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Does taking hydroxychloroquine before and during exposure to patients protect frontline healthcare workers from coronavirus?

Submission date
06/04/2020

Recruitment status
No longer recruiting

Registration date
14/04/2020

Overall study status
Completed

Last Edited
20/07/2022

Condition category
Infections and Infestations

[_] 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
On 11 March 2020, the World Health Organization declared SARS-CoV-2 (commonly called COVID-19) a global pandemic. As in any pandemic, maintaining the health and safety of the healthcare workforce is of great importance as healthcare workers (HCW) remain a critical line of defence against the spread of COVID-19 and play a vital role in the recovery of those already infected. Frontline HCW, such as those in the emergency department (ED), are at high risk of contracting COVID-19 due to their close proximity to patients who may have the virus. The impact of frontline HCW becoming ill and thus unable to go to work is equally high, and of grave risk to the function of the healthcare system and the ability to minimize the impact of the current pandemic. This study aims to evaluate whether hydroxychloroquine (HCQ), a well-tolerated drug typically used in the prevention of malaria transmission and rheumatic disease, taken before and during exposure to patients with COVID-19, is effective at reducing COVID-19 infections among ED health care workers.

Who can participate?
ED health care workers from five hospitals in Toronto, Canada

What does the study involve?
Participants are randomly allocated to take either HCQ or a placebo (dummy) pill for 90 days and the researchers compare the number of people in each group who are infected with COVID-19. Throughout the study they will monitor each group with monthly visits, where they will monitor if the drug is safe and tolerable, the ability of participants to take the medication regularly, as well as their psychological well-being.

What are the possible benefits and risks of participating?
This study, if successful, has the potential to greatly benefit the health system on an individual, institutional, national, and international level. There may be no medical benefit to participants from participating in this study as the effectiveness of HCQ in the prevention of COVID-19 has yet to be shown. There may be non-medical benefits in contributing to research that might benefit others, and other emotional and social benefits, including empowerment that

participants are taking another measure to potentially reduce their risk of infection of COVID-19. Chloroquine (CQ) and hydroxychloroquine (HCQ) have a long history of safety when used for both malaria prevention and in rheumatic disease. Very commonly occurring (>10%) adverse events include gastrointestinal (abdominal pain and nausea), with less commonly (1-10%) occurring events including blurring of vision, diarrhea, vomiting, anorexia, headache, emotional lability and skin rash. There is a low incidence of serious adverse events, most commonly occurring during chronic use (>1-2 years), with the main risk being macular retinopathy (<1%), which depends on the cumulative dose and permanent damage can be prevented with regular vision exams during treatment. Other rare events (<1%) include liver dysfunction and while HCQ can increase the QT interval, the frequency of this event is not known.

Where is the study run from?
1. Toronto General Hospital (Canada)
2. Toronto Western Hospital (Canada)
3. St. Michael's Hospital (Canada)
4. Sunnybrook Health Sciences Centre (Canada)
5. Mount Sinai Hospital (Canada)

When is the study starting and how long is it expected to run for?
March 2020 to February 2022

Who is funding the study?
1. Canadian Institutes of Health Research
2. National Research Council Canada

Who is the main contact?
1. Dr Megan Landes
megan.landes@utoronto.ca
2. Dr Kevin Kain
kevin.kain@uhn.ca
3. Dr Julie Wright
julie.wright@one-mail.on.ca

Contact information

Type(s)
Scientific

Contact name
Dr Megan Landes

ORCID ID
https://orcid.org/0000-0003-2944-0491

Contact details
200 Elizabeth Street
12 NU-1320
Toronto
Canada

M5G 2C4
+1 (0)416 340 4800
megan.landes@utoronto.ca

Type(s)
Scientific

Contact name
Dr Kevin Kain

ORCID ID
https://orcid.org/0000-0001-6068-1272

Contact details
MaRS, Toronto Medical Discovery Tower
101 College St, Ste 10-360A
Toronto
Canada
M5G 1L7
+1 (0)416 340 4800
kevin.kain@uhn.ca

