DISCREPANCIES AND INADEQUATE REPORTING IN RANDOMIZED CLINICAL TRIALS OF TRADITIONAL CHINESE MEDICINE(TCM)

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SOURCES

Liu JP, Han M, Li XX, Mu YJ, Lewith G, Wang YY, Witt CM, Yang GY, Manheimer E, Snellingen T, Berman B, Gluud C.(2013) ; Prospective registration, bias risk and outcome-reporting bias in randomized clinical trials of traditional Chinese medicine: an empirical methodological study.BMJ Open. 2013 Jul 16; Volume 3 Issue 7 pii: e002968. doi: 10.1136/bmjopen-2013-002968. Saved from http://www.ncbi.nlm.nih.gov/pubmed/23864210

ABSTRACT

Background: Bias might occur due to the clinical research study structures, endogenous bias, and to the investigators' intention, external bias, on selecting only the positive outcomes and published them. So the publication bias still widespread in TCM clinical, but TCM are not unique cases, therefore study conclusions ought to be interpreted with caution.

Objective: to review the article ''Prospective registration, bias risk and outcome-reporting bias in randomized clinical trials of traditional Chinese medicine: an empirical methodological'' regarding the contents, strengths, structures and limitations of Traditional Chinese Medicine (TCM) Clinical trials. In addition to outcome-reporting bias in randomized clinical trials.

Results: The number of Chinese randomized trials registration increases from 1999 to 2012, as well as the countries where these Chinese trials registered. As well as the frequency of the type of TCM intervention included in each registry. Classification of disease based on the International Classification of Diseases (ICD-10) has been used to classify medical conditions. Only (46.1%)= 505 out of 1096 registered randomized trials were completed studies. Only has found 29% of registered TCM trials presented selective outcome-reporting bias in between the outcomes registered and the outcomes published.

Conclusions: The quality of TCM clinical trials have developed through prospective international trial registration compared with previous methodological studies. Although there are some inconsistencies between the registered trial protocols and subsequent publications and inadequate reporting .Nevertheless it is indistinct how the study designs have got better-quality.

KEYWORDS

Chinese Medicine, Clinical Trials, Acupuncture, Conventional Medicine, Medical Journals, Herbal Medicine

INTRODUCTION

This review critically reviews the article 'Prospective registration, bias risk and outcome-reporting bias in randomized clinical trials of Traditional Chinese Medicine (TCM): an empirical methodological study 'published in16 July 2013 in The British Medical Journal (BJM open).

Publication bias as a consequence of selective outcome reporting is still widespread and similar to conventional medicine. In herbal medicine trials, it would be inappropriate if a trial design does not utilize syndrome differentiation, and participants may not be properly treated.

"Syndrome differentiation (Bian Zheng) in traditional Chinese medicine (TCM) is the comprehensive analysis of clinical information gained by the four main diagnostic TCM procedures: observation, listening, questioning, and pulse analysis, and it is used to guide the choice of treatment either by acupuncture and/or TCM herbal formulae". 1

The review will first include a literature review. Secondly, will summarize the article. Thirdly, it will briefly analyze the article in order to see if the information in the article is quite enough to disclose how the TCM empirical studies methodological quality of randomized clinical trials carried out , avoiding the risk of external and external biases .Fourthly, the review will critique the article through evaluating its authority, currency, accuracy, objectivity, stability and coverage. The review will also analyze the tables before finally evaluating the article's accessibility and credibility.

REVIEW OF LITERATURE

TCM has long been herbal medicine used to treat diabetes2, diabetic peripheral neuropathy, gastrointestinal disorders including irritable bowel syndrome3, non-operative therapy to treat small-bowel obstruction (SBO) 4, HIV infection and AIDS5, viral myocarditis6 and etc. Also, some conventional non-pharmacological and pharmacological treatments for insomnia used as an alternative therapy such as acupuncture7. There are others traditional Chinese non- pharmacological treatments

like; moxibustion, cupping, tuina, qigong, tiaichi, guasha, etc8, have been used to treat diseases and medical condition.

There is increased numbers of clinical trials investigating a variety of TCM interventions have been registered in international trial registries. Publications on TCM trials are uniformly positive a matter that raised the concerns to investigate the TCM which published if they have positive results. One of the ways to improve trial quality is to prospectively register clinical trial protocol in international trial registers such as clinical trials.gov, international clinical trial registry platform, established by World Health Organization (WHO) in 2005.In addition to that there are several peer –reviewed journals such as Lancet and Trials .

