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ORIGINAL ARTICLE

Mean platelet volume as an inflammatory marker in patients with severe periodontitis

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Abstract

Periodontitis has become the leading cause of tooth loss in adults, and the host's immunologic and inflammatory response to the bacteria can lead to periodontal destruction. In patients with periodontitis, platelets possess an increased activation status compared with platelets from healthy controls. Mean platelet volume (MPV) has been considered an important index of platelet activity and an inflammatory marker in many infectious diseases. The present study investigated the relationship between MPV and disease activity in subjects with severe periodontitis. Forty-five patients with periodontitis and 45 age and sex-matched healthy subjects were enrolled into the study. All subjects received periodontal and hematological examinations. The periodontitis patients were administered active periodontal treatment (APT). At baseline, a statistically significant decrease in MPV was noted in patients with periodontitis (9.73 ± 1.06 fL) compared with healthy controls (10.24 ± 1.07 fL). At 1 month post-APT, MPV was substantially increased (10.11 ± 1.04 fL). Positive correlation was found between increase of MPV and decrease of periodontal probing depth after treatment ($r = 0.377$; $p = 0.014$). In conclusion, the decrease of MPV was related to the severe periodontal inflammation, and the value inversed shift after APT. MPV might reflect the disease activity of periodontitis.

Introduction

Periodontitis is a widespread infectious disease of the periodontium that leads to gingival inflammation and bleeding. It has become the leading cause of tooth loss in adults. The primary etiologic factor of periodontitis is subgingival infection by a group of periodontal pathogens, and the host's immunologic and inflammatory response to the bacteria can also result in periodontal destruction. Cross-sectional studies suggest that patients with periodontitis have elevated levels of systemic inflammation markers including leukocytes [1, 2], neutrophils, and serum globulin [3] and C-reactive protein [1, 4, 5] compared to healthy controls. Papapanagiotou et al. have shown that platelets from patients with periodontitis have an increased activation status compared with platelets from healthy controls [6]. Many epidemiological studies have identified statistically significant associations between established periodontitis and cardiovascular diseases (CVD) [7, 8]. It was reported elevated WBC counts, C-reactive protein levels and platelet activation may partly explain the epidemiological association between periodontitis and CVD [1, 2, 5, 6].

Mean platelet volume (MPV), an important index of platelet activity, reflects platelet production rate and stimulation. Recently, MPV has been considered an inflammatory marker in many chronic diseases. Further, it has been observed that MPV level decreased in patients with ankylosing spondylitis, rheumatoid arthritis [9], ulcerative colitis [10], and chronic obstructive pulmonary disease exacerbation [11]. Up until now, only one study on MPV values in periodontitis patients has been reported and a slight increase in MPV level was observed. However, the patients enrolled in the study were adolescents with mild periodontitis [12]. It was known that elevated MPV is associated with CVD [13, 14]. It was valuable to investigate the relationship of MPV and severe periodontitis.

The aim of the present study was to investigate the relationships between MPV and severe periodontitis and short-term effects of active periodontal treatment (APT) on MPV level.

Materials and methods

A total of 90 unrelated Chinese subjects, including 45 patients with severe periodontitis and 45 periodontally healthy subjects were recruited from the Department of Periodontology, Peking University School and Hospital of Stomatology. All subjects were of Han ethnicity and signed written consent forms to participate in this research. The study was approved by ethic committee of Peking University Health Science Center.

At baseline, the inclusion criteria of the severe periodontitis group were [15]

(1) at least two interproximal sites with clinical attachment loss (CAL) ≥6 mm, not on the same tooth;
(2) One or more interproximal sites with pocket depth (PD) ≥5 mm.

Individuals with PD <3 mm or no obvious attachment loss (AL) were defined as healthy controls.

Exclusion criteria of all subjects were

(1) current or previous smoker,
(2) history of periodontal therapy or antimicrobial therapy within 6 months, or history of orthodontic therapy,

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(3) systemic disease (e.g. diabetes mellitus, nephrosis, hepatopathy, hypertension, neutropenia), or pregnant, or under medication known to affect the periodontium.

Clinical examinations and treatment

At the first visit before therapy (baseline), all participants were asked to complete a questionnaire to determine height and weight, smoking status, dental history, and systemic history. Body mass index (BMI) of subjects was calculated as weight/height^2 (kg/m^2) using patient-reported values. After clinical, radiographic, and blood examinations, all patients received APT consisting of anti-infective therapy (metronidazole 0.2 g and amoxicillin 0.5 g, 3 times/day for 7 days) with supragingival scaling and subgingival debridement under local anesthesia. At 1 and 6 months after APT, periodontal and blood examinations were re-evaluated and periodontal debridement was performed if necessary. No patient received periodontal surgery.

