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龈沟液炎症因子及 TSP-1 在拔牙正畸患者中的表达情况 及发生牙周疾病的影响因素分析*

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摘要 目的:探讨龈沟液炎症因子及 TSP-1 在拔牙正畸患者中的表达情况及发生牙周疾病的影响因素。**方法:**选取我院 2020 年 8 月到 2023 年 8 月收治的 80 例拔牙正畸治疗患者进行回顾性分析,分别取所有患者正畸前、正畸后 1 个月、3 个月及正畸结束时的龈沟液样本检测肿瘤坏死因子- α (TNF- α)、白细胞介素-1 β (IL-1 β)、白细胞介素-6(IL-6)、血小板反应蛋白-1(TSP-1)表达水平。随后依照患者正畸治疗过程中是否患有牙周疾病将其分为牙周疾病组($n=36$)及非牙周疾病组($n=44$),对比两组患者正畸前及正畸结束时的 TNF- α 、IL-1 β 、IL-6、TSP-1 表达水平,对比两组患者一般情况,采用 logistics 回归模型分析拔牙正畸患者牙周疾病的影响因素。**结果:**80 例拔牙正畸患者中正畸后 1 个月、3 个月 TNF- α 、IL-1 β 、IL-6、TSP-1 水平升高,正畸后 3 个月到正畸结束时 TNF- α 、IL-1 β 、IL-6、TSP-1 水平趋于平稳,但正畸后 1 个月、3 个月及结束时明显高于正畸前($P<0.05$);牙周疾病组与非牙周疾病组患者正畸前、正畸后 TNF- α 、IL-1 β 、IL-6、TSP-1 表达水平对比差异显著,牙周疾病组明显高于非牙周疾病组($P<0.05$);牙周疾病组及非牙周疾病组患者性别、年龄、BMI 对比无明显差异($P>0.05$),牙周疾病组及非牙周疾病组患者正畸治疗时间、拔牙数量、正畸方式、口腔清洁度对比差异显著($P<0.05$);logistic 回归分析结果表明:TNF- α 、IL-1 β 、IL-6、TSP-1、正畸方式、口腔清洁度为拔牙正畸患者牙周疾病的独立危险因素($P<0.05$)。**结论:**拔牙正畸患者随着正畸时间延长龈沟液炎症因子及 TSP-1 水平明显升高,且 TNF- α 、IL-1 β 、IL-6、TSP-1、正畸方式、口腔清洁度为拔牙正畸患者牙周疾病的独立危险因素。

关键词:龈沟液;炎症因子;血小板反应蛋白-1;拔牙正畸;牙周疾病;炎症反应

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Analysis of the Expression of Inflammatory Factors and TSP-1 in Gingival Crevicular Fluid in Orthodontic Patients Undergoing Tooth Extraction and the Influencing Factors of Periodontal Disease Occurrence*

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ABSTRACT Objective: To explore the expression of inflammatory factors and TSP-1 in gingival crevicular fluid in patients undergoing orthodontic extraction, and the influencing factors of periodontal disease. **Methods:** Eighty patients admitted to our hospital from August 2020 to August 2023 for orthodontic treatment of extracted teeth were retrospectively analyzed, and gingival sulcus fluid samples were taken from all the patients before orthodontic treatment, 1 month after orthodontic treatment, 3 months after orthodontic treatment, and at the end of orthodontic treatment to detect the tumor necrosis factor-alpha (TNF-alpha), interleukin-1beta (IL-1beta), interleukin-6 (IL-6), and platelet reactive protein-1 (TSP-1) expression levels. Subsequently, the patients were divided into periodontal disease group ($n=36$) and non-periodontal disease group ($n=44$) according to whether they suffered from periodontal disease during orthodontic treatment, compared the expression levels of TNF- α , IL-1 β , IL-6, and TSP-1 of the patients in the two groups before orthodontic treatment and at the end of orthodontic treatment, and compared the general conditions of the patients in the two groups, and then analyzed the influence factors of periodontal diseases in patients with extracted teeth in orthodontics with the use of logistic regression model. **Disease Influencing Factors. Results:** TNF- α , IL-1 β , IL-6, and TSP-1 levels were elevated at 1 month and 3 months after orthodontic treatment in 80 patients with extracted teeth, and TNF- α , IL-1 β , IL-6, and TSP-1 levels leveled off from 3 months to the end of orthodontic treatment, but were significantly higher than those before orthodontic treatment at 1 month, 3 months, and at the end of orthodontic treatment ($P<0.05$); there were significant differences in the expression levels of TNF- α , IL-1 β , IL-6, and TSP-1 in patients in the periodontal diseases group compared to those in the non periodontal diseases group, and the expression levels in the periodontal diseases group were significantly higher than those in the non periodontal diseases group ($P<0.05$). There were significant differences in the expression levels of TNF- α ,

