Review Article

Point of Care testing: The future of periodontal disease diagnosis and monitoring

Mohamad Khorshid[1*]

1Mississauga Smiles Dentistry, 102-90 Burnhamthorpe Rd West, Mississauga, Ontario, Canada.

* Correspondence: mohamad.khorshid@gmail.com

Received date: 12-09-2022
Accepted date: 15-10-2022
Published date: 15-12-2022

https://doi.org/10.26477/jbcd.v34i4.3277

Abstract: Manual probing and periodontal charting are the gold standard for periodontal diagnosis that have been used in practice over a century. These methods are affordable and reliable but they are associated with some drawbacks that cannot be avoided. Among these issues is their reliance on operator's skills, time-consuming and tedious procedure, lack sensitivity especially in cases of early bone loss, and causing discomfort to the patient. Availability of a wide range of biomarkers in the oral biofluids, dental biofilm, and tissues that potentially reflect the periodontal health and disease accurately encouraged their use as predictive/diagnostic/monitoring tools. Analysing biomarkers during care-giving to the patient using chairside kits is known as Point of Care (POC) testing. Introduction of POC in periodontal practice could provide more flexibility and add further dimensions to the process of diagnosis and tailoring more precise treatment plan for the patients. This review aimed to highlight available POC testing used for periodontal diagnosis and disease prediction/monitoring.

Keywords: Periodontal disease, periodontitis, saliva, gingival crevicular fluid, biomarkers, diagnosis, prognosis.

Introduction

Periodontitis is one of the most chronic prevalent disease, affecting over 45% of the populations worldwide [1]. This disease is considered as a "silent killer" of the teeth and ranked in the second place among the main reasons for tooth loss [2]. This disease has a huge economic impact and seriously associated with many systemic diseases such as diabetes mellitus, cardiovascular disease, and psychological disorders [3, 4]. Early detection and close monitoring are the most successful approaches to limit the negative outcomes of periodontitis.

Conventionally, diagnosis of periodontal disease depends on measuring periodontal parameters including bleeding on probing, clinical attachment level, and probing pocket depth together with radiographs. Although these methods are reliable and cost-effective, they suffer from inherited drawbacks such as their dependence on the operator's skills, probing force/direction, and dimensions of the probe [5, 6]. In addition, 3D radiographic machines are sophisticated, expensive, and exposing the patients to unnecessary radiations [7]. Availability of a wide range of proteins i.e., biomarkers in the oral tissues, dental biofilm, and oral fluids including saliva, gingival crevicular fluid (GCF), oral rinse samples, and peri-implant sulcular fluid (PISF), encouraged their use as diagnostic/prognostic tools [8]. Advantages of biomarkers over conventional techniques is the ability to provide information about active disease sites, anticipate progression rate, determine the susceptibility of the individuals, and tailoring the treatment

plan in more accurate way [8]. These tests that performed during providing care to the patients are known as Point of Care (POC) testing.

Several chairside tools were invited over the last decades to exploit a single or range of biomarkers in oral fluids to predict, diagnose, and monitor periodontal disease. The aim of this review was to summarize available POC testing commercially available that could be used in periodontal diagnosis and monitoring.

Biological sources for biomarkers

Oral cavity exhibits different biologic sources readily available for analysis such as saliva, GCF, plaque biofilm, tissues, and PISF. Saliva is the most popular biofluid used for clinical and experimental purposes due to its abundance, easily and non-invasively collected, enriched with biomarkers that reflect many local/systemic states, and can be collected without ethical issues [9]. Use of saliva as a source of biomarkers is rapidly expanding particularly after recent transcriptomic and proteomic studies that added considerable number of biomarkers that support the use of saliva as an alternative to blood and urine samples [10, 11]. However, the main problem with saliva is the reflection of the whole mouth condition without the ability to pinpoint sites with active disease process. In addition, the biomarkers are highly diluted in saliva which render their detection process difficult.

