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• 临床研究 •

根管治疗术改善牙髓炎患者外周血炎性细胞因子水平及焦虑抑郁状态的研究

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【摘要】 目的 探讨根管治疗术对牙髓炎患者外周血炎性因子的改善及焦虑抑郁情绪的影响。**方法** 选取2021年6月至2022年6月在第四军医大学口腔医院牙体牙髓病科收治的155例牙髓炎患者为试验组, 采用根管治疗术治疗; 另选同期接受健康体检且口腔健康的155例人员为对照组, 比较两组的广泛性焦虑障碍量表(Generalized Anxiety Disorder-7, GAD-7)评分、抑郁症筛查量表(Patient Health Questionnaire-9, PHQ-9)评分; 同时观察试验组治疗前与治疗第3、6周后的GAD-7评分、PHQ-9评分与疼痛评分, 其中疼痛用视觉模拟量表(visual analogue scale, VAS)评定; 比较试验组治疗前与治疗第3、6周后外周血的炎性细胞因子白细胞介素-8(interleukin-8, IL-8)、白细胞介素-1 β (interleukin-1 β , IL-1 β)、肿瘤坏死因子- α (tumor necrosis factor- α , TNF- α)、C反应蛋白(C-reactive protein, CRP)水平。**结果** 试验组治疗前GAD-7评分、PHQ-9评分均高于对照组($P < 0.05$); 试验组治疗第3、6周后的GAD-7评分、PHQ-9评分均低于治疗前($P < 0.05$), 治疗第3周后与治疗第6周后的GAD-7评分以及PHQ-9评分差异无统计学意义($P > 0.05$); 试验组治疗第3、6周后的疼痛评分均低于治疗前($P < 0.05$), 治疗第6周的疼痛评分比治疗第3周低($P < 0.05$); 试验组治疗第3、6周后外周血的IL-8、IL-1 β 、TNF- α 、CRP水平均低于治疗前($P < 0.05$), 治疗第6周后外周血的IL-8、IL-1 β 水平低于治疗第3周后($P < 0.05$), 治疗第6周后外周血的TNF- α 、CRP水平与治疗第3周后差异无统计学意义($P > 0.05$)。**结论** 牙髓炎患者外周血存在较高的炎症水平与明显的焦虑、抑郁情绪, 根管治疗术能降低牙髓炎患者的炎症水平, 改善焦虑、抑郁情绪。

【关键词】 根管治疗术; 牙髓炎; 外周血; 炎性因子; 焦虑; 抑郁; 广泛性焦虑障碍量表; 抑郁症筛查量表; 视觉模拟量表; 白细胞介素; 肿瘤坏死因子- α ; C反应蛋白

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【Abstract】 Objective To investigate the effect of root canal therapy (RCT) on inflammatory cytokines level in peripheral blood, anxiety, and depression in patients with pulpitis. **Methods** A total of 155 patients with pulpitis admit-

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ted to the Stomatology Hospital of the Fourth Military Medical University from June 2021 to June 2022 were treated with root canal therapy. Another 155 persons who received health examinations during the same period were selected as the control group. The Generalized Anxiety Disorder-7 (GAD-7) scores and the Patient Health Questionnaire-9 (PHQ-9) scores of the two groups were compared. The GAD-7, PHQ-9 and pain scores of the test group before treatment and 3 and 6 weeks after treatment were compared. Pain was assessed with a visual analog scale (VAS). Inflammatory cytokine [interleukin-8 (IL-8), interleukin-1 β (IL-1 β), tumor necrosis factor- α (TNF- α), c-reactive protein (CRP)] levels in the test group before treatment and 3 and 6 weeks after treatment were compared. **Results** The GAD-7 and PHQ-9 scores in the test group were higher than those in the control group before treatment ($P < 0.05$). The GAD-7 and PHQ-9 scores in the test group at 3 and 6 weeks after treatment were lower than those before treatment ($P < 0.05$); there was no significant difference between the GAD-7 and PHQ-9 scores at 3 and 6 weeks after treatment ($P > 0.05$). The pain scores of the experimental group at 3 and 6 weeks after treatment were lower than those before treatment ($P < 0.05$), and the pain scores 6 weeks after treatment were lower than those at 3 weeks after treatment ($P < 0.05$). The levels of IL-8, IL-1 β , TNF- α and CRP in the peripheral blood of the experimental group were lower 3 and 6 weeks after treatment than before ($P < 0.05$), and the levels of IL-8 and IL-1 β in the peripheral blood at 6 weeks after treatment were significantly lower than at 3 weeks after treatment ($P < 0.05$). The levels of TNF- α and CRP in the peripheral blood at 6 weeks after treatment were not significantly different from those at 3 weeks after treatment ($P > 0.05$). **Conclusion** The peripheral blood of patients with pulpitis has a high level of inflammatory cytokines, and the patients suffer from obvious anxiety and depression. Root canal therapy can relieve their anxiety and depression by reducing their level of inflammatory cytokines in peripheral blood.

