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The hydroxychloroquine debate: a therapeutic dilemma for general practitioners

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France has been at the epicenter of the worldwide debate about hydroxychloroquine, as the main advocacy for its use to treat COVID-19 comes from a research unit led by Didier Raoult in Marseille. Among a national panel of 2940 general practitioners, we found that physicians in the areas most strongly affected by the epidemic or closest to the epicenter of the controversy reported that the hydroxychloroquine debate had made it difficult for them to deal with patients' treatment requests. Their adherence to official recommendations was also lower. It will be necessary to examine the conditions producing so strong a conflict.

Introduction

Epidemics create a rush for treatment. In this context, the endorsement of pharmaceutical drugs by public figures before proper evaluation can have dire consequences, as was the case with hydroxychloroquine.

In the USA, President Trump's unbridled advocacy led to an increase in its off-label sales, shortages for patients with indications for which its efficacy is established, and an increase in its reported cardiac side effects.[1] France has been at the epicenter of this heated worldwide debate as the main advocacy for its use against COVID-19 has come from a team of infectiologists led by Didier Raoult in Marseille. Hydroxychloroquine's continued prominence in the news since mid-March has persuaded a significant proportion (48%) of the French public to believe in its efficacy.[2]

The impact of these highly visible debates has also affected healthcare providers. Doctors may be affected by patients' demands for a prescription for hydroxychloroquine or swayed by the arguments presented in favor of its prescription to patients with COVID-19, despite contrary recommendations from the French public health authorities.[3] Doctors can espouse beliefs at odds with public health authorities' recommendations and scientific consensus on various subjects ranging from vaccination[4] to Lyme disease[5].

We conducted a flash survey on COVID-19 among a representative sample (on age, gender and workload) of 1200 French self-employed general practitioners (GPs)—who were responsible for diagnosing and managing patients with COVID-19 in the community—to better understand the impact of controversies on their practices. The present article sought to evaluate the extent to which they may face dilemmas in epidemic contexts where uncertainty is substantial, prominent experts disagree and medical issues become politicized.

Methods

We used data collected from a national panel of 3300 self-employed GPs established in late 2018. They were randomly selected from the French National Registry of Health Care Workers (Health Ministry). The 2940 GPs (89.1%) still participating in the panel in April 2020 were asked to take this online cross-sectional survey. The questionnaire included the following question: 'Does the current controversy over hydroxychloroquine make it difficult for you to respond to requests for treatment by your patients positive for COVID-19?' (yes/no/do not know). It also collected participants' opinions about the official recommendations of the French health authorities on the diagnosis and management of patients with COVID-19: are they clear, sufficient, applicable or changed too often, four items, yes/no, Cronbach alpha = 0.66. We weighted data according to GPs' age, gender and workload to obtain a sample representative of this population for these variables.

Results

From 9 April to 20 April 2020, 1200/2940 GPs (40, 8.4%) participated in the cross-sectional survey. More than one doctor in four (27%) reported difficulties with their patients due to this polemic. This figure was significantly higher in Southeastern France (50%), especially in Marseille, and in the areas most affected by the epidemic (40%), compared with 25% in those least affected (Table 1). This opinion was significantly less frequent in group practices than in solo practices (aRR = 0.67, 95% CI = 0.49–0.90).

Moreover, the official recommendations of the Ministry of Health site for the overall management of patients with suspected or proven COVID-19 infection were clear for 69.5% of the doctors. More than half considered them sufficient (54.7%) or applicable (56.7%), but 64.2% felt that they changed too frequently. Multiple Poisson regression adjusted on age, gender and region found that overall adherence to these recommendations (score adding up GPs' answers to the four items; range 0–4) was significantly lower (aRR = 0.61, 95% CI = 0.47–0.80) among those physicians who felt that the controversy about hydroxychloroquine made it difficult for them to respond to these patients' requests (Table 1).

