

Hydroxychloroquine: the situation is critical

Drawing on research by Chinese doctors, an academic from Marseille, France, claimed, in a video aimed at the general public in February 2020, that thanks to *hydroxychloroquine*, covid-19 was (our translation) "*probably the most easily treated respiratory infection of all*" (1-3). Over subsequent weeks, medical evaluation experts, the World Health Organization (WHO), European drug regulatory agencies, major medical journals, and pharmacovigilance centres asked for evidence, issued warnings about the adverse effects of *hydroxychloroquine*, and advised against its use except as part of a clinical trial (4).

This situation was incomprehensible to many healthcare professionals and patients, especially in France: how could so much criticism have been levelled at a research scientist, described as one of the best, who had authored a series of studies in thousands of persons which, in his opinion, showed that *hydroxychloroquine* cures 92% of patients? Explanations abounded: he is a victim of Paris's anti-Marseille bias, of the "system", of Big Pharma, the government, bureaucratic doctors, the media, and so on. Explanations that revealed but also exacerbated the prevailing mood of mistrust and even hatred, judging by the invective online.

The explanation is simple, however. As far back as 1865, Claude Bernard, one of the pioneers of experimental medicine, wrote: "*Physicians often pride themselves on curing all their patients with a remedy that they use. But the first thing to ask them is whether they have tried doing nothing, i.e. not treating other patients; for how else can they know whether it was the remedy or nature that cured them?*" (5).

The reason comparative clinical trials exist is to eliminate this uncertainty. According to the methodological principles of clinical evaluation, acknowledged internationally for several decades now, comparative trials provide the most reliable evidence when evaluating treatments. The lowest-level evidence comes from expert opinions, case series, other observational studies and empiricism (6). This is still true in 2020 – and also in covid-19.

As of late July 2020, a substantial amount of data has been amassed from comparative trials of *hydroxychloroquine* in the treatment of covid-19. They show no evidence of efficacy, but patients have been harmed by this drug.

Healthcare professionals are taught critical appraisal to help them understand the pitfalls of various scientific procedures, and the factors that make it difficult to demonstrate cause-and-effect relationships. But the widespread lack of understanding among the public also shows the need to boost educational efforts, in schools in particular, to help citizens become critical thinkers, develop healthy scepticism and understand cognitive bias, as well as which scientific methods generate robust evidence. This would better equip the public to stand up to arguments from those who are presumed to be authorities.

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EDITORIAL