DOI: 10.7860/JCDR/2017/24260.9631

Review Article

Dentistry Section

Patient Centered Outcomes in Periodontal Treatment-An Evidenced Based Approach

EKTA BHARATBHAI SHAH[1], BHAVESH BHUPENDRABHAI MODI[2], MONALI AMIT SHAH[3], DEEPAK HARISHBHAI DAVE[4]

ABSTRACT

Transformation of research into clinical practice is the most challenging step in evidence based dental practice. Designing the most reliable research with applicable endpoint evaluation is very important as it can lead to successful research outcomes that can be accepted in clinical practice. In the periodontal research few accepted endpoints are used frequently as they are believed to be the gold standard in measuring the periodontal disease and the treatment outcomes. However, a wide range of endpoints used are surrogate endpoints and these endpoints have no direct correlation with the patient centered outcomes. Hence, a direct relationship of surrogate endpoints with true endpoints needs to be established. This review highlights the importance of true endpoints and challenges in implementing these in clinical research. Importance of patient's centered outcomes are also reviewed and duly discussed here. Need for conducting research which includes the true endpoints or the surrogate endpoints with clinical applicability and tangible outcomes, was also suggested in this review.

Keywords: Periodontal research, Surrogate endpoints, True endpoints, Tangible outcomes

INTRODUCTION

Evidenced based practice is one of the most desirable approaches to the treatment options, as it involves the patient centered outcomes along with the highest level of evidence for any problem encountered in the clinical practice. Evidence based dentistry involves decision making with four different parameters that include patient values, scientific evidence, clinician knowledge and experience and judgment [1]. Among these parameters, patient values should be attended with utmost priority during planning of the treatment as well as for the future research to achieve patient centered outcomes.

Conventional periodontal treatments are clinically significant but cannot measure the longevity in aspects of tangible outcomes. There is a need of scientific research with a long term follow up that directly correlates the severity of periodontitis to patient centered outcomes. True endpoints like tooth loss, reduction in mobility or sensitivity, pain during and after the surgical treatment, postoperative compliance of the patient to the therapy should be emphasized.

Patients' oral health, periodontal diseases, tooth loss and quality of life: The periodontal disease is one of the commonly seen oral health disease [2] where multiple anaerobic species of bacteria play a significant role in its progression and severity. In its initial stages, subjects are ignorant of their periodontal status and underestimate the treatment needs as suggested by dental professionals [3]. In more advanced stage of periodontal disease, difficulty in mastication, halitosis, tooth mobility and loss of interproximal papillae with food lodgement are routinely noticed by the individuals [4].

The global burden of disease represented by chronic periodontitis is verified by its position as the sixth most prevalent disease [5]. The periodontal disease activity and severity is routinely measured by research clinicians using different clinical parameters such as probing pocket depth, bleeding on probing and clinical attachment level [4]. On the other hand, other clinical parameters of periodontitis such as redness of gingiva, bleeding while brushing, loosening of teeth, and constant bad breath are the consequences of chronic inflammation and the destruction of tooth supporting tissue. From the research point of view such symptoms are not normally documented [6], however they are highly relevant from the patients' perspective and often have a considerable adverse impact on quality of life.

As patient centered approach is becoming more accepted nowadays, increased attention is given to assess the effects of the human health situations on an individual's overall quality of life. Various measures have been used to measure the effect of treatment on quality of life in other fields of dentistry but little has been reported about the effects of periodontal disease and its treatment outcome so far on quality of life. Quality of life assessing the effect of periodontal disease on the daily life activities was expressed by means of simple questionnaire surveys [7].

Patients' preference and needs are given equal weightage in implementing research outcome in evidence based practice. So a complete knowledge of periodontal disease and further consequences of the treatment on patients' perceptions will have added advantage on treatment planning and evaluation of periodontal care as it addresses patients' needs and concerns [7,8]. There is an extensive debate on the use of traditional outcome indicators vs patients' centered outcomes in periodontal therapy. Hujoel PP et al., commented that clinical as well as other periodontal parameters widely used in research are not more than just surrogate outcomes and not the true endpoints [9]. Such indications are not patient centered. Several researchers have started various studies to find out the relationship between patient satisfaction and periodontal treatment that is patient centered outcomes [10-14].

