

# Hypothesis: Delivery of Drug (hydroxychloroquine Sulphate) through Nebulizer may be used in Treatment or Prevention of Corona Virus

P.S. Devadkar<sup>1</sup>, P.S.Kale<sup>1</sup>, S.R.Thorat<sup>1</sup>, S.A.Kardule<sup>1</sup>, H.R.Gupta<sup>1</sup>,  
S.C.Karpe<sup>1</sup>, G.B.Parkhe<sup>1</sup>, T.S.Sonawane<sup>1</sup>, N.R.Rajankar<sup>1</sup>

<sup>1</sup>Department of pharmacology

DBATU University ,Raigad ,Maharashtra ,India.

**Abstract:-** Corona virus is an infectious disease caused by newly discovered SARS CoV2 Virus, this corona virus now reached almost all part of the world affecting more than 180 countries around the world. The first case of novel corona virus Found in Wuhan (China) in the mid of December 2019 . Now the countdown of cases has reached more than 3 million cases across the world and number of corona cases increasing rapidly day by day. Still there is no approved vaccine for the novel corona virus. even there is also no completely approved treatment for this newly found virus. we made hypothesis on the basis of ongoing research all around the world on corona virus which may be helpful in prevention and treatment of disease.

**Keywords:-** covid-19, treatment, Hypothesis, Novel ROA.

## I. INTRODUCTION

The COVID-19 pandemic, also known as the coronavirus pandemic, is an ongoing pandemic of corona virus disease 19 caused by SARS- CoV2 (severe acute respiratory syndrome Corona virus2). The outbreak was found in Wuhan ,Hubei, China, in December 2019.The WHO declared the outbreak a Public health emergency of

international concern on 30 January, and corona virus pandemic on 11 March. As of 4 May 2020, more than 3.6 million cases of COVID-19 have been reported in over 187 countries and territories , with more than 251000 deaths around the world . More than 1.16 million people have also recovered from the disease. The virus is primarily spread between people during direct contact through small droplets produced by coughing, sneezing, talking, or even breathing. or indirect contact with surface used by infected person . The droplets usually fall to the ground or onto surfaces rather than remaining in the air over long period .People may also become infected by touching a contaminated surface and then touching their face. On surfaces, the amount of virus declines over time until it is insufficient to remain infectious, but it may be detected for hours or days. It is most infectious during the first three days after the onset of symptoms, although spread may be possible before symptoms appear and in later stages of the disease.

Common symptoms include :

- Fever
- Cough
- Fatigue
- Shortness of breath

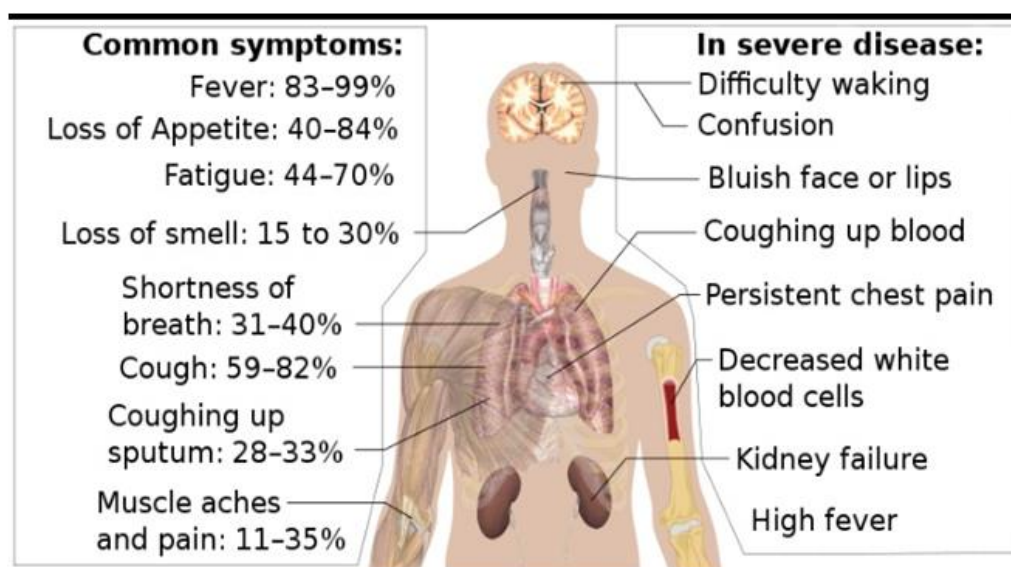


Fig 1

Complications may include: Pneumonia and acute respiratory syndrome. The time from exposure to onset of symptoms is typically around five days, but may range from two to fourteen days. FDA has granted emergency Authorisation to Hydroxychloroquine for treatment of corona virus disease. Hydroxychloroquine not only cost effective but also providing promising result in many part of the world in treatment of corona virus. Some in vitro studies also providing the evidences for the use of the hydroxychloroquine in treatment. In this paper we have proposed new route of delivery of HCQ in body which may be helpful in treatment and prevention of the disease.

