

doi: 10.13241/j.cnki.pmb.2017.09.044

布洛芬联合甲硝唑对慢性牙周炎龈沟液中细胞因子的影响

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摘要 目的:研究布洛芬联合甲硝唑对慢性牙周炎的疗效和对龈沟液中细胞因子的影响。**方法:**选择2013年1月~2015年12月在我院进行诊治的慢性牙周炎患者82例,随机分为两组,观察组给予布洛芬联合甲硝唑治疗,对照组给予甲硝唑治疗,比较两组的临床疗效、龈沟液中细胞因子的变化和抗氧化作用。**结果:**观察组的有效率为82.93%(34/41),明显高于对照组的65.85%(27/41)($P<0.05$);两组治疗后的龈沟出血指数、牙菌斑指数、附着水平和牙周袋深度均明显降低($P<0.05$),且观察组降低的更为明显($P<0.05$);两组治疗后的超敏C反应蛋白、肿瘤坏死因子、白介素-6和白介素-8水平均明显降低($P<0.05$),且观察组降低的更为明显($P<0.05$);两组治疗后的超氧化物歧化酶和谷胱甘肽过氧化物酶水平均明显升高($P<0.05$),丙二醛和一氧化氮水平均明显降低($P<0.05$),且观察组更为明显($P<0.05$);两组不良反应发生率相比无明显差异($P>0.05$)。**结论:**布洛芬联合甲硝唑对慢性牙周炎疗效显著,可以有效降低炎症水平,减少自由基损伤,有助于牙周组织的重建及恢复。

关键词:布洛芬;甲硝唑;慢性牙周炎;炎症因子;氧化应激

中图分类号:R781.4 **文献标识码:**A **文章编号:**1673-6273(2017)09-1763-04

Effect of Ibuprofen Combined with Metronidazole on Cytokines in Gingival Sulcus Fluid of Chronic Periodontitis

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ABSTRACT Objective: To study the effect of ibuprofen combined with metronidazole on chronic periodontitis and cytokines in gingival sulcus fluid. **Methods:** 82 patients with chronic periodontitis who were treated in our hospital from January 2013 to December 2015 were selected and divided into two groups randomly. The patients in observation group were treated with ibuprofen combined with metronidazole, and the patients in control group were treated with metronidazole. The curative effect, the changes of cytokines in gingival sulcus fluid and the antioxidation effect were compared. **Results:** After treatment, the effective rate of the observation group was 82.93% (34/41), significantly higher than 65.85% (27/41) of the control group ($P<0.05$); sulcus bleeding index, dental plaque index, attachment loss, depth of pocket were significantly decreased ($P<0.05$), and it was decreased more significantly in observation group ($P<0.05$); the superoxide discrimination enzymes and glutathione peroxidase levels were significantly increased ($P<0.05$), malondialdehyde and nitric oxide levels were significantly reduced ($P<0.05$), and it was more significantly observation group ($P<0.05$); the adverse reactions of two groups had no significant difference ($P>0.05$). **Conclusions:** Ibuprofen combined with metronidazole have significant effect on chronic periodontitis, which can effectively reduce the level of inflammation, reduce free radical damage, and contribute to the reconstruction and recovery of periodontal tissue.

Key words: Ibuprofen; Metronidazole; Chronic periodontitis; Inflammatory factor; Oxidative stress

Chinese Library Classification(CLC): R781.4 **Document code:** A

Article ID: 1673-6273(2017)09-1763-04

前言

慢性牙周炎是由于牙菌斑中的微生物引起的一种感染性疾病,属于口腔科的常见病和多发病。临床表现主要包括牙周袋形成、牙龈炎症、牙龈出血、牙槽骨吸收,甚至牙齿脱落^[1]。由

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(收稿日期:2016-07-13 接受日期:2016-07-30)

