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Original Research Paper

Periodontology

RESEARCH IN CLINICAL PERIODONTOLOGY: CURRENT APPROACHES AND FUTURE PERSPECTIVES

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ABSTRACT Research in the field of periodontology has observed a huge upheaval in the last two decades unveiling newer alterations in techniques, methodologies, and material science. The recent centre of attention in periodontal research is an evidence-based approach which offers a bridge from science to clinical practice. Research inculcates scientific and inductive thinking and it promotes the development of logical habits of thinking and organization. In terms of research methodology, the article aim to inform the reader on topics relating to randomized controlled trials in periodontal research, evidence-based dentistry, calibration of clinical examiners and statistics relevant to periodontal research.

KEYWORDS :

INTRODUCTION:

Research is like lighting a matchstick in a dark room. Once the dark room is lit there are no blind-spots, everything is clear. Once the research is complete the facts obtained can shed light on the unknown.

Research in clinical periodontology helps clinician to obtain scientific knowledge, therefore improving the actions or clinical management (evidence- based dentistry). Research starts with defining a problem, formulating a hypothesis, followed by collection and evaluation of data, drawing deductions and conclusions from the data and finally testing the conclusions to determine they deny or justify the formulated hypothesis.

Periodontology in last few decades has observed a tremendous advancement in clinical, epidemiological and molecular research, solving the blind-spots of etiopathogenesis and treatment aspects of periodontal disease.

The first step in conducting a research is the formulation of a specific research problem and generation of hypothesis. A hypothesis is a statement based on belief of the researcher that can be proved or disproved by the research.

Null hypothesis (H_0) is based on consideration that there is no difference in the population or groups relating to research hypothesis. **Alternative hypothesis** (H_A) states that there exists a difference among the groups. So, the hypothesis helps us to approach the dark room with an open mind even before lighting the matchstick.

Clinical research can be either experimental study or observational study. In observational studies, the researcher only observes the patients at a point in time (cross-sectional studies) or over a period of time (longitudinal studies). In experimental studies, the researcher intervenes. Experimental studies are always prospective studies. Prospective studies are those which go forward in time whereas retrospective studies are those that go back in time. Observational studies may be either prospective or retrospective.

Current approaches for conducting clinical research can be broadly categorized as:

Observational Studies are used to monitor or describe the health status of a population. Types of observational studies include:

- Correlational study: These studies intend to explore a correlation between two variables such as relationship between periodontitis and diabetes mellitus.
- Case reports and case series: Study in which the possibility of an association is explored between an observed effect and a specific environmental exposure in a single individual (case report) or small group (case series). For example, presence of multiple gingival recession in a smoker (case report) or smokers (case series).
- Cross sectional study: These studies are like snapshot picture of a population at a point in time, for example prevalence of alveolar bone loss in patients treated with doxycycline.
- Case-control study: A case control study starts with patients who already have the outcome or disease and the possible exposures are investigated or explored. The study of outcome to exposure.
- Cohort study: These studies take large population who are already exposed or under a particular treatment, follow them prospectively and compare them for outcomes with a similar non-exposed group or a group not under the particular treatment being studied. Cohort studies can be either a *prospective cohort study* where patients are grouped as per the past or current exposure and are followed to observe the outcomes of interest or a *retrospective cohort study*, where the exposures and outcomes have already occurred before the study isconducted.
- Systematic Reviews: The studies related to a

predetermined review question are categorised, segregated, reviewed, analysed and the results are summarized. An extensive literature search is conducted. E.g: A systematic review of subepithelial connective tissue graft for root coverage.The results of a systematic review may be statistically pooled together to generate a *Meta-analysis*, when possible.

Experimental study or interventional study is a study in which the researcher intervenes in the study by using a treatment, strategy, or other intervention, that is recorded and then analyzed. Experimental studies can either be preventive (prophylactic) trial or therapeutic (clinical) trial. In preventive trials a strategy that prevents disease occurrence is investigated. In therapeutic trials a strategy that treats an existing condition is investigated. In experimental study, the investigator assigns subjects to two or more groups that either receive or do not receive the preventive or therapeutic agents. **Randomized, controlled clinical trials** (RCTs) are meticulously planned research that introduce a treatment or exposure on patients to examine and evaluate the efficacy of the treatment strategy. Randomization and blinding are very powerful tools of RCT that reduce the potential for bias and that allow for comparison between intervention groups and control groups (subjects receiving no intervention). The researcher randomly assigns the exposures and then follows patients forward to an outcome which provides the knowledge of outcome of specific treatment strategy. A randomized controlled trial can enlighten us by providing evidence of cause and effect.