Type(s)
Public

Contact name
Dr Julie Wright

ORCID ID
https://orcid.org/0000-0002-1554-9456

Contact details
MaRS, Toronto Medical Discovery Tower
101 College St, Ste 10-360A
Toronto
Canada
M5G 1L7
+1 (0)416 340 4800
julie.wright@one-mail.on.ca

Additional identifiers

Protocol serial number
HEROs Protocol 1.1

Study information

Scientific Title
Protecting frontline health care workers from COVID-19 with hydroxychloroquine pre-exposure prophylaxis: a randomized, placebo-controlled multi-site trial in Toronto, Canada

Acronym
HEalth care worker pROphylaxiS against COVID-19 (HEROs)

Study objectives
Pre-exposure prophylaxis (PrEP) with 400 mg hydroxychloroquine (HCQ), taken orally once daily by high-risk health care workers in the emergency department, is effective against COVID-19 disease.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 08/04/2020, Clinical Trials Ontario - University Health Network Research Ethics Board (10th Floor, Room 1056, 700 University Avenue, Toronto, ON, M5G 1Z5, Canada; +1 (0)416 581 7849; boardofrecord@uhnresearch.ca), ref: CTO Project ID: 2132

Study design
Multicentre double-blinded randomized placebo-controlled trial

Primary study design
Interventional

Study type(s)
Prevention

Health condition(s) or problem(s) studied
COVID-19 (SARS-CoV-2 infection)

Interventions
Intervention: Hydroxychloroquine 400 mg orally once a day as pre-exposure prophylaxis against COVID-19.
Control: Placebo.
Randomization details: Fixed 1:1 allocation ratio produced by a computer-based random number generator. Randomly permuted blocks of varying size will be used to ensure equal allocation to each group, stratified by site.

Intervention Type
Drug

Phase
Phase III

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

Primary outcome(s)
Microbiologically confirmed COVID-19 (i.e. SARS-CoV-2 infection). This is a composite endpoint which includes any validated SARS-CoV-2 diagnostic assay, including detection of viral RNA and seroconversion, performed on participant viral detection samples throughout the study period or venous samples for serologic testing collected at day 0, 30, 60, 90 and 120.

Key secondary outcome(s))
1. Adverse events assessed using the DAIDS Table for Grading the Severity of Adverse Events, at day 30, 60, 90, and day 120
2. Symptom duration of COVID-19, measured in days, collected from participants via self-report (questionnaire) weekly (every 7 days) from day 7 to 120
3. Days of hospitalization attributable to COVID-19: the number of days (or partial days) spent admitted to an acute care hospital during the study period. Collected from participants or designate via self-report (questionnaire) weekly (every 7 days) from day 7 to 120
4. Respiratory failure requiring ventilatory support attributable to COVID-19: the number of days (or partial days) requiring i) non-invasive and ii) endotracheal intubation with ventilation during the study period. Collected from participants or designate via self-report (questionnaire) weekly (every 7 days) from day 7 to 120
5. Mortality attributable to COVID-19 and all-cause mortality during the study period, collected from participants or designate via self-report (questionnaire) weekly (every 7 days) from day 7 to 120
6. Number of days ineligible/unable to work due to COVID-19, measured from symptom onset to return to work date, collected from participants or designate via self-report (questionnaire) weekly (every 7 days) from day 7 to 120
7. Seropositivity: reactive serology by day 120, blood collected at day 0, 30, 60, 90, 120
8. Short-term psychological impact of exposure to COVID-19 measured using the K10, a validated measure of non-specific psychological distress, with a standard cutoff score of ≥16, at the beginning of randomization (day 1), during the randomized period (day 60) and during the open-label period (day 120)

Note: In the case of death or other conditions rendering the participant unable to communicate or complete the weekly email survey, the outcome will be obtained by contacting the designate identified by the participant at enrolment. If it is not possible to reach this person, the participant will be considered lost to follow up.