Table 1. Factors associated, among general practitioners, with agreement that the controversy over hydroxychloroquine made it difficult for them to deal with requests for the treatment from patients who tested positive for COVID-19, modified Poisson regression, weighted data, April 2020 (Ref. Do not agree, $N = 1151$)

Factors	aRR	95% CI
Sex (ref. Male)		
Female	1.16	0.87–1.55
Region (ref. Rest of France)		
South-eastern France	2.10	1.58–2.80
Western France (Pays de la Loire)	0.86	0.58–1.27
Intensity of the Covid-19 epidemic in French districts (ref. low)		
Moderate	1.14	0.77–1.70
High	1.79	1.17–2.74
Age (ref. < 50 years old)		
50–59	0.80	0.55–1.15
≥60	0.94	0.66–1.33
General practitioners density (ref. low)		
Yes	1.18	0.86–1.61
Type of practice (ref. solo)		
Group	0.67	0.49–0.90
Workload (ref. Min-Q1)		
Q1–Q3	1.03	0.76–1.41
Q3–Max	1.23	0.85–1.78
Score of trust in the Health Ministry to manage the Covid-19 epidemic [0–12] (ref. low [0–7])		
High [8–12]	0.80	0.59–1.09

Discussion

These results are an indicator of the scale of the consequences of the controversy around hydroxychloroquine. Physicians reported more frequent difficulties in the areas most strongly affected by the epidemic and especially those closest to the epicenter of the controversy than elsewhere. In these areas, physicians saw more frequent requests from patients positive for SARS-CoV-2 for the treatment, linked to the hope inspired by the claimed therapeutic benefits of hydroxychloroquine.

More broadly, physicians increasingly face patients who make specific requests or even demands for treatment, based on their own search for information and on non-medical considerations (psychological, cultural, even political with the demand for greater local autonomy). This process of empowerment[6] through which patients have strengthened their willingness and ability to take effective care of their health has been underway in Western countries for several decades. The results of a qualitative survey that we conducted in Marseille suggests that patients played a crucial role in GPs' decision whether to prescribe hydroxychloroquine (when this was still possible), suggesting an increased horizontalization of the doctor–patient relationship in this situation of uncertainty.[7]

The gap between the requests of patients and the guidelines of the health authorities may have created a dilemma among GPs, reinforced by the intensity of the disagreements between experts, the media coverage and politicization of the debates, as well as the fairly widespread mistrust of the government. Dialogue with colleagues, facilitated in group offices, might have reduced the perception of this dilemma and probably also made it possible to better organize the response to patients' requests for this treatment or medication. The growing importance of collegiality in health care decision-making reflects structural changes in the organization of primary care in France with the generalization of group practice particularly among young GPs. Nonetheless, the negative association between the frequency of this problem among physicians and their confidence in the official management guidelines for COVID-19 suggests the second type of explanation. The physicians themselves may be sufficiently convinced by the evidence of the hydroxychloroquine defenders to question the official guidelines. Indeed, the debate as it took place in France opposed leading researchers against one another rather than representatives of mainstream science against outsiders; it is therefore different from the controversy about the association between autism and the MMR vaccine that has raged for two decades.[8]

On one side were experts (and health authorities) who considered it essential to await the results of randomized controlled trials before prescribing hydroxychloroquine to patients with COVID-19. In the UK, for example, the National Health Service strongly discouraged the use of off-licence treatments outside of a trial.[9]

On the other side, Didier Raoult, backed by other medical school professors, claimed that (i) the preliminary data and long experience with this substance for other conditions were sufficient to judge its safety, (ii) an RCT would take too much time and is not appropriate for the production of knowledge for decision-making in emergency situations and (iii) the physician's duty is to try to treat the patient. These arguments are particularly likely to have convinced some French GPs who in situations of uncertainty would tend to rely on their own judgment rather than clinical practice guidelines.[10] Our experience in recent months with physicians in southeastern France shows broad support by GPs, particularly in Marseilles, for the combined therapy recommended by Pr. Raoult and his colleagues. Many GPs have taken up the arguments of the duty to treat (rather than wait for the disease to worsen) and the doctor's freedom to prescribe. The French health authorities banned the prescription of hydroxychloroquine by GPs but allowed it for severely ill patients at hospital; as a result, the drug continued to be prescribed in hospitals to which GPs referred their patients infected with COVID-19 for indications well beyond simple compassionate protocols.

Conclusion

In due course, it will be necessary to examine the conditions producing so strong a conflict and its societal causes as well as its public health and social consequences. This reflection will need to involve all parties, including GPs and not only specialist scientists, to ensure better preparation for health management and for knowledge production in the not unlikely event of a future epidemic.

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Key points

- The hydroxychloroquine controversy created dilemmas for a significant portion of GPs: adhering to the instructions of the health authorities or prescribing the hydroxychloroquine that patients were asking for.
- These difficulties were less frequent among those in group compared with solo practices.
- Overall adherence to official recommendations was lower among physicians affected by the controversy.

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