Original Article

Clinical trials in dentistry in India: Analysis from trial registry

S. Gowri, Sridharan Kannan[1]

Departments of Oral Health and [1]Health Sciences, College of Medicine, Nursing and Health Sciences, Fiji National University, Suva, Fiji

Abstract

Introduction: Evidence-based practice requires clinical trials to be performed. In India, if any clinical trial has to be performed, it has to be registered with clinical trial registry of India. Studies have shown that the report of clinical trials is poor in dentistry. Hence, the present study has been conducted to assess the type and trends of clinical trials being undertaken in dentistry in India over a span of 6 years.

Methodology: All the clinical trials which were registered with the Central Trial Registry of India (CTRI) (www.ctri.nic.in) from January 1, 2007 to March 3, 2014 were evaluated using the keyword "dental." Following information were collected for each of the clinical trials obtained from the search; number of centres (single center/multicentric), type of the institution undertaking the research (government/private/combined), study (observational/interventional), study design (randomized/single blinded/double-blinded), type of health condition, type of participants (healthy/patients), sponsors (academia/commercial), phase of clinical trial (Phase 1/2/3/4), publication details (published/not published), whether it was a postgraduate thesis or not and prospective or retrospective registration of clinical trials, methodological quality (method of randomization, allocation concealment). Descriptive statistics was used for analysis of various categories. Trend analysis was done to assess the changes over a period of time.

Results: The search yielded a total of 84 trials of which majority of them were single centered. Considering the study design more than half of the registered clinical trials were double-blinded (47/84 [56%]). With regard to the place of conducting a trial, most of the trials were planned to be performed in private hospitals (56/84 [66.7%]). Most (79/84, 94.1%) of the clinical trials were interventional while only 5/84 (5.9%) were observational. Majority (65/84, 77.4%) of the registered clinical trials were recruiting patients while the rest were being done in healthy participants. From 2011, some of the postgraduate thesis trials had also been registered (2011-8; 2012-8; 2013-13; 2014-6). Inadequacy in reporting the method of randomization and allocation concealment was observed in 37/67 (55.2%) and 31/67 (46.2%) clinical trials respectively. A considerable number of postgraduate theses was also registered with CTRI in dentistry and majority of the clinical trials despite being completed are not yet published.

Conclusion: The number of clinical trials in dentistry are low in India, and more focus should be placed by dental investigators regarding the reporting standards. Furthermore, researchers and trial sponsors should aim at publication of the research findings so that it is made publically available for use. A clear-cut need exists for an increase in both the quantity and quality of clinical trials in dentistry.

Keywords: Clinical trial registry, Central Trial Registry of India, dental trials

Address for correspondence:
Dr. Kannan Sridharan, Department of Health Sciences, College of Medicine, Nursing and Health Sciences, Fiji National University, Suva, Fiji.
E-mail: skannandr@gmail.com

Access this article online	
Quick Response Code:	Website: www.picronline.org
	DOI: 10.4103/2229-3485.203039

How to cite this article: Gowri S, Kannan S. Clinical trials in dentistry in India: Analysis from trial registry. Perspect Clin Res 2017;8:95-9.

INTRODUCTION

Evidence-based practice (EBP) has become the sole treatment principle in dentistry. As believed by Von Claude Bernard (1813-1878), "when we meet a fact which contradicts a prevailing theory, we must accept the fact and abandon the theory, even when the theory is supported by great names and generally accepted."[1] EBP has been defined as combining best research evidence, along with clinical experience and patient preferences to improve treatment outcomes. These research evidences are available through clinical trials. The safety and efficacy of new treatment modalities are judged through these trials. EBP and clinical trials go hand in hand. Thus, in order to practice EBP, complete documentation of these clinical trials is essential which is of great concern in recent times.[2] The Food and Drug Administration reports inability to track bioresearch due to nonmaintenance and nonregistration of clinical trials.[3] As EBP is the need of the hour, registering and publishing the available research data becomes obligatory. In India, the Central Trial Registry of India (CTRI), a nonprofit organization was set up wherein all trials conducted in India should be mandatorily registered before recruiting the first patient for the trial. It registers all the trials and links it to World Health Organization International clinical trial registry platform where quality assurance is ensured and increases the certainty for availability for EBP.[2] Studies have publicized that the reporting of clinical trials is poor in dentistry.[4] Hence, the present study was conducted to assess the methodological design and trends of clinical trials that are being undertaken in the field of dentistry in India over a span of 6 years.