Completion date
28/02/2022

Eligibility

Key inclusion criteria
1. Health care worker (HCW) in the emergency department who is anticipated to work at least 10 shifts over the duration of the study period (minimum 6 hours per shift) and anticipated to remain in the emergency department for the duration of the study (i.e., not transferring to another unit). For the purposes of the study, “health care workers” are physicians (including residents), nurses, nurse practitioners, physician assistants, respiratory therapists, X-ray technicians, social workers and support staff (including but not limited to house-keeping, and porters)
2. Age ≥18 years
3. Ability to communicate with study staff in English

Participant type(s)
Health professional

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Total final enrolment
13

Key exclusion criteria
1. Currently pregnant, planning to become pregnant during the study period, and/or breast feeding
2. Known hypersensitivity/allergy to hydroxychloroquine or to 4-aminoquinoline compounds.
3. Current use of hydroxychloroquine for the treatment of a medical condition.
4. Known prolonged QT syndrome, or concomitant medications which simultaneously may prolong the QTC that cannot be temporarily suspended/replaced. These are including but not limited to Class IA, IC and III antiarrhythmics; certain antidepressants, antipsychotics, and anti-infectives; domperidone; 5-hydroxytryptamine (5-HT)3 receptor antagonists; kinase inhibitors; histone deacetylase inhibitors beta-2 adrenoceptor agonists.
5. Known pre-existing retinopathy.
6. Disclosure of self-administered use of hydroxychloroquine or chloroquine within 12 weeks prior to study. This window allows five half-lives of HCQ (i.e. 21 days) to pass before being reintroduced to the drug.
7. Confirmed symptomatic COVID-19 at time of enrollment, i.e. symptom of COVID-19 at enrollment with confirmation of SARS-CoV-2 infection by viral detection as performed according to local guidelines for symptomatic HCWs. All participants with COVID-19 symptoms at enrollment will be directed to have confirmatory testing (within the department or occupational health as per the site guidelines). Participants who are negative for SARS-CoV-2 will be redirected to enrollment procedures; those testing positive will be excluded.

Date of first enrolment
13/04/2020

Date of final enrolment
20/05/2020

Locations

Countries of recruitment
Canada

Study participating centre
Toronto General Hospital
200 Elizabeth Street
Toronto

Canada
M5G 2C4

Study participating centre
Toronto Western Hospital
399 Bathurst St
Toronto
Canada
M5T 2S8

Study participating centre
St. Michael's Hospital
30 Bond St
Toronto
Canada
M5B 1W8

Study participating centre
Sunnybrook Health Sciences Centre
2075 Bayview Ave
Toronto
Canada
M4N 3M5

Study participating centre
Mount Sinai Hospital
600 University Ave
Toronto
Canada
M5G 1X5

Sponsor information

Organisation
University Health Network

ROR
https://ror.org/042xt5161

Funder(s)

Funder type
Government

Funder Name
Canadian Institutes of Health Research

Alternative Name(s)
Instituts de Recherche en Santé du Canada, The Canadian Institutes of Health Research (CIHR), Canadian Institutes of Health Research (CIHR), Canadian Institutes of Health Research | Ottawa ON, CIHR - Welcome to the Canadian Institutes of Health Research, CIHR, IRSC

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
Canada

Funder Name
National Research Council Canada

Alternative Name(s)
Conseil national de recherches Canada, ResearchCouncilCan, NRC, CNRC

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
Canada

Results and Publications

Individual participant data (IPD) sharing plan
At the time of completion of the analysis of primary and secondary outcomes, the HEROS Steering Committee will review all applications for use of participant-level data and make recommendations. The contact will be Megan Landes (megan.landes@uhn.ca).

IPD sharing plan summary

Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article	structured summary of protocol	14/07/2020	17/07/2020	Yes	No