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Salivary Soluble CD14 and Elastase as Co-biomarkers for Periodontal Assessment

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ABSTRACT

Mixed saliva contains egress from gingival crevices or periodontal pockets, and thus it may be used as a medium for overall assessment of periodontal conditions. Our early studies showed that neutrophilic elastase in gingival crevicular fluid may be a marker of periodontal disease and that salivary soluble CD14 (sCD14) may be an indicator of oral and periodontal health. This study was to determine sCD14 and neutrophilic elastase in saliva and evaluate whether these molecules could be used for an overall periodontal assessment. The participants were 61 non-smoking adults with untreated chronic periodontitis and 11 periodontally healthy subjects as controls. Full-mouth probing depth (PD) and bleeding on probing (BOP) were recorded by the Florida Probe®. Stimulated whole saliva was collected by a standard spitting method immediately prior to clinical examination. sCD14 levels (ng/mL) were determined by ELISA. Neutrophilic elastase was analyzed with a neutrophil-specific substrate (pGluProVal-pNA) and the maximal rate of elastase activity (MR-EA, mAbs/min) was calculated. Salivary sCD14 levels in healthy controls were significantly higher than in the patients (p<0.02), while MR-EA in patients was significantly higher than in healthy controls (p<0.001). Overall, a moderate negative correlation existed between these two molecules (r= -0.371, p=0.0013). sCD14 was negatively correlated with sites% showing PD ≥ 5.0mm (r= -0.311, p=0.0208) and BOP (r= -0.368, p=0.0152). In contrast, MR-EA was positively correlated with these two parameters (r=0.610, p=0.0001; r=0.356, p=0.0191). Increased MR-EA or reduced sCD14 levels in saliva elevate the relative risk of a subject presenting with periodontitis to 4.26 or 2.21, respectively. This study suggests that salivary neutrophil elastase and sCD14 levels may serve as co-biomarkers for an overall periodontal assessment. Supported by the Hong Kong Research Grants Council (RGC, HKU 7310/00M). E-mail: ljjin@hkusua.hku.hk

INTRODUCTION

- Currently, there are no well-established simple and reliable biochemical indicators for overall assessment of periodontal conditions.
- Granulocyte elastase in gingival crevicular fluid (GCF), a marker of neutrophil influx into the crevicular environment, has previously been shown to be correlated with periodontal diseases and disease progression (Eley & Cox 1996, Jin et al. 1999, 2000, 2002). Oral elastase test could be a valuable adjunct in periodontal screening and assessment of periodontal status (Nieminen et al. 1993, Uitto et al. 1996), but not suitable for smokers, as cigarette smoking leads to lowered elastase and neutrophil levels in the oral cavity (Pauletto et al. 2000).
- Our recent study for the first time detected the levels of soluble CD14 (sCD14) in GCF and showed that sCD14 in GCF may be an indicator of periodontal health (Jin & Darveau 2001).
- Saliva is a complex mixture of oral fluid mainly arising from salivary glands and GCF. The GCF source may play a particularly important role in the utility of saliva in diagnosis of many infectious diseases (Thieme et al. 1994, Streckfus & Bigler 2002, Lamster et al. 2003).
- Saliva may therefore offer great potential as an easily obtainable and subject-based medium for overall assessment of periodontal conditions.

AIMS

- To determine granulocyte elastase and sCD14 in saliva and evaluate whether these molecules could be used for an overall periodontal assessment.

SUBJECTS & METHODS

- **Subjects:**
  - 61 non-smoking Chinese adults (45.3 ± 9.0 years) with untreated chronic periodontitis.
  - Eleven periodontally healthy subjects (21.4 ± 1.7 years) as controls. (sites% BOP < 15%, No sites with PD > 3 mm or clinical attachment loss > 1 mm.)
  - Good general health.
  - No antibiotics in preceding 6 months; No immunosuppressive drugs.
  - Written and oral informed consents obtained.
- **Examination & collection of samples:**
  - Full-mouth PD and BOP were recorded by Florida Probe.
  - Stimulated whole saliva was collected by a standard spitting method immediately prior to clinical examination.
  - Salivary sCD14 levels (ng/mL) in supernatant were determined by ELISA. Salivary granulocyte elastase activity was analyzed with a granulocyte-specific substrate (pGluProVal-pNA), and presented as the maximal rate of elastase activity (MR-EA, mAbs/min) (Jin et al. 1999, 2000, 2002).
  - ANOVA was used to determine the significance of difference between the patient and control groups. Correlation analysis with two-tailed significance testing was performed to assess the relationship between elastase and sCD14 as well as their relations with clinical data.

RESULTS

- Salivary sCD14 levels in healthy controls were significantly higher than in the patients (p<0.02)(Fig. 1a), while MR-EA in patients was significantly higher than in controls (p<0.001) (Fig. 1b).

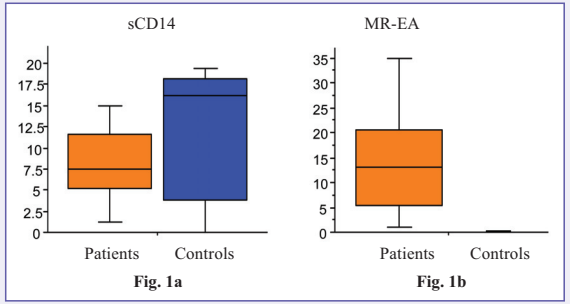

Fig. 1a **Fig. 1b**

- Overall, a moderate negative correlation existed between elastase and sCD14 levels in saliva (r= -0.371, p=0.0013) (Fig. 2).

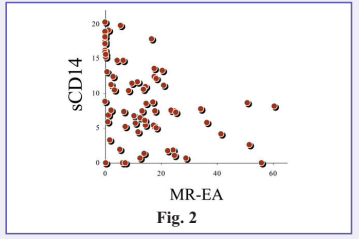

Fig. 2

- sCD14 was negatively correlated with sites% showing PD ≥ 5.0 mm (r= -0.311, p=0.0208) and BOP (r= -0.368, p=0.0152). In contrast, MR-EA was positively correlated with these two clinical parameters (r=0.610, p=0.0001; r=0.356, p=0.0191) (Table 1).
- Reduced sCD14 or increased MR-EA levels in saliva elevated the relative risk (RR) of periodontitis to 2.21 or 4.26, respectively. The combined test showed high sensitivity, specificity and RR (Table 2).

Table 1. Correlation between sCD14/elastase and clinical data

	Sites% BOP	Sites% PD ≥ 5.0mm	Mean PD (mm)
sCD14	-0.368**	-0.311*	-0.263
MR-EA	0.356**	0.61***	0.454**

*p<0.05; **p<0.02; ***p<0.001.

Table 2 . Sensitivity, specificity and relative risk for the diagnostic tests of sCD14 (< 15.3 ng/mL) and MR-EA (≥ 0.14 mAbs/min)

	Sensitivity	Specificity	Relative risk
sCD14	90.2%	72.7%	2.21
MR-EA	95.1%	90.9%	4.26
sCD14 & MR-EA	90.2%	100%	2.83

CONCLUSION

- This study suggests that salivary neutrophil elastase and sCD14 levels mights serve as co-biomarkers for an overall periodontal assessment.

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