Randomization or random allocation is process by which the subjects are randomly assigned the treatment groups. The advantage of randomization is that it distributes potential confounding factors evenly in the different intervention groups. Randomization is like asking an individual to sit in the dark room; the individual does not know where others are sitting.

For example, in a study of the effects of a chlorhexidine in the treatment of patients with periodontitis, random allocation of the subjects to the chlorhexidine and water or other mouthwash (control) would ensure that each group has equal distribution of other cofounding factors such as age, sex, genetic variation and others, ultimately removing bias.

Blinding or masking is a technique used to eliminate the occurrence of conscious and unconscious bias in a clinical trial. Blinding can remove predetermined polarisation or belief of the researchers as well as the subject. Fair conductance of the clinical trial helps to gain more accurate result. Blinding is like blindfolding in the individuals who are in the dark room, they cannot see the other person until and unless blindfold is removed even when the room is dimly lit (data retrieval and statistical analysis).

For example, in the previous mentioned study a subject knows about another control subject receiving other kind of mouthwash and does not appropriately use the treatment mouthwash then chance of error in the clinical trial will be more, once blinded the patient is devoid of any polarisation.

Bias is an "opinion or feeling that favors one side in an argument or one item in a group or series; predisposition; prejudice." In an epidemiological perspective, bias is present when the results from the study are systematically distorted and so are consistently above (or below) what they should be. Sackett in 1979 identified 24 biases and many more have now been identified. A Fewmajor Biases Are Listed As Follows:

Selection bias - When the study participants are not representive of the population of interest. This bias usually happens during the selection of subjects for control and test groups where the investigator assigns subjects such that they differ with respect to extraneous factors.

Observer or measurement bias - When an examiner consistently over/under reports a variable (a characteristic). This must be resolved in training and calibration sessions. Recall bias - An information bias in which the subjects with disease (cases) tend to recall past exposures better than controls.

Attrition bias - It happens when subjects quit the study before its completion. These drop outs in the clinical trial cause bias in the results due to the decreased sample size in one group or may be both, and also the decreased follow up time period.

Migration bias - Another kind occurs either when individuals drop out of study or move from one group to another. Publication bias - Studies which show significant results are more likely to be published in journals than those with insignificant or negative results.

Allocation bias - When treatment groups in an experimental study are not comparable with respect to the variables influencing the response of interest.

Confounding is a mixing of the effect of an exposure with the effect of another variable that is associated with the exposure and is an independent risk factor for the disease. Confounding factors are variables, which compete with the hypothesized risk factor as explanations for the observed response. For example, smoking and alcohol are together confounding factors in causing periodontitis. Smoking is a known risk factor for periodontitis. If a study is undertaken to associate between alcohol consumption and periodontitis and if the patients smoking status is not assessed in data analysis, it will appear as if alcohol is a strong risk factor for periodontitis when in fact it is not.

Hawthorne effect - It was first described by Roethlisberger and Dickson in 1939. The rationale of this is that in a research project, individual behaviours may be altered by the study itself, rather than the effects the study is researching. Subjects who are singled out to participate in a mouthwash trial consciously tend to improve their oral hygiene and may show lower plaque scores.

Rosenthal effect (Experimenter effect) - Research also demonstrates that the expectations and biases of an experimenter can be communicated to experimental subjects in unintentional ways and that these cues may significantly affect the outcome of the experiment. For example, differences in oral hygiene instructions given to patients can affect the response of the subjects. Experimenter effects can be avoided by using double blinded studies where the experimenters' expectations and biases are not communicated to the study subjects.

Data has to be collected from the subjects or participants of the research after the trial is over. This is the part where the matchstick has ignited but it is not too bright so that the whole picture in the dark room is visible. Data is like pieces of a jigsaw puzzle, collection of data is like collecting the pieces, when the data from all the individuals are collected all the pieces of puzzle is present.

Data can be quantitative or qualitative. Quantitative data represents an amount or a count. For example, amount of recession coverage post operatively can be measured. Qualitative data is like describing something or that provides the quality of observations. For example, researcher is enquiring about the taste of the mouthwash, the data will be

pleasant or unpleasant. Qualitative data can be further divided into –

a) Nominal or Categorical data: Variables that cannot be ranked or put in a sequence, for example an individual's gender. Dichotomous or Binary data is a type of categorical data where only two possibilities can be present, the data can be either this or that, such as male or female, present or absent.
b) Ordinal/rank data: Variables that can be put in an ordered sequence and can be ranked, it is an extension of categorical data. The different categories of data can be ranked as one better or worse than the other. For example, prognosis of a tooth can be ranked as good, fair, poor, hopeless, or stages of periodontitis as mild, moderate, or severe.
c) Interval scale: Interval variables do not have a true zero but has an arbitrary zero. The arbitrary zero is a considered value depending on lowest value.
d) Ratio scale: The variables have a definite zero as the starting point is true zero point. For example, a person having a recession of 4mm has twice the amount of recession than a person having 2mm because of the absolute zero point.

