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Short Communication

Clinical trials in Ayurveda: Analysis of clinical trial registry of India

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ABSTRACT

Ayurveda is one of the complementary and alternative systems of medicine requiring generation of high quality evidence for rational practice. Evidence can be generated from study designs and the present study is an attempt to critically assess the registered studies in the field of Ayurveda from clinical trial registry of India. We found low number of trials conducted with more focus required on the quality of these studies to contribute to high quality evidence.

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1. Introduction

Clinical trials form the main source of evidence-based medicine (EBM) and thereby forming the backbone of clinical practice. Evidence-Based Practice (EBP) has become the treatment of choice and is a combination of research, clinical experience and patient preferences. The most common definition of EBP is from Dr. David Sackett “EBP is the conscientious, explicit and judicious use of current best evidence in making decisions about the care of the individual patient. It means integrating individual clinical expertise with the best available external clinical evidence from systematic research.” [1] Traditional, theoretical, anecdotal reasoning has to be replaced by high quality evidence which becomes possible only by publication of high quality research data [2]. The strength of recommendation depends on the type of evidence generated and generally it forms a pyramid. Usually, the least in the cadre is the expert’s opinion followed by observational study, randomized controlled trial and finally at the top of the pyramid, meta-analysis [3]. A recent study conducted on clinical trials in the field of dentistry reported poor publication details of the research being conducted. [Unpublished manuscript] EBP in the ancient era used anecdotes which were transmitted by means of stories. This in the current scenario is in the form of publications. Some of knowledge regarding traditional medicines was codified and available in form

of books like-Ayurveda, Siddha, Unani, Tibetan medicine, Chinese traditional medicine Acupuncture and Korean traditional medicine which was based on evidence that was not robust in scientific methodology [4]. EBP in Ayurveda is not being considered because of the lack of good quality clinical trials and enough publications [5]. Bridging EBP and Ayurveda is a task because this empowers researchers and clinicians’ decision making. Considering this the present study was conducted to identify the scope of EBP in Ayurveda and obtain a holistic view on the methodological characteristics of the studies carried out in this field of medicine.

2. Methodology

The study was conducted on trials that were registered and available as public domain in Clinical Trial Registry of India [CTRI (www.ctri.nic.in)] and so was waived from obtaining ethics committee approval. All filters with regard to phase, type, recruitment status and place of trial were eliminated. Search was made with the key word “Ayurveda” and the following information was collected for each of the obtained clinical trials: number of centres (single/multicentre), type of institution (government/private/combined), study design (randomized/single/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), postgraduate thesis or not, nature of sponsors (academic/commercial), prospective or retrospective registration of clinical trials and

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methodological quality [details about randomization (method, concealment of allocation)]. Descriptive statistics were used to analyze these parameters. Trend analysis was done for all these parameters for the entire duration. Chi-square for trend analysis was employed to assess the trend difference between types of sponsors (academic/commercial). $P \leq 0.05$ was considered significant.

3. Results

3.1. Number of clinical trials

The search yielded a total of 208 trials registered in Ayurveda over the specified time period (3–2010; 35–2011; 52–2012; 71–2013, 35–2014; 12–2015). Of this 167/208 (80.2%) were single centered and only 41/208 (19.7%) were multi-centered. A total of 13/208 (6.25%) of the registered studies were sponsored by the pharmaceutical companies and no significant trend ($P = 0.6$) was observed in this category over the years.

3.2. Characteristics of registered clinical trials

Nearly two-thirds (130/208, 62.5%) of the studies were randomized controlled designs while 2/208 (0.96%) were non-randomized interventional trials. Only 9/208 (4.3%) were observational and reported in the year 2010 and 2011. More incline towards interventional trials was reported over the years. Considering the study design, only 21/130 (16.2%) were double blinded, 18/130 (13.8%) were single blinded and 8/130 (6.2%) were triple blinded. Despite this 70/208 (33.6%) of the randomized interventional trials did not describe blinding technique and 43.75% (91/208) of the studies were open labeled. Majority of clinical trials were conducted on patients 196/208 (94.2%) and the rest were on healthy volunteers. Diabetes [17/208 (8.1%)], bronchial asthma [12/208 (5.7%)], Anemia [8/208 (3.8%)] and hypertension [7/208 (3.3%)] were the most common conditions over which trials were conducted. Most of the trials were done in an academic set up [195/208 (93.7%)] while the rest in private set up. The phase of the trial was unclear in [37/208 (17.7%)] of the trials. Of the remaining, 3/208 (1.4%) belonged to Phase I, 87/208 (41.8%) in Phase II, 13/208 (6.25%) in Phase III, 11/208 (5.2%) in Phase IV. 21/208 (10.1%) trials were unclear whether it belonged to Phase I or II, 31/208 (14.9%) in Phase II or III, and 2/208 (0.96%) in Phase III or IV. A total of 168/208 (80.8%) were registered retrospectively.

