

## Case Report

# Acute hepatitis induced by a single dose of hydroxychloroquine

Presenjit Raut\*

Department of Pharmacology, CIMS, Bilaspur, Chhattisgarh, India

**Received:** 08 May 2020

**Revised:** 19 June 2020

**Accepted:** 01 July 2020

**\*Correspondence:**

Dr. Presenjit Raut,

E-mail: [presenjit@gmail.com](mailto:presenjit@gmail.com)

**Copyright:** © the author(s), publisher and licensee Medip Academy. This is an open-access article distributed under the terms of the Creative Commons Attribution Non-Commercial License, which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

### ABSTRACT

Hydroxychloroquine (HCQ) is considered the drug of choice for prophylaxis of COVID-19. It is supposed to be a safe drug. Herein we describe a case where a single dose of HCQ has led to acute toxic hepatitis. A junior of CIMS, Bilaspur while working at surgery department took a single dose of HCQ and suffered from jaundice. This suggests that we cannot label any drug to be safe and should take drug only after proper medical consultation and prescription without which even a single dose can cause hypersensitivity reaction.

**Keywords:** Hydroxychloroquine, COVID-19, Icterus, Hypersensitivity

### INTRODUCTION

Coronavirus disease-2019 (COVID-19) is a public health emergency of international concern. Patients contracting the severe form of the disease constitute approximately 15% of the cases. As of this time there was no known specific, effective, proven, pharmacological treatment. *In-vitro* studies have suggested that chloroquine, a drug traditionally used to treat malaria, is effective in reducing viral replication in other infections, including the SARS-associated coronavirus (CoV) and MERS-CoV. Chloroquine had been used worldwide for more than 70 years, and it is part of the World Health Organization (WHO) model list of essential medicines. It was also cheap and had an established clinical safety profile.<sup>1</sup>

Chloroquine had an immune-modulating activity and could effectively inhibit this virus *in vitro*. Clinical controlled trials had shown that chloroquine was proved to be effective in the treatment of patients with COVID-19.<sup>2</sup> Hydroxychloroquine is a slow acting antirheumatic drug. The efficacy of hydroxychloroquine was similar to that reported for other disease modifying antirheumatic drugs, with 60-80% of adult rheumatoid arthritis improving with hydroxychloroquine therapy.<sup>3</sup>

Since the structure and mechanism of action of chloroquine and hydroxychloroquine (HCQ) are exactly same except an additional hydroxy moiety in one terminal in HCQ, both act as a weak base that can change the pH of acidic intracellular organelles including endosomes/lysosomes, essential for the membrane fusion. It was believed that both the agents could be effective tools against SARS-CoV-1 and SARS-CoV-2. However, an important question that still remains was whether HCQ has a similar effect on SARS-CoV-2 infection. Some data show HCQ effectively inhibited both the entry, transport and the post-entry stages of SARS-CoV-2, similar to the chloroquine and one study found HCQ to be a more potent agent than chloroquine in inhibiting SARS-CoV-2 *in vitro*.<sup>4</sup> Herein we report acute toxic hepatitis by a single dose of hydroxychloroquine.

### CASE REPORT

A 26 year old female junior resident of our college CIMS, Bilaspur, Chhattisgarh, was working at surgery department. While working she thought of the danger of contacting COVID-19 disease in the hospital, hence she decided to take prophylactic dose of HCQ-400 mg BD on first day followed by 400mg every next week. So without

any further consultation with a physician she took a single tablet of HCQ-400 mg on 26 March 2020.

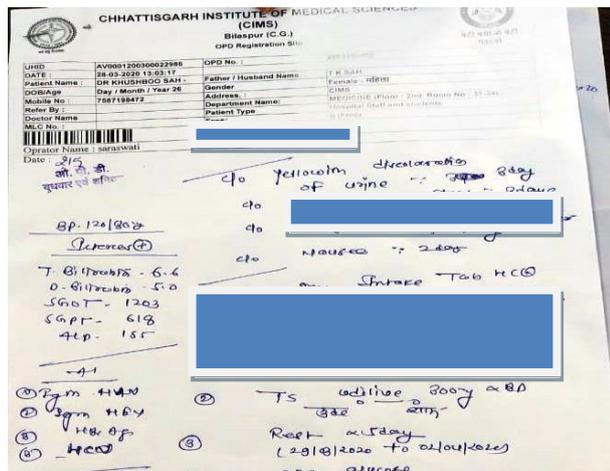


Figure 1: Prescription.

Next day morning she had yellow urine with greyish stool which she ignored and went to work. But next day i.e. on 28 March she developed nausea, vomiting and watery diarrhoea 6-8 times on that single day and consulted physician at CIMS who ordered for some laboratory investigations(LFT, CBC, random glucose, viral markers, RFT, serum electrolytes, etc).

Total bilirubin was raised 6.6 mg%, bilirubin(direct) was 5 mg%, SGOT was 1203 U/l, SGPT was 618 U/l, and alkaline phosphatase was 155 U/l (Table 1).

Table 1: Laboratory investigation results.

LFTs	
Bilirubin (total)	6.6 mg/dl
Bilirubin-direct	5 mg/dl
SGOT	1203 U/l
SGPT	618 U/l
Alkaline phosphatase	155 U/l

Reports indicated towards diagnosis of acute onset of toxic hepatitis (drug induced) as all the viral markers were negative. (IgMHEV, HBsAg, HCV, IgMHAV) (Table 2).

Table 2: Viral markers.

