TRANSLATIONAL ERRORS IN THE ARTICLE – 'PANAX GINSENG C.A MEYER ROOT EXTRACT FOR MODERATE CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD): STUDY PROTOCOL FOR A RANDOMISED CONTROLLED TRIAL'

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SOURCE

Xue, C. C., Shergis, J. L., Zhang, A. L., Worsnop, C., Fong, H. Story, D. Da Costa, C. Thien, F. C. K. (2011). Panax ginseng C.A Meyer root extract for moderate Chronic Obstructive Pulmonary Disease (COPD): study protocol for a randomised controlled trial. Trials, 12(164). doi:10.1186/1745-6215-12-164.

KEYWORDS

Ginseng extract, COPD, Clinical research translation, CAM, translational research, Complementary and Alternative Medicine

INTRODUCTION

The review will assess the article: 'Panax ginseng C.A Meyer root extract for moderate Chronic Obstructive Pulmonary Disease (COPD): study protocol for a randomised controlled trial', published in 2012 by Xue et al. in the E-journal, Trials, volume 12 number 164. The assessment will focus on the knowledge contribution of the article to the field of translational medicine and evidence based research for use of Complementary and Alternative Medicine (CAM).

Translational medicine, a research dissemination tool for advancing gains of basic laboratory discoveries to populations via clinical studies, has come to be a very useful tool for the practice of conventional medicines. This paradigm has also found usefulness as an emerging trend in the

development and practice of CAM. CAM, though older than conventional medicine, have found rebirth in the healing sphere owing to public demand and based on successful psychometric evaluations using various rigorous study designs of Randomised Controlled Trials (RCT).

The goal of designing a study protocols is to obtain a tool for measuring and evaluating how an intervention, medical device or diagnostic contribute to improvement in health status or knowledge. Hence, this review will assess the scientific rigour and proof of principles demonstrated by the author in developing the study design.

The article will be summarised, assessed on presentation effectiveness and the depth of literature on current knowledge. A critique on authority, currency, relevance, accuracy, objectivity and stability will be carried out and the conclusion will present the statement of scientific value of the article.

REVIEW OF LITERATURE

The article cited twenty six (26) literary works in the key subjects of COPD, CAM and properties of panax ginseng. The literature review dwelt largely on the state of COPD disease such as Global Initiative for Chronic Obstructive Lung Disease (GOLD) consensus report, (Rabe, et al. 2007); COPD prevalence and its measurement (Halbert, et al. 2006), issues of early diagnosis in primary care treatment, (Price, et al 2011), etc. Measurement literatures cited dealt with measurement of health-related quality of life (HRQoL), COPD respiratory symptoms (Ferrer, 1997), application of confidence intervals for multiple inference, (Ludbrook, 2000).

Considering that the article was written to present a RCT protocol and in line with the authors desire as stated ‘to guide the future development of quality clinical trials’ protocols on herbal medicine by other investigators’, it would be expected that the authors should have an expanded review of works on protocol development. Works such as Walker and Anderson (1999) and Elder et al. (2006) are examples of protocol literatures relating to CAM studies that provide relevant insight of the research experience of other workers. Added to the cited works of Gross et al. (2002) and others, the emphasis of the literature survey would be on the subject of clinical studies’ protocol developments.

Notwithstanding that the original study could generate several publication outcomes, the content and structure of each publication should be determined from the title. This literature survey failed to objectively focus on aspects that are very relevant to the topic: ‘study protocol for a randomised controlled trial’. The literature review fell short of providing adequate evidence of a rigorous background study necessary for educating readers on one of the articles critical goal of guiding researchers in designing clinical trials of herbal medicines. Readers must thus search other protocol and translational literatures to obtain necessary information to be able to exploit the full value of the article.

ARTICLE SUMMARY

The stated objective of the article is to evaluate the safety profile and therapeutic value of a standardised ginseng root extract on symptomatic relief, and focusing on QoL improvements in patient with moderate COPD. This objective refers to the outcome of the article when applied in a study to evaluate standardised ginseng extract. The article in itself was written to present a protocol designed for an evaluation comparing standardised ginseng extract to placebo. The design is a randomised, double-blinded parallel clinical trial in multi-centres with a placebo-controlled arm.

