The looming pandemic of COVID-19: What therapeutic options do we have now?

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Dear Editor,

The world came to know about a new corona virus infection spreading from Wuhan, China, in December 2019. Over the following 3 months, this respiratory pathogen, named as nCoV-2019, SARS CoV-2, or Covid-19, has affected many in the most populous regions of the world and there are growing concerns about it being a pandemic. World Health Organization (WHO) has reported infection in all continents in its Situation Report-42 published on 2 March 2020 and >3000 deaths (https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200302-sitrep-42-covid-19.pdf?sfvrsn=224c1add_2). Although it causes a flu-like respiratory illness, the mortality is low among previously healthy, young individuals but high in elderly and critically ill.[1] However, the low percent mortality has already transformed into a big absolute number (>3000 individuals) and counting. Each life is precious and there is a global movement to find treatment for this disease.

As yet, no definite prevention or cure is available for COVID-19. Lately, some reports have surfaced about various drugs indicated for other viral illness, being tried for this disease due to existing evidence in two related disorders, SARS-CoV and MERS-CoV. To critically evaluate the existing options, an attempt has been made to list the drugs considered potentially useful in corona virus infections including the previous outbreaks of SARS and MERS and are tabulated (Table 1) to derive lessons from the existing scientific literature.

This is highly imperative that although new drug and vaccine development is in progress, existing treatment may be applied to save precious lives. The information in media that corona virus has no effective treatment has already created panic in the masses and resultant lock down in many parts of the world. Hence, it could be helpful to mitigate the impression of "no treatment" and resultant fear around the world.

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Table 1

Syndromes related to corona virus and their management

Disease	Ref.	Sample (sample size)	Drugs	Strengths	Limitations	Comments
nCoV 2019	Lu[2]	Human bronchoalveolar isolates (9)	...	Genetic homology modelling; nCoV 2019 is distinct from SARS and MERS viruses. Identified angiotensin-II receptors as possible pathogen receptor.	In vitro study; small sample size.	Role of AT_1 receptor blockers in reducing virus transmission should be explored.
nCoV 2019	Lim[3]	Human patient (1)	Lopinavir/ritonavir	Drug trial. Patient recovered.	Treatment started late (day 10) and outcome may have been independent of the treatment.	Lopinavir/ritonavir may be effective.
MERS-CoV	Chan[4]	Animal study in primates (12)	IFNβ1b + lopinavir/ritonavir	Drug trial in primates.	Small sample size; human study needed.	Efficacy of IFNβ1b and lopinavir/ritonavir established.
nCoV 2019	Wang[5]	In vitro study in cell lines	Chloroquine	Efficacy established in SARS CoV and also in cell lines at standard doses.	In vitro study; drug trial needed.	Chloroquine may be an effective drug.
nCoV 2019	Wang[5]	In vitro study in human and primate cell lines	Remdesivir	Efficacy established in nCoV 2019 sensitive human cell lines and in primates at doses comparable with therapeutic concentrations.	In vitro study; drug trial needed.	Remdesivir may be an effective drug.
MERS-CoV	de Wit[6]	Animal study (18)	Remdesivir	Efficacy established in MERS-CoV infection in primates.	Needs testing for nCoV 2019.	Remdesivir may be an effective drug.
MERS CoV	Hart[7]	In vitro study in cell lines	IFNβ+ mycophenolate	MPA and ribavirin both inhibited viral replication but MPA was more potent. Similarly, IFNβ was much more potent than other interferons.	In vitro study; drug trial needed.	IFNα2b + ribavirin may be effective but IFNβ + MPA could be better.
MERS CoV	Falzarano[8]	In vitro study in cell lines	Ribavirin + IFN α2b	Individual drugs are effective at high doses, whereas a combination is effective at lower doses comparable with those achievable clinically.	In vitro study; drug trial needed.	IFNα2b + Ribavirin may be effective in a synergistic fashion.
MERS CoV	Khalid[9]	Human patients (6)	Ribavirin + IFN α2b	The efficacy of the combination was observed. Early treatment appeared beneficial.	Small sample size; case series; three cases with comorbidities died.	IFNα2b + Ribavirin may be effective in a synergistic fashion.
MERS CoV	Arabi[10]	Human patients (349)	Ribavirin ± IFN (IFN-α2a, IFN-α2b, or IFN-β1a)	Large number of patients.	Retrospective cohort study; no randomization; mixed treatment groups; no consistency in terms of initiation of therapy and cointervention; multiple confounders.	Observational study; No therapeutic advantage seen but the potential benefit of IFN + ribavirin may be obscured by the study design.
SARS CoV	Wu[11]	In vitro study in cell lines	Niclosamide	A series of experiments showed dose-dependent inhibition of corona virus replication.	In vivo testing and human trials needed.	Niclosamide could be effective in treating nCoV 2019.
MERS CoV	Arabi[12]	Human patients (309)	Steroids	Large number of patients.	Retrospective study; no randomization; mixed treatment groups; no consistency in terms of initiation of therapy and cointervention; multiple confounders. Patients were critically ill. No data on efficacy of inhaled steroids in this condition.	Observational study; no advantage seen; steroid use may reduce inflammation at the cost of delayed viral clearance. Steroids may still be considered on case-to-case basis. Efficacy of inhaled steroids should be studied in this regard.
Viral upper respiratory infection	Hemilä[13]	Meta-analysis (7 studies; 575 human patients of common cold)	Zinc supplements	Zinc supplements lead to faster recovery in flu.	Zinc dose was >75 mg/d; not directly applicable to many available formulations of zinc lozenges.	Zinc supplements may positively influence patient outcome.
SARS CoV	Wen[14]	In vitro assay	Chinese herbs	Potential for drug development.	Difficult to assign therapeutic benefit to a single agent.	Effectively inhibit viral replication; may prove to be beneficial as a herbal product.

IFN = interferon; MPA = mycophenolic acid.