The object of the study in this article stated strengths and limitations ;1- systemic searches of all available international trial registries for any clinical trials of TCM .2- all interventions involving any TCM were included as was the diagnosis,3- the registered information for clinical trials not uniform across the registries and important methodological information may be missing, 4- subsequent publications were obtained for those studies recorded as ‘ completed ‘ in the registry. This may not represent the true situation for trials if the registry data not updated by the researchers. The study design of registered TCM trials has improved in estimating sample size, use of blinding and placebos. However, selective outcome reporting is widespread and similar to conventional medicine and therefore study conclusions should be interpreted with caution

ARTICLE SUMMARY

TCM has long been used to treat a number of diseases and medical conditions with pharmacological and non –pharmacological treatments. The clinical data of TCM specialty and treated disease/conditions extracted from the registries and searched for subsequent publications in PubMed and Chinese databases. Then, TCM clinical trials in registries were systematically assessed and evaluated, and also their subsequent publications. Also, the characteristics of TCM trials were estimated for bias risk and outcome-reporting bias.

Fifteen trial registries were searched from their inauguration to July 2012 to identify randomized trials on TCM which included treatments with herbs, acupuncture and/or moxibustion, cupping, tuina, qigong, etc.

The information in the registries of completed trials compared with their publications focusing on study design, sample size, randomization, and bias risk including reporting bias from the register protocol.

Publication bias as a consequence of selective outcome reporting is still widespread and similar to conventional medicine, therefore study conclusions should be interpreted with caution. In herbal medicine trials, it would be inappropriate if a trial design does not utilize syndrome differentiation, and participants may not be properly treated.

The article finalized that the study design and the quality of reporting of TCM trials have improved through prospective international trial registration compared with previous methodological studies, although there are some inconsistencies between the registered trial protocols and subsequent publications and insufficient reporting on syndrome differentiation.

ARTICLE STRUCTURE

The article was introduced with an abstract providing a brief overview of main points in the original study as well as an article summary emphasizing article focus, key message of article and strengths and limitations of this study. The paragraphs were of suitable lengths and the idea in each one was well developed and the information was easy to access. The background or the introduction to the article came immediately without special heading after the conclusion of the abstract.

Then and there were six headings, which meant that there was a lot of quite detailed information contained under each heading. The six sections include; methods, inclusion and exclusion criteria. Any TCM clinical trials with singly or combined intervention were included. Non- randomized such as quasi randomized studies, cohort, phase trial, retrospective studies were excluded. The method explained that there were no limitations on study type.

Data source ; any TCM trial listed as ‘completed’ in the registered records of a 15 major international trial registries (14 linked to WHO –International clinical trial registry platform from their inception to July 2012. Other sources; articles published in PubMed, three Chinese Electronic Bibliographic Database, China National Knowledge Infrastructure and Chinese VIP Information.

The data extracted from each trial registry by two researchers using a standard, piloted data extraction form which was based on general characteristics of clinical trials, methodology and the 20minmum items required for WHO trial registration. The main information collected included all the information that have to be in research protocol and ethics required to carry out the researches. Results of the study summarized in flow diagram and figure and four tables. The article was well developed and it was HMLT rather than scanned PDF document and include many links that help to make the information accessible. Authors, citation, references journals and subjects links were provided to the readers.

ARTICLE CRITIQUE

AUTHORITY

BMJ is a weekly open-access 9 peer-reviewed medical journal. Open access (OA) is the practice of providing unrestricted access via the Internet to peer-reviewed scholarly research. BJM is one of the world's oldest general medical journals and has been described as among the most prestigious10. Originally called the British Medical Journal, the title was officially shortened to BMJ in 1988.

The journal is published by the BMJ Group, a wholly owned subsidiary of the British Medical Association. It has publication history from 1840 to present. The author's credibility established in; they have affiliations of some of the universities, institution, centers and hospital in China, UK, Germany, USA and Denmark. The article was published in peer- reviewed journals and data of the study extracted from major international trial registrie

ACCURACY

The final article is available for use under the terms of the Creative Commons Attribution Non – Commercial 3.0 License 11. So the research was current project .It was backed up and supported by comprehensive and recent 16 references. All authors have read and approved the final manuscript. Authors; J_PL, MH, X-XK, Y-JM, Y-YW and G-YY were supported by the grant number 2011-CXTD-09 from Beijing University of Chinese Medicine. BB, J-PL and EM were partially funded by the grant number R24 AT001293 from the National Institutions of Health .J-PL and MH were partially funded by the grant number 2011ZX09302-006-01-03(5) by the Ministry of Science and Technology of China.

Author affiliations and refereeing processes also contributed to the article's accuracy as did the links to other expert sources; http:// bmjopen.bjm.com.http://dx.doc.org/10.1136/bjmopen-2013-002968).