Alternatively, GCF and PISF are good source of biomarkers that specifically reflecting the condition of the site which is more useful tools to assess the efficacy of periodontal therapy [12]. Nevertheless, collection procedure is technically demanding and the strips are highly prone to contamination. Additionally, only small volume could be retrieved that add further complications to assaying procedure [12].

Subgingival biofilm samples considered as the main source for studying putative periodontal pathogens which, like GCF sampling, is subjected to contamination and technical issues to isolate and culture certain fastidious microorganisms [13]. The POC assays are based on microbiological, biochemical, and genetic test performed on different biological samples available (Figure 1)

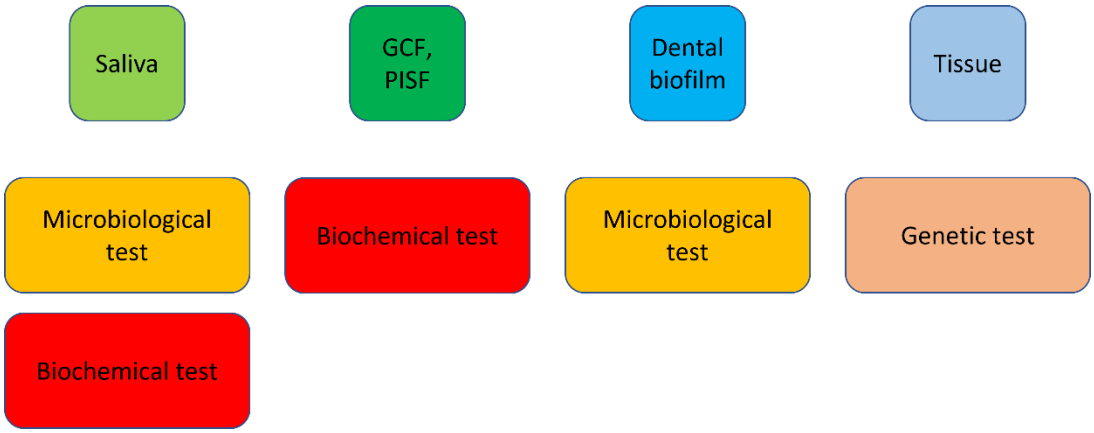

Figure 1: Biological source of biomarkers in the oral cavity and the corresponding assays used for Point of Care testing.

Commercial Point of Care testing in periodontics

Integrated microfluidic platform for oral diagnostics (IMPOD)

This microfluidic diagnostic platform was designed to detect salivary biomarkers (MMP-8, IL-6, TNF-α) indicative of periodontal disease using electrophoretic immunoassays approach [14]. This portable device allows analysis of multiple analytes using small volumes of saliva (10 μL) with a relatively short time (less than 250 sec) and low cost [14].

MyPerioPath®

This DNA polymerase chain reaction-based test is mainly used to detect periodontal pathogens, in salivary samples, responsible for initiation and progression of periodontal disease and could be associated with other systemic diseases such as diabetes and adverse pregnancy outcomes. These pathogens are divided according to their risk into high (*Aggregatibacter actinomycetemcomitans*, *Porphyromonas gingivalis*, *Tannerella forsythia*, and *Treponema denticola*), moderate (*Eubacterium nodatum*, *Fusobacterium nucleatum/periodonticum*, *Prevotella intermedia*, *Campylobacter rectus*, and *Peptostreptococcus*), and low (*Eikenella corrodens*, and *Capnocytophaga* species) [15, 16].

OMNIgene®

It is a DNA probe system used for quantitative profile analysis for eight periodontal bacteria (*P. gingivalis*, *P. intermedia*, *A. actinomycetemcomitans*, *F. nucleatum*, *E. corrodens*, *C. rectus*, *T. forsythia*, and *T. denticola*). The targeted samples are collected from subgingival plaque biofilm [17].

