Chloroquine/ hydroxychloroquine prevention of coronavirus disease (COVID-19) in the healthcare setting; a randomised, placebo-controlled prophylaxis study

Dosing of hydroxychloroquine v2.0, 1st July 2020

MORU Tropical Health Network

wellcome

UNIVERSITY OF OXFORD

UNIVERSITY OF OXFORD DIABETES TRIALS UNIT
The Oxford Centre for Diabetes, Endocrinology and Metabolism

brighton and sussex medical school

Tablets used in the study

- Hydroxychloroquine sulphate 200 mg
  - 155 mg OHCQ BASE

- Loading dose – 10 mg/kg BASE on the first day

- Thereafter – 1 tablet/day

Dosing for all subjects

Weight (Kg)	Number of tablets	Dose (base) received mg	Dose (base) in mg/kg
40 - <55	3	465	8.61-11.63
55 - <70	4	620	8.99-11.27
≥70.1	5	770	≤11.07

Taking the loading dose

- Take with a snack or taken with a meal
  - Reduces upper GI upset

<u>Loading dose is:</u>

- 3 tabs as a single dose or
- If 4 or 5 tabs
  - 2 tabs then 2 tabs or
  - 3 tabs then 2 tabs
    - separated by ≥ 1 hour, second dose does not need to be witnessed
    - study nurse records initial dose (if split) on the CRF
- Participant records all other doses on App

Vomiting of loading dose

- ≤ 30 minutes of loading dose (initial dose if split*)
  - dose should be repeated
  - taken when feeling better and with his/her next meal/snack
  - If vomiting recurs, subject withdrawn

- Vomiting > 30 minutes
  - No redosing

* No redosing of the 2nd half of the split dose

Side-effects (short-term use)

- Well tolerated, mild SE
  - Abdominal discomfort
  - Loss of appetite
  - Nausea / Vomiting
  - Dizziness
  - Headache
  - Itching (more common in individuals of African descent)
  - Rashes
  - Blurred vision/difficultly focusing (transient)

Tolerability of COPCOV dosing

- Boulware reported 40% of healthcare workers got side-effects with HCQ (17% placebo)
  - Esp. nausea/GI upset etc. - 22%
  - But under 50% correctly thought they were on HCQ
- Of note visual disturbance v uncommon in HCQ arm (0.9%)
- Awareness of the Boulware findings could put off participants
  - Boulware regimen was 7 tablets on day 1 then 3 tablets daily
  - Note the COPCOV dosing much lower (3-5 tabs day 1, then 1 tablet daily), around half that used in rheumatoid

Boulware DR et al NEJM 2020

Cardiotoxicity

- Life-threatening in overdose but well tolerated at therapeutic doses
- Anti-arrhythmic and used in the past to treat AF and protective against AV block and SVT in SLE (Teixeira 2014)
- HCQ used extensively at high dose for many years for rheumatological conditions
- Prolongs QT predictably
  - Cases of arrhythmias attributable to the drug are rare and only in conditions where myocarditis may occur
- CQ in SLE Exclusion – Known prolonged QT syndrome
  - Cardiac history or unexplained faints
- COPCOV exclusion criteria selected to ensure participants are at low risk of QT prolongation
- GP/Medical Information letter covers actions should a participant become unwell and need risk assessment for cardiac risk, any QT prolonging meds and unblinding if necessary

Teixeira, R. A., E. F. Borba, A. Pedrosa, S. Nishioka, V. S. Viana, J. A. Ramires, R. Kalil-Filho, E. Bonfa and M. Martinelli Filho (2014). "Evidence for cardiac safety and antiarrhythmic potential of chloroquine in systemic lupus erythematosus." Europace **16**(6): 887-892.

Additional Information

Reference Documents:

- COPCOV UK Protocol
- COPCOV UK HCQ Dosing SOP

Always refer to https://www.copcov.org/sites.html for correct version of documents

If you have any further questions please contact copcov@dtu.ox.ac.uk