3.3. Methodological quality and publication of the registered clinical trials

A total of 130/208 (62.5%) studies were conducted using the randomization design. Regarding the method of randomization sequence generation, 43/130 (33.1%) followed coin toss, lottery and throw of dice, 60/130 (46.1%) used computer generated list, 12/130 (9.2%) used random number table and 1/130 (0.7%) used stratified block randomization and 2/130 (1.5%) followed adaptive randomization. A total of 4/130 (3.1%) mentioned that randomization was not applicable when it was actually applicable. The various methods of concealment of allocation used were alternation [1/208 (0.4%)], case record number [6/208 (2.9%)], centralized [3/208 (1.4%)], on-site computer system [3/208 (1.4%)], pharmacy controlled [3/208 (1.4%)] and pre-numbered or coded [9/208 (4.2%)]. A total of 94/208 (45.1%) of the studies did not use any form of allocation concealment. Out of the 52/208 (25%) of the completed trials only 1 was published which needs to be highlighted. A total of 195/208 (93.7%) were done for academic purposes and 161/208 (77.4%) were post-graduate thesis studies of which only one had been reportedly published.

4. Discussion

This study aimed at identifying the status of clinical trials being conducted in the field of Ayurveda. This study also emphasizes the significance of documenting these trials in the form of publications which would end up in improving the quality of treatment provided in the form of EBP. Although majority of the trials were randomized, double blinded and single centered, still not all of these have mentioned the nature of randomization and allocation concealment. Majority of the studies were conducted for academic purposes. Considerable numbers of trials were conducted on patients with unclear phase and rarely were they published. Few trials inadequately reported the method of randomization and allocation concealment.

Ayurveda has its roots in Srilanka and India 3500 years ago and is one of the commonly practiced complementary and alternate systems of medicine (CAM). The use of Ayurvedic medicine has increased tremendously worldwide due to cost and consumer preference. Despite Asian origin, a recent study in the United States of America has shown nearly 59% of the study population used Ayurveda and almost all were aware of Ayurveda [6]. Patients with chronic pain, cancer and infection by human immunodeficiency virus were estimated to use Ayurveda more commonly [7]. As defined, EBM is all about analyzing and publishing the data which would help in final decision making [1]. Despite a widespread acceptance of EBP, there is a potential for the emergence of various types of biases that mainly includes limited patient involvement in the trials [8]. The practice of evidence-based medicine requires integrating individual clinical experience with the best available external clinical evidence [9]. The four main aspects of deciding treatment in Ayurveda include “tradition (inherited from ancestors), conventional (from other examples), belief (with the formula of dravya, guna, virya and karma)” and EBM, a combination of all these parameters to personalize the treatment [10]. The complexities involved in carrying out trials in Ayurveda are well-known such as treatment plan based on *prakriti*; difficulty in using blinding technique due to the odor and taste of Ayurveda medicine; holistic approach such as modification of behavior and dietary regimens associated with Ayurveda treatment and the differential assessment of outcomes based on doshas; lack of standardization of Ayurveda medicines and variation in the method and mode of drug administration [11]. Furthermore, there is limited support from various organizations in terms of granting funds to conduct trials in Ayurveda [12]. Despite these limitations, generation of good quality evidence pertaining to Ayurveda is essential for rational use. Initiatives such as consolidated standards of reporting trials in herbal interventions can be utilized by the investigators/researchers while drafting protocol and registering studies that will aid them to perform these tasks credibly [13]. More than 400,000 registered Ayurvedic physicians at more than 250 government-accredited universities or colleges form a major resource for carrying out clinical trials related to the field [14]. But, a recent review of 225 original studies published in Indian Ayurveda journals concluded a non-satisfactory diagnoses and inconclusive outcomes being used in nearly 90% of the published studies [15]. Experts suggest that Ayurvedic medicine needs more rigorous scientific research for evaluating safety, quality and efficacy to be acceptable to the scientific communities [16,17]. Few other researchers in the field of Ayurveda even suggest that instead of hierarchical approach, a circular approach to keep a balance between internal and external validity is better especially for trials evaluating CAM [18]. A similar analysis in the World Health Organization – International Clinical Trial Registry Platform lead to similar results in Ayurveda [19]. Not only in Ayurveda, similar findings in the study methodology and characteristics have been reported in dentistry as well [20]. CTRI is

an open registry of all the studies related to the field of biomedical research conducted in India. Interventional studies related to various medical and para-medical fields such as allopathy, dentistry, complementary and alternative systems of medicine and pharmacy carried out in India have to be registered in CTRI. Hence, for novice researchers, an update on the various aspects of Ayurvedic clinical studies such as study design, nature of intervention, details of funding and the institutions/investigators carrying out research will be available to fill their knowledge gap, avoid duplication of research that is being carried out in other centers and improving the research transparency.

5. Conclusions

We found that only few clinical trials are being carried out in the field of Ayurveda in India and more focus has to be on the quality of studies to generate high quality evidence based on which firm recommendations shall be made.

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Conflict of interest

None of the authors have any conflict of interest.

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