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IL-1 β , IL-6, and TSP-1 between patients in the pre-orthodontic and post-orthodontic groups, and the periodontal disease group was significantly higher than the non-periodontal disease group ($P<0.05$); there were no significant differences in the comparison of gender, age, and BMI between patients in the periodontal disease group and the non-periodontal disease group ($P>0.05$), and there were no significant differences in the duration of orthodontic treatment, number of extractions, oral cavity, oral cavity, and oral health of patients in the periodontal disease group and the non-periodontal disease group ($P<0.05$). number, orthodontic method, and oral cleanliness were compared significantly ($P<0.05$); logistic regression analysis showed that TNF- α , IL-1 β , IL-6, TSP-1, orthodontic method, and oral cleanliness were independent risk factors for periodontal disease in patients with extracted teeth and orthodontic treatment ($P<0.05$). **Conclusion:** Inflammatory factors of gingival crevicular fluid and TSP-1 levels increased significantly in orthodontic patients with prolonged orthodontic time, and TNF- α , IL-1 β , IL-6, TSP-1, orthodontic mode and oral cleanliness were independent risk factors for periodontal disease in orthodontic patients.

Key words: Gingival crevicular fluid; Inflammatory factors; Platelet reactive protein-1; Tooth extraction orthodontics; Periodontal diseases; Inflammatory reaction

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前言

口腔正畸治疗作为治疗牙齿和口腔颌面部畸形的重要方式,但正畸治疗过会改变牙周组织,尤其是需拔牙正畸治疗的患者,清洁牙齿困难程度加大,导致大量细菌积蓄,引发炎症。长期口腔环境的改变会增加牙槽骨吸收风险,诱发骨流失^[1-3]。因此,及时分析拔牙正畸患者正畸治疗过程中牙周炎症反应水平,及时采取措施进行干预,预防牙周疾病的发生具有重要价值。牙周疾病的病理表现为组织液渗出、炎症细胞浸润及牙周组织破坏,据报道^[4],龈沟液中炎症细胞可分泌多种细胞因子,参与口腔炎症反应。血小板反应蛋白-1(thrombospondin-1, TSP-1)广泛分布于多种组织的胞外基质中,是一种生长因子,能够促进血管内皮细胞增殖和新生血管生成^[5]。研究发现^[6],隐形矫治器正畸患者龈沟液 TSP-1 水平随着正畸时间延长,其水平显著升高,从而诱导牙周炎症反应发生。因此,本研究以我院 80 例拔牙正畸治疗患者进行回顾性分析,探讨龈沟液炎症因子及 TSP-1 在拔牙正畸患者中的表达情况及发生牙周疾病的影响因素,具体报道如下。

1 资料与方法

1.1 一般资料

选取我院 2020 年 8 月到 2023 年 8 月收治的 80 例拔牙正畸治疗患者进行回顾性分析。80 例患者中男性 36 例,女性 44 例;年龄为 10~32 岁,平均(21.25 \pm 3.64)岁。本研究经我院伦理委员会批准。

1.2 纳排标准

纳入标准:符合正畸治疗指征,且需要拔牙正畸^[7];首次进行口腔正畸治疗;临床资料完整;患者对本研究知情同意。

排除标准:正畸前合并牙周疾病者;合并认知功能障碍或精神类疾病依从性差者;合并颌骨囊肿、畸形者;合并严重脏器功能障碍者;合并血液相关疾病者。

1.3 方法

龈沟液炎症因子及 TSP-1 检测方法:分别取所有患者正畸前、正畸后 1 个月、3 个月及正畸结束时的龈沟液样本在零下 80 $^{\circ}$ C 并向内冻存,待样本提取完成后进行统一检测,取出样本放置在零下 4 $^{\circ}$ C 下解冻,离心取上层清液,应用 ELISA 检测样