【Key words】 root canal therapy; pulpitis; peripheral blood; inflammatory cytokines; anxiety; depression; Generalized Anxiety Disorder-7; Patient Health Questionnaire-9; visual analog scale; interleukin; tumor necrosis factor- α ; C-reactive protein

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牙髓炎是细菌感染引起的口腔颌面部最常见的炎症性疾病^[1],患者在发病过程中常伴有不同程度的疼痛和肿胀^[2],一般止痛药对患者疼痛缓解效果不佳,牙髓炎如果不及时进行有效治疗,很容易发生牙髓坏死甚至波及到根尖周组织,进一步加重患者的疼痛^[3]。剧烈或放散性的疼痛易使大多数患者产生焦虑、烦躁等不良情绪。如果牙髓炎未得到有效治疗,长期的疼痛可能会引发患者产生抑郁倾向,进一步危害身体健康,因此,降低或消除疼痛是减少牙髓炎患者不良情绪的前提条件^[4]。

目前,根管治疗术是牙髓炎最有效的治疗方法^[5],通过机械预备和化学消毒的方法清除髓腔内的感染物,通过药物消毒以及严密充填清除感染,封闭空腔,消灭细菌的生存空间,防止根管再感染^[6]。根管治疗可减轻牙髓炎患者的疼痛,提高其生命质量;但根管治疗术是否能够减轻牙髓炎患者由于疼痛和疾病原因产生的不良情绪仍鲜有

报道。

本研究通过比较牙髓炎患者根管治疗前后的外周血炎性细胞因子水平及广泛性焦虑障碍量表 (Generalized Anxiety Disorder, GAD-7) 评分、抑郁症筛查量表 (Patient Health Questionnaire-9, PHQ-9) 评分、疼痛评分,探讨牙髓炎患者根管治疗前后的外周血炎性因子及焦虑抑郁情绪的变化。

1 资料和方法

1.1 研究对象

选取2021年6月至2022年6月由第四军医大学口腔医院牙体牙髓病科收治的155例牙髓炎患者为试验组,进行根管治疗术,其中急性牙髓炎114例,慢性牙髓炎41例。纳入标准:①参照《维护牙周健康的中国口腔医学多学科专家共识(第一版)》^[7],确诊为牙髓炎;②认知正常;③无传染性疾病。排除标准:①合并其他口腔疾病;②精神疾病

患者;③缺少重要的临床资料;④恶性肿瘤患者;⑤存在传染性疾病。另选同期接受健康体检且口腔健康(口腔卫生良好,全口牙齿未见明显异常)的155例人员作为对照组,纳入标准:①无任何口腔疾病;②成年人;③认知正常。排除标准:①口腔健康的未成年人;②精神疾病患者;③存在口腔

疾病;④重要器官功能障碍患者。患者对研究知情并自愿签署知情同意书。本研究通过第四军医大学口腔医院伦理委员会批准(批准号:IRB-REV-2020088)。

对比两组研究对象的性别、年龄、受教育程度等一般资料,差异不具有统计学意义($P > 0.05$,表1)。

表1 牙髓炎患者与对照组的一般资料比较

Table 1 Comparison of general data between pulpitis patients and control group

 $n(\%) \bar{x} \pm s$

Group	n	Gender		Age (year)	Education level			
		Male	Female		Primary school and below	Junior high school	High school	College degree or above
Pulpitis group	155	84 (54.19)	71 (45.81)	38.65 $\pm$ 2.12	25 (16.13)	57 (36.77)	49 (31.61)	24 (15.49)
Control group	155	78 (50.32)	77 (49.68)	38.74 $\pm$ 2.16	20 (12.90)	52 (33.55)	53 (34.19)	30 (19.36)
χ^2/t	-	0.300		0.370	0.420	0.227	0.151	0.520
P	-	0.584		0.712	0.517	0.633	0.698	0.471