## II. MOA OF HCQ

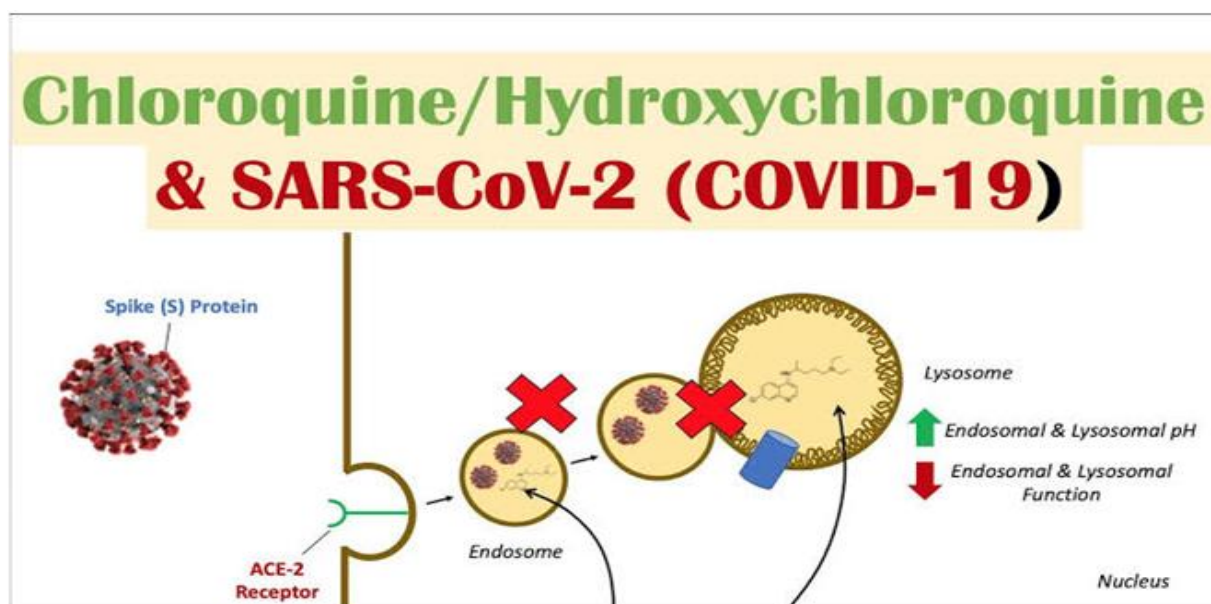
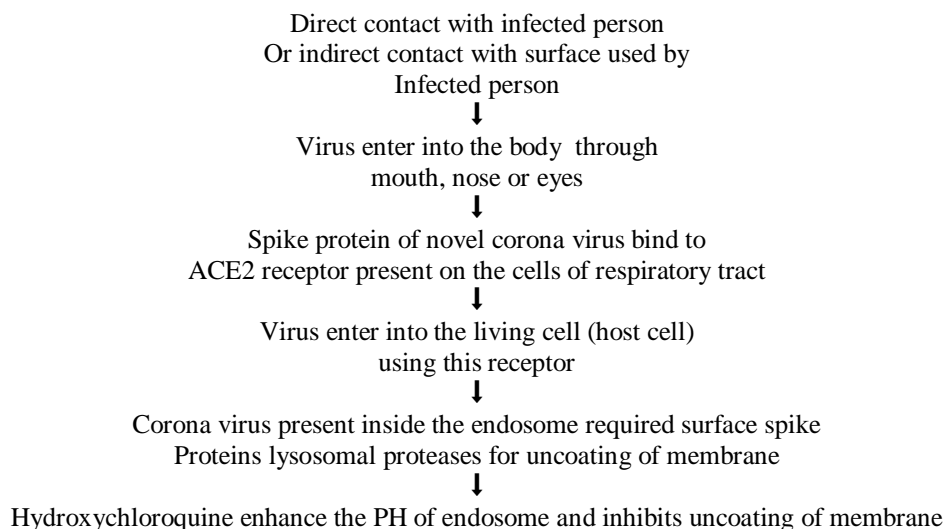


Fig 2

## III. MOA OF NEBULIZER

A nebulizer is a breathing machine used to treat lung conditions such as asthma, cystic fibrosis, and other respiratory illnesses. Nebulizer convert medication in the form of a mist that's inhaled into the lungs and are often used in situations in which using an inhaler is difficult or ineffective. Nebulizer treatment works by atomizing liquid medicine into an inhalable gas form, which can then be easily inhaled by the patient using a nebulizer mask. Nebulizer medicine also reach into the lungs faster and provide relief as fast as possible.