本中肿瘤坏死因子- α (TNF- α)、白细胞介素-1 β (IL-1 β)、白细胞介素-6(IL-6)、血小板反应蛋白-1(TSP-1)表达水平。

牙周疾病诊断标准:牙周炎诊断标准,^① X 线片检查提示牙槽骨出现不同程度吸收情况;^② 牙周袋内的牙周联合点位置 1 处及 1 处以上;^③ 牙周切口出血点数 2 个以上;牙周袋深度 \geq 4 mm。满足上述 2 项或以上可诊断为牙周炎。牙龈炎诊断标准,^④ 牙石或牙菌斑在牙齿表面可见;^⑤ 牙龈萎缩;^⑥ 牙龈软组织肿胀或增厚;^⑦ 牙龈出现疼痛与不适感;^⑧ 出现牙龈出血情况,在刷牙后更为明显;^⑨ 牙龈充血及红肿,满足上述 2 项或以上可诊断为牙龈炎^[8]。

1.4 统计学方法

采取 SPSS 23.0,计数资料以(n/%)表示, χ^2 检验;计量资料用($\bar{x}\pm s$)表示,t 检验;以 $P<0.05$ 为差异有统计学意义。

2 结果

2.1 正畸前后龈沟液炎症因子及 TSP-1 水平对比

80 例拔牙正畸患者中正畸后 1 个月、3 个月 TNF- α 、IL-1 β 、IL-6、TSP-1 水平升高,正畸后 3 个月到正畸结束时 TNF- α 、IL-1 β 、IL-6、TSP-1 水平趋于平稳,但正畸后 1 个月、3 个月及结束时明显高于正畸前($P<0.05$),如表 1 所示。

2.2 拔牙正畸治疗合并牙周疾病患者龈沟液炎症因子及 TSP-1 水平分析

牙周疾病组与非牙周疾病组患者正畸前、正畸后 TNF- α 、IL-1 β 、IL-6、TSP-1 表达水平对比差异显著,牙周疾病组明显高于非牙周疾病组($P<0.05$),如表 2 所示。

2.3 拔牙正畸患者牙周疾病单因素分析

牙周疾病组及非牙周疾病组患者性别、年龄、BMI 对比无明显差异($P>0.05$),牙周疾病组及非牙周疾病组患者正畸治疗时间、拔牙数量、正畸方式、口腔清洁度对比差异显著($P<0.05$),如表 3 所示。

2.4 拔牙正畸患者牙周疾病多因素分析

对表 2 及表 3 中具有统计学差异的指标进行赋值,logistic 回归分析结果表明:TNF- α 、IL-1 β 、IL-6、TSP-1、正畸方式、口腔清洁度为拔牙正畸患者牙周疾病的独立危险因素($P<0.05$),如表 4 所示。

表 1 正畸前后龈沟液炎症因子及 TSP-1 水平对比($\bar{x} \pm s$)

Table 1 Comparison of inflammatory factors and TSP-1 levels in gingival crevicular fluid before and after orthodontics($\bar{x} \pm s$)

Group	n	TNF- α (ng/L)	IL-1 β (ng/L)	IL-6(ng/mL)	TSP-1(ng/mL)
Before orthodontic treatment	80	21.46 \pm 2.46	30.80 \pm 3.82	3.27 \pm 0.35	90.53 \pm 6.84
One month after orthodontic treatment	80	26.34 \pm 4.75	35.57 \pm 8.24	4.23 \pm 1.16	103.54 \pm 7.93
3 months after orthodontic treatment	80	30.53 \pm 5.23	39.64 \pm 5.74	4.63 \pm 1.42	153.57 \pm 18.48
End of orthodontic treatment	80	28.68 \pm 4.75	39.24 \pm 6.85	4.32 \pm 1.05	148.85 \pm 23.65
F	-	55.287	36.493	33.964	45.365
P	-	<0.001	<0.001	<0.001	<0.001

表 2 拔牙正畸治疗合并牙周疾病患者龈沟液炎症因子及 TSP-1 水平分析($\bar{x} \pm s$)

