ISSN 2220-3176 (online)

World Journal of

Clinical Infectious Diseases

World J Clin Infect Dis 2020 October 28; 10(4): 47-57

Published by Baishideng Publishing Group Inc

WJCID

World Journal of Clinical Infectious Diseases

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ABOUT COVER

Peer reviewer for *World Journal of Clinical Infectious Diseases*, Dr. Chun-Feng Xiao is a psychiatrist and medical editor with expertise in Psychiatry and Mental Health, with over 120 publications. He serves as the Bentham Science Ambassador of Bentham Science Publishers and as the Junior Ambassador of the Universal Scientific Education and Research Network (USERN) in China. His research involving the psychological impact of global public health emergencies (particularly of infectious disease pandemic) led to his role as Organizing Committee Member for the upcoming Coronavirus and Research conference (March 29-30, 2021, Rome, Italy). He is the sole inventor of structured letter therapy (SLT), a novel approach to consultation on COVID-19-related psychological and mental problems that is expected to become a bond of transition from traditional psychiatry to digital psychiatry. He is also founder of the SLT Multidisciplinary Collaboration Group, an official organization dedicated to long-term planning and operation for SLT. (L-Editor: Filipodia)

AIMS AND SCOPE

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WJCID mainly publishes articles reporting research results and findings obtained in the field of infectious diseases and covering a wide range of topics including community-acquired infections, cross infection, eye infections, focal infection, infectious gingivitis, intraabdominal infections, laboratory infection, Ludwig's angina, necrotizing ulcerative periodontitis, opportunistic infections, pelvic infection, pregnancy complications, *etc*.

INDEXING/ABSTRACTING

World Journal of Clinical Infectious Diseases is now indexed in China National Knowledge Infrastructure (CNKI), China Science and Technology Journal Database (CSTJ), and Superstar Journals Database.

RESPONSIBLE EDITORS FOR THIS ISSUE

NAME OF JOURNAL
World Journal of Clinical Infectious Diseases

ISSN
ISSN 2220-3176 (online)

LAUNCH DATE
December 30, 2011

FREQUENCY
Irregular

PUBLICATION DATE
October 28, 2020

World Journal of Clinical Infectious Diseases

Submit a Manuscript: https://www.f6publishing.com

World J Clin Infect Dis 2020 October 28; 10(4): 55-57

DOI: 10.5495/wjcid.v10.i4.55

ISSN 2220-3176 (online)

LETTER TO THE EDITOR

Top ten tips for perfect corona-2 prophylaxis

Ahmad Abul-Ainine, Ali A Sadek

ORCID number: Ahmad Abul-Ainine 0000-0001-5087-111X; Ali A Sadek 0000-0002-7276-5403.

Author contributions: Abul-Ainine A wrote the manuscript, revised it, made the dosing software, and made the submission; Sadek AA discussed all items principles, reviewed and corrected the manuscript and tested the software.

Conflict-of-interest statement: The authors have no any conflicts of interest.

Manuscript source: Unsolicited manuscript

Received: June 11, 2020
Peer-review started: June 11, 2020
First decision: July 4, 2020
Revised: August 2, 2020

Ahmad Abul-Ainine, Consultant Paediatrician, Paediatric Department, Thuwal, Jeddah 23955, Saudi Arabia

Ali A Sadek, Consultant Public Health and Medical Statistics, MOH, Kuwait

Corresponding author: Ahmad Abul-Ainine, CCST, FRCP, Consultant Paediatrician, Paediatric Department, Thuwal, Jeddah 23955, Saudi Arabia. ainine@doctors.net.uk

Abstract

The current corona-2 pandemic has stimulated wide research for hydroxychloroquine (Quine) therapy and lately, prophylaxis. To optimize prophylaxis proper methods of use are explained. The focus is on tools of assessment and robust comparison; defining infection objectively; loading and maintenance dose designing based on pharmaco-viro-kinetics; confirming Quine threshold-levels and its sufficiency; and Quine side-effects vigilance/amelioration. Attention to statistics to study valid endpoints of goals in appropriately-sized population is essential. Mass interactive quine dose auto designer software is built to simplify, optimize and help collaboration of complex Quine dosing system. A similar chloroquine software can be built.

Key Words: Corona-2; COVID-19; Hydroxychloroquine; Prophylaxis; Dose; Mass interactive quine dose auto designer

Core Tip: Quine's role in corona-2 pandemic prophylaxis can be assured *via* designing correct loading doses (LD)/ maintenance doses (MD), therapy duration, and volumetric absorptive microsampling (VAMS) concentrations, assuring human IC_{50} and Liver and Heart safety thresholds of TC_L10 and TC_H10. Surely, good care will translate VeroE6 Viro-kinetics into human Viro-kinetics and help human-tailored dosing; not misguided by improper models, malaria, or rheumatology doses. Mass interactive quine dose auto designer (MIQDAD), viral count, and VAMS test help initial Quine LD/MD designing and human-tailored LD/MD dosing.