于慢性牙周炎症状重,病程长,组织破坏不可逆,对人们的日常工作、生活和学习造成严重影响。传统采用的牙周刮治、拔除患牙等机械除菌方法,不仅会加重患者的疼痛程度,严重损害患者牙根,而且复发率和不良反应发生率均较高,治疗效果较差^[2]。布洛芬可以通过抑制前列腺素的合成,减少对牙槽骨的吸收,有效控制牙周炎性反应^[3]。造成慢性牙周炎的主要致病菌为厌氧菌,因而甲硝唑对慢性牙周炎有较好的疗效^[4],但目前临床上尚未见关于这两种药物联合使用的研究报道。本研究主要探讨

了布洛芬联合甲硝唑对慢性牙周炎的疗效和对龈沟液中细胞因子的影响。

1 资料和方法

1.1 一般资料

选择 2013 年 1 月~2015 年 12 月在我院进行诊治的慢性牙周炎患者 82 例,患者均无严重全身性疾病,接受治疗前 3 个月均未使用过非甾体类药物和抗生素,5 mm< 牙周袋探诊深度<8 mm。随机分为两组,观察组 41 例,男 24 例,女 17 例;年龄 35~56 岁,平均(45.32± 12.25)岁。对照组 41 例,男 23 例,女 18 例;年龄 36~57 岁,平均(46.62± 11.03)岁。本研究获得我院伦理委员会的批准,所有患者均签署知情同意书。两组患者的年龄和性别分布比较无统计学差异(P>0.05),具有可比性。

1.2 研究方法

所有患者均进行根面平整、龈上洁治和龈下刮治,并给予常规的口腔卫生指导。对照组按照牙周袋的深度剪下合适大小的甲硝唑控释药膜,放入牙周袋底部,两天 1 次。观察组在此基础上,将布洛芬缓释凝胶缓慢注入牙周袋内,直至药物袋口溢出时停止注入,每周 1 次。两组均治疗 1 个月。

1.3 观察指标

比较两组患者治疗前后的龈沟出血指数、牙菌斑指数、附着水平和牙周袋深度;用 ELISA 法检测龈沟液中超敏 C 反应蛋白、肿瘤坏死因子、白介素 -6 和白介素 -8 水平;采用硫代巴比妥比色法检测丙二醛水平,黄嘌呤氧化酶法检测超氧化物歧化酶水平,DTNB 直接法检测谷胱甘肽过氧化物酶水平,硝酸还原酶法检测一氧化氮水平。

疗效标准:① 痊愈:牙龈疼痛和出血症状均消失;② 显效:牙龈疼痛和出血症状均明显改善,牙周袋深度降低超过 2 mm,牙龈指数降低 40% 以上;③ 有效:牙龈疼痛症状有所减轻,牙龈局部出血减少;④ 无效:各项症状均无任何改善。总有效率=(痊愈+显效+有效)/总数× 100%。

1.4 统计学分析

采用 SPSS15.00 软件进行统计学分析,计量资料以 $\bar{x} \pm s$ 表示,两组间对比用 t 检验,计数资料用 χ^2 检验,P<0.05 为差异有统计学意义。

2 结果

2.1 两组临床疗效比较

观察组的有效率为 82.93%(34/41),明显高于对照组的 65.85%(27/41)(P<0.05),见表 1。

表 1 两组临床疗效比较[例(%)]

Table 1 Comparison of the clinical effect between two groups [n(%)]

Groups	n	cured	Effective	Valid	Invalid	The total effect rate
Observation group	41	6	15	13	7	82.93 %*
Control group	41	4	12	11	14	65.85 %

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

2.2 两组牙周一般指标比较

两组治疗后的龈沟出血指数、牙菌斑指数、附着水平和牙

周袋深度均明显降低(P<0.05),且观察组降低的更为明显(P<0.05),见表 2。

表 2 两组牙周一般指标比较($\bar{x} \pm s$)

Table 2 Comparison of the periodontal general indexes between two groups($\bar{x} \pm s$)

Groups	n		Sulcus bleeding index(SBI)	Dental plaque index(PLI)	Attachment loss (AL,mm)	Depth of pocket (PD,mm)
Observation group	41	Before treatment	3.82± 0.13	2.53± 0.17	4.26± 0.17	5.53± 0.24
		After treatment	0.62± 0.07**	0.95± 0.06**	2.02± 0.20**	2.46± 0.12**
Control group	41	Before treatment	3.79± 0.12	2.61± 0.15	4.28± 0.19	5.48± 0.25
		After treatment	1.16± 0.16 [#]	1.24± 0.09 [#]	3.15± 0.12 [#]	4.12± 0.21 [#]

Note: Compared with control group, *P<0.05; compared with before treatment, [#]P<0.05.

