International Journal of Case Studies in Clinical Research

BIOCORE
EXPLORING SCIENTIFIC COMMUNITY

Volume 5 Issue 4,
July 2021

Citation
ManickavasagamRengaraju et.al.(2021), An Open labelled RCT to Evaluate the Efficacy and Safety of Siddha Supplement (MAM Granules) along with Standard Allopathy Treatment in the management of RT PCR Positive Pre Symptomatic COVID 19 patients –A Structured Summary of A Study Protocol. Int J Clinical & Case. 5:4, 49-53

ISSN 2572-102X

Published by
Biocore Group | https://www.biocoreopen.org/ijcc/archive.php

Declaration Of Conflicting Interest
The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Short Communication

An Open labelled RCT to Evaluate the Efficacy and Safety of Siddha Supplement (MAM Granules) along with Standard Allopathy Treatment in the management of RT PCR Positive Pre Symptomatic COVID 19 patients –A Structured Summary of A Study Protocol

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Article History: **Received:** May 31, 2021;
Accepted: June 07, 2021;
Published: XXXX, 2021.

Abstract

Background: COVID19 is emerging as a major health care challenge of this Century globally. Till date, there is no proven direct medication is declared to combat the COVID 19.Individual Ingredients of the MAM Granules are already having effective anti-viral activities in recent Pre-clinical studies. The outcome of these studies will really useful to explore the suitable Supplementary Siddha drug in the Management of COVID 19.

Methods:

Objectives: The primary objectives are to evaluate the efficacy of MAM Siddha Granules as a supplement along with standard Allopathy Supplement (Vit C and Zinc) to compared with standard Allopathy Supplement (Vit C and Zinc) in the management of Pre - Symptomatic COVID 19 patients and also determine the efficacy of Standard of care along with MAM Granules in reducing the onset of clinical symptoms in asymptomatic patients, Reduction in the duration of SARS CoV-2 viral infections and reduction of Viral load from the baseline. The secondary objectives are to evaluate the efficacy on immunity by selected immunological markers and safety of the trial medicines and their effects in reduce the risks of the disease. In addition, to document the profile of Pre-Symptomatic COVID 19 patients based on Siddha system Principles.

Trial Design: An open Labelled, Double arm, Single Centre, Exploratory and comparative Randomized Controlled Trial.

Participants: Patients tested RT PCR Positive COVID- 19 at COVID Care Centre at Govt. Institute of Medical Sciences. Noida, India will be recruited.

Primary outcomes: Negative conversion of SARS CoV - 2 by 7/14 days Reduction in Viral load at the end of treatment period .Reduction in incidence of clinical symptoms like fever, cough and breathlessness Effect of Supplement in Immunology and inflammatory markers (IL6,) at the end of treatment .

Secondary outcomes : Reduction in incidence of complications (ARDS, other Respiratory Illness).Mean changes in Laboratory markers (Hematological & Bio – Chemical Markers).

Trial Registration: This trial was registered with (Clinical Trial Registry of India) CTRI (Registration number - CTRI/2021/02/031420 on 19.02.2021.

Keywords

COVID 19, RCT, Protocol, Siddha Medicine, MAM Granules, CAM

Introduction

COVID19 is emerging as a major health care challenge of this Century globally. Even Developed countries are trailing and lack behind the treatment and management of COVID 19 to their own people. Till date, there is no proven direct medication is declared to combat the COVID 19.World community are keenly waiting for the proven solution for this killer disease.

AYUSH Systems of Medicines are traditional indigenous systems which are practicing in India through the centuries. Siddha system is one among the traditional Indigenous medical system existing in Southern India. This is the need of hour to integrate the Siddha Medications/Diet along with allopathic medications as Prophylactic/Management/Supplementary to combat the viral infections especially Corona viral infections. As all of us aware, Siddha system is not only dealing with treatment, also mentioning about the Prophylactic/ Supplementary Methods to combat viral infections through the years.

"Food is medicine; Medicine is Food" is one of the popular quote about its Diet based Techniques in Siddha. Lots of Culinary spices also used as a medicine based on their natural healing properties in Siddha. Siddha System Classified some of these Culinary spices as "Thirithoda Samana Porutkal" which are having both anti –dote and therapeutic effects. Lots of antiviral Herbs and spices are also used by Tamil people in their day today life in diet.

MAM Granules is one of the Siddha Health Supplement, is made up of Some Siddha Herbs like Turmeric (Curcuma Longa), Aswagadha(Withania Somnifera) and Black Pepper (Piper Nigrum) etc. (1),(2),(3)

Preclinical In vitro Anti Viral Studies which were done at ICGEB, New Delhi (MTT & Anti – Viral Assays) showed marked Efficacy of the MAM Granules in COVID 19 Cell-line level. Preclinical Acute animal Toxicity studies which were done at Dabur Research Foundation, Ghaziabad Showed the safety profile of the MAM Granules in Lab Animals.