Periogard

Death of the cells is highly associated with the release of the cytoplasmic enzyme aspartate aminotransferase (AST) as a by-product. This principle was used in the development of Periogard to detect active site exhibiting remarkable periodontal tissue destruction [18-20]. A multicenter trial aimed to validate Periogard kit by measuring AST levels in GCF sample collected from patients treated by scaling and root planing. The results of showed consistency reported by this chairside tool over different locations [20]. The GCF sample containing this enzyme is used for analysis; however, this assay is considered technically demanding which limits its use in clinical practice [15].

Periocheck®

This chairside device obtained Food and Drug Administration (FDA) approval in the United States. The principle of this technique relies on the presence of natural protease activity within GCF. Briefly, strips containing GCF samples are placed on a gel containing insoluble dye-labelled collagen fibrils which would be digested by the proteases in the GCF. The reaction outcome appears as a blue color [15]. Results of a clinical trial aimed to evaluate diagnostic and prognostic potentials of this device indicated that Periocheck® lacks diagnostic and predictive reliability as compared to clinical methods [21]. In addition, the GCF samples from interproximal surface are prone to salivary contamination which further reduces the efficacy of this test.

MMP dipstick

Irreversible periodontal tissue destruction is associated with upregulation of active-matrix metalloproteinases (MMP)-8 in the GCF of natural dentition and peri-implant sulcular fluid with increasing

neutrophil activity. This fact was used to develop a chair-side dipstick test containing monoclonal antibodies to MMP-8 [22]. This tool exhibited high accuracy in differentiating periodontal health from disease, predicting and monitoring periodontal/peri-implant disease [8].

Perioscan (BANA)

The basic of this test depends on the presence of trypsin-like proteases secreted by red complex putative pathogens *P. gingivalis*, *T. denticola*, *T. forsythia* in subgingival biofilm samples which hydrolyzing the trypsin substrate [23]. Although results from clinical studies encouraged the use of BANA to monitor the outcome of periodontal therapy [24], another study showed opposite results [21].

Evalusite™ Periodontal Test

Subgingival biofilm plaque samples are used for analysis to detect three periodontal pathogens (*A. actinomycetemcomitans*, *P. gingivalis* and *P. intermedia*). This assay is based on sandwich-ELISA in which the presence of these bacteria is indicated by pink spots [15]. This assay is prone to subjectivity and its limitation to detect narrow range of putative pathogens are the main drawbacks [25]. However, it is highly sensitive for detecting the aforementioned bacteria, rapid, and user-friendly [26, 27].

Toxicity prescreening assay (TOPAS)

This assay can indirectly detect the presence of putative pathogens via their toxins and proteins. Indeed, actively dividing bacteria and increasing mass of the biofilm are associated with increased metabolic activity/product in the GCF that can discriminate between active and inactive periodontal destruction sites [28].

Periodontitis susceptibility trait test

This test is one of few commercially available genetic-based assays which identifies the genetic predisposition of individuals to severe periodontitis by detecting polymorphisms of IL-1α at +4845 and 1β +3954 loci. However, ambiguity is associated with the predictive potential of this assay and the results must be interpreted with caution [29].

MyperioID

Another IL-1-based genetic assay which predicts the susceptibility of patients at higher risk to develop periodontal disease via taking salivary samples that shipped and analysed in the laboratory [15].

Conclusions

Chairside diagnostic kits available in the market showed encouraging outcomes with decent sensitivity and specificity to predict, diagnose, and monitor periodontal disease on a community level. These tools could reduce treatment time, accurately diagnosing the disease; hence, help in tailoring personalized treatment plan with more predictable outcomes. However, each assay suffers certain drawback(s) that should be solved before recommended for use as a routine dental practice by general practitioners.

Conflict of interest: None.

References

1. Nazir M, Al-Ansari A, Al-Khalifa K, Alhareky M, Gaffar B and Almas K. Global Prevalence of Periodontal Disease and Lack of Its Surveillance. ScientificWorldJournal. 2020;2020:2146160.