An experienced self-calibrated periodontist conducted all periodontal examinations and treatments. Periodontal examinations included plaque index (PLI), PD, bleeding index (BI) [16], and CAL at six sites (mesial, distal, and middle sites of the buccal and lingual sides) for all teeth except the third molars.

Blood examinations

A total of 5 ml of fasting blood was obtained by venipuncture from each participating subject, half of which was injected into a vacuum tube with or without anticoagulant (ethylenediaminetetraacetic acid [EDTA]) separately. The blood samples were sent to the testing laboratories of Peking University School and Hospital of Stomatology within 30 minutes. A technician who was blinded for case status performed the blood test. Blood samples in the vacuum tubes with EDTA were used for complete blood cell analysis in a calibrated Sysmex XS-1,000 automated hematology analyzer (Sysmex, Kobe, Japan), while blood samples in coagulant-containing tubes were used to analyze other hematological parameters such as albumin (ALB, g/l), globulin (GLB, g/l), and albumin/globulin ratio (A/G) in a HITACHI 7180 Automatic Analyzer (HITACHI, Tokyo, Japan). The reference values for MPV ranged between 7.7 and 13.1 fL.

Statistical analysis

Statistical analysis was performed using SPSS software, version 13.0 (SPSS, Chicago, IL). All data were tested for normal distribution by Kolmogorov–Smirnov test. Student *t*-test was used to compare values of periodontitis patients at baseline and controls. Comparisons of clinical and blood parameters of patients with periodontitis between baseline and 1 month post-APT were performed by paired-samples *t*-test, while comparisons among baseline, 1 month, and 6 months post-APT were performed by analysis of variance with the Bonferroni *post hoc* test. Partial correlation analysis was used to investigate the relationship between change of MPV and changes of clinical parameters before and after treatment after controlling for age, gender, and BMI as potential confounders. A two-tailed *p* value below 0.05 was considered statistically significant.

Results

In this study, all patients had a complete set of clinical and hematological data at baseline and 1 month post-APT. However, at 6 months post-APT, 15 patients were lost to follow-up: 10 refused to undergo subsequent examinations, two sought continuing treatment elsewhere, and three could not be contacted. As a result, 30 patients were included into the clinical and hematological analyses at 6 months post-APT. Demographic features and

Table I. Demographic features and clinical parameters of patients and controls.

	Periodontitis group (*n* = 45)	Control group (*n* = 45)	*p*
Age (year)	35.3 ± 10.3	34.8 ± 12.0	0.841
Gender (F/M)	21/24	20/25	0.835
BMI	21.68 ± 2.79	21.41 ± 2.12	0.601
PLI	2.10 ± 0.57	1.33 ± 0.31	0.000
PD (mm)	6.18 ± 0.97	1.91 ± 0.52	0.000
BI	3.70 ± 0.49	1.31 ± 0.36	0.000
AL (mm)	5.51 ± 0.99	0.00 ± 0.00	0.000

BMI, body mass index; PLI, plaque index; PD, pocket depth; BI, bleeding index; AL, attachment loss.

Table II. Comparison of hematological parameters between groups.

	Periodontitis group (*n* = 45)	Control group (*n* = 45)	*p*
ALB (g/l)	49.31 ± 2.31	49.38 ± 2.30	0.891
GLB (g/l)	28.93 ± 3.37	26.58 ± 3.18	0.001
A/G	1.72 ± 0.21	1.89 ± 0.26	0.001
WBC (× 10^9/l)	6.42 ± 1.90	5.94 ± 1.33	0.172
NEUT%	62.69 ± 6.98	58.78 ± 9.22	0.026
NEUT (× 10^9/l)	4.09 ± 1.51	3.51 ± 1.03	0.037
PLT (× 10^9/l)	252.20 ± 52.09	232.04 ± 50.95	0.098
PLCR (%)	0.23 ± 0.08	0.28 ± 0.08	0.007
MPV (fL)	9.73 ± 1.06	10.24 ± 1.07	0.026

ALB, albumin; GLB, globin; A/G, ratio of albumin and globin; WBC, white blood cell; NEUT%, percentage of neutrophil granulocyte; NEUT, number of neutrophil granulocyte; PLT, platelet; PLCR, platelet large cell ratio; MPV, mean platelet volume.

clinical parameters of the periodontitis and control groups at baseline are shown in Table I. Age, gender, and BMI were similar in both groups.