1.2 主要试剂和仪器

根管测量仪(Raypex5, VDW, 德国); NiTi器械 ProTaper Gold(Dentsply Sirona, Ballaigues, 瑞士); 超声器械(Komet Dental, Lemgo, 德国); 氢氧化钙糊剂(ApexCal®, Ivoclar Vivadent, Liechtenstein); AH Plus 封闭剂(Dentsply Sirona, 瑞士); 肿瘤坏死因子- α (tumor necrosis factor- α , TNF- α) ELISA 试剂盒(#PT518, Beyotime Biotechnology, 中国); 白细胞介素-8(interleukin-8, IL-8) ELISA 试剂盒(#PI641, Beyotime Biotechnology, 中国)、白细胞介素-1 β (interleukin-1 β , IL-1 β) ELISA 试剂盒(#PI305, Beyotime Biotechnology, 中国); C反应蛋白(C-reactive protein, CRP)检测试剂盒(#PC190, Beyotime Biotechnology, 中国)。

1.3 方法

1.3.1 根管治疗术 对试验组患牙采用根管治疗术, 步骤如下: 牙齿常规开髓, 建立直线入路, 使用根管测量仪确定根管工作长度, NiTi器械 ProTaper Gold 进行根管的机械预备, NaOCl(2.5%)溶液结合超声器械荡洗根管, 纸尖干燥根管, 使用氢氧化钙糊剂消毒根管。2周后复诊, 采用热熔垂直加压技术(Schilder 技术)和 AH Plus 封闭剂充填根管。2周后患牙进行嵌体或者冠修复, 定期随访。

1.3.2 GAD-7评分 GAD-7量表共包括7个条目, 每个条目评分标准为0~3分: 0分代表“完全不会”; 1分代表“好几天”; 2分代表“超过一周”; 3分代表“几乎每天”。总分为7个条目评分之和: 0~4分代

表没有焦虑症状; 5~9分代表轻度焦虑症状; 10~14分代表中度焦虑症状; 15~21分代表重度焦虑症状。量表获取方法参照卯骏聪^[8]等的研究。

1.3.3 PHQ-9评分 PHQ-9量表共包括9个条目, 每个条目评分标准为0~3分: 0分代表“几乎不会”; 1分代表“有几天”; 2分代表“一半以上”; 3分代表“几乎每天”。总分为9个条目评分之和: 0~4分代表没有抑郁症状; 5~9分代表可能存在轻度抑郁症状; 10~14分代表可能存在中度抑郁症状; 15~19分代表可能存在中重度抑郁症状; 20~27分代表可能存在重度抑郁症状。量表获取方法参照韦振媚^[9]等的研究。

1.3.4 疼痛评分 疼痛评分采用视觉模拟量表(visual analogue scale, VAS)进行评估^[10], 总分范围为0~10分: 0分代表“无痛”; 1~3分代表“轻度疼痛”; 4~6分代表“中度疼痛”; 7~10分代表“剧烈疼痛”; 评分与疼痛程度呈正比。

1.3.5 炎症因子检测 在治疗前和治疗第3、6周后抽取患者空腹外周静脉血, 采用酶联免疫吸附法测定患者血清炎症因子IL-8、IL-1 β 、TNF- α 的表达水平, 免疫比浊法测定CRP水平。

1.4 观察指标

比较对照组与试验组治疗前的GAD-7评分以及PHQ-9评分; 比较试验组治疗前与治疗第3、6周后的GAD-7评分、PHQ-9评分、疼痛评分及炎症细胞因子水平。

1.5 统计学分析

采用SPSS21.0软件进行统计学分析, 进行正态

性检验,符合正态分布的计量资料用均数 $\pm$ 标准差表示,两组比较用 t 检验,多组比较用方差分析;计数资料采用卡方检验验证进行比较, $P < 0.05$ 为差异有统计学意义。

