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Comparing cotrimoxazole to standard care for the treatment of severe coronavirus (COVID-19) infection in hospitalised patients

Submission date
05/02/2021

Recruitment status
No longer recruiting

Registration date
09/02/2021

Overall study status
Completed

Last Edited
15/11/2022

Condition category
Infections and Infestations

[X] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[_] Record updated in last year

Plain English summary of protocol

Background and study aims
COVID-19 is a condition caused by the coronavirus (called SARS-CoV-2) that was first identified in late 2019. This virus can infect the respiratory (breathing) system. Some people do not have symptoms but can carry the virus and pass it on to others. People who have developed the condition may develop a fever and/or a continuous cough among other symptoms. This can develop into pneumonia. Pneumonia is a chest infection where the small air pockets of the lungs, called alveoli, fill with liquid and make it more difficult to breathe. At least 15-20% of those who are infected progress to severe COVID-19 disease.

In a small number of patients, there may be a misdirected immune response to the infection, causing inflammation of the lungs and respiratory failure. This response may also cause increased clotting of the blood. Currently, there is no evidence-based, specific anti-viral treatment available for COVID-19, and recommended treatment is supportive with steroids and low molecular weight heparin.

Co-trimoxazole (combination of trimethoprim and sulphamethoxazole) is an antibiotic that kills bacteria. Co-trimoxazole is effective against a wide range of bacterial infections including respiratory tract infections. It has been used for over 80 years and is well-tolerated, inexpensive, and readily available. In addition to having fighting bacterial infections, co-trimoxazole has an effect on the immune system and anti-inflammatory properties. Therefore, co-trimoxazole may be a potential treatment option severe COVID-19.

This study will investigate if starting cotrimoxazole treatment early in hospitalised COVID-19 patients could prevent the development of the disease to a critical stage.

Who can participate?
All adult patients admitted to Medical College Hospital, Kolkata with severe COVID-19 infection

What does the study involve?
Participants will be allocated to one of two groups, with an equal chance of being in either group

(like tossing a coin). Participants and researchers will not have a choice in the treatment given. The first group of participants will receive the study drug, cotrimoxazole, plus standard care. They will be asked to take cotrimoxazole by mouth, three times daily, for 7 days. Treatment with drugs or procedures that the clinician responsible for the participant feels is necessary and would be part of routine clinical practice will be allowed. The other group will receive only the necessary drugs or procedures in routine clinical practice according to the best standard of care and local guidance.

What are the possible benefits and risks of participating?
All participants in this study shall have the privilege of additional (beyond routine care) closer and more intense medical attention. Co-trimoxazole is a time-tested, relatively well-tolerated drug that has been in clinical use for around five decades. Appropriate cautions shall be exercised by the investigators to guard against the known side effects of the drug. In case of any rare serious complication, urgent treatment shall be provided free of cost.

Where is the study run from?
School of Tropical Medicine, Kolkata (India)

When is the study starting and how long is it expected to run for?
October 2020 to March 2023

Who is funding the study?
Department of Health and Family Welfare, Govt of West Bengal (India)

Who is the main contact?
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Contact information

Type(s)
Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Protocol serial number
CTRI/2021/02/031012

Study information

Scientific Title
Cotrimoxazole in hospitalised patients with severe COVID-19 infection compared to the standard of care – an investigator-initiated, randomised controlled trial

Acronym
CoTroxCov

Study objectives

Use of oral cotrimoxazole in patients with severe COVID-19 can prevent ‘higher’ oxygenation requirements through non-invasive and invasive mechanical ventilation, decrease in-hospital stays, and decrease death rate

Ethics approval required
Old ethics approval format

Ethics approval(s)
1. Approved 09/01/2021, Institutional Ethics Committee, Medical College Kolkata (88, College St, Calcutta Medical College, College Square, Kolkata, West Bengal 700073; +919433084372; no email address available), ref: MC/KOL/IEC/NON-SPON/863/01/2021
2. Approved 14/01/2021, Clinical Research Ethics Committee (Calcutta School of Tropical Medicine, 108 Chitta Ranjan Avenue, Kolkata 700073; +919433349332; smnaser2012@gmail.com), ref: CREC-STM/2020-AS-18

Study design
Single-centre randomized controlled trial

Primary study design
Interventional

Study type(s)
Prevention

Health condition(s) or problem(s) studied
Hospitalized patients with severe COVID-19 (SARS-CoV-2 infection)

Interventions
Current intervention as of 14/11/2022:

Randomisation to treatment arms cotrimoxazole plus standard of care or standard of care ony in a 1:1 ratio will be performed using an internet-based randomisation tool.