The authors presented an in-depth review on the prevalence of COPD and its global profile on mortality and morbidity stating that COPD was an emerging healthcare burden with a10% prevalence and global cause of death projections ranking by 2030 of 3rd. There is no cure for the disease, adverse effect limits use of available treatments, there is a growing interest and use of CAM for its management and ginseno sides from ginseng have been identified as an effective treatment. However, the lack of clinical evidence necessitates designing RCTs to evaluate safety and efficacy of ginseng in COPD.

The protocol design is defined with an objective of four key research questions. The authors elaborately discussed the design methodology under the following headings: Design, Study duration, subjects, inclusion and exclusion criteria, ethical issues, randomisation, sample size, treatment, outcome measures, adverse event reporting, and statistical analysis. A flow chart is used to demonstrate the study activities while a table indicate the time and nature of measurements.

ARTICLE STRUCTURE

The article opened with a structured abstract providing an overview of the content of the article under the subheadings of **Background, Aim, Methods and Discussion.** The main body of the article was laid out in four (4) key headings of background, objective, method and discussion.

The background presents a review of issues around the aetiology and prognosis of COPD as a public health challenge and dwelt largely on the state of COPD disease without discussing issues that borders on the core aim of the article which was the description of the design of a randomised, double-blinded, placebo controlled clinical trial. The authors highlighted the medicinal properties of ginseng as a probable treatment option for COPD.

Under the heading objective, the article stated its core objective. This stated objective is at variance with the content of the article. The Unstated objective can be deduced from a statement in the structured abstract under the subheading of Method as ‘to present the protocol of a randomised, double-blinded parallel clinical trial design with a placebo-controlled arm.

The article defined in a very cogent manner how the study hopes to achieve its stated objective by addressing a set of four questions. In defining the methodological approach to the proposed study, the authors described the various steps to be taken in order to obtain and analyse data. Although the

authors failed to provide a scholarly background on protocol development, the design presentation was quite articulate and easy to understand and use. A list of abbreviation was provided making the reading of the article easy. The references were unambiguously listed.

ARTICLE CRITIQUE

Authority:

The authors have the necessary professional background and are affiliated to international medical research institutions. Their interdisciplinary background suggests a widened scope of scholarly activity. The registration of the trial in Australia, the funding from three institutions (the National Health and Medical Research Council (NHMRC), the National Institute of Complementary Medicine Australia, and the Guangdong Provincial Academy of Chinese Medical Sciences, China) suggest a robust research evaluation hence a sound authority. Finally the article was published in the Trials. This is a peer-reviewed open access, E- journal encompassing all aspects including randomized controlled trials' findings and performance. It is included in PubMed. The article is thus considered of an authoritative source.

Accuracy:

The article is not considered very accurate due to the authors' neglect of relevant literature which is necessary to present an empirical basis for the protocol design. The authors planned to integrate rigorous clinical research methodology of contemporary science to design the protocol and went further to identify ethical principles and guidelines of Helsinki including Good Clinical Practice documents as evidence of their knowledge but failed to cite them. Next, the stated objective was of the outcome of the designed protocol for which the article was written and not that of the article. Lastly, the introductory part of the article discussed the proposed RCT while the later part discussed the protocol development. This imply presentation of two inconclusive papers; one on the study to evaluate the therapeutic value and safety profile of a standardised ginseng root extract and another describing an RCT protocol design. However, the reference listing is accurate.

Currency:

This article was published in 2011 and deals with clinical and translational research issues in CAM. CAM related translational studies are of scholarly demand owing to changing medical strategies. Owing to the few treatment options in COPD, the use of traditional Chinese medicines is considered an attractive opportunity however, there is a dearth of evidence bases for use, hence the need for this type of publications and considering that the protocol will guide other similar studies. The authors cited up to date references in the article and demonstrated current knowledge of principles and guidelines of ethics as it affects development of clinical research protocols.

