

## Research Article

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## Study of the Safety and Efficacy of the Hydroxychloroquine Protocol against COVID-19 in Algeria: Experience of the Gynaecology Department of the EHU Oran

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### ABSTRACT

In Algeria, the Scientific Council of the Ministry of Health has decided on the hydroxychloroquine protocol for the treatment of patients with COVID-19, as the hydroxychloroquine molecule has not been the subject of a randomized clinical trial and the therapeutic evidence remains uncertain. The safety of hydroxychloroquine remains dependent on a study to secure and evaluate the efficacy of this protocol in the management of COVID-19 infection. This is a prospective study of 55 patients with COVID-19 hospitalized in the gynaecology department at EHU Oran for a period of one month and confirmed by RT-PCR or thoracoabdominal CT scan. The safety indicator and therapeutic evaluation were based on active reporting of protocol adverse events. In conclusion, the COVID-19 therapeutic protocol is not devoid of adverse effects, even though it brings a benefit, whereas during our study some patients who did not benefit from the protocol showed the same remission rate.

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**Received:** November 24, 2020; **Accepted:** December 12, 2020; **Published:** December 10, 2020

**Keywords:** COVID-19, Hydroxychloroquine, Azithromycin, Safety, Efficacy

### Introduction

The emergence of the COVID-19 epidemic due to SARS-CoV-2, discovered in Wuhan, China in late December 2019, has shaken the world with its rapid spread outside of China to invade many countries around the world [1-3]. The WHO declared the outbreak of COVID-19 as a pandemic on March 12, 2020 (4-5). Algeria is now facing the wave of COVID-19 with a high contamination rate. Among candidate drugs to treat COVID-19, repositioning hydroxychloroquine is an interesting strategy because knowledge of the safety profile, adverse effects, dosage and drug interactions is well known [6,7]. Hydroxychloroquine has demonstrated anti-CoV2 SARS activity in vitro. The clinical safety profile of hydroxychloroquine is better than that of chloroquine and allows for a higher daily dose and has fewer concerns regarding drug interactions, as the hydroxychloroquine molecule has not been subjected to a randomized clinical trial and the anti-CoV2-SRAS therapeutic evidence remains uncertain. The treatment with hydroxychloroquine is recommended with azithromycin by the Algerian Ministry of Health since March 23, 2020, for the moment the results are encouraging however the treatment requires strict monitoring of safety and an estimate of the effectiveness of the molecule [8-10]. The objective of this work is to evaluate the efficacy and safety of the protocol in the treatment of COVID-19 in patients hospitalized in the gynaecology department at EHU Oran.

### Material and Method

#### Type of study

This is a prospective descriptive observational study carried out at the EHU Oran department of gynaecology for one month.

#### Study Population

COVID-19 in patients undergoing curative treatment were included in this study regardless of their clinical condition. Excluded patients are patients transferred during the treatment period, children hospitalized with their mothers under 12 years of age for preventive treatment.

#### Method

Data collection, medication and medication review are recorded on a chart and completed by the clinical pharmacy team (Appendix 1); adverse events, complications of hydroxychloroquine and signs of remission will be reported daily throughout the study period. Clinical and biological follow-up for each patient

#### Protocol for the treatment of COVID-19 in Algeria

For all patients presenting: a moderate form, a form with pneumonia and/or a severe form suspected of a COVID-19 infection: it will be prescribed, in the absence of contraindications and under medical supervision (10).

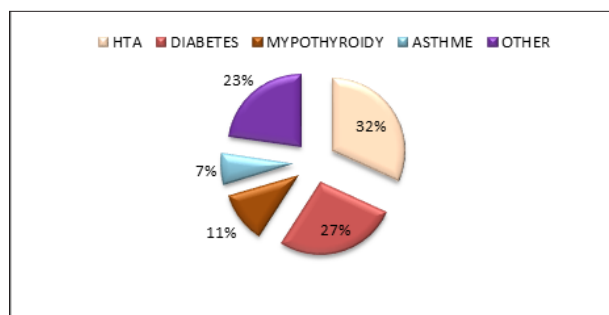
-Hydroxychloroquine: 200mg, 3 times daily for 10 days.