Table 2 Analysis of inflammatory factors and TSP-1 levels in gingival crevicular fluid in patients with periodontal disease($\bar{x} \pm s$)

Groups	n	TNF- α (ng/L)		IL-1 β (ng/L)		IL-6(ng/mL)		TSP-1(ng/mL)	
		Before orthodontic treatment	After orthodontic treatment	Before orthodontic treatment	After orthodontic treatment	Before orthodontic treatment	After orthodontic treatment	Before orthodontic treatment	After orthodontic treatment
Periodontal disease group	36	25.67 \pm 5.02	31.65 \pm 4.54*	35.75 \pm 4.95	45.50 \pm 5.14*	3.68 \pm 4.62	5.30 \pm 1.28*	83.58 \pm 6.15	166.26 \pm 29.42*
Non periodontal disease group	44	20.52 \pm 4.95	25.75 \pm 5.23*	24.35 \pm 5.02	33.60 \pm 4.86*	2.27 \pm 3.75	4.00 \pm 1.05*	98.36 \pm 10.52	130.51 \pm 28.37*
t		5.702	9.227	7.566	8.336	8.104	9.939	7.472	8.343
P		<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001

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

表 3 拔牙正畸患者牙周疾病单因素分析

Table 3 Single factor analysis of periodontal disease in orthodontic patients undergoing tooth extraction

Category	Periodontal disease group(n=36)	Non periodontal disease group(n=44)	χ^2/t	P
Gender				
Male	16	20	0.270	0.604
Woman	20	24		
Age (years)	25.30 \pm 3.57	25.21 \pm 3.42	0.063	0.946
BMI(kg/m ²)	23.14 \pm 2.34	23.19 \pm 3.29	0.063	0.950
Orthodontic treatment time (months)	25.54 \pm 4.31	18.48 \pm 4.51	7.105	<0.001
Number of extracted teeth (pieces)	2.13 \pm 0.42	1.43 \pm 0.32	8.458	<0.001
Orthodontic methods				
Twin-Block Appliance	10	14	8.780	0.012
Implicit orthodontic appliances without brackets	8	21		
Straight wire arch correction technique	18	9		
Oral cleanliness				
Differ from	11	4	15.510	<0.001
Same as	20	16		
Good	5	24		

表 4 拔牙正畸患者牙周疾病多因素分析

Table 4 Multivariate analysis of periodontal diseases in orthodontic patients undergoing tooth extraction

Variable	β	SE(β)	Wald χ^2	OR	95%CI	P
TNF- α	2.313	0.652	3.135	1.789	1.447~3.682	<<0.001
IL-1 β	2.457	0.584	5.265	2.791	1.457~5.745	<<0.001
IL-6	2.546	0.631	3.757	2.146	1.534~3.693	<<0.001
TSP-1	3.241	0.642	4.636	2.845	1.726~4.361	<<0.001
Orthodontic treatment time	1.245	0.326	1.536	0.658	0.431~1.221	0.424
Number of extracted teeth	1.231	0.412	1.787	0.857	0.542~1.336	0.425
Orthodontic methods	2.314	0.597	3.241	2.526	1.873~4.547	<<0.001
Oral cleanliness	1.645	0.554	5.642	1.726	1.321~3.564	<<0.001

3 讨论

正畸治疗会对牙周组织进行改建,导致牙周组织长期受到正畸力干预,破骨细胞生成活跃,发生牙槽骨吸收,诱发炎症^[9,10]。此外,长期佩戴矫治器可阻碍口腔清洁剂刷牙自洁,致使口腔环境变差,影响牙周健康状况,诱发牙周疾病^[11,12]。因此,本研究通过分析正畸治疗过程中龈沟液炎症因子及 TSP-1 水平,及时了解正畸治疗过程中患者牙周炎症反应情况,并分析牙周疾病的影响因素,以期对拔牙正畸治疗过程中牙周疾病的控制及预防提供参考意见。