### ➤ Hypothesis:

We hypothesis that corona virus disease can be prevent and treated in better way by using hydroxychloroquine Sulphate liquid formulation in nebulizer. Metabolism of drug can be prevent by using this route of administration. Drug can be delivered rapidly at the site where required most. Reason behind selection of this ROA is that corona virus mainly affect respiratory system and enter in the body through ACE 2 receptor present throughout the respiratory track, the use of nebulizer to deliver the medicine in the track can be helpful to treat the patient with early signs and symptoms

or inhibit the entry of the virus present in the respiratory passage by enhancing the pH of endosome after the entry of virus in living cell.

➤ *Probable Disadvantages of Ongoing Treatment:*

- Corona virus mainly affect respiratory tract. To enhance the pH of endosome and inhibit the further multiplication of corona virus in the body it is necessary to reach a drug at alveolar site in required concentration however drug can be made available at alveolar site by increasing the dose of the drug But the amount of dose is directly related to side effects of drug including the accumulation of drug in liver, kidney and other body part . By using above mentioned route, drug can be made available at alveolar site in appropriate concentration in short period of time.
- Hydroxychloroquine is partly metabolised by liver and slowly excreted in urine. the early plasma half life varies from 5 to 15 days Because of tight tissue binding, small amount of drug persist in body with terminal half life of 21 to 50 days.
- Higher dose and with long-term use of drug include following Side effects:
  - ✓ Long QT or QT prolongation (abnormal heart rhythm)
  - ✓ Irreversible visual changes
  - ✓ Muscle weakness or nerve pain
  - ✓ Hypoglycemia .

Note: delivery of drug through the nebulizer it doesn't mean it don't have side effects of drug but Side effects of drug can be lowered.

#### IV. CONCLUSION

The basic principle regarding the effectiveness of any drug is that promising result can be obtained if drug administered through appropriate Route. dose of drug can be lowered if medicine given through nebulizer delivered at site where required. Which ultimately help to reduce the side effects of drug. we made hypothesis on the basis of evidences of hydroxychloroquine sulphate in treatment of corona virus disease. To determine whether drug is effective or not in above mentioned Route further study required in appropriate direction.

#### REFERENCES

[1]. "Hydroxychloroquine Use During Pregnancy" . Drugs.com. 28 February2020. Retrieved 21 March 2020.

[2]. "Hydroxychloroquine Sulfate Monograph for Professionals" . The American Society of Health-System Pharmacists. 20 March 2020. Archived from the original on 20 March 2020. Retrieved 20 March 2020.

[3]. Cortegiani A, Ingoglia G, Ippolito M, Giarratano A, Einav S (March 2020). "A systematic review on the efficacy and safety of chloroquine for the treatment of COVID-19" . Journal of Critical