Individual Ingredients of the MAM Granules are already having effective anti-viral activities in recent Preclinical studies. The outcome of these studies will really useful to explore the suitable add -on/ Supplementary Siddha drug in the Management of COVID 19.

Objectives

Primary Objectives:

The primary objectives of this trial are to evaluate the efficacy of the MAM Siddha Granules(A combination of anti viral Siddha Herbs Like Turmeric, Pepper, Aswagandha)) as a supplement along with standard Allopathy Supplement (Vit C and Zinc) to compared with standard Allopathy Supplement (Vit C and Zinc)(in the management of Pre - Symptomatic COVID 19 patients and also determine the efficacy of Standard of care along with MAM Granules in reducing the onset of clinical symptoms in asymptomatic patients, Reduction in the duration of SARS CoV-2 viral infections and reduction of SARS CoV-2 Viral load from the baseline. (4)

Secondary Objectives:

The secondary objectives are to evaluate the efficacy in Specific on immune system in terms of selected immunological markers and safety of the trial medicines and their effects in the reduce the risks of the disease. In addition, to document the profile of Pre-Symptomatic COVID 19 patients based on Siddha system Principles.(4),(5)

Inclusion Criteria:

1. Laboratory Confirmed COVID – 19 with Asymptomatic Patient (as per ICMR Guidelines) 30 Patients in each group
2. Aged 18-65 years
3. Consenting to participate in the study and sign the informed consent

Exclusion Criteria:

1.Patients with severe primary respiratory disease or other pathogenic microbial pneumonia
2.Patient with Uncontrolled DM (≥ 350 mgs Fasting Sugar) Severe HT (180/120 mmHg as per JNC 8 Guidelines), Chronic BA (≥ 5 years Based on Clinical History), Renal Dysfunction (Known CKD ≥ 5 years eGFR Stage ≥ 3 as per NKA guidelines)
3.Pregnant and Lactating mothers
4.People who have history of allergic to Siddha medicine or intolerant to taking medication
5.Patients participating in other COVID-19 clinical trials
6.Patients already went under COVID 19 vaccination

Trial Design:

An open Labelled, Double arm, Single Centre, Exploratory and comparative Randomized Controlled Trial.

Participants:

Patients who tested RT PCR Positive COVID- 19 at COVID Care Centre at Govt. Institute of Medical Sciences. Noida in India will be recruited. These will be patients with Pre- symptoms (with or without symptom) with laboratory confirmed COVID 19 (RT – PCR Tested Positive) aged 18-65, consenting and willing to participate into the study.

Intervention and comparator

Arm I: Standard Allopathy Intervention(5),(6) (Vit C, Zinc and others) + Milk Morning and Night after Food, for 14 days.

Arm II: Standard Allopathy Intervention (Vit C, Zinc and others) + 2 Gms of MAM Granules Milk Morning and Night after Food, for 14 days.

The investigational drug MAM Granules is a registered products under the Govt.of India and bought from GMP Certified, Central Pharmacy, Siddha Central Research Institute, Chennai, Tamilnadu,India.

Main Outcomes

Primary outcomes:

1.Negative conversion of SARS CoV - 2 by 14 days Reduction in Viral load of SARS-CoV-2 at the end of treatment period (14 days).

2. Reduction in incidence of clinical symptoms like fever, cough and breathlessness .

3.Effect of Supplement in Immunology and inflammatory markers (IL6,) at the end of treatment (14 days).

Secondary outcomes:

1.Reduction in incidence of complications (ARDS, other Respiratory Illness).

2. Mean changes in Laboratory markers (Hematological & Bio – Chemical Markers)

Randomisation:

Randomization will be done following Simple randomization method.The Participants will be assigned into 2 Groups and will be allocated in 1:1 Ratio in each group through randomization blocks in Microsoft Excel by a Statistician after the assessment of eligibility and Informed consent procedures.

Blinding:

The Study is an open labelled. Participants and Investigators will not be blinded.

Numbers to be randomized (Sample size):

The design of the drug trial is exploratory in nature. Though a randomized selection of patients will be done to either of the two arms, the sample size is that of convenience and the same is not statistically powered however, sample size (30 patients in each arm) is sufficient to draw meaningful conclusions. The statistical significance $p<0.05$(two sided) is predefined for analysis. Statistical analysis will be performed using standard tests to compare the two interventional arms for primary and secondary efficacy measures. Safety events will be also analyzed. Both intent-to-treat and per protocol completer analysis will be performed. Regression analysis will be done to identify predictors of response. Clinical symptoms, Subjective parameters and Laboratory parameters will be subjected to Univariate and multivariate analysis using Statistical Package for Social Sciences (SPSS) 15.0 version with appropriate statistical methods.(7),(8).