Periodontal inflammation of the periodontitis group was significantly greater than that of the control group, as all clinical variables were higher in the periodontitis group than in the control group (*p* < 0.01). The results of the blood examinations are shown in Table II. Compared to the control group, significantly higher GLB level and neutrophil count and percentage were observed in the periodontitis group (*p* < 0.05), while A/G, platelet large cell ratio (PLCR), and MPV were significantly lower in the periodontitis group than in the control group (*p* < 0.05). Platelet count in patients with periodontitis was higher than that in controls, though not reached significant difference (*p* = 0.098).

Changes in clinical parameters post-APT

All periodontal clinical parameters had a statistically significant decrease at 1 month post-APT compared with baseline (Table III). A comparison of data 6 months post-APT and 1 month post-APT revealed further improvement in clinical parameters, but without significant difference (data not shown).

Changes in hematological parameters of patients post-APT

Compared with that at baseline, significantly lower white blood cell (WBC) count, neutrophil percentage, and neutrophil count accompanied by higher A/G, PLCR, and MPV levels were noted at 1 month post-APT (Table IV). At 1 month post-APT, MPV level was more similar to the control group (10.11 ± 1.04 fL vs. 10.24 ± 1.07 fL, *p* = 0.58). The serum GLB level reduction was nearly statistically significant (*p* = 0.057); A/G elevated from

1.72 ± 0.21 to 1.79 ± 0.25 ($p = 0.04$), while there was no obvious change in ALB level. At 6 months post-APT, compared to that at 1 month post-APT, all hematological parameters were similar to the control group (data not shown).

Table III. Changes in clinical parameters at 1 month post-APT of periodontitis group (mean $\pm$ SD).

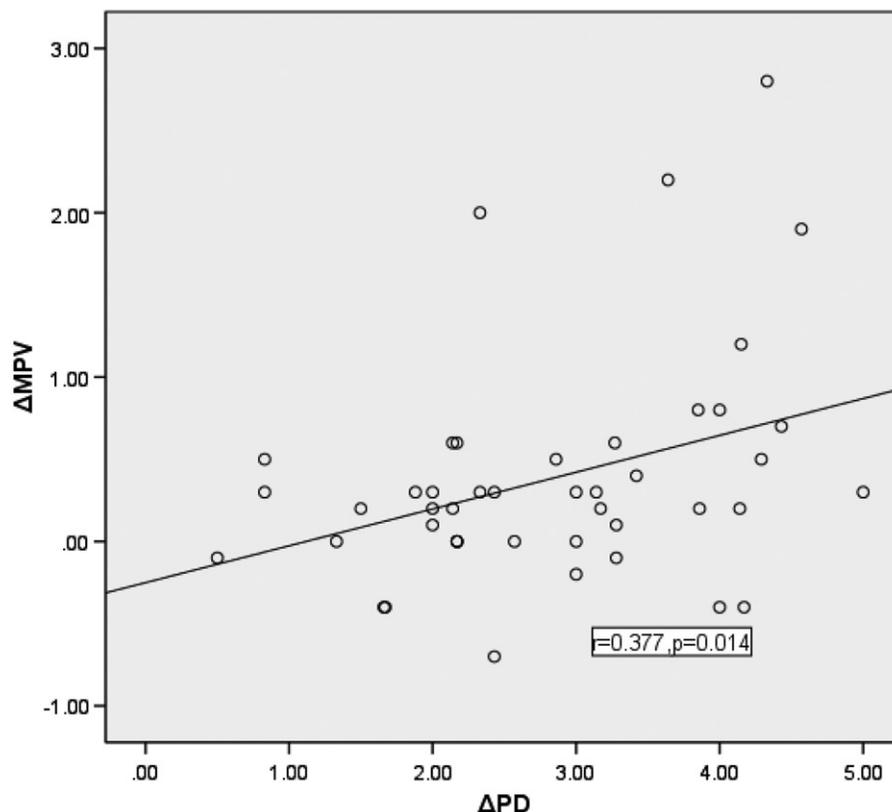|	Baseline ($n = 45$)	1 month post-APT ($n = 45$)	p
PLI	2.10 ± 0.57	1.50 ± 0.61	0.000
PD (mm)	6.18 ± 0.97	3.36 ± 0.72	0.000
AL (mm)	5.51 ± 0.99	3.56 ± 1.21	0.000
BI	3.70 ± 0.49	1.77 ± 0.68	0.000

PLI, plaque index; PD, pocket depth; BI, bleeding index; AL, attachment loss.