2.3 两组炎症因子的比较

两组治疗后的超敏 C 反应蛋白 (hs-CRP)、肿瘤坏死因子

(TNF-α)、白介素 -6(IL-6)和白介素 -8(IL-8)水平均明显降低(P<0.05),且观察组降低的更为明显(P<0.05),见表 3。

表 3 两组炎症因子的比较($\bar{x} \pm s$)

Table 3 Comparison of the inflammatory factors between two groups($\bar{x} \pm s$)

Groups	n		hs-CRP(μmol / L)	TNF-α(ng / mL)	IL-6(ng / L)	IL-8(μg / L)
Observation group	41	Before treatment	23.12± 4.58	21.35± 10.12	6.42± 1.34	11.76± 0.24
		After treatment	9.26± 2.13**	10.13± 5.12**	2.02± 0.20**	2.46± 0.12**
Control group	41	Before treatment	22.75± 4.39	21.53± 11.26	6.45± 1.23	5.48± 0.25
		After treatment	13.45± 3.12 [#]	16.39± 6.17 [#]	3.54± 0.96 [#]	4.12± 0.21 [#]

Note: Compared with control group, *P<0.05; compared with before treatment, [#]P<0.05.

2.4 两组氧化应激指标的比较

两组治疗后的超氧化物歧化酶(SOD)和谷胱甘肽过氧化物酶(GSH-Px)水平均明显升高($P<0.05$),丙二醛(MDA)和一氧化

氮(NO)水平均明显降低($P<0.05$),且观察组更为明显($P<0.05$),见表4。

表4 两组氧化应激指标的比较($\bar{x} \pm s$)

Table 4 Comparison of the oxidative stress indexes between two groups($\bar{x} \pm s$)

Groups	n		SOD(nU/mL)	MDA(mmol/L)	eNO(μ mol/L)	GSH-Px(mg/L)
Observation group	41	Before treatment	21.42 $\pm$ 11.39	6.72 $\pm$ 1.35	62.31 $\pm$ 12.37	7.53 $\pm$ 2.16
		After treatment	48.32 $\pm$ 12.31 [#]	3.12 $\pm$ 0.23 [#]	27.45 $\pm$ 10.37 [#]	17.25 $\pm$ 2.37 [#]
Control group	41	Before treatment	22.15 $\pm$ 11.26	6.68 $\pm$ 1.26	61.53 $\pm$ 11.42	7.15 $\pm$ 2.26
		After treatment	34.17 $\pm$ 10.25 [#]	4.69 $\pm$ 1.32 [#]	39.15 $\pm$ 11.36 [#]	12.19 $\pm$ 2.53 [#]

Note: Compared with control group, ^{*} $P<0.05$; compared with before treatment, [#] $P<0.05$.

2.5 不良反应

观察组出现5例一过性疼痛,3例一过性红肿,对照组出现4例一过性疼痛,3例一过性红肿,经涂抹碘甘油后症状均消失。两组不良反应发生率相比无明显差异($P>0.05$)。

3 讨论

慢性牙周炎常见于牙骨质、牙周韧带和牙龈等部位,其主要发病机制为慢性牙龈炎症向牙周深部扩散而导致,如果治疗不及时易造成牙齿松动,甚至脱落,对患者的发音、美观和咀嚼功能造成严重影响,并且具有缓慢持续加重的临床特征,会继发性的破坏患者感染的牙槽、牙龈、牙骨质和牙周膜^[5-7]。慢性牙周炎的常规治疗方法主要包括牙周刮治、牙周洁治及根面平整等,能有效去除已发生病变的牙骨质及牙龈上下的牙菌斑,但仅使用上述机械方法的治疗效果往往不佳,因此需要配合药物进行治疗^[8-10]。

