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Anti-COVID property of subcutaneous ivermectin in synergy with zinc among midlife moderately symptomatic patients: a structured summary of a study protocol for a randomised controlled trial

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Abstract

Objectives: The study objective is to quantify the effectiveness of ivermectin (subcutaneous/oral IVM) in the presence or absence of zinc (Zn) for clinical and radiological improvement in coronavirus disease 2019 (COVID-19) patients with moderate severity.

Trial design: This quadruple-blinded, placebo-controlled randomized clinical trial will be a multiarmed multi-centered study with superiority framework.

Participants: Quinquagenarian and sexagenarian patients with moderate COVID-19 symptoms and positive severe respiratory syndrome coronavirus -2 (SARS-CoV-2) PCR will be included. Participants with co-morbidities and pregnant women will be excluded.
Patient recruitment will be done in Shaikh Zayed Medical Complex, Doctors Lounge and Ali Clinic in Lahore (Pakistan).

Intervention and comparator: The registered patients will be allocated in 6 groups (30 participants each). Patients will be taking subcutaneous IVM at 200 μg/kg/48 h (Arm A) or subcutaneous IVM at 200 μg/kg/48 h and oral Zn 20mg/8 h (Arm B) or oral IVM at 0.2 mg/kg/day (Arm C) or oral IVM at 0.2 mg/kg/day and oral Zn 20mg/8 h (Arm D) or alone oral Zn 20mg/8 h (Arm E) or placebo alone (Arm X). Patients in all arms will receive standard care and respective placebo (empty capsule 8 hourly and/or subcutaneous normal saline 2ml/48 h).

Main outcomes: Primary endpoints will be duration of symptomatic phase and SARS-CoV-2 clearance along with high resolution CT (HRCT) chest score and clinical grade scale (CGS) on day 6. 30-day mortality will be documented as a secondary endpoint. SARS-CoV-2 clearance will be calculated by second PCR on day 7. HRCT chest score will be measured by the percentage and lung lobes involvement on day 6 with a maximum score of 25. CGS will be recorded on a seven-point scale; grade 1 (not hospitalized, no evidence of infection and resumption of normal activities), grade 2 (not hospitalized, but unable to resume normal activities), grade 3 (hospitalized, not requiring supplemental oxygen), grade 4 (hospitalized, requiring supplemental oxygen), grade 5 (hospitalized, requiring nasal high-flow oxygen therapy and/or noninvasive mechanical ventilation), grade 6 (hospitalized, requiring ECMO and/or invasive mechanical ventilation) and grade 7 (death).

Randomisation: A simple lottery method will be used to randomly allocate scrutinized patients in 1:1:1:1:1:1 ratio in 6 groups.

Blinding (masking): Patients, primary care physicians, outcome assessors and the data collection team will be blinded.

Numbers to be randomised (sample size): 180 participants will be randomized into six arms with five investigational and one placebo group.

Trial Status: Institutional Review Board Shaikh Zayed Post-Graduate Medical Complex, Lahore, Pakistan has approved the protocol (version 2.3) with ID SZMC/IRB/Internal0056/2020. The trial was approved on July 14, 2020, and enrolment started on July 30, 2020. The estimated completion date is October 30, 2021.

Trial registration: Clinical Trial has been retrospectively registered on www.clinicaltrials.gov with registration ID NCT04472585 dated July 16, 2020.

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: Ivermectin, Zinc, Subcutaneous Ivermectin, Pakistan, COVID-19, Randomised controlled trial, protocol

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s13063-021-05487-z.

Additional file 1. Full protocol.

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Authors' contributions

SA, SoA, IF, SiA, MA, MAI, LK, RA, RK, MG and SR contributed equally to this paper and share joint first authorship. SA, ShA, SA, MA, and AA are joint corresponding authors. KA, and UNS contributed equally and share joint second authorship. SA, SoA, MA, SA, MAI, LK, RK and MG added to the conception, designing and manuscript drafting. SA, SoA and MoA proposed the hypothesis and study design. MA, MuA, SiA, MKA, MG, ZH, MKA, SR, SSHS and 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, AM, ZS, ZA, TA, AmA, SA, MH, QuAI, AmA, ARV, MeG, TM, and MU contributed significantly to designing the final methodology. MKA, and AH provided statistical inputs. SZ, SS, SSA, MIA, TM, AH, 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

Dr. Sohaib Ashraf will have access to the final trial dataset, and this could be available from the author on reasonable request, but the dataset is subject to data protection regulations. (Email address: sohaib@skzmdc.edu.pk Mobile Number: +1 (857) 316 7995)

Declarations

Ethics approval and consent to participate

Ethics Committee of Shaikh Zayed Post-Graduate Medical Complex, Lahore, Pakistan has approved the study on July 14th, 2020 with ID SZMC/IRB/Internal0056/2020. I certify that this trial has received ethical approval from the appropriate ethical committee as described above. Prior to enrolment, participants will be fully informed of the study and asked to sign the consent form in order 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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