Table IV. Changes in hematological parameters at 1 month post-APT of periodontitis group (mean $\pm$ SD).

	Baseline ($n = 45$)	1 month post-APT ($n = 45$)	p
ALB(g/l)	49.31 ± 2.31	49.27 ± 2.03	0.899
GLB(g/l)	28.93 ± 3.37	27.98 ± 3.92	0.057
A/G	1.72 ± 0.21	1.79 ± 0.25	0.040
WBC($\times 10^9$/l)	6.42 ± 1.90	5.69 ± 1.84	0.018
NEUT%	62.69 ± 6.98	58.38 ± 7.39	0.002
NEUT($\times 10^9$/l)	4.09 ± 1.51	3.40 ± 1.61	0.014
PLT($\times 10^9$/l)	250.20 ± 52.09	242.02 ± 57.50	0.097
PLCR(%)	0.23 ± 0.08	0.26 ± 0.08	0.000
MPV(fL)	9.73 ± 1.06	10.11 ± 1.04	0.001

APT, active periodontal treatment; ALB, albumin; GLB, globin; A/G, ratio of albumin and globin; WBC, white blood cell; NEUT%, percentage of neutrophil granulocytes; NEUT, number of neutrophil granulocytes; PLT, platelet; PLCR, platelet large cell ratio; MPV, mean platelet volume.

Figure 1. Partial correlation between ΔMPV and ΔPD in periodontitis patients. ΔMPV $=$ MPV at 1 month post-APT $-$ MPV at baseline; ΔPD $=$ PD at baseline $-$ PD at 1 month post-APT.

After controlling for age, gender, and BMI as potential confounders, positive relationship between ΔMPV (ΔMPV $=$ MPV at 1 month post-APT-MPV at baseline) and ΔPD (ΔPD $=$ PD at baseline $-$ PD at 1 month post-APT) was identified by partial correlation analysis ($r = 0.377$, $p = 0.014$, Figure 1).

Discussion

Several studies have demonstrated that adult patients with periodontitis frequently present with significant differences in blood parameters when compared to healthy controls. Loos et al. found that the number of peripheral WBCs increased with increasing severity and extent of periodontitis [2]. Shi et al. reported that the number and percentage of neutrophils and serum GLB level in patients with aggressive periodontitis (AgP) were much higher than those in healthy controls, and ALB level and A/G were lower in the AgP group than in the control group [3].

Similar to previous studies, in this study, we observed that serum GLB level, the number and percentage of neutrophils in peripheral blood were higher, and A/G was lower in the controls. Moreover, we also found that MPV levels in patients with severe periodontitis were significantly lower than those in the control group (9.73 ± 1.06 fL vs. 10.24 ± 1.07 fL, $p < 0.05$). In accordance with MPV, PLCR was also decreased in patients compared with that in controls ($p < 0.05$). Although not reached significant difference, platelet count was increased in patients group, which was in agreement with other studies [6, 17]. MPV is readily measured by clinical hematology analyzers and is a reliable marker of platelet function and activation. It has been demonstrated that MPV plays an important role as a marker of inflammation, disease activity and efficacy of anti-inflammatory treatment in several chronic inflammatory disorders. However, there were still controversies about MPV trends in different infectious diseases. It has been reported that MPV level in peripheral blood increases in early rheumatoid arthritis [18] and septicemia [19]. In patients with ulcerative colitis and acute

exacerbation of chronic obstructive pulmonary disease, which were associated with high-grade systemic inflammation, a lower MPV was recorded compared with controls [11, 20]. Gasparyan et al. found that high-grade inflammation accompanies a decrease of MPV in rheumatoid arthritis, possibly due to the increased consumption of platelets at the sites of rheumatoid inflammation. A reverse shift of MPV results from the suppression of inflammation by disease-modifying and anti-tumor necrosis factor-α agents [21]. The authors proposed that the size of circulating platelets was dependent on the intensity of systemic inflammation, with contrasting features of MPV in high- and low-grade inflammatory disorders and in the course of anti-inflammatory treatment. In high-grade inflammatory disorders, large amount of highly reactive large-sized platelets migrated to inflammatory sites, where they were intensely consumed, then MPV decreased; in low-grade inflammatory disorders, large-sized platelets came into the circulation and involved in thrombi, not consumed in inflammatory sites, which resulted in increase of MPV level [14].