布洛芬能通过抑制慢性牙周炎患者组织内白三烯及前列腺素E2的释放,减轻牙周的炎症程度,从而减少牙槽骨的吸收,有效治疗慢性牙周炎^[11]。致病菌通过寄生于牙周袋内菌斑中,不断合成和释放毒素,破坏结合上皮细胞,并进入牙槽骨和牙龈组织,其所含的抗原成分可导致局部的免疫反应,严重破坏牙周组织,因而有效清除牙周袋内的细菌、控制感染是治疗慢性牙周炎的关键^[12,13]。甲硝唑主要用于对革兰阳性及革兰阴性厌氧菌造成的感染,可以通过透过厌氧菌微生物的细胞膜,破坏DNA链而抑制DNA的合成,进而阻断DNA转录,造成细菌死亡^[14,15]。慢性牙周炎的主要致病菌为牙龈单胞菌、普氏菌等厌氧菌,而甲硝唑主要作用于厌氧菌,从而有效治疗慢性牙周炎,对牙龈类杆菌具有较高的抑制率^[16,17]。本研究采用的甲硝唑控释药膜,不仅发挥药效时间长,提高病灶药物浓度,还能减少全身用药的副作用^[18]。

结果显示,观察组的有效率为82.93%(34/41),明显高于对照组的65.85%(27/41)($P<0.05$),两组治疗后的龈沟出血指数、牙菌斑指数、附着水平和牙周袋深度均明显降低($P<0.05$),且观察组降低的更为明显($P<0.05$),提示布洛芬联合甲硝唑对慢性牙周炎疗效显著,可有效改善患者的牙周状况,可能是由于二者作用机制不同,可以发挥协同作用,兼具减少骨吸收、缓解牙周炎症、广谱抗菌等功效。慢性牙周炎的发生发展与牙周袋中的微生物和牙菌斑紧密相关,当炎症发作时牙菌斑中的微生物

与脂多糖等分泌物可以通过受损的上皮进入到血液系统中,激活细胞免疫及体液免疫,并活化单核巨噬细胞,释放超敏C反应蛋白、肿瘤坏死因子、白介素-6和白介素-8等炎症因子^[19]。结果显示,两组治疗后的超敏C反应蛋白、肿瘤坏死因子、白介素-6和白介素-8水平均明显降低($P<0.05$),且观察组降低的更为明显($P<0.05$),提示布洛芬联合甲硝唑可以有控制慢性牙周炎患者的炎症反应。

局部浸润炎症反会有氧化产物生成,而自由基反应是造成牙周炎损伤的重要原因,自由基可以破坏生物膜,加重脂质过氧化反应^[20]。超氧化物歧化酶和谷胱甘肽过氧化物酶能清除超氧阴离子,保护细胞结构和功能免受损伤。牙周炎发生时,局部组织大量自由基产生,超氧化物歧化酶和谷胱甘肽过氧化物酶下降,造成超氧阴离子生成增多,两者的过表达可减轻这种损伤^[21]。一氧化氮在牙周病的病理过程中起到了重要的作用,随着牙周炎症的发生和发展,牙周组织内一氧化氮产量增多,一氧化氮通过龈沟上皮弥散至龈沟内,使龈沟液内的一氧化氮含量呈现逐渐升高的趋势^[22]。本文结果显示,两组治疗后的超氧化物歧化酶和谷胱甘肽过氧化物酶水平均明显升高($P<0.05$),丙二醛和一氧化氮水平均明显降低($P<0.05$),且观察组更为明显($P<0.05$),提示布洛芬联合甲硝唑可以有效减轻氧化应激反应,抑制氧自由基的生成及脂质过氧化,从而保护抗氧化酶,降低了自由基诱导的细胞毒性反应,降低超氧化物歧化酶和谷胱甘肽过氧化物酶的消耗,有效保护牙周组织。

综上所述,布洛芬联合甲硝唑对慢性牙周炎疗效显著,可以有效降低炎症水平,减少自由基损伤,有助于牙周组织的重建及恢复。

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