METHODOLOGY

The study was conducted using the data, available as public domain and so waived from obtaining Institutional Ethics Committee approval. All trials which were registered with the CTRI (www.ctri.nic.in) from January 1, 2007 to March 3, 2014 were evaluated. No filters were used with regard to phase, type, recruitment status, and place of clinical trials. Search was made using the keyword "dental." Following information were collected for each of the clinical trials obtained from the search; number of centres (single center/multicentric), type of the institution undertaking the research (government/private/combined), study design (randomized/single blinded/double-blinded), type of study (observational/interventional), type of participants (healthy/patients), type of health condition, phase of clinical trial (Phase 1/2/3/4), publication details (published/not published), whether it was a postgraduate thesis or not, nature of sponsors (academic/commercial), prospective or retrospective registration of clinical trials and methodological quality (details about randomization [method, concealment of allocation]). Descriptive statistics was used to analyze these parameters. Trend analysis was done for all these parameters for the entire duration. Chi-square for trend analysis was employed for assessing the trend difference between types of sponsors (academic/commercial). A $P < 0.05$ was considered significant.

RESULTS

Number of clinical trials

The search yielded a total of 133 clinical trials, of which 84 trials (3-2007; 4-2008; 4-2009; 6-2010; 22-2011; 16-2012; 21-2013 and 8 in 2014 till 3rd March) have been found to belong to the field of dentistry. Of these, in the years 2007, 2013, and 2014, all the registered clinical trials were single centered. In general, majority of the clinical trials were single centered (only two each in the year 2010, 2011 and one each in 2008, 2009, and 2012 were multicentric). The trend analysis of total registered clinical trials as well as, whether it was a single or multicentered is depicted in Figure 1.

Characteristics of the registered clinical trials

Considering the study design more than half of the registered clinical trials were double-blinded (47/84 [56%]). Despite this, a clear description regarding the use of blinding technique is unavailable for few registered clinical trials, though showing a declining trend over the years as shown in Figure 2. Most (79/84, 94.1%) of the clinical trials were interventional while only 5/84 (5.9%) were observational.

Table 1 lists the health conditions in which the clinical trials have been reported to be conducted and it can be observed that maximum number of clinical trials are being conducted in the condition of dental caries (9/84, 10.7%). Table 2 describes types of study participants, institutions, sponsors, and interventional studies in the registered clinical trials over the study period. Majority (65/84, 77.4%) of the registered clinical trials were recruiting patients while the rest were being

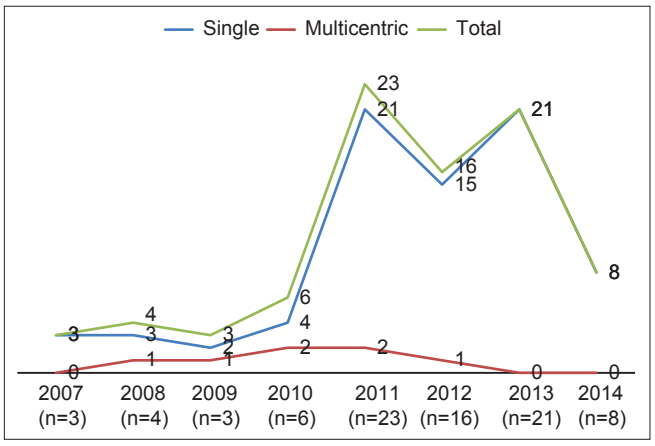

Figure 1: Trend analysis of registered clinical trials in dentistry between 2007 and March 2014

Table 1: Dental health conditions mentioned in the registered clinical trials

Health condition	2007 (*n*=3)	2008 (*n*=4)	2009 (*n*=3)	2010 (*n*=6)	2011 (*n*=23)	2012 (*n*=16)*	2013 (*n*=21)	2014 (*n*=8)
Stains and discoloration	1							
Dental hypersensitivity	1						1	
Plaque and calculus	1	1			1	1	2	1
Premalignant/malignant oral lesions		1			2		1	
Dental defects		2						
Chronic periodontitis			1				3	3
Caries			1	1	2	2	3	
Acute soft tissue injury			1	1	3			
Tooth extraction				1	2	3		1
Postoperative dental pain/wound healing				1		1		
Root canal filling				1	2			
Gingivitis/gum disease/gum surgery					5	1		
Sub-mucosal fibrosis					1	1		
Oral candidiasis					1			
Deciduous teeth/immature lost teeth					1	1		
Dental implants/orthodontic treatment					3	1		
Denture						2	1	
Cavity						1		
Others (tooth movement, halitosis, oral pruritis, indirect pulp cap, enamel subsurface lesion, oral health program, oral health training)				1		3	5	1
Tempero mandibular joint							3	
Facial deformity							2	1
Oral antiseptics								1