2 结果

2.1 牙髓炎患者根管治疗前与对照组的焦虑、抑郁情绪评分比较

牙髓炎患者根管治疗前GAD-7评分以及PHQ-9评分均高于对照组,差异具有统计学意义($P < 0.05$,表2)。

表2 牙髓炎患者根管治疗前与对照组的焦虑、抑郁情绪评分比较

Table 2 Comparison of anxiety and depression scores between patients with pulpitis before root canal therapy and the control group $n=155, \bar{x} \pm s$		
Group	GAD-7	PHQ-9
Pulpitis group	13.58 ± 0.96	10.55 ± 0.83
Control group	4.12 ± 0.13	3.15 ± 0.37
t	121.574	101.382
P	< 0.001	< 0.001

GAD-7: Generalized Anxiety Disorder-7; PHQ-9: Patient Health Questionnaire-9

2.2 牙髓炎患者根管治疗前与治疗第3周、第6周后的焦虑、抑郁情绪评分比较

治疗第3、6周后,牙髓炎患者的GAD-7评分以及PHQ-9评分均低于治疗前,差异有统计学意义($P < 0.05$);治疗第3周后与治疗第6周后的GAD-7评分以及PHQ-9评分差异无统计学意义($P > 0.05$,表3)。

表3 牙髓炎患者根管治疗前与治疗第3、6周后的焦虑、抑郁情绪评分比较

Table 3 Comparison of anxiety and depression scores of pulpitis patients before root canal therapy and at 3 and 6 weeks after treatment $n=155, \bar{x} \pm s$		
Group	GAD-7	PHQ-9
Before treatment	13.58 ± 0.96	10.55 ± 0.83
After 3 weeks of treatment	$6.54 \pm 0.13^{(1)}$	$4.77 \pm 0.56^{(1)}$
After 6 weeks of treatment	$6.51 \pm 0.15^{(1)}$	$4.64 \pm 0.61^{(1)}$
F	165.743	189.215
P	< 0.001	< 0.001

GAD-7: Generalized Anxiety Disorder-7; PHQ-9: Patient Health Questionnaire-9. 1): compared with before treatment, $P < 0.05$

2.3 牙髓炎患者根管治疗前与治疗第3、6周后的疼痛评分比较

与治疗前相比,牙髓炎患者治疗第3、6周后的疼痛评分呈下降趋势,均低于治疗前,差异有统计学意义($P < 0.05$);治疗第3周与治疗第6周的疼痛评分比较,差异有统计学意义($P < 0.05$,表4)。

表4 牙髓炎患者根管治疗前与治疗第3、6周后的疼痛评分比较

Table 4 Comparison of pain scores of pulpitis patients before root canal therapy and at 3 and 6 weeks

after therapy $n=155, \bar{x} \pm s$	
Group	Pain score
Before treatment	8.76 ± 1.04
After 3 weeks of treatment	$4.84 \pm 0.21^{(1)}$
After 6 weeks of treatment	$2.49 \pm 0.05^{(1)(2)}$
F	97.732
P	< 0.001

1): compared with before treatment, $P < 0.05$; 2): compared with after 3 weeks of treatment, $P < 0.05$

2.4 牙髓炎患者根管治疗前与治疗第3、6周后外周血的炎性细胞因子水平比较

治疗第3、6周后,牙髓炎患者外周血的IL-8、IL-1 β 、TNF- α 、CRP水平均低于治疗前,差异有统计学意义($P < 0.05$);治疗第6周后外周血的IL-8、IL-1 β 水平低于治疗第3周后,差异有统计学意义($P < 0.05$);治疗第6周后外周血的TNF- α 、CRP水平与治疗第3周后差异无统计学意义($P > 0.05$),见表5。

