PROTOCOL

Protocol for Systematic Review of Efficacy and Safety of Ayurveda Interventions in Bronchial Asthma

Anagha Ranade[1], Rasika Kolhe[2], Goli P Prasad[3]

Abstract

Introduction: A systematic review is planned to investigate the safety, efficacy, and effectiveness of Ayurvedic interventions in the management of *Tamaka Shwasa*/bronchial asthma through systematic analysis of published clinical researches.

Materials and methods: A systematic review of the published clinical work for Ayurvedic interventions for *Tamaka Shwasa*/bronchial asthma will be conducted. Electronic searches, such as, EMBASE, MEDLINE, COCHRANE and AYUSH Research Portal, DHARA, Shodhganga Databases on dissertation works, conference proceedings, print journals, and reference list of articles, will be considered in the search strategy. All studies as per inclusion criteria including study design and participants will be analyzed by two investigators individually; in case of ambiguity, it will be discussed by a senior expert (investigator). The population (P in PICO) will include diagnosed cases of bronchial asthma/*Tamaka Shwasa,* where intervention (I) will be Ayurveda stand alone or as add-on with conventional therapy and (C) comparator will be Ayurveda and non-Ayurveda interventions or placebo. The primary outcome (O) will be improvement evident by a decrease in dyspnea, rhonchi, number of attacks, and classical symptoms of *Tamaka Shwasa*. Risk of bias assessment using Robin's tool will be used for non-randomized clinical trials, whereas CONSORT statement will be used for quality assessment of randomized clinical trials.

Dissemination: This review is ongoing, and upon completion, the review will be published in a peer-reviewed journal. The review will be updated to inform and guide healthcare practice and policy. The results will be presented in terms of high risk, moderate or low/unclear risk in risk of bias assessment.

Trial registration number: PROSPERO 2019 CRD42019123886.

Keywords: Ayurveda, Bronchial asthama, Systematic Review, *Tamaka Shwasa*.

Journal of Research in Ayurvedic Sciences (2019): 10.5005/jras-10064-0093

Introduction

Bronchial asthma is a global burden for developed as well as developing countries per the World Health Organization.[1] With the increasing use of traditional medicinal systems in the past two decades, there has been a considerable shift in the preference of patient population toward Ayurveda in the management of asthma. The clinical features of bronchial asthma have close resemblance with the condition named '*Tamaka Shwasa*' in Ayurveda.[2] Ayurveda caters to the management strategy by its unique way of diagnosis and treatment with various therapeutic interventions/procedures. Ayurvedic management of *Tamaka Shwasa* consists of *Shodhana* (purification) and *Shamana* (pacify). *Shodhana* is detoxification procedure consisting of purgation and induced emesis. *Shamana* consists of administration of medicated *Ghrita* (ghee), *Guti-Vati* (tablets), *Kwatha* (decoctions) and *Asava* (self-generated medicated alcoholic preparations) along with dietary recommendations. There are copious publications in Ayurveda fraternity that have documented and reported the clinical efficacy of Ayurveda interventions—vis-à-vis modern regimen in bronchial asthma. There are experiential evidences by physicians that report clinical efficacy of *Shamana* and *Shodhana* therapies of Ayurveda in treatment of bronchial asthma. But still, there are always queries raised regarding the effectiveness of Ayurveda in the management of asthma. The recent highest level of evidence is considered to be reported from systematic review and meta-analysis.[3] In the case of bronchial asthma, many systematic reviews and meta-analyzes have been published in light of modern regimens.[4–7] Some systematic reviews are also available for complementary and alternative medicines.[8–10] Exclusive systematic reviews on efficacy of Ayurvedic interventions are meagre. In order to establish the recommendation of Ayurveda interventions in bronchial asthma, it is the utmost need of the hour to report the results of all documented clinical trials with the help of systematic review and meta-analysis.

Review Question

This review seeks to establish, through the available literature, the effectiveness of Ayurvedic intervention in the management of *Tamaka Shwasa* (bronchial asthma). The specific review question to be addressed is:

"Are Ayurveda interventions efficacious and safe as standalone or as add-on therapy in comparison to conventional treatment in bronchial asthma?"

[1–3]Regional Ayurveda Institute for Fundamental Research, Kothrud, Pune, Maharashtra, India

Corresponding Author: Anagha Ranade, Regional Ayurveda Institute for Fundamental Research, Kothrud, Pune, Maharashtra, India, Phone: +91 9422767076, e-mail: anagharanade11@gmail.com

How to cite the article: Ranade A, Kolhe R, Prasad GP. Protocol for Systematic Review of Efficacy and Safety of Ayurveda Interventions in Bronchial Asthma. J Res Ayurvedic Sci 2019;3(4):140–143.

