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## 牙周炎患者正畸治疗前后龈沟液中弹性蛋白酶的变化 \*

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**摘要 目的:**探讨牙周炎患者正畸治疗前后龈沟液中弹性蛋白酶的变化价值,希望为早期预测患者预后提供参考。**方法:**2016 年 12 月到 2019 年 10 月选择在本院就诊的牙周炎患者 68 例作为研究对象,所有患者都给予正畸治疗,检测正畸治疗前后弹性蛋白酶、探诊深度(probing depth, PD)、出血指数(bleeding on probing, BOP)、附着丧失(attachment loss, AL)的变化,记录患者的病情变化、判定预后并进行相关性分析、影响因素分析。**结果:**所有患者完成治疗,对于正畸治疗的美观、固位、稳定性均满意。治疗后 1 个月与治疗后 3 个月患者的 PD、BOP、AL 都低于治疗前( $P<0.05$ ),治疗后 3 个月也低于治疗后 1 个月( $P<0.05$ )。治疗后 1 个月与治疗后 3 个月患者的龈沟液弹性蛋白酶值都低于治疗前( $P<0.05$ ),治疗后 3 个月也低于治疗后 1 个月( $P<0.05$ )。Spearman 分析显示治疗前与治疗后 3 个月的龈沟液弹性蛋白酶变化差值与 PD、BOP、AL 变化差值存在显著正相关性( $P<0.05$ )。多因素 Logistic 回归显示 PD、BOP、AL 变化差值作为影响龈沟液弹性蛋白酶变化差值的主要因素( $P<0.05$ )。**结论:**牙周炎患者正畸治疗前后龈沟液中弹性蛋白酶水平显著下降,与患者的病情变化显著相关,也是反映与预测患者预后的重要指标。

**关键词:**牙周炎;正畸治疗;弹性蛋白酶;探诊深度;出血指数

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## Changes of Elastase in Gingival Crevicular Fluid before and after Orthodontic Treatment in Patients with Periodontitis\*

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**ABSTRACT Objective:** To investigate the value of elastase in gingival crevicular fluid before and after orthodontic treatment in patients with periodontitis, it hope to provide reference for early prediction of patient prognosis. **Methods:** From December 2016 to October 2019, 68 cases of patients with periodontitis in our hospital were selected as the research target. All patients were given orthodontic treatment, and the changes of elastase, Probing depth (PD), bleeding on probing (BOP), attachment loss (AL) at before and after orthodontic treatment were detected, and were to determine the patient's condition and prognosis, and they given correlation analysis and influencing factor analysis. **Results:** All patients were completed the treatment and were satisfied with the aesthetics, retention and stability of orthodontic treatment. The PD, BOP, AL gingival crevicular elastase values at 1 month after treatment and 3 months after treatment were lower than before treatment ( $P<0.05$ ), and the 3 months after treatment were also lower than 1 month after treatment ( $P<0.05$ ). The gingival crevicular elastase values at 1 month after treatment and 3 months after treatment were lower than before treatment( $P<0.05$ ), and the 3 months after treatment were also lower than 1 month after treatment( $P<0.05$ ). Spearman analysis showed that there were significant positive correlation between the difference in the change of sputum fluid elastase and the difference of PD, BOP and AL before treatment and 3 months after treatment( $P<0.05$ ). Multivariate logistic regression showed that the difference of PD, BOP and AL were the main factor affected the difference of eosinase change in gingival crevicular fluid ( $P<0.05$ ). **Conclusion:** The level of elastase in gingival crevicular fluid of patients with periodontitis are significantly decreased before and after orthodontic treatment, which are significantly correlated with the patient's condition and are important indicators to reflect and predict the prognosis of patients.

