



Clinical Studies

On the diagnostic discrimination ability of mouthrinse and salivary aMMP-8 point-of-care testing regarding periodontal health and disease☆☆☆

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ABSTRACT

This study investigated the diagnostic utility of mouthrinse and saliva in aMMP-8 measurements to analyze patients' risk for active periodontal tissue destruction and progression of periodontal disease among 47 adolescents. Results show that measurements from mouthrinse produce better discrimination and should be used instead of saliva measurements.

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Oral fluids (saliva, mouthrinse, gingival crevicular fluid [GCF], and peri-implant sulcular fluid [PISF]) provide a matrix for periodontitis and dental peri-implant biomarker diagnostics as recently studied by Schmalz et al. (2019). In periodontitis and peri-implantitis, elevated levels of neutrophil collagenase or collagenase-2, especially in active/activated form, reflect, predict, and monitor the diagnosis, course, and treatment of these diseases. Oral fluid active matrix metalloproteinase-8 (aMMP-8)/neutrophil collagenase is a potential point-of-care (PoC)/chairside biomarker for these diseases, and commercially available aMMP-8 PoC tests have been developed and are in

use. GCF and PISF have often been sampled at individual sites using filter papers and/or micropipettes (Rathnayake et al. 2017), but there is an alternative way to sample GCF: a wash using a mouthrinse technique (Drouin et al. 1988; Gangbar et al. 1990). This simpler technique utilizing mouthrinse has been developed to collect GCF from periodontitis patients (Gangbar et al. 1990; Nwhator et al. 2014; Heikkinen et al. 2016; Räisänen et al. 2019a). The aim of this note is to provide more accurate assessment of the efficiency of mouthrinse vs. salivary aMMP-8 analysis in discrimination of periodontal health and disease.

Fig. 1 illustrates the ability of aMMP-8 PoC mouthrinse test compared to aMMP-8 IFMA measured from saliva, and it clearly shows how saliva is inferior to mouthrinse in aMMP-8 measurements related to identifying periodontal health and disease. There is a significant association between the aMMP-8 PoC mouthrinse test result and aMMP-8 IFMA levels in saliva in this sample of adolescents, as has been shown recently by Räisänen et al. (2019b). However, if patient's periodontal health is considered, the distinction of salivary aMMP-8 IFMA measurements is far from perfect between a positive and negative test result. aMMP-8 IFMA concentrations vary between similar maximum and minimum levels independent of the patient's number of sites (0 or 1, and 2 or more) with ≥ 4 mm periodontal pockets. On the contrary, the aMMP-8 mouthrinse test is very sensitive for at least 2 sites with

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☆☆ Ethical approval This study was approved by the Ethical Committee of Helsinki University Central Hospital, Helsinki, Finland (Diary number 260/13/03/00/13, 17.12.2013). The study was conducted according to the principles of the Declaration of Helsinki (2008). Participants provided a written informed consent in this study.

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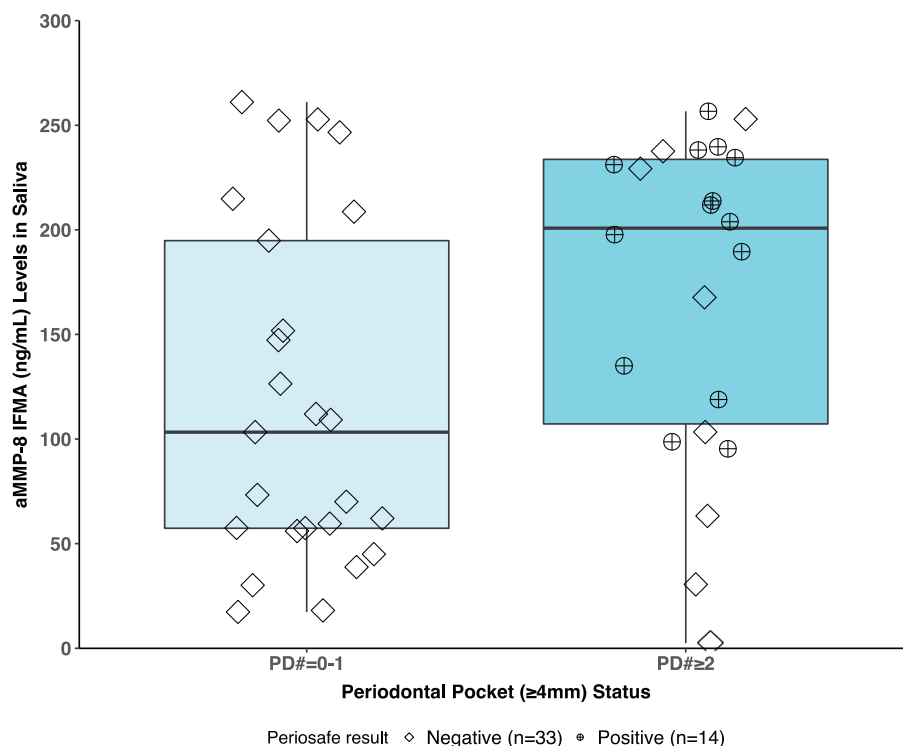


