NEWS

Covid-19: Doctors criticise Indian research agency for recommending hydroxychloroquine prophylaxis

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Doctors in India have decried the Indian health research agency's intransigence on its recommendation of hydroxychloroquine prophylaxis against covid-19 to hospital healthcare workers, saying that the agency has breached principles of medical ethics.

The doctors have accused the Indian Council of Medical Research of resisting calls from the medical community for randomised control trials to assess hydroxychloroquine prophylaxis against covid-19 and for relying on weak evidence to justify its recommendation.

In an advisory dated 22 May the council expanded hydroxychloroquine prophylaxis to healthcare workers in hospitals and police personnel deployed on covid-19 duty throughout the country. In March the council had recommended it to frontline healthcare workers treating covid-19 patients and to household contacts of patients.

Existing studies

The advisories recommend two regimens: for healthcare workers and police, 400 mg twice a day on the first day followed by once weekly for seven weeks; and for household contacts, 400 mg twice a day on the first day followed by 400 mg once weekly for three weeks.

In favour of these treatments the council has cited in vitro studies, the safety profile of hydroxychloroquine, and an observational study of healthcare workers in a public hospital in New Delhi that "showed that those on prophylaxis had lower incidence of SARS-CoV-2 infection than those not taking it."¹

Balram Bhargava, the council's director general, said this week, "We thought it may be a useful drug for prophylaxis, taking [into account] biological plausibility, in vitro data, and the availability and safety of the drug . . . We looked at the data from observational studies and found that it may be working."

But many clinician researchers have expressed surprise at the council's stance, saying that no peer reviewed or published data support its advice and that the recommendations will expose thousands of healthy healthcare workers and police personnel to a drug known to be associated with adverse effects on cardiac function.

Ethics and science

The council has asserted that its observational studies have found hydroxychloroquine to be safe, although the drug needs to be taken under medical supervision and people taking it have been asked to have electrocardiography once during the eight week regimen.

But Shriprakash Kalantri, director professor of medicine at the Mahatma Gandhi Institute of Medical Sciences in the central Indian town of Wardha, told *The BMJ*, "It is unfortunate—we're seeing the country's top health research body abandoning ethics and science."

In the eight weeks since the council issued its first advisory, said Kalantri, it could have organised a large study with several thousands of healthcare workers randomly assigned to a hydroxychloroquine arm and a control arm. "The council could have easily done this: had it done so and shown positive results, it would have earned accolades and not the criticism it is facing now," he said.

Some researchers say that the council's resistance to randomised clinical trials is even more worrying than the recommendation on prophylaxis itself. The council has not responded to a proposal by researchers at New Delhi's George Institute for Global Health for a randomised clinical trial in hospitals in Mumbai and Chennai, including around 5000 health workers in the two arms.

Vivekanand Jha, director of the George Institute, told *The BMJ*, "Their stance is mystifying and bothersome. However, while it is possible that a group of doctors is convinced about its prophylactic use, we also see an attempt to stall legitimate research."

Jha said it was "disturbing" that the Indian science ministry's department of biotechnology had rejected his institute's proposal for a randomised clinical trial of hydroxychloroquine prophylaxis, saying that under the council's advisory it would be difficult to get a control arm for the trial.

Amar Jesani, a physician-researcher and editor of the *Indian Journal of Medical Ethics*, commented, "When the Indian Council of Medical Research issues an advisory, it comes with some authority. That makes it even more important for the council to adhere to principles of science and ethics."

A senior council official told *The BMJ* that an expert panel would review the recommendation on hydroxychloroquine therapy for covid-19 patients, after the World Health Organization's decision to temporarily pause the hydroxychloroquine arm in the global Solidarity Trial.² "The review is only for use as treatment," the official said.

- 1 Ministry of Health and Family Welfare, Government of India. Revised advisory on the use of Hydroxychloroquine (HCQ) as prophylaxis for COVID-19 infection (in supersession of previous advisory dated 23 Mar 2020). <https://www.mohfw.gov.in/pdf/RevisedadvisoryontheuseofhydroxychloroquineasprophylaxisforSARSCoVID19infection.pdf>.
- 2 Mahase E. Covid-19: WHO halts hydroxychloroquine trial to review links with increased mortality risk. *BMJ* 2020;369:m212610.1136/bmj.m2126.

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