True endpoints and surrogate endpoints: True endpoints are tangible outcomes to the patient. True endpoints are those outcomes that directly measure patient's perception and how a patient feels about treatment. The word tangible is defined as capable of being precisely identified or realized by the mind. True endpoints also include subjective oral health related quality of life measurements [15] or simple self reported symptoms such as bleeding after brushing, mobility of teeth, foul smell from mouth, food lodgment, sensitivity, tooth loss etc. True endpoints are sometimes referred to as clinically relevant endpoints, clinically meaningful endpoints, terminal endpoints, or ultimate endpoints [16].

Surrogate endpoints are intangible outcomes to the patient. Surrogate endpoints are being used as a substitute for true endpoints

[17]. Changes measured in periodontal pocket depth, clinical attachment level, gingival crevicular fluid markers, inflammatory markers, microbiological and immunologic parameter are examples of intangible outcomes [18]. Surrogate endpoints are recorded by the clinician or in laboratory as they are objective and do not rely on patient's subjective views. They are sometimes referred to as intermediate endpoints, biological markers, or biomarkers [16].

True endpoint trials may also provide a first mover advantage. The first mover advantage is the one where outcomes measured after the clinical trial itself motivates vast number of patients to undergo the same treatment therapy with positive outcomes [16]. Various drug trials which have shown positive impact; presently they are widely accepted and used in their specific field. Periodontal research done with such tangible benefit can lead to self motivation and drastic increases in further treatment among the target population with a first mover advantage.

For example, following root coverage procedure more weightage is given to recession measurement than the amount of patient satisfaction achieved by self reported aesthetic improvement [16]. So the endpoints measured for any disease condition should be from patient's perspective and not from clinician's point of view.

True endpoints and surrogate endpoints in periodontal research: All clinical trials that measure true endpoints are generally of a long duration and require the enrollment of more number of patients. From a periodontal point of view few parameters like pain management are taken care of within few weeks of trial while some parameters like tooth loss takes decades to establish any outcome to the treatment. If any clinical trial requires years to complete, hypothesis becomes out dated by the time they get into practice.

Surrogate endpoints at times are not concluding because the direct connections between treatments to surrogate endpoints are not established with true endpoints [Table/Fig-1]. The use of surrogate endpoints can lead to both false positive and false negative results.

Surrogate endpoints	True endpoints	Patients perception/ Tangible outcomes
Bleeding on probing	Bleeding while brushing	Bleeding while brushing
Probing depth/ clinical attachment level	Masticatory efficiency	Satisfactory mastication
GCF Markres	Life span of tooth	Tooth loss
Microbial load	Halitosis	Bad breath
Intrabony defects and furcation defects fill	Masticatory efficiency, Life span of tooth, dental comfort	Tooth loss and satisfactory mastication without pain
Position of gingival margin	Complete root coverage	Aaesthetic outcomes and satisfaction

[Table/Fig-1]: Correlation of surrogate endpoints with true endpoint and patients perception.

Clinical trials and real life scenario: Generally, routine dental treatment care is planned in a way that it focuses on the well being of an individual. Along with the present clinical condition, patient's desire and financial condition are also considered. In contrast, a research design for any trial is done with an aim to test the given hypothesis where a conclusion can be drawn according to the results achieved. Such conclusion can lead to outcomes that are applicable to a large group of population.

The concept of evidence based decision making in medicine was introduced in 1990s and it's based on providing outcomes using four sources of information which are scientific evidence, clinician knowledge, experience and judgment, patient's values and patient's clinical circumstances [1].

It is known that many times patients' perception for subjective symptoms is different from the test hypothesis which is provided by health care provider. Such clinical trials may not measure parameters that are significant for the patient. Information gained from these clinical trials might be important to the patient but different from what patient perceives [19]. Because as a clinician our goal is to improve the quality of life of the patients by the treatment offered, but randomized control clinical trial have been designed that includes parameters that are important to the research hypothesis.

Challenges to implement true endpoints and the importance of surrogate endpoint validation in periodontal clinical trials: The foremost challenge in implementing the true endpoints in clinical trials is the blind faith in currently used surrogate endpoints. The feasibility for few true endpoints like surgical procedures done for aesthetic outcomes or splinting as treatment for mobility to measure the masticatory efficiency or the use of NSAIDs for pain control in acute conditions could be easily done with short term goals. Any trial that has pain as a true endpoint outcome can be an example that implementing a true endpoint is not a real challenge and that such endpoints are relevant as well as feasible for further periodontal research. But challenges do lie on the pathway to true endpoint if we measure parameters like tooth loss that have a long term outcomes but still its achievable and can't be neglected or avoided as the inference drawn is much more important than the short term gains measured like probing depth reduction or attachment gain.