Source of support: Central Council for Research in Ayurvedic Sciences

Conflict of interest: None

Methods and Study Design

Objective

This systematic review aims to assess safety and efficacy of Ayurvedic interventions in management of *Tamaka Shwasa*/ bronchial asthma.

Study Selection Criteria

Participants/population

Diagnosed cases of bronchial asthma using the standard criteria of modern medicine. Also, studies having data of patients who were selected based on Ayurveda criteria of diagnosis; provided the majority of participants had features approximating similar criteria of modern medicine.

Intervention

Ayurveda stand alone or as add on therapy with conventional therapy. This will include trials consisting of *Shodhana* therapy such as *Vamana*/*Virechana*; *Shamana* therapy consisting of *Vati*, *Guti*, *Asava*, *Kwatha*, *Avaleha*, etc. Also, trials including dietary restrictions (*Pathyapathya*), *Pranayama* as an intervention will also be included.

Control

Non-Ayurveda interventions, namely, conventional management (inhaled corticosteroids, long-acting beta-2 agonists, leukotriene receptor antagonists, long-acting anti-muscarinic agent etc.), placebo, or sham therapy.

Outcomes

Primary Outcome

The primary outcome will be improvement evident by a decrease in dyspnoea, rhonchi, number of attacks, and classical symptoms of *Tamaka Shwasa*.

Secondary Outcome

The secondary outcome will be change in pulmonary function tests, eosinophil count, spirometry values, quality of life, need of rescue medications, and a prolonged period of exacerbation tendency where symptoms severity increases.

Study Design

This systematic review will consider published interventional studies consisting of randomized controlled trials (RCTs), quasi-randomized controlled trials, controlled clinical trials, multiple arm clinical trials, and placebo comparator type studies.

Search Strategy

All the published research works in English available online will be considered in the literary review. Electronic searches, namely, PubMed, EMBASE, MEDLINE, COCHRANE and AYUSH Research Portal, DHARA, Shodhganga Databases on dissertation works, Conference proceedings, Print journals, the Reference list of articles, will be considered in the search strategy. Search strategy combining MeSH terms and free-text words using the Boolean operators "AND" and "OR", using key words like bronchial asthma, *Tamaka Shwasa*, parallel arm, multiple arm clinical trial, randomized controlled trials, quasi-randomized controlled trials, Ayurveda interventions, *Shodhana*, Ayurvedic management, etc. will be used for the search. In addition, the reference section in the studies will be examined for additional relevant articles.

Data Collection and Analysis

Selection of Studies

The titles and abstracts identified during literature search satisfying the inclusion and exclusion criteria for the study will be assessed independently by two authors. Disagreements will be settled with the help of opinion of third author separately.

Data Extraction

The data will be mined by two authors separately and will be cross-checked for any discrepancies that will be resolved later. Data will be extracted in a pre-designed word format from the selected trials to study the following information:

- General information: data related to title, authors, year, study design, risk of bias, patients randomized, patients analyzed, and funding agency if any.
- Participant characteristics: age, sex, disease duration, and concurrent treatments.
- Intervention characteristics: posology, methods of administration, time of administration, duration of treatment, withdrawals, and dropouts.
- Control characteristics: active or placebo; if active, then drug name, dosages, methods of administration, frequency, duration of treatment, withdrawals, and dropouts.
- Data on outcome variables: all outcomes assessed by the authors.

Risk of Bias (Quality) Assessment

Two authors will independently assess the risk of bias. For assessment, the Cochrane Collaboration's Robins' tool recommendations will be followed. Incongruities among the authors will be resolved through discussions among them in timely meetings. The third author will have the right to express final opinion in case of any discrepancies. The risk of bias assessment will be summarized for every outcome included within the study.

Treatment Effect Measurement

The mean difference or standardized mean difference will be measured to compare the same outcomes measured with different scales for the continuous data. The confidence intervals (95%) will be estimated for all measures of treatment effect. For safety outcomes, an intention-to-treat model will be adopted for data analysis.

Dealing with Missing Data

If missing data is found, efforts will be made to derive information by contacting the original authors. If not possible, the data will be analysed as it is and reported as limitations of study.