*In 2012, the total number of clinical trials registered is 16 but a clinical trial has been conducted in both gum diseases and plaque. Hence, the total number of health conditions amounts to 17

Table 2: Setting and phases of registered clinical trials in dentistry

Year (number of clinical trials)	Types of participants		Type of institution			Type of sponsors*		Type of interventional studies				
	Healthy individuals	Patients	Only government	Only private	Combined	Academic	Commercial	Phase 1	Phase 2	Phase 3	Phase 4	Unclear
2007 (*n*=3)	3	0	0	3	0	1	2	0	0	3	0	0
2008 (*n*=4)	1	3	0	3	1	2	2	1	1	1	1	0
2009 (*n*=3)	1	2	1	1	1	1	2	0	0	1	0	2
2010 (*n*=6)	2	4	2	4	0	3	3	0	0	2	1	2
2011 (*n*=23)	5	18	8	15	0	18	5	1	2	1	6	10
2012 (*n*=16)	0	16	0	10	6	14	2	0	2	0	2	12
2013 (*n*=21)	4	17	9	12	0	20	1	0	0	2	4	15
2014 (*n*=8)	3	5	3	5	0	8	0	0	0	2	2	3

*$P<0.05$ by Chi-square for trend analysis

conducted on healthy participants. With regard to the place of trial, most of the trials were planned to be performed in private institutions/hospitals (61/84 [72.6%]), 53 were only in private while 8 were combined. There were no registered clinical trials solely conducted in any of the government organizations in the year 2007, 2008 and 2012. In addition, with the rise in the number of trials over the years, the rise was mainly in the private sector. Most of the clinical trials were being undertaken as academic studies (67/84, 79.8%), and a significant trend ($P < 0.05$) was observed for clinical trials to be more of academia than sponsored by a commercial company as shown in Table 2. Similarly, the phase of clinical trials was unclear in 44/79 (55.7%) of the registered clinical trials. Of the remaining clinical trials, 16/35 (45.7%) were of Phase 4, 12/35 (34.3%) were Phase 3, 5/35 (14.3%) were Phase 2, and 2/35 (5.7%) were Phase 1. From 2011, some of the postgraduate thesis had also been registered (2011-9; 2012-8; 2013-13; 2014-6). Similarly, there was more retrospective registration of clinical trials (2011-15; 2012-13; 2013-17; 2014-7).

Methodological quality and publication of the registered clinical trials

A total of 67/79 (84.8%) interventional clinical trials has been conducted using a randomization technique in their study methodology. Regarding the method of randomization sequence generation, 22/67 (32.8%) have used computer-generated randomization sequence, and 8/67 (11.9%) have used random number table. Inadequacies in reporting randomization method were observed in the rest (37/67, 55.2%) of which, 24/67(35.8%) reported coin toss, lottery, toss of dice, and shuffling cards, 2/67 (3.0%)