-Azithromycin: 500mg on the first day then 250mg per day for 4 days.

-Zinc and vitamin C supplementation

## Results and Discussion

In this study we recruited 55 patients out of 75 respondents to the inclusion criteria with an average age of 44 years ranging from 12 to 82 years among them six pregnant women. Associated pathologies, hypertension is the most common pathology with a percentage of 32%, of which 45% are under an ACE inhibitor (converting enzyme inhibitor) / ARBII (angiotensin II receptor blocker), then diabetes with a percentage of 27%, of which 20% are insulin-dependent and the others under ADO (oral antidiabetic drugs); hypothyroidism 11%, asthma 7%, other complications estimated at 23% such as ACFA, liver metastasis, breast neoplasia, hypercholesterolemia, chronic gastritis, osteoarthritis and seasonal allergies (See Figure 1).



**Figure 1:** Percentage of associated co-morbidities

In our population, 93% of symptomatic patients and 7% asymptomatic patients represent the distribution of clinical signs of hospitalized patients respectively; Asthenia 44%, cough 36%, anosmia 36%, dyspnea 33%, agueusia 31%, aches and pains 25%, fever 24%, other signs mainly respiratory, chest pain (DT), runny nose, sneezing with 16% and the other signs with a lower frequency pharyngitis 13%, headache 11%, exacerbation 9%, chills, vomiting, and the others with (7%) (Visual disturbances, sore throat, abdominal pain, muscle pain, loss of appetite) (See Table 1).

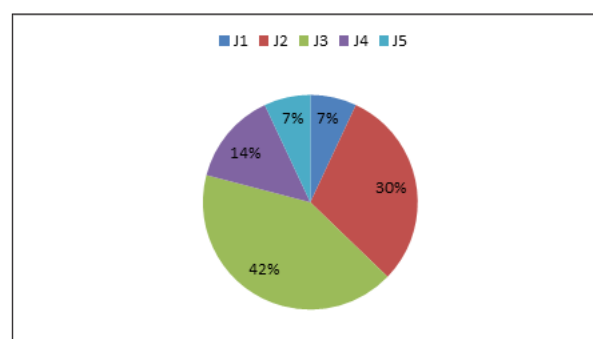
**Table 1:** Clinical signs of COVID 19 and their frequencies

Clinical signs	Case	%
Asthenia	24	44
All	20	36
Anosmia	20	36
Dyspnea	18	33
Agueusie	17	31
Curvature	14	25
Fever	13	24
Diarrhea	10	18
DT	9	16
sneeze	9	16
Nasal discharge	9	16
Pharyngitis	7	13
Headache	6	11
Exacerbation	5	9
vomiting	4	7
Frisson	4	7
Asymptomatic	4	7
others	4	7

The duration of hospitalization of patients is five days according to the ministerial instruction, except for severe and critical cases (pregnant women, respiratory distress, cardiac disorders) 90% of the forms observed are considered benign and are mainly anosmia, agueusia, chest pain, cough, headache, and asthenia, for the remaining 10% developed a moderate to severe form, of which 3% required respiratory assistance.

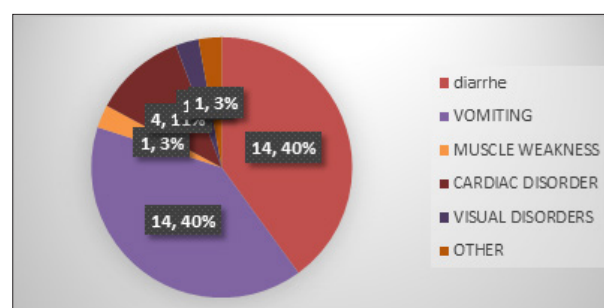
Thus, according to our study, 84% of hospitalized patients are under hydroxychloroquine protocol, 30% of which saw a decrease in fever and chills after the first two days, 42% of the main signs that disappear on the 3rd day are agueusia, anosmia, chills, fever, dyspnea and aches and pains, for some symptoms persist until the 4th or even the 5th day of treatment, mainly respiratory signs including cough and dyspnea 21%.

