Review Article

An overview of evidence-based dentistry and randomized controlled trials: Importance in the current orthodontic research

ABSTRACT

Evidence-based dentistry (EBD) was developed to help dental care professionals in incorporating the current, valid, and bias-free research into their clinical practice. It is equally important to review and critically appraise the evidence before its adoption into clinical decision-making. In orthodontics, as there are emerging innumerable appliances, materials, and treatment approaches, there is an urgent need to conduct new trials to determine their effectiveness. Recently, randomized controlled trials (RCTs) are considered as the most powerful and strongest research design for the comparison of various treatment interventions. This article gives a brief overview about EBD and RCTs and their importance in the field of orthodontics.

Keywords: Evidence-based dentistry, orthodontics, randomized controlled trials

INTRODUCTION

Orthodontics is defined as an area of dentistry concerned with the supervision, guidance, and correction of the dentofacial structures and various tooth malpositions. Each individual orthodontic patient deserves the best treatment which is possible only through the judicious use of the best available information.[1] During the 20th century, some aspects of orthodontic treatment planning consistently failed to be resolved and became the topic of controversies in spite of all efforts to clarify the underlying principles by clinical and academic research, for example, one-phase versus two-phase treatment and extraction versus nonextraction treatment. This showed that there is a need to incorporate science into clinical practice to aid in better decision-making. Ackerman stated, "the challenge facing orthodontists in the 21st century is the need to integrate the accrued scientific evidence into clinical orthodontic practice."[2] This resulted in the development of evidence-based dentistry (EBD) which enables the clinician to search, critically evaluate the evidence and its adoption.[3] According to Turpin, "The purpose of using the evidence-based approach is to close the gap between what is known and what is practiced, and to improve patient care based upon informed decision making."[4] The systematic reviews of randomized controlled trials (RCTs) are accepted as the most reliable source of evidence for orthodontic practice.[5]

WHAT IS EVIDENCE-BASED DENTISTRY?

The foundation for evidence-based practice was laid by Dr. David Lawrence Sackett who has defined it as –"Integrating individual clinical expertise with the best available external clinical evidence from systematic research." Evidence-based

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decision-making involves scientific evidence, patient preferences and values, clinical patient circumstances, experience, and judgment.[6,7] Five A's of EBD are as follows: [8,9]

1. Ask – asking answerable questions. Research question consists of four elements "PICO" which include population, intervention, comparison, and outcome
2. Acquire – searching for the best evidence. Various orthodontic journals and websites such as the American Association of Orthodontists and sources such as PubMed and Cochrane Collaboration provide adequate information
3. Appraise – critically appraising the evidence. International evidence-based groups have develop various appraisal forms and checklists such as Consolidated Standards of Reporting Trials (CONSORT) and Preferred Reporting Items for Systematic Reviews and Meta-Analyses
4. Apply – applying the evidence. Decide whether the evidence can be applied to your patient. Patient preferences and values should be taken into consideration, and any risk associated with treatment should be fully discussed
5. Assess – evaluating the outcome.

William R. Proffit stated that, "Professional excellence requires a commitment to critical evaluation and cannot be maintained in a climate of uncritical clinical experimentation."[10] Results of high-quality, double-blinded, multicentered RCTs are considered to be the strongest evidence in evidence-based orthodontic practice and are recognized as the "gold standard" for providing clinical research evidence. It is considered as one of the most powerful research tools.[11,12]

WHAT ARE RANDOMIZED CONTROLLED TRIALS?

RCTs are studies that randomly assign individuals to an intervention group or to a control group to measure effects of the intervention. By allocating participants randomly, patient characteristics are likely to be similar across the groups at the start of the treatment (at the baseline) which eliminates selection bias. Thus, any significant differences between groups in the outcome event can be attributed to the intervention and not to some other unidentified factors.[13] The first RCT in medicine is credited to Sir Austin Bradford Hill, an epidemiologist for England's Medical Research Council. The trial tested whether streptomycin is effective in treating tuberculosis or not.[14] Since Hill's pioneering achievement, the methodology of the RCTs has been increasingly accepted, and the number of RCTs reported has grown exponentially.

RCTs can be broadly classified as "explanatory" or "pragmatic" trials. Explanatory RCTs test efficacy in a research setting with highly selected participants and under highly controlled conditions. In contrast, pragmatic RCTs test effectiveness in everyday practice with relatively unselected participants and under flexible conditions. For example, an efficacy trial answers the question: "Does this intervention work under optimal conditions?" An effectiveness trial answers the question: "Does this intervention work under usual conditions?"[15]

A multicenter trial is a collaborative effort that involves more than one independent center in the task of enrolling and following study participants. The number of centers varies depending on the requirements of the study, for example, studies requiring hundreds of participants usually cannot be done at one center. A multicenter study enables investigators with similar interests and skills to work together on a common problem, also gives opportunity to capable, clinically oriented persons, who might otherwise not become involved in research activities or contribute to science.[16]

IMPORTANT STEPS OF RANDOMIZED CONTROLLED TRIALS

Although the experimental model is unquestionably the most appropriate approach to scientific problem, ethical considerations often prevent its application to the study of disease in humans. Therefore, before launching any human experiments, the benefits of the experiment have to be weighed against the risks involved.[17] It is important that the existing literature does not already suggest that one intervention is better or more effective than another. The operators in the study should not have a preference for any of the interventions being tested. This is called as "equipoise." Ethically, it may not always be possible to randomize to a control group and not provide treatment to some patients. Therefore, most RCTs in the field of orthodontics compare two or more treatments or interventions called as "randomized clinical trials." Once ethical committee approval has been obtained, patient registration is done. Patients should be informed of the theoretical risks and benefits of the interventions under test both verbally and in writing.[18] Adequate sample size is calculated, and study sample is selected from target population using inclusion and exclusion criteria. Sample is allotted to experimental and control group using randomization technique.