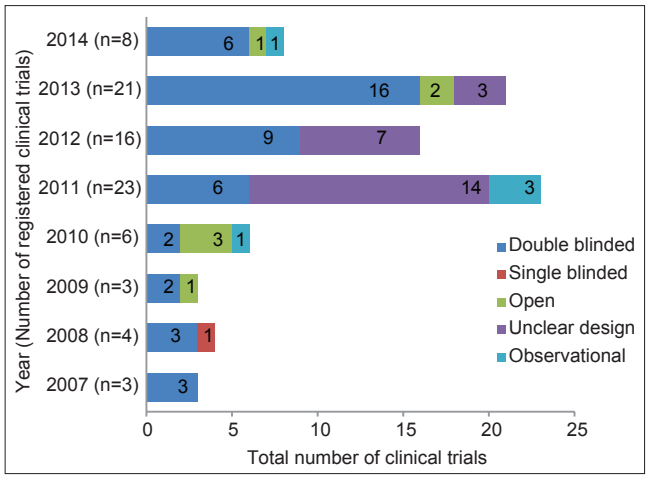

Figure 2: Use of blinding techniques in the registered clinical trials

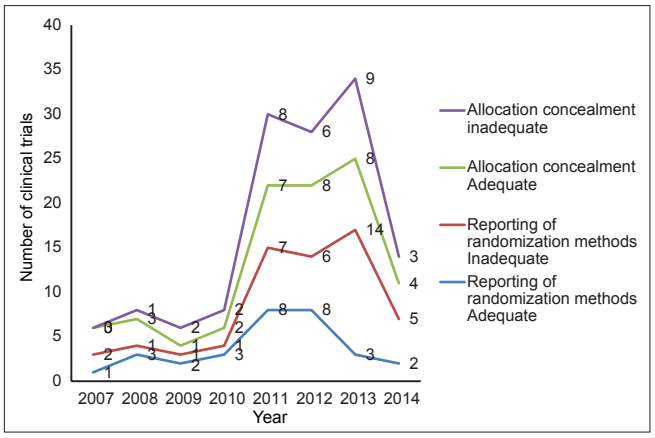

Figure 3: Trends in the methodological quality of registered clinical trials

each have mentioned as "others" and "not applicable," when in fact it is applicable and 9/67 (13.4%) have mentioned the type of randomization incorrectly (stratified/permuted) instead of method of generation. Figure 3 depicts the changes in reporting standards of randomization and allocation concealment between 2007 and 2014. Similarly, only 36/67 (53.7%) randomized clinical trials have reported an appropriate method of concealing the allocation (sequentially numbered opaque sealed envelope [19/36, 52.8%], centralized [5/36, 13.9%], coded identical containers [10/36, 27.8%] and pharmacy controlled [2/36, 5.6%]).

A total of 52 clinical trials (38 from academia and 14 from commercial sponsors) has been found to be concluded, out of which only few have been reported to be published (2007-3; 2008-2; 2010 and 2011-1 each). Of these 38 academic clinical trials, only 3 (7.9%) were published while 4/14 (28.6%) in the commercial sponsored studies were published. Sixteen (48.5%) out of 33 unpublished academic clinical trials have been reported to be post graduate thesis. Of the total 36 postgraduate thesis that have been registered as clinical trials, 18 have been completed, of which only 2 (10.9%) were published.

DISCUSSION

This paper discusses the importance of registering clinical trials and the significance of documenting trials in the form of publications in order to practice EBP in the field of dentistry. We found a low number of clinical trials being conducted in this field although an increasing trend in the recent years. Majority of the clinical trials were interventional, single centered, used double blinding and were conducted in private hospitals. Considerable number of trials had an unclear phase, retrospectively registered, and rarely published. Furthermore, slightly more than half of registered clinical trials have inadequately reported the method of randomization and allocation concealment.

Evidence-based practice in any field requires adequate clinical evidence, for which clinical trials are mandatory. We found that number of clinical trials in dentistry in India is found to be less, albeit a steady increase over time. To the best of our knowledge, this is the first study that assessed with reference to the clinical trials in dentistry. Since there were no data available for comparison with our data, we did a crude search in Clinical Trials.gov, a registry of clinical trials from around 187 countries, with the keyword "dental," category "mouth and tooth diseases" between Jan 1, 2007 and March 3, 2014.[5] We found a total of 1086 studies; certainly not all of these belong to dentistry. Hence, it seems like there are relatively less number of clinical trials being conducted in the field of dentistry in India. Oral health plays a significant role in maintaining quality-of-life and self-esteem of individuals. Oral problems have been one of the commonly reported health issues by Indian patients. A World Health Survey that was conducted in many of the Indian states assessed a prevalence of oral health problems to the extent of 28%.[6] Various other studies have shown a prevalence of periodontal diseases between 11% and 98% in Indian population.[7] In addition, the field of dentistry is surfacing at a rapid pace.[8] Surprisingly, the number of clinical trials being conducted in this field is relatively less in India as per the present study. An analysis of CTRI for trials registered in the field of medicine has also lead to a similar conclusion where the authors have reported that India is contributing only to 2.7% of the global clinical trials.[9] Lack of trained researchers in dentistry and sponsors (both private and government), poor patient awareness about clinical trials in India reducing the chance of their recruitment are some of the speculations for the low rate of dental clinical trials in India. Furthermore, the present study found a poor quality reporting of methods in the dental clinical trials. This can be due to poor understanding of research principles as shown in the study

involving a cohort of dental faculty in the Middle East.[10] Trials shall be registered in CTRI only after obtaining approval from the concerned ethics committee. Having more than half of the dental trials with these errors may raise suspicion regarding the quality of the review of these protocols by the approved ethics committees. Alternatively, anyone involved in a clinical trial may register the trial, not necessarily the principal investigator or a scientific person involved in the study. This may also be one of the reasons for such poor reporting value. Hence, there is a need to train dental fraternity toward the essential principles of clinical research/trials and to strengthen their knowledge gap in the same arena. Of course, considering the recent amendments in Indian law related to compensation in case of serious injury or death and audio-visual consenting process, clinical trials may take a setback due to these complexities especially in dentistry.