Statistical analysis is when the matchstick burns bright and the dark room is clearly visible. Statistics is stitching together the jigsaw puzzle pieces to form a clear picture. Statistical analysis may be descriptive or inferential.

Descriptive statistics include the numbers, tables, charts, and graphs used to describe, organize, summarize, and present raw data. They are routinely used in reports which contain a significant amount of qualitative or quantitative data.

Inferential statistics are used to draw conclusions and make predictions based on the analysis of numeric data. Inferential statistics are frequently used to answer cause-and-effect questions. They are also used to investigate differences between and among groups.

Statistical inference is achieved usually by means of hypothesis testing using P value (Probability value). P-value refers to the probability of detecting a statistically significant difference that is not the result of the treatment but the result of chance. In other words, the P level determines the probability of obtaining an erroneously significant result. The P value gives the researcher a dichotomous significance and non-significance, estimation gives an idea of 'how much' one intervention works better than the other.

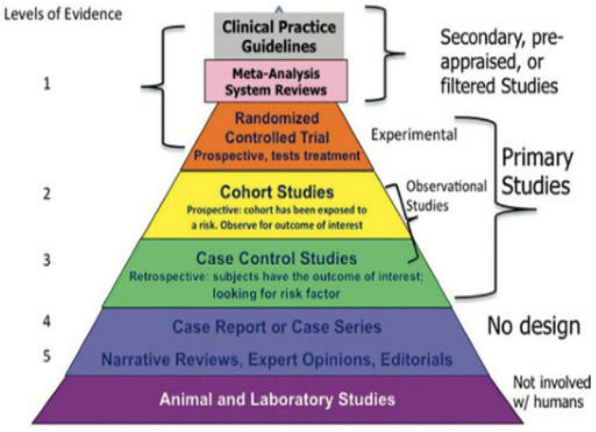
Statistical tests are used to draw inferences about a population from a sample. These are classified into parametric and non-parametric tests.

Parametric tests - A statistical test which concerns population parameters and requires assumptions about these parameters. Parametric data have an underlying normal (Gaussian) distribution which allows for more conclusions to be drawn as the shape can be mathematically described. T-test, correlation, regression, analysis of variance (Anova), and Chi-square test are a few frequently used parametric tests.

Non-parametric tests - Used in cases when the researcher knows nothing about the parameters of the variable of interest in the population (hence the name nonparametric). These tests rely more on the differences in medians rather than on the estimation of parameters (such as the mean or the standard deviation) and hence also referred to as distribution-free methods. Non-parametric methods are often employed when measurements are available only on a nominal (categorical) or ordinal (rank) scale. A formal statistical test (Kolmogorov-Smirnoff test) can be used to test whether the distribution of the data differs significantly from a Gaussian distribution.

Application of clinical research - Clinical periodontology can utilise the results of the research for decision making for better and more recent protocol that has proven efficacy clinically. Hence better treatment and management for the patient, more benefitted is the society.

The decision making relies on the hierarchy of the research, higher the level of evidence more is the reliability of treatment mentioned in the evidence.



Hierarchy of research and levels of clinical evidence

Problems & Future remedy - Most of the research conducted during the post- graduation course of Periodontology is RCT, the reason being the time required for reaching conclusion in a RCT is less as investigator can intervene the study and control various factors. But the most common problem that we face is subject related. The subjects are required to be monitored and regulated. For example, the researcher asks the subject to use a mouthwash for 14days but subject discontinued the use after 10days. Though these errors can be avoided by using large number of subjects. As the number increases the project becomes more tedious, time-consuming and resource-consuming for a single researcher.

Had there been a way to ensure proper subject related factors, there will be less subject required for the research, hence less time and resource. At this day and age, we are restricted only by thoughts and imagination.

Is nanorobotics too far in the future? These robots of microscopic scales are already in application in clinical periodontology. Can we not precisely create nanorobots to monitor the subject, deliver the drug at precise time for precise duration, to record the outcome, measure quantitative and qualitative data without asking the subject? Can these nanorobots render a clinical research devoid of errors? Answer though lies in the future, I will be a strong believer that the advancing technology will create a perfect world.

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