The remaining 16% of patients who did not benefit from the national protocol had a contraindication to hydroxychloroquine (ACFA, extended TQ); these benefited from treatment with lovenox as a preventive measure, azithromycin, vitamin C, zinc; the reduction in signs was similar to those under treatment with hydroxychloroquine (Figure 2). Our study is similar to the study by Gautret et al. on the clinical efficacy of the hydroxychloroquine and azithromycin protocol, however in our study there was no significant difference between patients treated with the hydroxychloroquine and azithromycin protocol and patients without hydroxychloroquine.



**Figure 2:** Percentage remission of clinical signs of COVID-19 as a function of time

Regarding safety indicators, the adverse events reported daily are mainly digestive; diarrhea and vomiting 14.40% in the first 3 days, heart problems, palpitations 4.11% and only one case of QT wave lengthening, the latter was the subject of a pharmacovigilance investigation whose accountability studies proposed close clinical monitoring and close ECGs, other cases noted (visual disturbances, muscle weakness, bruising of the lower limb). Although the pregnancy safety data for hydroxychloroquine are insufficient, our patients did not develop any serious adverse effects and were tolerant to treatment with tolerable diarrhea.



**Figure 3:** Percentage of reported cases of adverse events

In conclusion, through this work, we wanted to make our modest contribution in the field of management of patients contaminated by SARS-CoV 2. In this work we evaluated the impact of remission through the symptomatology that are the first signs that disappear after treatment with the hydroxychloroquine protocol. We were surprised to find that a segment of the population without treatment had recovered from their COVID-19.

Finally, our study is a first step towards strengthening the immunity of patients.

### Study Bias

Short study time; hence insufficient sample size to obtain conclusive results

### References

1. CC Lai, TP Shih, WC Ko, HJ Tang, PR Hsueh (2020) Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and coronavirus disease-2019 (COVID-19): The epidemic and the challenges. *Int J Antimicrob Agents* 55: 105924.
2. LS Wang, YR Wang, DW Ye, QQ Liu (2020) Erratum to “A review of the 2019 Novel Coronavirus (COVID-19) based on current evidence” [International Journal of Antimicrobial Agents 55/6 (2020) 105948]. *Int J Antimicrob Agents* 56: 106137.
3. Philippe Gautret, Jean-Christophe Lagier, Philippe Parola, Van Thuan Hoang, Line Meddeb, et al. (2020) Hydroxychloroquine and azithromycin as a treatment of COVID-19: results of an open-label non-randomized clinical trial, *International Journal of Antimicrobial Agents* 56: 105949.
4. WHO Director-General’s opening remarks at the media briefing on COVID-19 - 11 March 2020. <https://www.who.int/dg/speeches/detail/who-director-general-s-opening-remarks-at-the-media-briefing-on-covid-19-11-march-2020-11-march-2020>.
5. Z Wu, JM. McGoogan (2020) Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: summary of a report of 72 314 cases from the Chinese Center for Disease Control and Prevention. *JAMA* 323: 1239-1242.
6. Public Health France. Infection with the new Coronavirus (SARS-CoV-2), COVID-19, France and World <https://www.santepubliquefrance.fr/maladies-et-traumatismes/maladies-et-infections-respiratoires/infection-a-coronavirus/articles/infection-au-nouveau-coronavirus-sars-cov-2-covid-19-france-et-monde>.
7. P Colson, JM Rolain, D Raoult Chloroquine for the 2019 novel coronavirus SARS-CoV-2 *Int J Antimicrob Agents* (2020 Feb15) Article 105923, 10.1016/j.ijantimicag.2020.105923.
8. M Wang, R Cao, L Zhang, X Yang, J Liu, M Xu, et al. Remdesivir and chloroquine effectively inhibit the recently emerged novel coronavirus (2019-nCoV) in vitro *Cell Res* (2020), pp. 10-0282.
9. J Gao, Z Tian, X Yang (2020) Breakthrough: Chloroquine phosphate has shown apparent efficacy in treatment of COVID-19 associated pneumonia in clinical studies *Biosci Trends* (2020 Feb 19) 14: 72-73.
10. Note N012 of March 23, 2020 relating to the implementation of the COVID-19 patient management system.

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