2. Tonetti MS, Jepsen S, Jin L and Otomo-Corgel J. Impact of the global burden of periodontal diseases on health, nutrition and wellbeing of mankind: A call for global action. J Clin Periodontol. 2017;44:456-62.

3. Reynolds I and Duane B. Periodontal disease has an impact on patients' quality of life. Evid Based Dent. 2018;19:14-5.

4. Winning L and Linden GJ. Periodontitis and systemic disease. BDJ Team. 2015;2:15163.

5. Gupta N, Rath SK and Lohra P. Comparative evaluation of accuracy of periodontal probing depth and attachment levels using a Florida probe versus traditional probes. Med J Armed Forces India. 2015;71:352-8.

6. Shapoff CA. Understanding the limitations of dental radiographs--implications for soft-tissue management programs. Compend Contin Educ Dent. 2004;25:338-40, 42, 44 passim.

7. Kamburoğlu K. Use of dentomaxillofacial cone beam computed tomography in dentistry. World J Radiol. 2015;7:128-30.

8. Gul SS, Abdulkareem AA, Sha AM and Rawlinson A. Diagnostic Accuracy of Oral Fluids Biomarker Profile to Determine the Current and Future Status of Periodontal and Peri-Implant Diseases. Diagnostics (Basel). 2020;10.

9. Malamud D. Saliva as a diagnostic fluid. Dent Clin North Am. 2011;55:159-78.

10. Genco RJ. Salivary diagnostic tests. The Journal of the American Dental Association. 2012;143:3S-5S.

11. Haririan H, Andrukhov O, Bertl K, Lettner S, Kierstein S, Moritz A and Rausch-Fan X. Microbial analysis of subgingival plaque samples compared to that of whole saliva in patients with periodontitis. J Periodontol. 2014;85:819-28.

12. Barros SP, Williams R, Offenbacher S and Morelli T. Gingival crevicular fluid as a source of biomarkers for periodontitis. Periodontol 2000. 2016;70:53-64.

13. Nickles K, Scharf S, Röllke L, Dannewitz B and Eickholz P. Comparison of Two Different Sampling Methods for Subgingival Plaque: Subgingival Paper Points or Mouthrinse Sample? J Periodontol. 2017;88:399-406.

14. Herr AE, Hatch AV, Giannobile WV, Throckmorton DJ, Tran HM, Brennan JS and Singh AK. Integrated microfluidic platform for oral diagnostics. Ann N Y Acad Sci. 2007;1098:362-74.

15. Srivastava N, Nayak PA and Rana S. Point of Care- A Novel Approach to Periodontal Diagnosis-A Review. J Clin Diagn Res. 2017;11:Ze01-ze6.

16. Javaid MA, Ahmed AS, Durand R and Tran SD. Saliva as a diagnostic tool for oral and systemic diseases. J Oral Biol Craniofac Res. 2016;6:66-75.

17. Van Arsdell SW, DiFronzo F, Backman KC and Mahler PH. Selling biotechnology in the dental medicine marketplace: the OmniGene Diagnostics DNA probe tests for periodontal pathogens. Technol Health Care. 1996;4:339-46.

18. Persson GR, DeRouen TA and Page RC. Relationship between gingival crevicular fluid levels of aspartate aminotransferase and active tissue destruction in treated chronic periodontitis patients. J Periodontal Res. 1990;25:81-7.

19. Chambers DA, Imrey PB, Cohen RL, Crawford JM, Alves ME and McSwiggin TA. A longitudinal study of aspartate aminotransferase in human gingival crevicular fluid. J Periodontal Res. 1991;26:65-74.

20. Persson GR, Alves ME, Chambers DA, Clark WB, Cohen R, Crawford JM, DeRouen TA, Magnusson I, Schindler T and Page RC. A multicenter clinical trial of PerioGard in distinguishing between diseased and healthy periodontal sites. (I). Study design, methodology and therapeutic outcome. J Clin Periodontol. 1995;22:794-803.

