

Hydroxychloroquin for COVID-19 Why was so much hype?

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At the time of writing coronavirus disease 2019 (COVID-19) outbreak has affected more than 8 million persons worldwide with India contributing over 380,000. The disease has taken more than 450,000 and still counting.

As of now there is neither a specific drug nor a vaccine that can treat or prevent the it.

On the strength of in vitro¹ and some observational trials anti malarial drug chloroquine and its analog hydroxychloroquin (HCQ) with or without microlide azithromycin has been touted by some agencies as a treatment/ prophylactic agent for COVID 19. Its recommendations for treatment and prevention has been undergoing sea saw movement by various investigators and health and research organizations like WHO, Indian Council of Medical Research (ICMR).

Perhaps no other drug has attracted so much of a research and controversy in such a short span of 4 months since the spread of pandemic. Hope of cure was given by some of the in vitro observations. HCQ was shown to inhibit SARS-CoV-2 virus by acting at the angiotensin converting enzyme 2 receptor which is the binding site for the virus.

Further in the earlier observational data from France the drug when combined with microlide Azithromycin showed promising reports.

It is not surprising that even in the absence of any large observational registry or randomized controlled trial the drug has been used and abused considering desperate pandemic situation with no alternate available treatment.

Unfortunately 2 studies published in Lancet and New England Journal of Medicine respectively which were reported to be negative trials for HCQ had to be retracted by lead author Mandeep Mehra after flaws were pointed out in the studies. Promptly after the publication of Dr. Mehra's article in Lancet, WHO as a knee jerk reaction stopped HCQ arm in SOLIDARITY trial that is evaluating the efficacy of various drugs for COVID-19.

Soon after retraction of these 2 publications by the authors WHO with another knee jerk reaction reincluded HCQ in the SOLIDARITY trial!

While all studies focused on the treatment efficacy of HCQ data on prevention remained blank. However Boulware et² al have published their data on the efficacy of HCQ for prevention of COVID-19 in New England Journal of Medicine. It is a randomized placebo controlled double blind trial from USA and Canada. Investigators enrolled 812 asymptomatic individuals with 87.6% being exposed to high risk COVID-19 contacts. Individuals were assigned to receive placebo or 800 mg of HCQ as loading dose followed by 600 mg in 6-8 hours with maintenance of 600 mg daily for 4 days.

Primary outcome was the incidence of laboratory positive COVID-19 or symptoms compatible with COVID-19 within 14 days.

There was no significant difference between 2 arms. New illness compatible with diagnosis of COVID-19 occurred in 49 of 414 (11.8%) in those who received HCQ versus 58 of 407 (14.3%). Side effects occurred in 40% of treatment arm versus 16.8% placebo arm. While the design of the trial may be open to criticism as of now it is the only worthwhile randomized control trial for HCQ in prevention of COVID -19 published in peer reviewed journal.³

So where does HCQ go from here?

Despite so much controversy and doubts about value of HCQ, ICMR came out with new guidelines on 22 nd May 2020 expanding its indication for prevention of COVID 19 to asymptomatic-health care workers in non COVID hospitals, non COVID areas of COVID hospitals, asymptomatic front line workers which would include surveillance workers, in containment zones, paramilitary and police force involved in COVID-19 related activities.

ICMR claims 1) its recommendation are only for prevention of COVID 19 in health workers and front line workers and not for treatment 2) Its recommendations are based on observations of about 300 plus health care workers in All India Institute of Medicine and few other hospitals. It claims that the trial showed that those who received HCQ did better than those who did not receive HCQ. A case control study has been published with lightening speed.⁴ Numbers are too few, one does not know whether ICMR followed strict protocols of research which it has set in the past for other studies. There could be selection bias for those who were prescribed HCQ. Use of PPEs was more frequent in treatment arm. Was the article peer reviewed? Above all would ICMR have accepted such a trial and data if it was conducted and published during non COVID-19 period?

Unfortunately Maharashtra task force for COVID had been following these recommendations and HCQ was being given to front line workers and police force. Already more than 2500 police force personnel is COVID-19 positive and about 25 of them have unfortunately died. This despite HCQ!!

One understands the gravity of the prevailing pandemic situation. But we should not lose sight of the fact France has banned its use in COVID-19. UK has abruptly stopped HCQ arm in the RECOVERY trial since the initial data revealed that 1542 patients who were treated with HCQ when compared with 3132 treated with usual standard of care had similar outcomes (Mortality 25.7% HCQ arm versus 23.5% control arm). As per news appearing in media USA is loaded with tons of surplus HCQ due to its non use in COVID-19 and India has lifted ban on export of HCQ.

A long awaited action is again taken –HCQ is out from SOLIDARITY trail!!!

Will HCQ survive to treat or prevent COVID-19?

Since USA and France have banned its use for COVID-19 and UK has withdrawn HCQ arm from RECOVERY trial the case for its use in COVID -19 as a treatment has very little hope to survive.

Mercifully last nail in the coffin of HCQ as treatment is put.

What about prevention?

Though its use in healthy frontline health workers has not resulted in any serious adverse effects annoying symptoms have been reported in virtually all the trials including from Poona as per news paper reports.

As of now there are 203 COVID 19 trials with HCQ and 60 of them are for prevention !!

Results of a very large trial Healthcare Worker Exposure Response and Outcomes of Hydroxychloroquin (HERO-HCQ) that would recruit 15000 health care workers are awaited. Unfortunately currently HCQ has become a favourite topic for media, social and therefore political circles clouding scientific data obtained so far. Media seems to be knowing more about HCQ and COVID -19 than medical profession!

There is no robust scientific data to recommend its use for prevention of COVID-19 as of now. Until then it will be unscientific and unfair to give false hopes of protection to our health care and front line workers by advising them HCQ

References

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