The intervention group, cotrimoxazole plus standard of care, will receive oral cotrimoxazole 960 mg three times daily for 7 days. Treatment with drugs or procedures in routine clinical practice that the clinician responsible for the patient deems necessary is allowed.

The control group will receive drugs or procedures in routine clinical practice according to the best standard of care as per local protocol.

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Previous intervention:

Randomisation to treatment arms cotrimoxazole plus standard of care or standard of care ony in a 2:1 ratio will be performed using an internet-based randomisation tool.

The intervention group, cotrimoxazole plus standard of care, will receive oral cotrimoxazole 960 mg three times daily for 7 days. Treatment with drugs or procedures in routine clinical practice that the clinician responsible for the patient deems necessary is allowed.

The control group will receive drugs or procedures in routine clinical practice according to the best standard of care as per local protocol.

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
cotrimoxazole

Primary outcome(s)
Current primary outcome measure as of 15/11/2022:

Number of in-patient deaths measured from patient records between baseline and hospital discharge or death

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Previous primary outcome measure:

1.Clinical status, the number of patients requiring escalation of care to non-invasive ventilation (CPAP and HFNC) and invasive ventilation measured using the 7-point ordinal scale (scored from 1 to 7 as follows: 1= death; 2= hospitalised, requiring invasive mechanical ventilation or extracorporeal membrane oxygenation (ECMO); 3= hospitalised, requiring non-invasive ventilation or high flow oxygen devices; 4= hospitalised, requiring supplemental oxygen; 5= hospitalised, not requiring supplemental oxygen, but in need of ongoing medical care (COVID-19 related or otherwise), 6= hospitalised, not requiring supplemental oxygen and no longer requires ongoing medical care (independent); or 7= not hospitalised) between baseline and hospital discharge or death
2. Duration of hospitalisation measured from patient records between baseline and hospital discharge or death
3. Number of in-patient deaths measured from patient records between baseline and hospital discharge or death

Key secondary outcome(s))
Current secondary outcome measures as of 15/11/2022:

1. Clinical status, the number of patients requiring escalation of care to non-invasive ventilation (CPAP and HFNC) and invasive ventilation measured using the 7-point ordinal scale (scored from 1 to 7 as follows: 1= death; 2= hospitalised, requiring invasive mechanical ventilation or extracorporeal membrane oxygenation (ECMO); 3= hospitalised, requiring non-invasive ventilation or high flow oxygen devices; 4= hospitalised, requiring supplemental oxygen; 5= hospitalised, not requiring supplemental oxygen, but in need of ongoing medical care (COVID-19 related or otherwise), 6= hospitalised, not requiring supplemental oxygen and no longer requires ongoing medical care (independent); or 7= not hospitalised) between baseline and hospital discharge or death
2. Time to recovery measured from patient records between baseline and hospital discharge or death
1. Changes in COVID-19 severity measured using the following at baseline, 3, and 7 days:

1.1. Body temperature measured using a thermometer
1.2. Respiratory rate measured using manual method
1.3. Serum levels of C-reactive protein (CRP) measured from blood samples
1.4. Oxygen saturation measured using a pulse oximeter
2. Incidence of serious and non-serious adverse events measured from patient records between baseline and hospital discharge or death

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Previous secondary outcome measures:

1. Changes in COVID-19 severity measured using the following at baseline, 3, and 7 days:
1.1. Body temperature measured using a thermometer
1.2. Respiratory rate measured using manual method
1.3. Serum levels of C-reactive protein (CRP) measured from blood samples
1.4. Oxygen saturation measured using a pulse oximeter
2. Incidence of serious and non-serious adverse events measured from patient records between baseline and hospital discharge or death