MPV value in severe periodontitis has not been assessed up till now. López et al. investigated whether adolescent cases of periodontitis present with hemogram findings different from those observed in control subjects, and they found that periodontitis cases presented with 5% higher values for MPV than controls [12]. However, in their study, the periodontal inflammation was mild; only 49.4% of patients had a PD of ≥ 5 mm in the mouth, with a mean percentage of sites with a PD of ≥ 5 mm being only 1.4. In our study, the patients with periodontitis developed severe inflammation, with a mean PD of 6.18 mm, a mean AL of 5.51 mm, and a mean BI of 3.70, the clinical parameters were significantly higher than those of the control group. Deep pockets, higher AL, and the BIs suggested that the periodontal disease was active, while MPV value was found to be decreased. Recent studies have demonstrated that in patients with severe periodontitis, the serum level of interleukin-6, tumor necrosis factor-α, and other proinflammatory cytokines are elevated in response to the inflammation [22, 23]. Consequently, the overproduction of proinflammatory cytokines and acute-phase reactants can suppress the size of platelets by interfering with megakaryopoiesis and a subsequent release of small-sized platelets from the bone marrow [24]. Another possible explanation of the decreased size of circulating platelets in active periodontitis relates to the intensive consumption of large platelets at sites of inflammation.

It was interested that one month post-APT, the hematological parameters in patients group were approaching the level of the healthy controls. Following the decrease of serum GLB level, A/G obtained significant elevation compared with that at baseline ($p = 0.040$). Significant reductions of WBC count and number and percentage of neutrophils also indicated alleviation of inflammation. Moreover, statistically significant increases in MPV and PLCR were observed after treatment. Positive correlation was found between increase of MPV and decrease of PD (a very import clinical parameter reflecting periodontal inflammation). This trend suggests that the change of MPV in periodontitis was associated with the status of inflammation.

Periodontitis, as a chronic inflammatory disease, shared many risk factors with CVD such as age, gender, smoking, diabetes and obesity. Many cross-sectional and longitudinal epidemiological studies have provided evidence that there is an association between periodontitis and elevated risk for cardiovascular disease [7, 8, 25]. Some studies suggested the link between periodontal disease and cardiovascular disease is probably inflammation [26]. MPV, besides an inflammatory marker, was also a reflection of prothrombotic conditions. Increased levels of MPV have been shown to be an independent risk factor for CVD [13, 14]. It was meaningful to find MPV change in periodontitis. In a recent study,

Androsz-Kowalska reported that MPV was significantly higher in the patients with previously diagnosed CVD and coexisting chronic periodontitis ($n = 19$) than that in the control group, and the correlation between clinical parameters of periodontal disease and MPV in patients with coronary artery disease was found [27]. However, the authors did not find significant difference in MPV between patients with periodontitis and controls, which may be due to that the periodontal inflammation of the enrolled patients was less severe than our patients. As the authors mentioned, there were some limitations of their study: the study groups comprised a small number of patients; the distribution of the sexes in the studies groups was uneven. In our study, MPV level was lower in patients with severe periodontitis comparing with healthy controls, while the MPV level of patients increased after treatment, which seemed in contrast to the link between periodontitis and CVD as well as the association between increased MPV and CVD. However, it should be mentioned that MPV level in patients after treatment was closer to but still lower than that in controls (10.11 ± 1.04 fL vs. 10.24 ± 1.07 fL). The studies regarding the relationship between MPV and CVD showed that MPV level in CVD patient group was higher than that in control group [28–30]. In a cohort study, MPV above the 10.35 fL cut-off level predicted unstable angina and myocardial infarction with 78.3% sensitivity and 74.6% specificity [31]. Therefore, it could be deduced that increase of MPV after periodontal treatment did not mean elevated risk for CVD. Interestingly, the same tendency was also found in rheumatoid arthritis, which was in relation to CVD as well [21]. In addition, the definitive etiologic relationship between periodontitis and CVD has not been established yet. Elevated markers for systemic inflammation such as CRP, WBC were thought to be the association between periodontitis and CVD in many studies [26, 32]. In the present study, periodontal inflammation was relieved and WBC counts were reduced after treatment, which could lower the risk for CVD. In further clinical studies, it is valuable to investigate MPV value among patients with periodontitis only, with CVD only, with CVD and coexisting chronic periodontitis and the healthy controls to find the definite role of MPV in periodontitis and CVD.

In conclusion, the present study showed that the decrease of MPV was related to the severe periodontal inflammation, and the value inversed shift after APT. The findings suggest that MPV was related with inflammatory status of patients with severe periodontitis.

Declaration of interest

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