A total Number of 60 Patients, 30 each in two groups will be recruited in 1:1 Ratio.

Data collection:

At the time of recruitment, we will collect socio-demographics, history of illness and clinical examination. At every Visit we will do systematic clinical examination, determine adherence to interventions and assessment about any complaints and any adverse events.

Trial Status:

Protocol Number: SCRUND GIMS Noida MAM Granules Study 2,Version: 5.0 Protocol Date : 17.02.2021. The Trial started its recruitment on 27.02.2021. The study is ongoing and investigators are still collecting, or analyzing data. We anticipate study including data analysis will finish in May 2021 with in a period of 2 months.

Trial Registration:

This trial was registered with (Clinical Trial Registry of India) CTRI and the registration number is CTRI/2021/02/031420 on 19.02.2021

Full Protocol:

The full Protocol is attached as an additional file, Accessible from the Journal website (Additional file 1).the protocol Version is 5.0 dated 17.02.2021. In the interest in expediting dissemination of this material, the usual familiar formatting has been eliminated .this letter serves as a summary and outline of the key elements of the full protocol. The Study protocol has been reported in accordance with the SPIRIT guidelines.

DECLARATIONS

Acknowledgements: (Steering Committee):
1.Brigadier Dr. Rakesh Kumar Gupta, Director, Government Institute of Medical sciences, (GIMS) Greater Noida, UP.
2.Prof. Dr. K. Kanakavalli, Director General, Central Council for Research in Siddha, Chennai.
3.Prof.Dr. Jugal Kishore, Director, HOD- Department of Community Medicine, VMMCH & Safdarjung Hospital, New Delhi.
4.Dr.P. Sathiyarajeshwaran, Director- in-Charge, Siddha Central Research Institute, Central Council for Research in Siddha, Chennai.

Authors Contribution:

MR, AS conceived the study. MR, AS and VN initiated the study at trial site. VG Contributed to incorporate all lab investigations and Lab parameters. MR, AS,VN, SS, RU,VG and SS contributed to Protocol writing. RG, KK,JK and PS given their inputs to finalize the Study Protocol. This protocol read and approved by all authors.

Authors Information:

AS, SS, RU,VG and SS possess the background of Allopathy
MR and VN possess the background of Siddha (An Ancient Traditional medical system of India).

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Funding:

The Trial is funded by the Central Council for Research in Siddha (CCRS), Min.of AYUSH, Govt.of India and Government Institute of Medical sciences, (GIMS) Greater Noida, UP. study protocol has undergone peer-review by the funding body by experts.

Availability of Data and Materials:

All participant data will be kept confidential and personal identifiers of the study participants will not be disclosed to the public. only the Investigator will have access to the trial data. All the procedures will be carried out by adherence of the Good Clinical Practices (GCP).The monitor will have access to the study documents.

Ethics Approval and consent to participate:

The trial received the ethical approval from the Institutional Ethical Committee of Siddha Clinical Research Unit, Safdarjung Hospital, New Delhi on 16.02.2020. This is to state that the appropriate ethical committee approval was taken. Written Consent will be taken from all eligible and willing participants before their participation into the trial. Any Deviations from protocol should be approved by Ethics Committee with amendments and that will be also updated in CTRI website.

Consent for Publication: Not Applicable.

Ethical Considerations:

The purpose of the trial will be explained to all eligible SARS-CoV-2 confirmed patients. Informed consent will be obtained from all eligible participants willing to participate in the trial. Each participant will be informed that participation in the trial is voluntary and that s/he is free to withdraw, without justification, from the trial at any time without consequences and without affecting professional responsibilities. Informed consent will seek approval to collect blood samples and clinical data for the intended purpose of this trial. Study should be conducted according to GCP and AYUSH GCP guidelines.

Risks and benefits for subjects:

This investigation poses minimal risk to participants, involving the collection of a small amount of blood. The direct benefit to the participant is the ability to detect SARS-CoV-2 viral load which would allow for appropriate monitoring and treatment. The primary benefit of the study is indirect in that data collected will help to find an intervention for the management of COVID-19.Any ADR will occur during the study period,participants will be provided with compensation.ADR events should also be informed to Ethics Committee,AYUSH DSMB and Pharmaco Vigilance Reporting.

Confidentiality:

Participant confidentiality will be maintained throughout the investigation. All subjects who participate in the investigation will be assigned a study identification number by the investigation team for the labelling of questionnaires and clinical specimens. The link of this identification number to individuals will be maintained by the investigation team and the CCRS & GIMS and will not be disclosed elsewhere

Related Articles Published:

There were no publications containing the results of this study have already been published or submitted to any journal.

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