Assessment of Heterogeneity

I^2 and X^2 tests will be used to measure heterogeneity. If the value of $I^2 \leq 50\%$, heterogeneity will be considered insignificant but if found ≥50%, then narrative summary will be provided instead of meta-analysis.

Assessment of Reporting Bias

The methodological quality of the RCTs and parallel-group studies will be assessed by following the CONSORT 2010 statement.[11] The internal validity and risk of bias for RCTs will be assessed using Cochrane Handbook for Systematic Reviews of Interventions[12] and ROBINS-i for non-randomized studies of interventions.[13]

Data Synthesis and Analysis

Firstly, only the qualitative synthesis of studies will be focussed which meet criteria. The software named 'RevMan' 5.3 will be used for the analysis part.

Subgroup Analysis

If significant heterogeneity is observed, subgroup analysis will be made to explore the reasons for

- Duration of bronchial asthma (less than 6 months; 6 months to two years; more than 2 years)
- Type of Ayurvedic intervention (therapy or medicines only)
- Therapy that is more useful as per Ayurveda (*Shodhana* or *Shamana*)
- Agewise

Sensitivity Analysis

If sufficient trials are found during the study, it is planned to conduct a sensitivity analysis comparing the results using all trials quality wherein studies will be classified as having a 'low risk of bias' vs those having a 'high risk of bias'.

Discussion

Systematic review generates data which is a reproducible and transparent procedure. In this protocol, describe the participants, interventions, comparators, and outcomes will be described. Also, the sources of data, search strategy, data extraction methods (including quality assessment), and methods of combining data will be mentioned. By publishing the research protocol, clarity of the strategy and minimize the risk of bias will be emphasized. This flexible approach was essential due to the paucity of available research on this topic. Results of the review may aid future researchers, clinicians, and policy makers. The study will review published literature on the management of bronchial asthma/*Tamaka Shwasa* with Ayurveda and might aid in developing reporting guidelines Ayurveda clinical trials.

Ethics and Dissemination

As primary data were not collected, ethical clearance is not necessary. The results will be made available widely through a peer-reviewed publication.

Trial Registration Number

International Prospective Register for Systematic Reviews (PROSPERO) number - CRD42019134041.

Strengths and Limitations of This Study

- This protocol will help reduce the possibility of duplication, thereby giving transparency. It will reduce possible biases and allow peer review.
- This study will help generate level of evidence from this systematic review of randomized controlled trials as well as non-randomized controlled trials. It will pave a way for defining guidelines for reporting of the clinical studies in Ayurveda.

Amendments

Any modifications to this protocol will be documented and recorded in excel templates for data collection and synthesis.

Author Contribution

AR and RK have prepared the protocol; GP has inspired the idea of this study and monitored the research entirely. AR and RK prepared the draft document, GP have finalized the manuscript. AR and RK have conducted primary searches for literature.

Acknowledgments

The authors would like to thank Prof Vaidya KS Dhiman (Director-General, CCRAS) and Dr Narayanam Shrikanth (Deputy Director-General, CCRAS) for their continuous support and guidance in the entire study.