It is a real time problem that such subjective or tangible outcomes are never used only because of the belief that objective or intangible outcomes are superior to the subjective outcomes. Subjective endpoint at times defers from patient to patient or as it's believed that subjective parameters are never universal to all the patients. For example, if the patient complains of pain/sensitivity it is very difficult to measure the severity of pain/sensitivity as it can vary from patient to patient. Various scales available to measure the same also have their own drawbacks.

Criteria to validate surrogate endpoints are essential for clinical trials. Prentice RL has given the criteria to validate the surrogate endpoint that are [20]:

1. Surrogate endpoints must correlate to the true clinical outcome;
2. Treatment offered should have effect on surrogate endpoint leading to the true clinical outcome.

Various explanations for failure of surrogate endpoints are described [21], where the surrogate endpoints may correlate with disease progression or they might not involve in pathophysiologic process that result in clinical outcome. If the surrogate endpoint does not correlate to the disease progression then such endpoints fail to get relevant outcomes in the research methodology. If the intervention done is directly related to the disease pathopysiology and surrogate endpoint which in turn leads to true clinical outcome is the most desired endpoints for the clinical trials for any intervention study. Sometimes the intervention does not correlate to the surrogate endpoints anywhere, leading to failure of using it in the clinical trial. Interventions at times may mediate through unintended mechanism which inturn directly relate to true clinical outcomes independent of the actual disease pathophysiology or surrogate endpoints.

Example: Osteoporosis in Postmenopausal Women.

Severe bone destruction along with osteoporosis is a common finding in postmenopausal women, which ultimately leads to increase risk of fractures. Various treatment modalities like sodium fluoride are used to increase the bone mass by stimulating more bone formation but according to the study done by Riggs BL and his colleagues in a group of postmenopausal women having osteoporosis, it was concluded that the same causes increase in skeletal fragility apart from increasing bone mass [22]. The present situation describes the use of surrogate endpoints like bone mineral density to measure the clinical outcome to osteoporosis but the true outcomes from patient's perception is to have reduced risk of fracture is not taken into consideration during the treatment trial.

Future perspective and further research: No direct correlation has been established between surrogate endpoints like probing depth or clinical attachment level with tangible outcomes like tooth loss and mobility. On the contrary true endpoints like bleeding on brushing or pain management measures outcomes from patients' perception. Such true endpoints do not require longer duration for any evaluation during the clinical trial. Hence studies should be conducted which includes the true endpoints or the surrogates that inturn give true clinically desired outcome. Direct relationship of surrogate endpoints with true endpoints should be established based on high quality longitudinal study.

CONCLUSION

Surrogate endpoints can be used cautiously where use of true endpoints is not feasible. Screening and evaluation of phase 2 trials for promising new therapies can include surrogate endpoint. Results following such trial inturn can guide us in decision making whether the intervention is effectively potential to rationalize the conduct of large scale and longer term clinical trials. This need to be supported by trials using true endpoints, which are more tangible and patient centered. The primary goal is to obtain direct evidence of the intervention's effect on true clinical outcomes.

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PARTICULARS OF CONTRIBUTORS:
1. Senior Lecturer, Department of Periodontology, K.M.Shah Dental College, Sumandeep Vidyapeeth University, Vadodara, Gujarat, India.
2. Senior Lecturer, Department of Periodontology, K.M.Shah Dental College, Sumandeep Vidyapeeth University, Vadodara, Gujarat, India.
3. Professor, Department of Periodontology, K.M.Shah Dental College, Sumandeep Vidhyapeeth University, Vadodara, Gujarat, India.
4. Professor and Head, Department of Periodontology, K.M.Shah Dental College, Sumandeep Vidyapeeth University, Vadodara, Gujarat, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Dr. Ekta Bharatbhai Shah,
132, Ashutosh Society, Karelibaug, Vadodara-390018, India.
E-mail: e_shah_ekta@yahoo.co.in

FINANCIAL OR OTHER COMPETING INTERESTS: None.

Date of Submission: **Sep 19, 2016**
Date of Peer Review: **Nov 19, 2016**
Date of Acceptance: **Dec 31, 2016**
Date of Publishing: **Apr 01, 2017**