Care. doi:10.1016/j.jcrc.2020.03.005 . PMID 32173110

- [4]. Grady D (1 April 2020). "Malaria Drug Helps Virus Patients Improve, in Small Study" . The New York Times. Archived from the original on 1 April 2020. Retrieved 1 April 2020.
- [5]. Smolen, J. S. et al. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2013 update. *Ann. Rheum. Dis.* 73, 492–509 (2014).
- [6]. Fanouriakis, A. et al. 2019 update of the EULAR recommendations for the management of systemic lupus erythematosus. *Ann. Rheum. Dis.* 78, 736–745 (2019).
- [7]. Pons-Estel, B. A. et al. First Latin American clinical practice guidelines for the treatment of systemic lupus erythematosus: Latin American Group for the Study of Lupus (GLADEL, Grupo Latino Americano de Estudio del Lupus)-Pan-American League of Associations of Rheumatology (PANLAR). *Ann. Rheum. Dis.* 77, 1549–1557 (2018).
- [8]. Gordon, C. et al. The British Society for Rheumatology guideline for the management of systemic lupus erythematosus in adults. *Rheumatology* 57, e1–e45 (2018).
- [9]. Tektonidou, M. G. et al. EULAR recommendations for the management of antiphospholipid syndrome in adults. *Ann. Rheum. Dis.* 78, 1296–1304 (2019)
- [10]. Romanelli F, Smith KM, Hoven AD. Chloroquine and hydroxychloroquine as inhibitors of human immunodeficiency virus (HIV-1) activity. *Curr Pharm Des.* 2004. 10(21): 2643-8.
- [11]. Keyaerts E, Vijgen L, Maes P, Neyts J, Van Ranst M. In vitro inhibition of severe acute respiratory syndrome coronavirus by chloroquine. *Biochem Biophys Res Commun.* 2004. 323(1): 264-8.
- [12]. Vincent MJ, Bergeron E, Benjannet S, et al. Chloroquine is a potent inhibitor of SARS coronavirus infection and spread. *Virology* 2005. 2: 69.
- [13]. Ooi EE, Chew JS, Loh JP, Chua RC. In vitro inhibition of human influenza A virus replication by chloroquine. *Virology* 2006. 3: 39.
- [14]. Li C, Zhu X, Ji X, et al. Chloroquine, a FDA-approved Drug, Prevents Zika Virus Infection and its Associated Congenital Microcephaly in Mice. *EBioMedicine.* 2017. 24: 189-194.
- [15]. Zheng, N., Zhang, X. & Rosania, G. R. Effect of phospholipidosis on the cellular pharmacokinetics of chloroquine. *J. Pharmacol. Exp. Ther.* 336, 661–671 (2011).
- [16]. Ohkuma, S. & Poole, B. Fluorescence probe measurement of the intralysosomal pH in living cells and the perturbation of pH by various agents. *Proc. Natl Acad. Sci. USA* 75, 3327–3331 (1978).
- [17]. Popert, A. J. Chloroquine: a review. *Rheumatology* 15, 235–238 (1976).
- [18]. Laaksonen, A. L., Koskiahde, V. & Juva, K. Dosage of antimalarial drugs for children with juvenile rheumatoid arthritis and systemic lupus erythematosus. A clinical study with determination of serum concentrations of chloroquine and

- hydroxychloroquine. *Scand. J. rheumatol.* 3, 103–108 (1974).
- [19]. Huang, C. et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet* 395, 497–506 (2020).
- [20]. Kuznik A, Bencina M, Svajger U, Jeras M, Rozman B, Jerala R. Mechanism of endosomal TLR inhibition by antimalarial drugs and imidazoquinolines. *J Immunol* 2011; 186:4794–4804. doi:10.4049/jimmunol.1000702
- [21]. Willis R, Seif AM, McGwin G Jr, et al. Effect of hydroxychloroquine treatment on pro-inflammatory cytokines and disease activity in SLE patients: data from LUMINA, a multiethnic US cohort. *Lupus* 2012; 21(8):830–835. doi:10.1177/0961203312437270
- [22]. Fox R. Anti-malarial drugs: possible mechanisms of action in autoimmune disease and prospects for drug development. *Lupus* 1996; 5(suppl 1):S4–S10. pmid:8803903
- [23]. Ruiz-Irastorza G, Ramos-Casals M, Brito-Zeron P, Khamashta MA. Clinical efficacy and side effects of antimalarials in systemic lupus erythematosus: a systematic review. *Ann Rheum Dis* 2010; 69(1):20–28. doi:10.1136/ard.2008.101766
- [24]. Cass, L. M., Efthymiopoulos, C., & Bye, A. (1999). Pharmacokinetics of zanamivir after intravenous, oral, inhaled or intranasal administration to healthy volunteers. *Clinical pharmacokinetics*, 36(1), 1-11.
- [25]. Chen, I. Y., Moriyama, M., Chang, M. F., & Ichinohe, T. (2019). Severe acute respiratory syndrome coronavirus viroporin 3a activates the NLRP3 inflammasome. *Frontiers in microbiology*, 10.
- [26]. Chen Y. Adjunctive Corticosteroid Therapy for Patients with Severe Novel Coronavirus Pneumonia (COVID-19): a Randomized Controlled Trial. <http://www.chictr.org.cn/showproj.aspx?proj=48777> [Accessed 03 April 2020].
- [27]. Colson, P., Rolain, J. M., Lagier, J. C., Brouqui, P., & Raoult, D. (2020). Chloroquine and hydroxychloroquine as available weapons to fight COVID-19. *Int J Antimicrob Agents*, 105932