Markers	Results
IgM HEV	Negative
HBsAG	Negative
HCV	Negative
IgM HAV	Negative

Considering this as an important case we reported it to IPC, Ghaziabad on 15 April 2020, as probable after calculating the causality score from Naranjo algorithm (total score after calculation=5).<sup>5</sup>

## DISCUSSION

Although hydroxychloroquine is considered to be a safe drug. The most common adverse effects encountered with the use of this drug were blood and lymphatic system disorders such as hemolysis reported in individuals with glucose-6-phosphate dehydrogenase (G-6-PD) deficiency, cardiac disorders like cardiomyopathy, QT interval prolongation. Ear and labyrinth disorders that include vertigo, tinnitus, nystagmus, nerve deafness, deafness. Eye disorders such as irreversible retinopathy with retinal pigmentation changes (bull's eye appearance), visual field defects (paracentral scotomas) and visual disturbances (visual acuity), maculopathies (macular degeneration). Gastrointestinal disorders like nausea, vomiting, diarrhoea, abdominal pain. Hepatobiliary disorders such as liver function tests abnormal, acute hepatic failure. Immune system disorders like urticaria, angioedema, bronchospasm. Metabolism and nutrition disorders that include decreased appetite, hypoglycemia, porphyria, weight decreased. Musculoskeletal and connective tissue disorders like sensorimotor disorder, skeletal muscle myopathy or neuromyopathy leading to progressive weakness and atrophy of proximal muscle groups, depression of tendon reflexes and abnormal nerve conduction. Nervous system disorders particularly headache, dizziness, seizure, ataxia and extrapyramidal disorders such as dystonia, dyskinesia, tremor. Psychiatric disorders this include affect/emotional lability, nervousness, irritability, nightmares, psychosis, suicidal behaviour. Skin and subcutaneous tissue disorders that include rash, pruritus, pigmentation disorders in skin and mucous membranes, hair colour changes, alopecia; dermatitis bullous eruptions including erythema multiforme, Stevens-Johnson syndrome, and toxic epidermal necrolysis, drug reaction with eosinophilia and systemic symptoms (DRESS syndrome), photosensitivity, dermatitis exfoliative, acute generalized exanthematous pustulosis (AGEP).<sup>6</sup>

As per above list it was common to have abnormal LFTs with the use of HCQS, but herein we have encountered an unusual case where only a single dose of HCQS had caused hepatic toxicity. This can be thought of as a hypersensitivity reaction to HCQS as the course of treatment was not completed and it occurred with only one single dose of the drug.

Hydroxychloroquine had not been associated with significant serum enzyme elevations during therapy of rheumatologic diseases. Furthermore, clinically apparent liver injury from hydroxychloroquine was rare. A single case series (two cases) of acute liver failure attributed to hydroxychloroquine was published twenty years ago, but case reports of clinically apparent liver injury have not appeared subsequently. Thus, acute liver injury with jaundice due to hydroxychloroquine must be very rare, if it occurs at all.<sup>7</sup>

One case of hydroxychloroquine induced toxic hepatitis in a patient of SLE was reported by Galil in 2015. But increased levels of liver enzymes are a common finding in patients of SLE.<sup>8</sup>

In another case described by Galvan et al. women with mixed connective tissue disorder who developed a reversible acute hepatitis shortly after the initiation of low dose HCQS. It seemed to be a dose dependent, idiosyncratic & molecule specific toxic effect.<sup>9</sup>

## CONCLUSION

To conclude this should be always kept in mind that treating or giving HCQS to any person without taking proper history of any type of hypersensitivity to these drug could lead to a possible toxic reaction which if not treated properly or on time could be fatal. This is a case report but it will serve as an important case of hypersensitivity/Idiosyncratic reaction to any drug

*Funding: No funding sources*

*Conflict of interest: None declared*

*Ethical approval: Not required*

## REFERENCES

1. Cortegiani A, Ingoglia G, Ippolito M, Giarratano A, Einav S. A systematic review on the efficacy and safety of chloroquine for the treatment of COVID-19. *J Crit Care.* 2020;57:279-83.
2. Li-Sheng W, Yi-ru W, Da-wei Y, Qing-quan L. A review of the 2019 Novel Coronavirus (COVID-19) based on current evidence. *Int J Antimicrobial Agents.* 2020;55(6):105948.
3. Tett SE, Cutler DJ, Day RO, Brown KF. Bioavailability of hydroxychloroquine tablet in healthy volunteers. *Br J Clin Pharmacol.* 1989;27:771-9.
4. Singh AK. Diabetes and Metabolic Syndrome. *Clin Res Rev.* 2020;14(3):241-6.
5. Naranjo CA, Busto U, Sellers EM, Sander P, Ruiz I, Roberts EA et al. A method for estimating the probability of adverse drug reaction. *Clin Pharmacol Ther.* 1981;30:239-45.
6. Roque RM. Chloroquine and Hydroxychloroquine toxicity. *Medscape.* Available at: <https://emedicine.medscape.com/article/1229016-overview>. Accessed on 2 May 2020.
7. Liver Tox: Clinical and Research information on drug induced Liver Injury. Bethesda. National Institute of Diabetes and Digestive and Kidney disease. Available at <https://www.niddk.nih.gov/news/archive/2013/livertox-new-online-resource-information-drug-induced-liver-injury>. Accessed on 2 May 2020.
8. Abdel GSM. Hydroxychloroquine induced toxic hepatitis in a patient with SLE: A case report. *Lupus.* 2015;24(6):638-40.
9. Galvañ VG, Oltra MR, Rueda D, Esteben MJ, Redon J. Severe acute hepatitis related to hydroxychloro-quine in a woman with mixed connective tissue disease. *Clin Rheumatol.* 2007;26:971-2.

**Cite this article as:** Raut P. Acute hepatitis induced by a single dose of hydroxychloroquine. *Int J Sci Rep* 2020;6(10):413-5.