21. Hemmings KW, Griffiths GS and Bulman JS. Detection of neutral protease (Periocheck) and BANA hydrolase (Perioscan) compared with traditional clinical methods of diagnosis and monitoring of chronic inflammatory periodontal disease. J Clin Periodontol. 1997;24:110-4.

22. Sorsa T, Mäntylä P, Rönkä H, Kallio P, Kallis GB, Lundqvist C, Kinane DF, Salo T, Golub LM, Teronen O and Tikanoja S. Scientific basis of a matrix metalloproteinase-8 specific chair-side test for monitoring periodontal and peri-implant health and disease. Ann N Y Acad Sci. 1999;878:130-40.

23. Loesche WJ, Syed SA and Stoll J. Trypsin-like activity in subgingival plaque. A diagnostic marker for spirochetes and periodontal disease? J Periodontol. 1987;58:266-73.

24. Dhalla N, Patil S, Chaubey KK and Narula IS. The detection of BANA micro-organisms in adult periodontitis before and after scaling and root planing by BANA-Enzymatic™ test kit: An in vivo study. J Indian Soc Periodontol. 2015;19:401-5.

25. Mikx FH and Renggli HH. [How sensible are bacteriological tests in periodontology?]. Ned Tijdschr Tandheelkd. 1994;101:484-8.

26. Boyer BP, Ryerson CC, Reynolds HS, Zambon JJ, Genco RJ and Snyder B. Colonization by Actinobacillus actinomycetemcomitans, Porphyromonas gingivalis and Prevotella intermedia in adult periodontitis patients as detected by the antibody-based Evalusite Test. J Clin Periodontol. 1996;23:477-84.

27. Nakagawa T, Saito A, Takahashi J, Komiya A, Hosaka Y, Yamada S and Okuda K. Evaluation of EvalusiteTM Periodontal Test for Detecting Periodontopathic Bacteria. Nihon Shishubyo Gakkai Kaishi (Journal of the Japanese Society of Periodontology). 1995;37:312-6.

28. Pucau CG, Dumitriu A and Dumitriu HT. Biochemical and enzymatic diagnosis aids in periodontal disease. OHDMBSC. 2005;4:19-25.

29. Greenstein G and Hart TC. A critical assessment of interleukin-1 (IL-1) genotyping when used in a genetic susceptibility test for severe chronic periodontitis. J Periodontol. 2002;73:231-47.

اختبار نقطة الرعاية: مستقبل تشخيص أمراض اللثة ومراقبتها

الباحثون: محمد خورشيد

المستخلص:

يعتبر الفحص اليدوي المعيار الذهبي لتشخيص امراض دواعم الأسنان التي تم استخدامها في الممارسة العملية على مدى قرن من الزمان. هذه الطرق ميسورة التكلفة وموثوقة ولكنها مرتبطة ببعض العيوب التي لا يمكن تجنبها. من بين هذه المشكلات اعتمادهم على مهارات الطبيب، والإجراءات التي تستغرق وقتًا طويلاً ومملا

بالنسبة للمراجع والمعالج، ونقص الحساسية خاصة في حالات فقدان العظام المبكر، والتسبب في إزعاج المريض. إن توافر مجموعة واسعة من المؤشرات الحيوية في السوائل الحيوية في الفم والأغشية الحيوية للأسنان والأنسجة التي من المحتمل أن تعكس صحة اللثة ومرضها شجع استخدامها كأدوات تنبؤية / تشخيصية / مراقبة. يُعرف تحليل المؤشرات الحيوية أثناء تقديم الرعاية للمريض باسم اختبار نقطة الرعاية (POC). يمكن أن يوفر إدخال POC في ممارسة اللثة مزيدًا من المرونة وإضافة أبعاد أخرى لعملية التشخيص وتصميم خطة علاج أكثر دقة للمرضى. تهدف هذه المراجعة البحثية إلى تسليط الضوء على اختبار POC المتاح المستخدم في تشخيص اللثة والتنبؤ بامراضها ومراقبتها.