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Prophylactic potential of honey and Nigella *sativa* L. against hospital and community-based SARS-CoV-2 spread: a structured summary of a study protocol for a randomised controlled trial

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Abstract

Objectives: Considering the therapeutic potential of honey and Nigella sativa (HNS) in coronavirus disease 2019 (COVID-19) patients, the objective of the study is defined to evaluate the prophylactic role of HNS.

Trial design: The study is a randomized, placebo-controlled, adaptive clinical trial with parallel group design, superiority framework with an allocation ratio of 1:1 among experimental (HNS) and placebo group. An interim analysis will be done when half of the patients have been recruited to evaluate the need to adapt sample size, efficacy, and futility of the trial.

Participants: All asymptomatic patients with hospital or community based COVID-19 exposure will be screened if they have had 4 days exposure to a confirmed case. Non-pregnant adults with significant exposure level will be enrolled in the study

- High-risk exposure (<6 feet distance for >10min without face protection)
- Moderate exposure (<6 feet distance for >10min with face protection)

Subjects with acute or chronic infection, COVID-19 vaccinated, and allergy to HNS will be excluded from the study. Recruitment will be done at Shaikh Zayed Post-Graduate Medical Institute, Ali Clinic and Doctors Lounge in Lahore (Pakistan).

Intervention and comparator: In this clinical study, patients will receive either raw natural honey (0.5 g) and encapsulated organic Nigella sativa seeds (40 mg) per kg body weight per day or empty capsule with and 30 ml of 5% dextrose water as a placebo for 14 days. Both the natural products will be certified for standardization by Government College University (Botany department). Furthermore, each patient will be given standard care therapy according to version 3.0 of the COVID-19 clinical management guidelines by the Ministry of National Health Services of Pakistan.

Main outcomes: Primary outcome will be Incidence of COVID-19 cases within 14 days of randomisation. Secondary endpoints include incidence of COVID-19-related symptoms, hospitalizations, and deaths along with the severity of COVID-19-related symptoms till 14^{th} day of randomization.

Randomisation: Participants will be randomized into experimental and control groups (1:1 allocation ratio) via the lottery method. There will be stratification based on high risk and moderate risk exposure.

Blinding (masking): Quadruple blinding will be ensured for the participants, care providers and outcome accessors. Data analysts will also be blinded to avoid conflict of interest. Site principal investigator will be responsible for ensuring masking.

Numbers to be randomised (sample size): 1000 participants will be enrolled in the study with 1:1 allocation.

Trial Status: The final protocol version 1.4 was approved by institutional review board of Shaikh Zayed Post-Graduate Medical Complex on February 15, 2021. The trial recruitment was started on March 05, 2021, with a trial completion date of February 15, 2022.

Trial registration: Clinical trial was registered on February 23, 2021, www.clinicaltrials.gov with registration ID NCT04767087.

Full protocol: The full protocol is attached as an additional file, accessible from the Trials website (Additional file 1). With the intention of expediting dissemination of this trial, the conventional 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 Standard Protocol Items: Recommendations for Clinical Interventional Trials (SPIRIT) guidelines.

Keywords: Honey, Nigella Sativa, Prophetic Medicine, Pakistan, COVID-19, Randomised controlled trial, Protocol

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s13063-021-05510-3.

Additional file 1: Full protocol.

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DOCTORS LOUNGE Consortium

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Authors' contributions

SA, ShA, MA, AM, SA, MAI, LK, UNS, NM, IF, RK, and MG contributed equally to this paper and share joint first authorship. SA, ShA, MA, AM, and AA are joint corresponding authors. KAUNS, NM, IF and RA contributed equally and share joint second authorship. SA, ShA, MA, AM, SA, MAI, LK, RK and MG added to the conception, designing and manuscript drafting. SA, ShA and MoA proposed the hypothesis and study design. MA, MuA, SiA, MKA, NM, MG, ZH, MKA, SR, ZH, ZS, contributed biochemical, dosimetry, pharmacological as well as pharmaceutical inputs. SA, MoA, SR, AZ, RK and SR drafted the first version of the manuscript. Doctors Lounge Consortium IF, RA, MSS, SR, AH, AM, ZS, ZA, AK, KH, GAm, MiK, SA, MH, QuAI, AmA, ABA, MU,, ABH, SSHS, ZS, AnA, MK, TM and MU contributed significantly to designing the final methodology. MKA, SoA, and AH provided statistical inputs. AAM, UsI, MSu, SZ, SS, SSA, MIA, AmM, TM, AH, YMA, QAS, AA, MoA and MI have contributed to intellectual inputs in the study protocol and methodology along with final manuscript write up. All authors are responsible for their contributions, providing critical edits and final authorization of the article. The corresponding authors attest trial validity and authenticity. All authors read and approved the final manuscript.

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Availability of data and materials

All required data will be posted along with the trial results and final trail dataset requests can be made to Dr. Sohaib Ashraf which could be available from the author on reasonable appeal subject to data protection regulations. (Twitter: SohaibAshrafMD, email address: sohaib@skzmdc.edu.pk, Mobile Number: +92 3334474523)

Declarations

Ethics approval and consent to participate

The trial was approved by institutional ethical review board of Shaikh Zayed Post-Graduate Medical Complex (IRB ID # SZMC/IRB/Internal/273/2021) on February 15, 2021. Authors certify that the study has received ethical approval from the appropriate ethical committee as stated above. Before enrolment, all partakers will be fully informed of the study and asked to sign the consent form to be eligible for randomization and participation.

Consent for publication

Not applicable

Competing interests

The authors declare that they have no competing interests.

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