**Key words:** Periodontitis; Orthodontic treatment; Elastase; Depth of probing; Bleeding index

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### 前言

俗话说“貌美牙为先”,只有拥有一口整齐、漂亮、健康的牙齿,才可以让人拥有美好的容颜和自信的笑容。牙周炎是细

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菌感染导致的慢性进展性疾病,其发生是由于牙周炎原菌和宿主防御机制复合物之间的复杂交互作用<sup>[1,2]</sup>。由于牙周组织再生能力有限,因此早期诊断疾病与进行早期治疗对改善患者的预后具有重要的临床意义<sup>[3]</sup>。牙周炎患者采用正畸治疗除了可以消除咬合创伤,与可为牙槽骨修复再生提供了可能<sup>[4,5]</sup>。随着口腔种植科学的发展,种植体支抗技术得以发展起来,并逐渐得到广大正畸医生的接受。其中片段弓矫治技术灵活性大,可迅速达到临床预定的矫治目标<sup>[6,7]</sup>。龈沟出血指数和牙龈指数是检查牙齿健康的重要指标,作为龈沟液组织中重要的组成成分,弹性蛋白酶(elastase, EA)是来源于中性多形核白细胞的一种丝氨酸中性蛋白水解酶,与牙周炎关系密切,能广泛破坏牙周组织中的骨和结缔组织,也可作为辅助评定预后的重要客观指标<sup>[8,9]</sup>。本文具体探讨了牙周炎患者正畸治疗前后龈沟液中弹性蛋白酶的变化,希望为早期预测患者预后提供参考。

## 1 资料与方法

### 1.1 研究对象

2016年12月到2019年10月选择在本院就诊的牙周炎患者68例,符合牙周炎分类国际研讨会制定的标准(X线片显示牙槽骨吸收超过根长的1/2);无全身系统性疾病;无妊娠、非哺乳期妇女;患者知情同意;临床资料完整。排除标准:妇女处于怀孕期及哺乳期,入院前半年内做过牙周基础治疗;有偏侧咀嚼习惯者。

其中男37例,女31例;年龄最小17岁,最大45岁,平均年龄 $34.20 \pm 4.21$ 岁;平均体重指数 $22.81 \pm 1.48$  kg/m<sup>2</sup>;平均病程 $1.48 \pm 0.36$ 年;平均收缩压 $128.14 \pm 12.58$  mmHg;平均舒张压 $76.25 \pm 12.58$  mmHg。

### 1.2 治疗方法

所有患者都给予正畸治疗,对患者实施X线片检查,压低处理上磨牙、下前牙,关闭处理对散在间隙,对排齐牙弓进行整

平,对牙颌关系进行细致调整,采取经且间断的方式增加正畸力,避免伤及患者的牙齿。治疗后1个月左右复查2次,治疗观察3个月,观察期间进行3~4次超声洁治或手动根面平整,指导合理进行手动刷牙。

### 1.3 常规指标检测

记录患者治疗前后与对照组入选者的PD、BOP、AL,所有检查均由同一检查者完成,测定三次取平均值。

### 1.4 龈沟液中弹性蛋白酶检测

在龈沟液取样前用气枪轻轻吹干受试牙面和周围牙龈粘膜,去除龈上菌斑,在取样中用镊子夹取在电子天平上称重的2 mm×10 mm滤纸条,将滤纸条轻轻插入龈沟,放置30 s后取出。将取出的滤纸条放入原EP管中封好,将样本送置-70℃低温冰箱中冻存待用;在检测中,样本自然解冻后加入100 μL PBS液,室温下振荡1 h后高速冷冻低温离心机4℃,1000 rpm条件下离心10 min。采用酶标仪法检测龈沟液中弹性蛋白酶相对含量,测定波长为405 nm。

### 1.5 统计方法

选择SPSS22.00,计量数据选择( $\bar{x} \pm s$ )表示,采用t检验与方差分析,而计数数据采用%表示,采用卡方分析,相关性分析采用Spearman分析,影响因素分析采用多因素Logistic回归分析, $P < 0.05$ 有统计学意义,检验水准为 $\alpha = 0.05$ 。

## 2 结果

### 2.1 治疗外观效果

所有患者均完成治疗,对于正畸治疗的美观、固位、稳定性均满意。

### 2.2 常规指标变化对比

治疗后1个月与治疗3个月患者的PD、BOP、AL值都低于治疗前( $P < 0.05$ ),治疗后3个月也低于治疗后1个月( $P < 0.05$ ),见表1。

表1 治疗前后不同时间点的常规指标变化对比( $\bar{x} \pm s$ )