We found that only few of the completed clinical trials in dentistry have been published. Documentation of any trial in the form of publication is an essential part of its completion. This aids in the availability of data for further use and also in EBP. Published data form the basis of EBP, one of the important objectives for establishing such trial registries.[11] Studies report that only one-third of the clinical trials ultimately gets published.[12] Lack of motivation to publish the study results especially when it is sponsored by a private company for a commercial purpose with negative study results and journal's rejection for various reasons are well-known.[13] In the present study, it seems that more of academic clinical trials are not published and around half-of these were post graduate thesis. In fact, only one-tenth of the postgraduate thesis that are registered as clinical trials are getting published. A recent study from India revealed that only 30% of the postgraduate thesis were published eventually in a journal and mean time taken for publication was 34 months.[14] Not publishing the results of a clinical trial shall also be considered a scientific misconduct. This emphasizes the need for increasing the awareness on documenting clinical trials among the investigators in dentistry.

This study has the following limitations: Although CTRI was initiated in 2007 clinical trials have mandatorily been made to register only from June 2009. Hence, before 2009, the registered clinical trials may not actually reflect all those undertaken in India. Second, our search was limited with the keyword "dental" without individual health condition like dental caries, cavity, etc., that may underestimate the number of clinical trials that are being undertaken in this field. With regard to the publication status, we just looked the status as mentioned in the trial registry without actually looking in the literature database. There is a possibility that trials may have been published, but the status may not have been updated in the trial registry. Despite these pitfalls, we conclude that the number of clinical trials in dentistry in India is low down, and more focus should be placed by dental investigators regarding the reporting standards. Furthermore, researchers and trial sponsors should aim at publishing the research findings so that it is made publically available for use. A clear-cut need exists for amplification in both the quantity and quality of clinical trials in dentistry.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Sackett DA, Strauss SE, Richardson WS, Rosenberg W, Haynes RB. Evidence-Based Medicine: How to Practice and Teach EBM Canberra: Churchill-Livingstone; 2000. p. 1.
2. Pandey A, Aggarwal AR, Maulik M, Gupta Y, Juneja A, Seth SD. Clinical trial registry: India: Redefining. Indian J Cancer 2008;45:79-81.
3. Baijpai V. Rise of clinical trial industry in India. An analysis. ISRN Public Health 2013. Doi:10.1155/2013/167059. Available from: http://www.hindawi.com/journals/isrn/2013/167059/cta/ [Last accessed on 2014 Aug 14].
4. Cairo F, Sanz I, Matesanz P, Nieri M, Pagliaro U. Quality of reporting of randomized clinical trials in implant dentistry. A systematic review on critical aspects in design, outcome assessment and clinical relevance. J Clin Periodontol 2012;39 Suppl 12:81-107.
5. Clinical trials.gov. Available from: http://www.clinicaltrials.gov. [Last accessed on 2014 Aug 30].
6. Gambhir RS, Brar P, Singh G, Sofat A, Kakar H. Utilization of dental care: An Indian outlook. J Nat Sci Biol Med 2013;4:292-7.
7. Agarwal V, Khatri M, Singh G, Gupta G, Marya CM, Kumar V. Prevalence of periodontal diseases in India. J Oral Health Community Dent 2010;4:7-16.
8. Poorni S, Ramachandran S, Rooban T, Kumar PM. Contributions of Indian conservative dentists and endodontists to the Medline database during 1996-2009: A bibliometric analysis. J Conserv Dent 2010;13:169-72.
9. Selvarajan S, George M, Kumar SS, Dkhar SA. Clinical trials in India: Where do we stand globally? Perspect Clin Res 2013;4:160-4.
10. El-Dessouky HF, Abdel-Aziz AM, Ibrahim C, Moni M, Abul Fadl R, Silverman H. Knowledge, awareness, and attitudes about research ethics among dental faculty in the middle east: A pilot study. Int J Dent 2011;2011:694759.
11. Slavicek G. Evidence based dentistry: Benefits, advantages and pitfalls. Available from: http://www.megabyte.utm.ro/articole/2010/info/sem1/InfoStraini_Pdf/2_EVIDENCE%20BASED%20DENTISTRY.pdf. [Last accessed on 2014 Aug 13].
12. Shaw G. Nearly one-third of large clinical trials go unpublished-in neurology, too. Neurol Today 2014;2:24-5.
13. DeCoursey TE. It's difficult to publish contradictory findings. Nature 2006;439:784.
14. Dhaliwal U, Singh N, Bhatia A. Masters theses from a university medical college: Publication in indexed scientific journals. Indian J Ophthalmol 2010;58:101-4.