Completion date
01/03/2023

Eligibility

Key inclusion criteria
Current inclusion criteria as of 14/11/2022:
1. Adult male or female individuals, age ≥18 years and ≤70 years
2. Patients giving written informed consent to participate in the study (i.e. GCS 15/15: conscious, alert, and oriented)
3. COVID-19 documented by a positive RT-PCR test/Rapid Antigen Test
4. Hospitalised patients with severe COVID-19, requiring supplemental oxygen through a non-re-Breath mask between 10-15 l/min maintaining saturations between 92-96% for up to 30 h and between 94-98% for the first 6 h
5. Clinical/radiological evidence of interstitial pneumonia requiring admission (optional)

Previous inclusion criteria as of 13/05/2021:

1. Adult male or female individuals, age ≥18 years and ≤65 years
2. Patients giving written informed consent to participate in the study (i.e. GCS 15/15: conscious, alert, and oriented)
3. COVID-19 documented by a positive RT-PCR test/Rapid Antigen Test
4. Hospitalised patients with severe COVID-19, requiring supplemental oxygen through a non-re-Breath mask between 10-15 l/min maintaining saturations between 92-96% for up to 30 h and between 94-98% for the first 6 h
5. Clinical/radiological evidence of interstitial pneumonia requiring admission (optional)

Previous inclusion criteria:

1. Aged between 18 and 65 years
2. COVID-19 infection documented by a positive RT-PCR test
3. Hospitalised with severe COVID-19 infection, characterized by fever (at the time of screening or when admitted) and requiring supplemental oxygen through non-rebreather mask between 10 and 15 l/ min
4. Clinical/radiological evidence of interstitial pneumonia requiring admission (optional)
5. Informed written consent given

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria
Current exclusion criteria as of 13/05/2021:

1. Patients who require invasive or non-invasive (including CPAP and high flow nasal cannula). ventilation at the time of inclusion
2. AST/ALT values >5 fold the upper normal limit
3. Impairment of renal function(creatinine clearance<30ml/min/m^2)
4. Absolute neutrophil count below 500 cells/mm^3
5. Absolute platelet count below 50,000 cells/mm^3
6. Documented sepsis or high clinical suspicion of superimposed severe bacterial or fungal infection
7. Concomitant acute medical emergencies, such as AMI, acute pericarditis, PE, stroke, acute Surgical and orthopaedic emergencies like acute abdomen and fractured neck of femur etc.
8. Comobidities or concomitant medications likely to be incompatible for cotrimoxazole use pregnancy or lactation
9. History of cotrimoxazole hypersensitivity
10. Patients participating in another clinical trial for SARS-CoV-2 infection

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Previous exclusion criteria:

1. Require invasive or non-invasive (including CPAP and high flow nasal cannula) ventilation at the time of inclusion
2. Aspartate transaminase (AST)/alanine transaminase (ALT) ratio >5 times the ULN
3. Documented impairment of renal function
4. Absolute neutrophil count <500 cells/mm^3
5. Absolute platelet count <50,000 cells/mm^3

6. Documented sepsis or high suspicion of superimposed severe bacterial or fungal infection
7. Comorbidities or concomitant medications likely to be incompatible for cotrimoxazole use
8. Pregnancy or lactation
9. History of cotrimoxazole hypersensitivity
10. Participating in another clinical trial for SARS-CoV-2 infection

Date of first enrolment
15/02/2021

Date of final enrolment
01/09/2022

Locations

Countries of recruitment
India

Study participating centre
Medical College and Hospital, Kolkata
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Study participating centre
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Sponsor information

Organisation
School of Tropical Medicine, Kolkata

Funder(s)

Funder type

Government

Funder Name
Department of Health and Family Welfare, Government of West Bengal

Alternative Name(s)

Funding Body Type
Government organisation

Funding Body Subtype
Local government

Location
India

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated and/or analysed during the current study during this study will be included in the subsequent results publication

IPD sharing plan summary
Other

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	version v1.0	09/02/2021	01/03/2021	No	Yes
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes
Protocol file	version v2.0	24/12/2020	01/03/2021	No	No