Table 1 Comparison of conventional index changes at different time points before and after treatment ( $\bar{x} \pm s$ )

| Time points              | n  | PD(mm)               | BOP(%)                 | AL(mm)               |
|--------------------------|----|----------------------|------------------------|----------------------|
| Before treatment         | 68 | $3.98 \pm 0.22$      | 39(57.4%)              | $4.54 \pm 0.24$      |
| 1 months after treatment | 68 | $2.13 \pm 0.20^{\#}$ | 16(23.5%) <sup>#</sup> | $2.45 \pm 0.33^{\#}$ |
| 3 months after treatment | 68 | $1.98 \pm 0.18^{**}$ | 3(4.4%) <sup>**</sup>  | $2.19 \pm 0.28^{**}$ |

Note: Compared with before treatment, <sup>#</sup> $P < 0.05$ ; compared with 1 month after treatment, <sup>\*</sup> $P < 0.05$ .

### 2.3 龈沟液弹性蛋白酶变化对比

治疗后1个月与治疗3个月患者的龈沟液弹性蛋白酶

值都低于治疗前( $P < 0.05$ ),治疗后3个月也低于治疗后1个月( $P < 0.05$ ),见表2。

表2 治疗前后不同时间点的龈沟液弹性蛋白酶变化对比( $\bar{x} \pm s$ )

Table 2 Comparison of changes in gingival crevicular fluid elastase at different time points before and after treatment ( $\bar{x} \pm s$ )

| Time points              | n  | Gingival crevicular fluid elastase |
|--------------------------|----|------------------------------------|
| Before treatment         | 68 | $0.301 \pm 0.010$                  |
| 1 months after treatment | 68 | $0.156 \pm 0.015^{\#}$             |
| 3 months after treatment | 68 | $0.017 \pm 0.002^{**}$             |

Note: Compared with before treatment, <sup>#</sup> $P < 0.05$ ; compared with 1 month after treatment, <sup>\*</sup> $P < 0.05$ .

## 2.4 相关性分析

在 68 例患者中, Spearman 分析显示治疗前与治疗后 3 个

月的龈沟液弹性蛋白酶变化差值与 PD、BOP、AL 变化差值存在显著正相关性( $P<0.05$ ), 见表 3。

表 3 牙周炎患者正畸治疗前后龈沟液中弹性蛋白酶变化与常规指标变化的相关性( $n=68$ )

Table 3 Correlation between changes of elastase in gingival crevicular fluid before and after orthodontic treatment in patients with periodontitis and changes in conventional indicators ( $n=68$ )

| Index | PD    | BOP   | AL    |
|-------|-------|-------|-------|
| r     | 0.424 | 0.445 | 0.443 |
| P     | 0.021 | 0.018 | 0.019 |

## 2.5 影响因素分析

在 68 例患者中, 以一般资料与 PD、BOP、AL 变化差值作为自变量, 以龈沟液弹性蛋白酶变化差值作为因变量, 多因素

Logistic 回归显示 PD、BOP、AL 变化差值作为影响龈沟液弹性蛋白酶变化差值的主要因素( $P<0.05$ ), 见表 4。

表 4 影响牙周炎患者正畸治疗前后龈沟液中弹性蛋白酶变化的因素( $n=68$ )

Table 4 Factors affecting the changes of elastase in gingival crevicular fluid before and after orthodontic treatment in patients with periodontitis ( $n=68$ )

| Index | B     | SE    | Wald  | P     | OR(95%CI)            |
|-------|-------|-------|-------|-------|----------------------|
| PD    | 3.367 | 1.398 | 5.378 | 0.016 | 28.492(1.848-44.781) |
| BOP   | 2.488 | 1.942 | 8.104 | 0.000 | 6.398(1.644-16.292)  |
| AL    | 2.783 | 2.001 | 7.433 | 0.006 | 4.583(1.782-9.771)   |

## 3 讨论

牙周炎是由多种因素致病, 临床发病率比较高, 常引起牙齿的继发性畸形和咬合创伤, 进一步损害牙周组织<sup>[10,11]</sup>。牙周炎治疗常采用的方法为局部及全身用药、菌斑控制、龈上洁治等, 短期内能较有效地控制牙周炎症, 但是常由于患者口腔卫生护理不佳, 导致其复发引发一系列的并发症, 而且很难恢复已经发生错位的牙齿<sup>[13]</sup>。