本研究结果表明,80 例拔牙正畸患者中正畸后 1 个月、3 个月 TNF- α 、IL-1 β 、IL-6、TSP-1 水平升高,正畸后 3 个月到正畸结束时 TNF- α 、IL-1 β 、IL-6、TSP-1 水平趋于平稳,但正畸后 1 个月、3 个月及结束时明显高于正畸前($P<0.05$),与 De Ridder L 等^[13]研究结果相符。De Ridder L 等研究发现,随着正畸治疗时间延长,龈沟液中炎症因子表达水平升高,代表正畸治疗可能对牙周健康产生一定负面影响。分析原因为,由于慢性牙周炎早期出现的急性炎症病变,大量炎症介质被释放到龈沟液及牙周组织中,而 TNF- α 、IL-1 β 、IL-6 同样也是慢性牙周病病理发展过程中的早期代表性炎症反应核心介质^[14,15]。另外,正畸牙齿移动初期阶段为机体急性炎症过程,虽然个体差异会导致炎症反应水平存在偏差,但研究表明^[16],TSP-1 为促进血管内皮细胞增殖的重要标志物,可诱导骨肿瘤增殖。然而,随着正畸治疗时间延长牙槽骨吸收 TSP-1 水平出现明显变化^[17]。另外,还可能与 TSP-1 介导炎症反应相关^[18];牙周疾病组与非牙周疾病组患者正畸前、正畸后 TNF- α 、IL-1 β 、IL-6、TSP-1 表达水平对比差异显著,牙周疾病组明显高于非牙周疾病组($P<0.05$),与 Wafaie K 等^[19]、Wang CW 等^[20]研究相符。Wafaie K 等研究发现,TNF- α 等炎症因子与牙槽骨吸收量成正比。Wang CW 等研究也发现,IL-1 β 、IL-6 等龈沟液炎症因子水平升高可介导牙周疾病发生。分析原因为,牙周组织在正畸治疗过程中由于清洁受限或正畸压力影响,容易受到损伤、细菌毒素及微生物刺激,巨噬细胞和单核细胞分泌 IL-1 β 、IL-6 进而激活破骨细胞,致使牙周结缔组织损害、牙槽骨吸收^[21,22]。TNF- α 可刺激趋化因子及

黏附因子表达,增强破骨细胞活性,使得基质细胞凋亡,牙周发生软组织损伤,同时阻碍牙周软组织修复^[23,24]。当前临床上针对 TSP-1 与牙周疾病的相关研究较少。但笔者认为,可能与 TSP-1 介导炎症反应相关;牙周疾病组及非牙周疾病组患者性别、年龄、BMI 对比无明显差异($P>0.05$),牙周疾病组及非牙周疾病组患者正畸治疗时间、拔牙数量、正畸方式、口腔清洁度对比差异显著($P<0.05$)。研究显示^[25],正畸治疗时间增加,患者牙周疾病发生率显著升高。分析原因为,随着正畸治疗时间进展,牙齿移动会对牙周膜造成紧张压迫,进而出现水肿、无菌性坏死以及炎症反应情况,促使牙周疾病发生^[26]。另外,在正畸治疗过程中,大多观点支持尽量不拔牙,但需要依照患者实际情况而定,而拔牙数量增加,对于患者牙龈及牙周组织造成损伤,再加上持续正畸治疗影响,牙周内细菌留存,增加牙周疾病发生率^[27]。Jedliński M 等^[28]研究显示,无托槽隐性矫治具有舒适性、清洁方便等优点,可改善牙周炎症反应,提升牙周健康水平^[29],与本研究结果相符。最后对于口腔清洁度来说,清洁程度越好,牙周细菌留存时间短,可进一步降低牙周疾病发生率;logistic 回归分析结果表明:TNF- α 、IL-1 β 、IL-6、TSP-1、正畸方式、口腔清洁度为拔牙正畸患者牙周疾病的独立危险因素($P<0.05$)。以往临床上针对拔牙正畸患者中牙周疾病影响因素尚无确切定论,而本研究提示,针对早期 TNF- α 、IL-1 β 、IL-6、TSP-1 水平升高患者,需及时采取相应措施,进行牙周清洁,避免牙周疾病发生^[30]。另外本研究发现,针对拔牙正畸患者需尽量采取无托槽隐性矫治,可进一步预防牙周疾病情况。

综上所述,拔牙正畸患者随着正畸时间延长龈沟液炎症因子及 TSP-1 水平明显升高,且 TNF- α 、IL-1 β 、IL-6、TSP-1、正畸方式、口腔清洁度为拔牙正畸患者牙周疾病的独立危险因素。

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