References

1. Anonymous, WHO news-Factsheets, Bronchial Asthma. Available at: https://www.who.int/mediacentre/factsheets/fs206/en/.
2. Gohel SD, Anand IP, Patel KS. A comparative study on efficacy of bharangyadi avaleha and vasa avaleha in the management of tamaka shwasa with reference to childhood asthma. Ayu 2011;32(1):82–89. DOI: 10.4103/0974-8520.85736.
3. OCEBM Levels of Evidence Working Group*. "The Oxford 2011 Levels of Evidence". Oxford Centre for Evidence-Based Medicine. Available from: http://www.cebm.net/index.aspx?o=5653.
4. Jadad AR, Moher M, Browman GP, et al. Systematic reviews and meta-analyses on treatment of asthma: critical evaluation. BMJ 2000;320(7234):537–540. DOI: 10.1136/bmj.320.7234.537.
5. Brocklebank D, Ram F, Wright J, et al. Comparison of the effectiveness of inhaler devices in asthma and chronic obstructive airways disease: a systematic review of the literature. Health Technol Assess 2001;5(26):1–149. DOI: 10.3310/hta5260.
6. Adams NP, Jones PW. The dose–response characteristics of inhaled corticosteroids when used to treat asthma: an overview of Cochrane systematic reviews. Respir Med 2006;100(8):1297–1306. DOI: 10.1016/j.rmed.2006.04.015.
7. Ram FS, Robinson SM, Black PN. Effects of physical training in asthma: a systematic review. Br J Sports Med 2000;34(3):162–167. DOI: 10.1136/bjsm.34.3.162.
8. McCarney RW, Lasserson TJ, Linde K, et al. An overview of two cochrane systematic reviews of complementary treatments for chronic asthma: acupuncture and homeopathy. Respir Med 2004;98(8):687–696. DOI: 10.1016/j.rmed.2004.05.005.
9. Singh BB, Khorsan R, Vinjamury SP, et al. Herbal treatments of asthma: a systematic review. J Asthma 2007;44(9):685–698. DOI: 10.1080/02770900701247202.
10. Passalacqua G, Bousquet PJ, Carlsen KH, et al. ARIA update: I—systematic review of complementary and alternative medicine for rhinitis and asthma. J Aller Clin Immunol 2006;117(5):1054–1062. DOI: 10.1016/j.jaci.2005.12.1308.
11. Schulz KF, Altman DG, Moher D, et al. CONSORT 2010 statement: Updated guidelines for reporting parallel group randomized trials. BMJ 2010;340(mar23 1):c332. DOI: 10.1136/bmj.c332.
12. Higgins JPT, Green S. Cochrane handbook for systematic reviews of interventions. 5.1.0 edition Cochrane Collaboration. Chichester, UK: John Wiley and Sons; 2016.
13. Sterne JA, Hernán MA, Reeves BC, et al. ROBINS-I: A tool for assessing risk of bias in non-randomized studies of interventions. BMJ 2016;355:i4919. DOI: 10.1136/bmj.i4919.

हिन्दी सारांश

ब्रोंकीयल अस्थमा / तमकश्वास मे आयुर्वेदिक उपचार की प्रभावकारिता एवं सुरक्षितता पर सिस्टेमेटिक रिव्यू प्रोटोकॉल

अनघा रानडे, रसिका कोल्हे, गोली पी प्रसाद

पृष्ठभूमि: सदर शोधपत्र में अस्थमा / तमकश्वास में आयुर्वेदीय उपचार पर पहले प्रकाशित नैदानिक शोध कार्यों पर व्यवस्थित विश्लेषण करने हेतु व्यवस्थित समीक्षा प्रोटोकॉल प्रस्तुत है|

विधी एवं विश्लेषण: इस अध्ययन हेतु विविध इलेक्ट्रोनिक डेटाबेसेस उदा: EMBASE, MEDLINE, COCHRANE तथा AYUSH Research Portal, DHARA, शोधगंगा, सम्मेलन कार्यवाही पत्र, प्रकाशित शोध पत्रिका आदि की खोज कार्यनीति में विचार किया जाएगा। सभी पत्रों को निहित समावेशन मापदंडो तथा स्टडी डिजाइन और प्रतिभागीयों के आधार पर दो शोधकर्ताओं द्वारा व्यक्तिगत रूप मे विश्लेषण किया जायेगा| कुछ संदेह हुआ तो वरिष्ठ विशेषज्ञ से चर्चा कर उस पत्र को अध्ययनार्थ आगे लिया जाएगा| सभी अध्ययन में प्रकाशित शोधपत्रों से PICO फॉर्मेट में डेटा देखा जाएगा। प्राथमिक परिणाम में दमा, वेगों की संख्या मे कमी तथा तमकश्वास के लक्षणों मे होने वाले सुधार को देखा जायेगा| नोन रेंड्माइज्ड क्लिनिकल ट्राइल की गुणवत्ता जांचने के लिए रिस्क ऑफ़ बायस असेसमेंट की जाएगी जिसके लिए रॉबिन्स टूल का इस्तेमाल किया जायेगा तथा रेंड्माइज्ड क्लिनिकल ट्राइल के लिए CONSORT statement का इस्तेमाल किया जायेगा|

प्रसार: समीक्षा अध्ययन जारी है और पूरा होने के बाद पीयर रिव्यूड जर्नल मे प्रकाशित किया जाएगा। स्वास्थ्य सेवा अभ्यास और नीति को सूचित करने और मार्गदर्शन करने हेतु समीक्षा को अध्यतित किया जाएगा। परिणाम उच्च, मध्यम या निम्न/ अस्पष्ट जोखिम के संदर्भ में पूर्वाग्रह मूल्यांकन के जोखिम में प्रस्तुत किए जाएंगे।

ट्राइल पंजीकरण संख्या: PROSPERO 2019 CRD42019123886.