本研究显示治疗后 1 个月与治疗前 3 个月患者的 PD、BOP、AL 值都低于治疗前, 治疗后 3 个月也低于治疗后 1 个月, 所有患者完成治疗, 对于正畸治疗的美观、固位、稳定性均满意。与 Mallikarjun S 与 Marinho MC 等学者的研究结果类似<sup>[14,15]</sup>, 也表明表明正畸治疗对牙周的刺激很小, 能促进口腔病原菌的清除, 不会引起牙周膜的增宽, 有利于游离端基牙的稳定和长期健康。从机制上分析, 牙周炎是一种多因素复杂性的炎症性疾病, 其发生是由于牙周炎原菌和宿主防御机制复合物之间的交互作用<sup>[16]</sup>。该病的发病因素包括菌斑、环境和宿主, 其中菌斑因素是始发因素, 宿主因素可能是决定因素, 环境因素是危险因素<sup>[16]</sup>。正畸治疗能重建良好咬合关系, 不仅有利于牙周炎的控制, 也改善了患者的面部美观和咀嚼功能, 也为牙槽骨修复再生提供了可能<sup>[17]</sup>。

本研究显示治疗后 1 个月与治疗前 3 个月患者的龈沟液弹性蛋白酶值都低于治疗前, 治疗后 3 个月也低于治疗后 1 个月, 与 Ramich T 等研究结果类似<sup>[18]</sup>。从机制上分析, 龈沟液的液体成分主要来自于血清, 其他成分则分别来自于血清、邻近的牙周组织及细菌。龈沟液在机体防御中发挥重要的作用, 筛选准确灵敏的龈沟液标志物有助于指导牙周炎的临床诊治<sup>[18,19]</sup>。龈沟液中弹性蛋白酶活性和牙周炎症的病情呈正比, 随着牙周组织炎症的加重而升高<sup>[20-22]</sup>。弹性蛋白酶可增强吞噬细

胞的吞噬作用, 对中性粒细胞具有调节作用, 可增强机体细胞对革兰阳性和阴性细菌的吞噬作用, 诱导内皮细胞致炎因子的表达, 可通过刺激宿主使其产生大量的炎症介质间接导致牙周炎的发生<sup>[23,24]</sup>, 表明正畸治疗能有效抑制龈沟液弹性蛋白酶的表达。

弹性蛋白酶是一种中性的丝氨酸蛋白酶, 不仅可以特异性水解弹性蛋白, 还可以水解蛋白多糖、胶原、纤维蛋白原等牙周组织结构<sup>[25-27]</sup>。弹性蛋白酶水平的波动易受到牙周炎病情的影响, 当前已有学者尝试通过弹性蛋白酶水平的变化对正畸各阶段牙周组织状况进行监控<sup>[28]</sup>。本研究 Spearman 分析显示牙周炎患者治疗前与治疗后 3 个月的龈沟液弹性蛋白酶变化差值与 PD、BOP、AL 变化差值存在显著正相关性; 多因素 Logistic 回归显示 PD、BOP、AL 变化差值作为影响龈沟液弹性蛋白酶变化差值的主要因素, 与 Hirschfeld J、Vannala V 等学者的研究结果类似<sup>[29,30]</sup>, 也说明龈沟液弹性蛋白酶的变化与临床常规指标显著正相关, 可考虑作为判断牙周炎患者预后的指标。从机制上分析, 龈沟液的液体成分主要来自于血清, 其他成分则分别来自于血清、邻近的牙周组织及细菌。当修复体周围发生炎症时, 修复体周围龈沟液分泌量增加。而酶在牙周组织改建中的作用早已受到学者们的重视, 而且龈沟液中的酶具有一定的稳定性, 但与牙周组织的活动性明显相关<sup>[31-33]</sup>。健康状态下绝大部分弹性蛋白酶存在于细胞浆内, 当组织破坏细胞坏死时, 则有大量弹性蛋白酶出现于细胞外环境, 并与牙周临床指数高度正相关; 而随着正畸治疗的进行, 弹性蛋白酶的水平会显著下降<sup>[34-36]</sup>。本研究也存在一定的不足, 纳入的入选者比较少, 且有关指标也相对少, 可能造成研究偏倚, 将在下一步进行深入分析。

总之, 牙周炎患者正畸治疗前后龈沟液中弹性蛋白酶水平显著下降, 与患者的病情变化显著相关, 也是反映与预测患者预后的重要指标。

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(上接第 3920 页)

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