3 讨论

牙髓炎引起的神经疼痛给患者带来极大痛苦,影响患者进食及日常生活^[11]。根管治疗术通过清除根管系统内的感染物质,封闭根管系统可以改善患者的临床症状^[12]。神经炎症在疼痛的产生中起着至关重要的作用,许多体外和动物疼痛模型已证明促炎细胞因子对外周和中枢疼痛感受的作用^[13-14]。在人体内,局部和全身表达的促炎细胞因子也被认为是疼痛的介质,其中,TNF- α 、IL-1 β 和IL-8在神经损伤后存在痛觉过敏效应,CRP是一种主要的急性期蛋白,在严重炎症状态下,其浓度可能增加1 000倍以上,因此观察其水平变化情况有助于了解评估患者的治疗效果^[15-16]。本研究

表5 牙髓炎患者根管治疗前与治疗第3、6周后外周血的炎性细胞因子水平比较

Table 5 Comparison of levels of inflammatory cytokines in peripheral blood before treatment and at 3 and

Group	6 weeks after treatment			
	IL-8/ (μg/L)	IL-1β/ (pg/mL)	TNF-α/ (μg/L)	CRP/ (mg/L)
Before treatment	30.45 ± 1.74	108.36 ± 2.33	10.47 ± 0.56	24.89 ± 1.96
After 3 weeks of treatment	13.82 ± 0.52 ¹⁾	92.35 ± 1.48 ¹⁾	6.21 ± 0.17 ¹⁾	7.32 ± 0.55 ¹⁾
After 6 weeks of treatment	12.56 ± 0.37 ¹⁾²⁾	91.88 ± 1.35 ¹⁾²⁾	6.18 ± 0.22 ¹⁾	7.26 ± 0.49 ¹⁾
<i>F</i>	124.658	95.329	107.984	113.593
<i>P</i>	< 0.001	< 0.001	< 0.001	< 0.001

IL-8: interleukin-8; IL-1β: interleukin-1β; TNF-α: tumor necrosis factor- α; CRP: C-reactive protein. 1): compared with before treatment, $P < 0.05$;

2): compared with after 3 weeks of treatment, $P < 0.05$

中, 试验组治疗第3、6周后的疼痛评分低于治疗前, 治疗第3、6周后外周血的IL-8、IL-1β、TNF-α、CRP水平低于治疗前, 证明根管治疗术治疗牙髓炎可显著减轻疼痛和机体的炎性反应, 降低炎性细胞因子水平。

近年来, 越来越多的证据表明应激诱导产生的炎症因子会促进抑郁, 可能加剧抑郁症状。研究表明, 促炎细胞因子升高会导致抑郁行为^[17]。本研究发现试验组GAD-7评分以及PHQ-9评分均高于对照组, 说明相比于健康人群, 牙髓炎患者存在严重的不良情绪, 以焦虑、抑郁为主, 与上述研究结果相符。Radat等^[18]通过流行病学研究发现42%的神经疼痛患者合并有抑郁症状, 而37%的抑郁患者也伴随疼痛症状。Zhu等^[19]认为患者疼痛缓解后, 其抑郁症状往往也相应得到缓解。

本研究试验组治疗第3、6周后的GAD-7评分以及PHQ-9评分低于治疗前, 表明根管治疗术使患者的疼痛及消极情绪得到有效控制, 可能与降低炎性因子水平有关。牙髓炎患者产生焦虑、抑郁等负面情绪的原因有多种, 除上述提到的疼痛、炎性因子水平过高外, 高昂的治疗费用、较低的医疗服务质量同样可引发负面情绪, 甚至中断治疗。另外, 急性牙髓炎患者与慢性牙髓炎患者的负面情绪产生原因及严重程度不同, 慢性牙髓炎病程长, 但疼痛程度没有急性牙髓炎剧烈, 本次研究纳入患者大多数为急性牙髓炎, 因此治疗前疼痛评分较高。本研究还显示随着治疗时间的延长, 患者炎性因子水平、疼痛评分逐渐下降, 焦虑抑郁症状逐渐减轻, 证明根管治疗术对改善牙髓炎患者炎性因子及焦虑抑郁状态有良好效果。

4 小 结

综上所述, 牙髓炎患者存在较高的炎症水平

与明显的焦虑、抑郁情绪, 根管治疗术能够在降低炎症水平的基础上改善焦虑、抑郁情绪。

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