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Trials

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A double blinded placebo controlled comparative clinical trial to evaluate the effectiveness of Siddha medicines, Kaba Sura Kudineer (KSK) & Nilavembu Kudineer (NVK) along with standard Allopathy treatment in the management of symptomatic COVID 19 patients - a structured summary of a study protocol for a randomized controlled trial

Anurag Srivastava[1], Manickavasagam Rengaraju[2*], Saurabh Srivastava[1], Vimal Narayan[2], Vivek Gupta[1] and Rashmi Upadhayay[1]

Abstract

Objectives: The primary objectives of the study are to determine the effectiveness of the Kaba Sura Kudineer (KSK) & Nilavembu Kudineer (NVK) along with standard Allopathy Treatment to compared with Placebo (Decaffeinated Tea) with standard Allopathy Treatment in the management of Symptomatic COVID 19 patients and also in reduction of Hospital Stay Time & Changes in Immunological (IL6) and Bio Chemical Markers (Ferritin, CRP, D-Dimer and LDH). The secondary objectives are to evaluate the safety of the trial medicines and their effects in the reduce the risks of the disease. In addition, to document the profile of Symptomatic COVID 19 patients as per Siddha Principles.

Trial Design: A Double Blinded, Three arm, Single Centre, Placebo Controlled, Exploratory and comparative Randomized Controlled Trial

Participants: Patients who were admitted to the COVID Care Centre at Govt. Institute of Medical Sciences. Noida in India will be recruited. These will be patients with Mild and Moderate symptoms with laboratory confirmed COVID 19 (RT – PCR Tested Positive) aged 18-65, willing and consenting to participate.

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* Correspondence: manick.siddha@gmail.com
[2]Siddha Clinical Research Unit, Safdarjung Hospital, A Unit of Central Council for Research in Siddha, New Delhi 110029, India
Full list of author information is available at the end of the article

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Intervention and comparator:

Arm I: Decaffeinated Tea (Placebo – similar in taste and appearance to the other Two Decoctions), 60 Ml Morning and Night after Food, along with standard Allopathy Treatment for 10 days.

Arm II: Nilavembu Kudineer (The Siddha Medicines which is used as a standard Anti-Viral drug for the past Pandemics by Siddha Physicians) 60 Ml Morning and Night after Food, along with standard Allopathy Treatment for 10 days.

Arm III: Kaba Sura Kudineer (The Siddha Medicine which is proposed to be used as a Treatment for COVID 19 based on Siddha Literature) 60 Ml Morning and Night after Food, along with standard Allopathy Treatment for 10 days.

The investigational drugs are registered products under the Govt.of India and bought from GMP Certified Manufacturing Units.

Main Outcomes:

Primary outcomes:

1. Reduction in Viral load of SARS-CoV-2 at the end of treatment (10 days). 2. Time taken to convert Patient from symptomatic to Asymptomatic based on Reduction in clinical symptoms (10 days). 3. Effect of drugs inflammatory markers (IL6,) at the end of treatment (10 days). 4. Reduction in hospital stay time (20 days follow up). (Based on RT PCR CT Value 3^{rd}, 6^{th} if needed 10^{th} day). (Based on IL 6 Value needed 10^{th} day or IL6 value on turning negative. (entry level/exit level).

Secondary outcomes (10 days):

1. Reduction in use of Intensive Supportive Care. 2. Reduction in incidence of complications (Acute Respiratory Distress Syndrome, other systemic complications). 3. MuLBSTA score for viral pneumonia (multinodular infiltration, hypo-lymphocytosis, bacterial co infection, Total Leucocyte Count (TLC $\leq 0.8 \times 10^9$/L), smoking history, hypertension and age) score. 4. Laboratory markers (Haematological & Biochemical Markers). 5. Adverse events/effects Siddha-based measurements. 6. Siddha Udaliyal assessment by using Yakkai Ilakkanam (YI) Tool to diagnose body condition for covid-19 patients.

Randomisation: The assignment of the participants into 3 Groups will be allocated in 1:1:1 Ratio through randomization Blocks in Microsoft Excel by a Statistician who is not involved in the study. The allocation scheme will be made by another statistician by using a closed envelope after the assessment of eligibility and Informed consent procedures. The groups will be balanced for age and sex with 3:1 Ratio in each group for mild: severe COVID-19 symptoms.

Blinding: The Study is Double Blinded. Participants and Investigators were blinded.

Numbers to be randomized (Sample size): Sample size could not be calculated, Since there are no prior trials on KSK and NVK as a comparative trial. In addition, there are no prior trials on KSK and NVK in this region.
A total Number of 120 Patients, 40 each in 3 groups will be recruited in 1:1:1 Ratio.

Trial Status: Protocol Number : SCRUND GIMS Noida Study 1,Version: 2.0 Protocol Date : 20.08.2020
The recruitment period is completed for the trial. The Trial started its recruitment on 22.8.2020. We anticipate study including data analysis will finish in January 2021.
This is to state that it was a late submission from authors for publication of the protocol to the BMC, after enrolment in the study was over.

Trial Registration: The trial protocol was registered with CTRI (Clinical Trial Registry of India) and number is CTRI/2020/08/027286 on 21.08.2020

Full Protocol: The full Protocol is attached as an additional file, Accessible from the Trials website (Additional file 1). In the interest in expediting dissemination of this material, the familiar formatting has been eliminated. This letter serves as a summary of the key elements of the full protocol. The Study protocol has been reported in accordance with the SPIRIT guidelines.

Keywords: COVID 19, Randomised Controlled Trial, Protocol, Siddha Medicine, Herbal, CAM,

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RG,KK,JK and PS given their inputs to finalize the Study Protocol.

Authors' Contributions
MR, AS conceived the study. MR, AS and VN initiated the study. VG Contributed to incorporate all lab investigations. MR, AS, VN, SS and RV contributed to Protocol writing. This protocol was read and approved by all authors.

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

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Availability of Data and Materials
All participant data will be kept confidential and personal identifiers of the study participants will be disclosed to the public. Only the Investigator will have access to the trial data. All the procedures will be carried out by adhering 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 20.07.2020 and Trial Site Ethics Committee on 04.08.2020.
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.

Consent for Publication
Not Applicable

Competing Interest
The authors declare that they have no competing interests.

Author details
[1]Government Institute of Medical sciences (GIMS), Greater Noida, UP 201310, India. [2]Siddha Clinical Research Unit, Safdarjung Hospital, A Unit of Central Council for Research in Siddha, New Delhi 110029, India.

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