Citation: Abul-Ainine A, Sadek AA. Top ten tips for perfect corona-2 prophylaxis. *World J Clin Infect Dis* 2020; 10(4): 55-57
URL: https://www.wjgnet.com/2220-3176/full/v10/i4/55.htm

Accepted: September 18, 2020
Article in press: September 18, 2020
Published online: October 28, 2020

P-Reviewer: Song G, Xiao C
S-Editor: Ma YJ
L-Editor: A
P-Editor: Wu YXJ

DOI: https://dx.doi.org/10.5495/wjcid.v10.i4.55

TO THE EDITOR

A good effort to study post-exposure hydroxychloroquine (Quine) prophylaxis was recently published[1]. Despite that it has decent statistical design, it has salient issues that need to be addressed to perfect the outcome of further Quine prophylaxis: (1) The primary outcome should involve viro-conversion from positive at entry to negative on exit (little testing in this study); (2) Primary outcome involves clinical symptoms reported by patients (was its percent reliability factored in sample-size calculations?) and was rated by 4 Infectious Disease doctors (without mention of inter-rater training or kappa of agreement reliability)[2]; (3) No data on further exposure to corona-2; other flu virus or having nasal allergy during the 2-wk study; (4) Using primary outcome as clinical symptoms is subjective, neither sensitive (as 80% are asymptomatic) nor specific to COVID19, (is it another flu virus or hay-fever?); (5) The Quine antimalarial dose is smaller than its antiviral loading doses (LD) calculated from the pharmaco-kinetics data held by FDA[3] (Table 1). Low LD will produce sub-inhibitory levels, so that patients are not protected for 1-4 d pre-enrollment and 4-5 d post-enrollment (treatment start 1 d after enrollment and might take 4 d to reach the level required for protection-threshold); (6) although measuring drug levels by using finger-prick to self-collect 10 µm blood samples (VAMS) is well-known, *in-vivo* Quine IC_{50} (= 50% Inhibitory Concentration) is never assured; pharmacokinetics from one study proposed VeroE6 cell IC_{50} of 4.5 µmol/L in 48 h of post-infection (mcM/hpi)[4,5], and another 6.3-5.9 in 24-48 mcM/hpi[6] requiring higher LD (15 and 20 tablets x 200 mg each, respectively); plus 2-3-wk maintenance doses (MD) or until patients develop their own immuno-protection; (7) Finding of safety-thresholds (10% Toxic Concentration = TC10) for liver enzymes elevation (= $TC_{Liver}10$), for heart QT-prolongation (= $TC_{Heart}10$), clinical hepatitis and dysrhythmia issues; (8) Since Quine is virostatic, its prophylactic-level must be maintained for at least 2-3 wk to build immunity that can clear virion particles (not possible in VeroE6 cell-kinetic cultures). So, dosing for 5 of 14 d is inadequate; (9) the folate-placebo helps one-carbon atom transfer to thymine to produce uracil, the rate-limiting substrate for RNA synthesis –undesired confounder; and (10) Although using sophisticated statistics to end the study early at a priori statistical power outcome is good, extending Quine prophylaxis (following correct LD) to achieve and define human IC_{50}, is a missed historical landmark in the human/corona-2 contest. Sadly, statistical passion forced ending at only 2.4% incidence reduction rather than a 7% reduction –glorifying statistical-significance sacrificed nearby finding/measuring the more clinically important IC_{50} –*cf. McNamara fallacy*.

CONCLUSION

Quine's role in corona-2 pandemic prophylaxis can be assured *via* designing correct LD/MD, therapy duration, and VAMS concentrations, assuring human IC_{50} and Liver and Heart safety thresholds of $TC_{Liver}10$ and $TC_{Heart}10$. Surly, good care will translate VeroE6 Viro-kinetics into human Viro-kinetics and help human-tailored dosing; not misguided by improper models, malaria, or rheumatology doses.

Mass interactive quine dose auto designer, viral count and VAMS test help initial Quine LD/MD designing and human-tailored LD/MD dosing.

Table 1 The mass interactive quine dose auto designer (MIQDAD,Download)

Body weight (kg)	60		Loading dose	Loading days if	Maintenance	Post-protect	Durations	Load/Maint	Protective nadir (mcM)	5
C rise/tab (mcM)	0.386	Target levels	Computed	6	7	5.0	Give to stay on peak doses for	6		
Half-life: T ½	22.4	Level in mcM	Tablets to load	Tablets used/d	Tablets/wk	Post-last-dose		Doses Ratio	Maintenance interval (d)	1
Well indications		1 Tab = 200 mg = 155 × 0.74		2 tablets /6 h						
Protection		5.0	14	2.3	2.5	0	Until becomes immuno-protected or the pandemic ends	5.5	Protective peak (mcM)	5.2
Community helper		6.0	17	2.8	3.0	6		5.5		
Exposed but well		7.0	20	3.3	3.5	11	2 wk	5.6	First dose (200 mg tablets)	13.4
Unwell indications										
Low Infection		8.0	23	4	4	15	2 wk	5.7	Maintain dose (tablets)	0.4
Medium infection		10.4	30	5	5	24	2 wk	5.8		
High infection		13.3	40	7	7	32	2 wk	6.0	PostCourse protected days	1.0

Assuming these doses for weights 40-60 kg: Each 600 mg or 3 tablets is replaced by: Child < 40 kg dose = 12 mg/kg or Adult > 60 kg idealised 3 tablets equivalent = kg/20 Tablets; Micro finger-prick testing (Volumetric Absorptive Micro-Sampling, VAMS) can be used to confirm or guide dosing; All red numbers are editable, so that user's can tailor to the needs and evolving data on effective inhibitory concentrations; Durations: For symptomatic infections, Quine (virostatic) should cover until immune system is able to inactivate the virus; C rise/tab (mcM): Drug concentration rise per tablet in micro-moles/L (mcM).

ACKNOWLEDGEMENTS

Dr. Osman Akhtar, Pharmacist in Thuwal Clinic for reviewing and testing the dosing software mass interactive quine dose auto designer.

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E-mail: bpgoffice@wjgnet.com
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