Fig. 1. aMMP-8 IFMA (ng/mL) concentrations in saliva according to periodontal pocket (≥ 4 mm) status (0 or 1 [PD# = 0–1], and 2 or more [PD# ≥ 2] periodontal pockets) categorized by the corresponding aMMP-8 PoC test result measured from oral mouthrinse.

periodontal pockets (Nwhator et al. 2014; Heikkinen et al. 2016; Räisänen et al. 2019a). It is instructive that the sensitivity regarding 2 sites with periodontal pockets of ≥ 4 mm had been reported in 2014 long before it was mentioned in the latest classification (Tonetti et al. 2018).

As indicated in Fig. 1, aMMP-8 PoC mouthrinse test functions much better and more precisely, which suggests that mouthrinse aMMP-8 measurements are the optimal way of analyzing patient's risk for active periodontal tissue destruction and progression of periodontal disease. Furthermore, the use of mouthrinse aMMP-8 to measure active collagenases avoids the interference by tissue inhibitors of metalloproteinase (TIMPs) when saliva is used (Drouin et al. 1988; Gangbar et al. 1990).

In accordance with the original findings of Drouin et al. (1988) and Gangbar et al. (1990), as well the recent studies using the aMMP-8 chairside PoC tests (Nwhator et al. 2014; Izadi Borujeni et al. 2015; Heikkinen et al. 2016; Johnson et al. 2016; Sorsa et al. 2016; Heikkinen et al. 2017; Lorenz et al. 2017; Alassiri et al. 2018; Leppilähti et al. 2018; Räisänen et al. 2018; Schmidt et al. 2018; Schmalz et al. 2019; Räisänen et al. 2019a), repeatedly and strongly indicate that aMMP-8 or active neutrophil collagenase present in mouthrinse is derived from GCF and neutrophils. Regarding saliva, there are multiple other potential sources for aMMP-8 in addition to neutrophils (Rathnayake et al., 2017). Overall, mouthrinse provides calibration and standardization of the GCF and its aMMP-8 biomarker to be quantitatively analyzed (Nwhator et al. 2014; Izadi Borujeni et al. 2015; Heikkinen et al. 2016; Johnson et al. 2016; Sorsa et al. 2016; Heikkinen et al. 2017; Lorenz et al. 2017; Sorsa et al. 2017; Alassiri et al. 2018; Leppilähti et al. 2018; Räisänen et al. 2018; Schmidt et al. 2018; Schmalz et al. 2019; Räisänen et al. 2019a). Additional studies have further shown that aMMP-8, but not total MMP-8, can predict and differentiate between “active” and “inactive” periodontal pockets (Lee et al. 1995; Mancini et al. 1999; Romanelli et al. 1999; Kiili et al. 2002; Sorsa et al. 2006), and standard-of-care treatment (i.e., scaling and root planing) reduces aMMP-8 levels in oral fluid (GCF and mouthrinse) and, at the same time, ceases the clinical progression of the disease (Mäntylä et al.

2003; Leppilähti et al. 2014; Leppilähti et al. 2015; Alassiri et al. 2018). Elevation of aMMP-8 (>20 ng/mL) by 2 or even 1 active deep site is required for the chairside PoC test to be positive to indicate increased risk for periodontitis and/or its development and progression, thus reflecting the high sensitivity of commercially available aMMP-8 PoC mouthrinse test (Nwhator et al. 2014; Heikkinen et al. 2016; Räisänen et al. 2019a). This was also originally observed for active collagenase activity by Gangbar et al. (1990). Salivary analysis of periodontitis biomarkers is on the other hand less exact and potentially erroneous (Fig. 1). Thus, the aMMP-8 oral fluid test is a mouthrinse—not salivary—test addressing GCF/PISF aMMP-8 in periodontal disease.

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