分为4级:牙龈正常为0分;牙龈有轻度炎症且探诊不出血为1分;牙龈有中度炎症且探诊出血为2分;牙龈有重度炎症且经常性出血为3分。(4)生活质量变化:健康检查简表(SF-36)对患者的生活质量进行评估分析,包含情感功能、生理功能、生理职能、躯体疼痛、社会功能、精力、精神健康、总体健康8个维度。每个维度总分均为100分,得分越高表示生活质量越好。

1.4 统计学方法

本研究数据均采用SPSS20.0软件进行检测分析,计量资料以均数 $\pm$ 标准差表示,实施t检验;计数资料以%表示,实施卡方检验。 $P<0.05$ 表明两组数据对比具有统计学意义。

2 结果

2.1 两组患者临床疗效比较

观察组临床治疗总有效率明显高于对照组,差异有统计学意义($P<0.05$),见表1。

2.2 两组患者治疗前后龈沟液中TNF- α 、IL-1 β 和IL-8水平比较

治疗前两组患者龈沟液TNF- α 、IL-1 β 、IL-8水平差异无统计学意义($P>0.05$),治疗后两组患者龈沟液TNF- α 、IL-1 β 、IL-8水平显著降低,观察组患者龈沟液TNF- α 、IL-1 β 、IL-8水平明显低于对照组,差异有统计学意义($P<0.05$),见表2。

2.3 两组患者治疗前后PLI、GI水平比较

治疗前两组患者PLI、GI比较差异无统计学意义($P>0.05$),治疗后两组PLI、GI均显著降低,且观察组患者低于对照组($P<0.05$),见表3。

表1 两组患者临床疗效比较[n(%)]

Table 1 Comparison of clinical efficacy between two groups of patients[n(%)]

Groups	n	Excellence	Better	Invalid	Total effective rate
Observation group	42	22(52.38)	16(38.10)	4(9.52)	38(90.48)
Control group	42	18(42.86)	13(30.95)	11(26.19)	31(73.81)
χ^2 value	-	-	-	-	3.977
P value	-	-	-	-	0.046

表 2 两组患者治疗前后龈沟液中 TNF- α 、IL-1 β 和 IL-8 水平比较($\bar{x}\pm s$)Table 2 Comparison of TNF- α , IL-1 β and IL-8 levels in gingival crevicular fluid between two groups before and after treatment($\bar{x}\pm s$)

Groups	n	TNF- α (pg/mL)		IL-1 β (pg/mL)		IL-8(pg/mL)	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Observation group	42	23.11 $\pm$ 3.42	14.01 $\pm$ 3.57*	23.63 $\pm$ 2.64	11.72 $\pm$ 6.51*	13.25 $\pm$ 2.85	7.28 $\pm$ 1.33*
Control group	42	22.94 $\pm$ 3.32	18.23 $\pm$ 3.91*	23.71 $\pm$ 2.75	15.34 $\pm$ 7.58*	13.49 $\pm$ 2.75	9.45 $\pm$ 1.28*
T value	-	0.231	4.627	0.136	2.841	0.514	4.824
P value	-	0.818	0.000	0.892	0.006	0.426	0.000

Note: Compared with before treatment,* $P<0.05$.表 3 两组治疗前后 PLI、GI 比较($\bar{x}\pm s$)Table 3 Comparison of PLI and GI before and after treatment in two groups($\bar{x}\pm s$)

Groups	n	PLI		GI	
		Before treatment	After treatment	Before treatment	After treatment
Observation group	42	1.32 $\pm$ 0.79	0.53 $\pm$ 0.13*	2.73 $\pm$ 0.78	1.02 $\pm$ 0.13*
Control group	42	1.31 $\pm$ 0.81	0.89 $\pm$ 0.34*	2.72 $\pm$ 0.79	1.66 $\pm$ 0.32*
T value	-	0.057	6.409	0.058	12.008
P value	-	0.955	0.000	0.954	0.000

Note: Compared with before treatment,* $P<0.05$.