Relevance:

This article is considered relevant to clinical research translation. This is especially so if we consider the dearth of evidence based studies in complementary and alternative medicines that are gradually becoming the option of choice for many different disease conditions.
The protocol design as presented considered all necessary aspects that will lead to data gathering, analysis and ethical consideration.

It is considered as a scholarly material contributing to knowledge and providing guidance for design of similar studies. It is important though for readers to carefully scrutinise the article and identify areas of relevance as it concern their interest considering the slight mix up in defining the real focus of the article.

Objectivity:

The area of core error of this article lies in the lack of objective focus in the writing of the paper. The title as given by the authors suggests that the paper will discuss the subject of developing a study protocol for RCT. However, the paper dwelt largely on the aetiology and prognosis of COPD. Its literature search largely neglected citations on RCTs and general reference guideline on clinical trials protocols. Although the article indicated a plan to utilise ethical principles and guiding documents, it failed to cite them. The authors thus failed to demonstrate systematic scientific approach in designing the presented protocol. This removes the power of scientific rigour from the article.

Stability:

Published in the journal Trials, the article is adjured stable considering that the Journal, though of open access, is a peer-reviewed journal specially dedicated to clinical trial research that encompasses all aspects of the performance and findings of randomized controlled trials, included in PubMed and enjoys a global readership audience

RECENT ADVANCES RELATED TO THE TOPIC

Although public health related research is ubiquitous, a large gap exists between the volume and its transformation into clinical application and practice (Brownson et al. 2006). In the era of evidence-based medicine and the advances of clinical research targeted at the improvement of clinical practice in the care of patients, systematic application of translational research remains a burning issue hence a steady influx of new translational studies based on RCT.

In the ‘omic’ and human genome era, the concept of personalised medicine, rooted in the translation of individual genetic or molecular mechanism, has shifted from principle to practice (Waldman and Terzic, 2009; Terzic and Waldman, 2010)

CAM is another emerging health practice that has enjoyed growing attention in recent time. (Frenkel and Borkan, 2003). This growing attention emanates from a global demand for quality care and a greater interest by patients in personal health issues as evidenced in Australia, UK and USA (Shergis et al. 2013). The clinical research community have had to deal with obtaining the needed evidence for use of CAM, (Ernst, et al. 2004; Verhoef, et al. 2006). This evidence is useful for the translation and integration of CAM into modern clinical practice. Researchers have coined a specialty field called, 'Translational Chinese Medicine' and it is a current developing arm of clinical research, (Sun, et al. 2011). According to Ware et al. (2006), MEDLINE indexed articles in the past two decade indicate an increasing number of RCTs being undertaken by researchers to determine the efficacy and safety of CAM interventions.

The technical difference between Translational Chinese medicine and translational medicine according to Sun, et al., (2011), is that while translational medicine takes data from laboratory to bedside, translational Chinese medicine on the other hand takes data from bedside to laboratory and back while seeking clinical evidence. To do this, CAM researchers have strived to achieve scientific rigour through the design of study protocols that meet global gold standards in Clinical research. The Goal of this effort has been to integrate CAM therapies of proven safety and efficacy into healthcare and clinical practice.

CONCLUSION

This review was aimed at assessing the scientific and literary merit of the article as a translational research literature. The objective was to determine the degree of exploitation of existing knowledge in substantiating the principles, ethics and theories of developing a clinical research protocol to achieve its goal of measuring the efficacy and safety of an intervention.

In the cause of the review, it was observed that the article in its elaborate literature review provided a bibliography that was skewed in favour of the disease (COPD) in terms of its aetiology, prognosis and the use of ginseng as probable treatment. The subject of the article 'study protocol for a randomised controlled trial' was not given adequate attention. As a result of this, even though the authors were quite rigorous and eloquent in presenting the details of the protocol, they failed to highlight the guiding principles and theories to the uninformed reader. This and the fact that the work had errors in objective accuracy marred the scholarly quality of the article. However, the article presented a very clear methodological sequence of the protocol which could be exploited in RCT to test medical interventions.

This review thus concludes that the article provides information on the subject of RCT's protocol development of complementary and alternative medicine. However, readers require seeking other necessary literature to fully appreciate the protocol.

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