Randomization

This stage is central to the mechanics of the trial. Through randomization, we allocate interventions to trial arms in such a way which ensures that neither the investigators nor the participants know or can predict ahead of time which treatment a subject will receive. Proper randomization procedure and reporting involves following

steps: generation of the random allocation sequence, allocation concealment, and implementation of the random allocation sequence. Popular methods that deliver true randomized allocation include simple, restricted or block, and stratified techniques.[19,20] Allocation concealment is an essential aspect of a randomized trial. The idea is that the person who generates the allocation sequence should not be the person who determines eligibility and entry of patients. If this is not carried out properly, there is a possibility that those responsible for recruiting participants could detect the upcoming treatment assignments and then channel individuals with a better prognosis to the experimental group and those with a poorer prognosis to the control group or vice versa. One popular method of allocation concealment is to transfer the randomization list to a series of sealed opaque envelopes each containing the allocation on a card.[18,21]

Blinding

Represents an important, distinct aspect of RCTs. The term "blinding" refers to keeping trial participants, investigators, or assessors (those doing data analysis) unaware of an assigned intervention so that they are not influenced by that knowledge. Blinding prevents bias at several stages of a trial. Single-blind trial – participants remain unaware of intervention assignments throughout the trial, double-blind trial – participants and investigators remain unaware of the intervention assignments throughout the trial, and triple-blind trial – usually means a double-blind trial that also maintains a blind data analysis.[22]

Stopping rules and data analysis

Stopping rules are defined at the start of the trial to ensure that there is a "safety valve," for example, if it becomes obvious during a trial that one or more treatments are significantly worse or better than another, then the trial should be stopped. Data analysis should only be carried out at the end of the study, except in cases where the interim analysis is planned at the start of the study. There are several software packages that can be used for data analysis. If dropout exceeds 20%, dropout analysis should be done.[18,21,23] Finally, when an RCT is written up, CONSORT guidelines should be used. In 1996, a group of epidemiologists, biostatisticians, and journal editors published "CONSORT" to improve the standards of reporting of RCTs.[24] Moher *et al.* describe the latest version of CONSORT which updates the reporting guideline based on new methodological evidence and accumulating experience.[25]

Limitations

RCTs may not always be feasible because of as follows:[26,27]

- Ethical reasons – RCTs provide the highest level of evidence; however, it is not always possible or ethical to conduct such a trial. When RCTs are not feasible or ethical, we must resort to observational studies
- Large sample size required – patient recruitment is a serious problem if the condition of interest is rare or the study population has large variations. An adequate size is needed to allow randomization to equal out potentially confounding variables. The sample should be large enough to detect a significant difference between the test and control groups and to prevent type II error
- High cost for conducting the trial
- Low compliance of patients or high dropouts – for studies that require long follow-up periods, there is a natural tendency for a high dropout rate and low compliance of patient
- Validity – "internal validity" is defined as the degree to which a study is free from bias and "external validity" is used to describe the extent to which results of RCT can be applied to reference population. RCTs in orthodontics have "high internal validity" but "low external validity"
- RCTs cannot intercept rare or unexpected complications – RCT study design is the gold standard to assess the efficacy of a therapy, but infrequent complications are better studied by surveys.

IMPORTANT HISTORICAL RANDOMIZED CONTROLLED TRIAL STUDIES IN ORTHODONTICS ON FUNCTIONAL APPLIANCES

Considerable amount of literature existed on the treatment timing of Class II malocclusion. In the 1990s, RCT methodology had been used by two major projects which were supported by the National Institute of Dental and Craniofacial Research (NIDCR) and carried out at the University of North Carolina and University of Florida.[28] Participants were randomly allotted to control group, headgear group, and functional appliance group. Results showed that children with Class II malocclusion experience considerable variation in growth during the preadolescent period, both with and without treatment. Early treatment with either headgear or functional appliance therapy reduced the severity of a Class II skeletal pattern with 75% chance of improvement in the jaw relationship. On average, headgear produces greater change in the maxilla, whereas functional appliance therapy produces greater mandibular change, but there is considerable variation in the effect with both appliance systems.[29,30] A third NIDCR supported trial at the University of Pennsylvania compared functional appliance and headgear treatment but did not include a control group. Results showed that both the headgear and function regulators are effective in correcting the Class II, Division 1 malocclusion of prepubertal children. The common mode of action of these appliances is the possibility to

generate differential growth between the jaws. The extent and nature of this effect, as well as other skeletal and occlusal responses differ.[31] An another important trial at the University of Manchester that was supported by the Medical Research Council of the United Kingdom had been reported in which the Class II patients were randomly allocated to twin block group and untreated control group. Data were collected at the start of the study and 15 months later. Results showed that early treatment with twin-block appliance resulted in reduction of overjet, correction of molar relationship, and reduction in severity of malocclusion. Most of this correction was due to dentoalveolar change, but some were due to favorable skeletal change. Results showed that early treatment with twin-block appliances resulted in an increase in self-confidence and a reduction of negative social experiences.[32,33]

CONCLUSION

Clinical orthodontic decision-making should involve the integration of skill, clinical experience, patient preferences, and the best-available evidence. An RCT is considered as the most powerful research tool which provides the highest level of evidence in the current evidence-based orthodontics and, therefore, also considered as the gold standard for evaluating the effectiveness of interventions. However, bias could arise when there are flaws in the design or management of a trial. CONSORT guidelines should be used as the standard framework for reporting the quality of RCTs.

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Conflicts of interest

There are no conflicts of interest.

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