2.4 两组患者治疗后 SF-36 评分对比

差异有统计学意义($P<0.05$)。见下表 4。

治疗后观察组 SF-36 量表各维度评分均显著高于对照组，

表 4 两组患者治疗后 SF-36 评分对比(分, $\bar{x}\pm s$)Table 4 Comparison of SF-36 scores between two groups after treatment(score, $\bar{x}\pm s$)

SF-36 scale	Observation group(n=42)	Control group(n=42)	T value	P value
Physiological function	84.4 $\pm$ 9.03	72.4 $\pm$ 7.82	6.530	0.000
Physiological function	80.2 $\pm$ 8.55	70.7 $\pm$ 7.46	5.463	0.000
Somatic pain	85.3 $\pm$ 9.18	73.5 $\pm$ 8.01	6.311	0.000
Social function	83.6 $\pm$ 8.62	74.7 $\pm$ 7.57	0.000	0.000
Energy	85.4 $\pm$ 9.16	72.5 $\pm$ 7.33	7.166	0.000
Emotional function	85.1 $\pm$ 8.48	72.8 $\pm$ 7.65	7.037	0.000
Emotional health	82.7 $\pm$ 8.53	72.8 $\pm$ 7.48	5.693	0.000
General health	84.4 $\pm$ 8.25	73.7 $\pm$ 7.39	6.316	0.000

3 讨论

慢性牙周炎多发于牙骨质、牙龈以及牙周韧带等部位,其中慢性牙龈炎症逐渐向牙周深部扩散是该病的主要发病机制^[14-16]。如不给予患者及时有效的治疗,易导致牙齿松动、脱落,进一步对患者发音、美观性以及咀嚼功能造成不同程度的影响^[17-19]。与此同时,该病患者普遍具有持续加重的临床特征,会继发性破坏患者感染的牙槽、牙龈、牙骨质以及牙周膜^[20-23]。目前,临床上治疗慢性牙周炎应用较为广泛的方法包括牙周洁治、牙周刮治以及根面平整等,上述治疗方式虽能在一定程度上清除已发生病变的牙骨质和牙龈上下的牙菌斑,但效果并不十分理想,因此通常需要配合药物进行治疗^[24,25]。近年来,随着口腔医学的不断发展,盐酸米诺环素软膏以及布洛芬作为治疗慢

性牙周炎的药物开始被广泛应用于临床上,且均有一定的效果。

本文研究结果发现,观察组临床治疗总有效率为 90.48%明显高于对照组的 73.81%,提示盐酸米诺环素软膏联合布洛芬治疗慢性牙周炎疗效更佳,与相关报道的结果类似^[26,27]。可能是由于盐酸米诺环素软膏属于一种新型的四环素,具有较强的抗菌活性,同时具有已渗透、低毒性等优点,可有效消灭牙周炎各种致病菌。而布洛芬不仅可增强患者的防御反应,同时还可在一定程度上减少炎症以及骨吸收,从而有效维持溶酶体膜的稳定性,进一步减少炎症因子的产生、分泌。两药联合具有一定的协同作用,因此可有效提高临床治疗效果。此外,治疗后观察组患者龈沟液细胞因子水平平均明显低于对照组,提示盐酸米诺环素软膏联合布洛芬可抑制慢性牙周炎患者的炎症反应,具有较强的抗炎效果。其主要原因在于盐酸米诺环素软膏可直接在

病变组织上进行治疗,从而促使病变的组织周围保持长久且有效药物浓度,进一步达到持续杀菌的作用。而其与布洛芬具有一定的协同作用,同时具有广谱抗菌、缓解牙周炎症的作用^[28,29]。这同时也表明盐酸米诺环素软膏联合布洛芬有利于改善慢性牙周炎患者全身免疫状态,改善慢性牙周炎患者的免疫功能。另外,治疗后观察组患者 PLI、GI 水平均明显低于对照组,说明盐酸米诺环素软膏联合布洛芬治疗有利于牙周组织的重建和恢复。究其原因,可能是布洛芬能通过对患者组织内白三烯与前列腺素 E2 的释放产生抑制作用,从而减轻牙周的炎症反应,减少牙槽骨的吸收,为患者牙周组织恢复创造了有力条件^[30]。本文结果还显示了治疗后观察组各维度 SF-36 评分均显著高于对照组,生活质量显著提高。

综上所述,盐酸米诺环素软膏联合布洛芬治疗慢性牙周炎的疗效确切,且有效降低患者龈沟液 TNF- α 、IL-1 β 、IL-8 水平,有利于牙周组织的重建和恢复,提高患者生活质量,值得临床推广应用。

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