CURRENCY

The prepublication history and additional material for this article is available online. The article received in 1 April 2013, revised 31May 2013 and accepted 17 June 2013.Therefore the research was current and the article cited up – to date references in the body of the text ranging from 1998- 2011. The journal has publication history from 1840 to present, and the article was accepted for publication in 17 June 2013.

The study' Prospective registration, bias risk and outcome-reporting bias in randomized clinical trials of Traditional Chinese Medicine (TCM): an empirical methodological study .These trial assessed with current measures to evaluate their ability to answer the contemporary concerns of clinicians and care provider.

RELEVANCE

The article concluded that the study design and the quality of reporting of TCM trials have improved through prospective international trial registration compared with previous methodological studies. The article stated that: there are some inconsistencies between the registered trial protocols and subsequent publications and insufficient reporting on syndrome differentiation. Selective outcome reporting in TCM in publications is still wide spread, careful interpretation for a study's conclusion is necessary.

In TCM herbal medicine trials, it would be inappropriate if the trial design does not utilise syndrome differentiation, and participants may not be properly treated. The article

Did not explain the meaning of the terminology of syndrome differentiation, a matter that might little bit difficulty to some readers to understand one the most important entity the TCM based to treat different diseases with same medicine and same disease with different treatments.

OBJECTIVITY

The information regarding the TCM was objectively developed; there are increasing numbers of clinical trials investigating a variety of TCM interventions have been registered in international trial registries and this supported with a current base with all evidence acknowledged and referenced.

The article disclosed that the study has some limitations; A- lack of standardized of the items required for registration in different registry: B- research only carried for 'completed 'and published trial of TCM, C-research undertook in PubMed and three Chinese databases only, there is lag time between completing a study and writing for publication, D- very large number of TCM trials were conducted without being registered, nothing could be said about their risks of random errors. Finally, it could be concluded that TCM trial have improved through prospective international trial registration compared with previous method logical studies.

STABILITY

Stability is supported by criteria of inclusion, exclusion, data sources, data extraction of the article, and being publishedin16 July 2013 in BJM open. With its sources of 15 major international trial registries, 14 of them linked to WHO ICTRP from their inception to July 2012 and three Chinese electronic bibliographic databases.

ANALYSIS

The article contained a flow diagram, figure 1, consisted of boxes that connected to one another, the boxes summarized the procedure used, from the sources of the data through the criteria of inclusion and exclusion to analysis. The Diagram supported with a key explained the abbreviation used. Figure 2 in the article showed the number of registered trials from the year 1999 to 2012, as well as the countries where these Chinese trials registered. Table 1 summarized the registered and randomized trials on TCM by registry and countries. It contained all the types of the randomized trials in TCM that valid for the purpose of the study "Table 1 shows the frequency of the type of TCM intervention included in each registry" Each registry is not shown in table 1, only the country of TCM intervention12.

Table 2 illustrates all the disease and medical conditions studied in the completed registered TCM. Classification of disease based on the International Classification of Diseases(ICD-10). Table 3 gave information of the methodological of only1096/1640 registered randomized trials were identified evaluating TCM, of which 505 were completed studies (46.1%). Table 3 does not show the variation across registries, only the methodological variation across TCM interventions.13 RCT ON TCM from

International Trial Registries. Table 4 constructed to illustrate if there is any reporting – bias in the methodological components between registered records and subsequent publications of RCTs
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CONCLUSION

The aim of this review is to review the article of 'Prospective registration, bias risk and outcome-reporting bias in randomized clinical trials of traditional Chinese medicine: an empirical methodological study'. The contents, strengths, structures and limitations were analyzed and critiqued. The article has contributed to the literature in terms of its valuable critique of current research measures that govern study on clinical trials and to investigate a variety of TCM interventions which have been registered in international trial registries14.

The study design of registered TCM trials has improved in estimating sample size, use of blinding and placebos. There are increasing number of clinical trial investigated TCV registered in international registries15 Bias might occur due to the clinical research study structures, endogenous bias, and to the investigators' intention, external bias, on selecting only the positive outcomes and published them. 16 .

So the publication bias still widespread in TCM clinical, but TCM are not unique cases, therefore study conclusions ought to be interpreted with caution .In herbal medicine trials, it would be inappropriate if a trial design does not utilize syndrome differentiation, and participants may not be properly treated .The article concluded that the quality of TCM trials have improved through prospective international trial registration compared with previous methodological studies. Although there are some discrepancies between the registered trial protocols and subsequent publications and insufficient reporting on syndrome differentiation. But it is unclear how the study design has improved12.

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