WEEKLY EPIDEMIOLOGICAL REPORT

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Treatments for COVID 19

Background

The COVID 19 infection is spreading at a fast pace around the world and affecting more than 200 countries at present. There are 3,349,786 people who were diagnosed to have COVID 19 infection and 238,628 people have already died up to 04th of May 2020. When compared to the more recent outbreaks of infectious diseases, the COVID 19 infection has already led to a more disease burden in terms of a number of cases and deaths. Therefore, many scientists and other experts are eagerly carrying out research on various drugs, which can potentially be used to cure this devastating infection caused by SARS-CoV-2. Finding appropriate treatment is essential as nearly 15% of SARS-CoV-2 infected patients are suffering from severe disease and hospitals are becoming overwhelmed in certain countries.

Rather than finding a new drug, it is worthwhile to repurpose drugs which have already been approved for other diseases, to treat patients affected by COVID-19. Scientists are especially looking at unapproved drugs which were found to be safe in animal studies and the drugs which were worked well against two recent coronavirus infections: Severe Acute Respiratory Syndrome (SARS) and Middle East Respiratory Syndrome (MERS). The drugs which can slow down the activity of novel coronavirus may save lives of severely ill patients as well as it can be used prophylactically to protect health care workers and others who are having a higher risk of infection. It may also reduce the time which patients spend in the intensive care units.

The WHO is currently focusing on four of the most promising therapies: the malaria medications - chloroquine and hydroxychloroquine; an antiviral compound called remdesivir; a combination of two HIV drugs: lopinavir and ritonavir; and the same combination plus interferon –beta. The main aim of this article is to give a brief account of various drug treatments experimented for the treatment of COVID-19 except for chloroquine and hydroxychloroquine since those were described in a previous article.

Remdesivir

Remdesivir is an intravenous drug with a broad-spectrum antiviral activity which is under investigation. It inhibits viral replication through premature termination of RNA transcription and has in-vitro activity against SARS-CoV-2 and in-vitro and in-vivo activity against related beta-coronaviruses. Although scientists found that remdesivir was not effective against the Ebola virus during the outbreak in Congo last year, researchers have found that remdesivir can inhibit the coronaviruses that cause SARS and MERS. Experimental data in mice infected with the related MERS virus have also shown that remdesivir performed better than a combination of lopinavir/ritonavir and interferon beta in improving lung function. In vitro studies, published in January 2020, have shown that remdesivir is active against a clinical isolate of SARS-CoV-2. According to a study published in the New England Journal of Medicine, remdesivir has shown clinical improvement in 36 out of 53 patients (68%) subjected to the study.[1] The remdesivir is most effective for patients with mild symptoms according to the currently available evidence. However, the usefulness of this drug in the treatment of patients with COVID 19 needs further studies. The need for an intravenous route and the high cost are the main drawbacks of this medication.

Ritonavir/lopinavir combination

Ritonavir/lopinavir combination which is a HIV medication has been used in China to treat COVID-19. It inhibits the protease of HIV, an enzyme that cleaves a long protein chain into peptides during the assembly of new viruses. Because lopinavir is quickly broken down in the human body by our own proteases, it is given with low levels of ritonavir, another protease inhibitor, that lets lopinavir persist longer and prolong its action.

The first trial regarding the effectiveness of ritonavir/lopinavir combination was conducted in Wuhan, China. However, the results were not very encouraging. The researchers had given two pills of lopinavir/ritonavir twice a day plus standard care or standard care alone to 199 patients. There were no significant differences observed between the two groups according to the New England Journal of Medicine.[2] The authors note that additional studies should be undertaken because the treatment may reduce serious complications such as acute kidney injury or secondary infections if given at a certain stage of illness. This drug is generally safe, but there's a risk of drug interactions and significant

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liver damage in critically ill patients.

Ritonavir/lopinavir and interferon-beta combination

Ritonavir/lopinavir and interferon-beta combination is a drug which regulates inflammation in the body and has been shown to be effective in patients with MERS. A randomized controlled trial has been conducted to assess the effectiveness of this drug for MERS in Saudi Arabia, but according to scientists, use of ritonavir/lopinavir and beta interferon combination for COVID -19 patients might be risky, since it can cause severe tissue damage.[3]

Favipiravir

Favipiravir, also known as "Avigan", is an antiviral and is designed to target RNA viruses which include the coronaviruses and influenza viruses. The mechanism of its actions is thought to be related to the selective inhibition of viral RNA-dependent RNA polymerase. According to an open-label cluster-randomized trial conducted in China, Favipiravir shows shorter viral clearance time and higher improvement in chest imaging compared to the control group.[4] This drug is available in both oral and intravenous forms.

Angiotensin-converting enzyme inhibitors and angiotensin receptor blockers

The diagnosed COVID 19 patients with comorbidities such as hypertension and cardiovascular diseases are commonly treated with renin angiotensin system blockers, such as angiotensin -converting enzyme inhibitors (ACEIs) or angiotensin-receptor blockers (ARBs). However, the use of ACEIs/ARBs in patients with COVID-19 or at risk of COVID-19 infection is currently a subject of intense debate. SARS-CoV-2 uses the ACE2 receptor for entry into target cells. Animal (mice) studies have shown that the expression of ACE2 is substantially increased in patients treated with ACEIs/ARBs. Based on these observations, some experts have speculated that the use of ACEIs/ARBs leading to increased expression of ACE2 could potentially facilitate infection with COVID-19. It is also postulated that increased levels of the soluble form of ACE2 may act as a competitive interceptor of SARS-CoV-2 and slow virus entry into the cells and protect from lung injury.[5] The usefulness of these drugs in the treatment of patients with COVID 19 needs further studies.

Non-steroidal anti-inflammatory drugs (NSAIDs)

The existing literature does not currently provide conclusive evidence for or against the use of NSAIDs in the treatment of COVID-19 patients, though there appears to be some evidence that corticosteroids may be beneficial if utilized in the early acute phase of infection.[6] The intermittent or occasional use of NSAIDS could help patients with COVID-19, mainly to relieve night symptoms and improvement of sleep which subsequently helps in improving immune function. Furthermore, patients with COVID-19 may need NSAIDs for other symptoms such as musculoskeletal pain.[7]
However, according to a rapid systematic review done by WHO, there is no evidence of severe adverse events, acute health care utilization, long-term survival in patients with COVID-19, as a result of the use of NSAIDs at present.

Treatment with convalescent plasma

Artificial antibodies against the novel coronavirus are also under investigation to treat patients with SARS-CoV-2. A patient, who has survived from a COVID-19 infection, is likely to produce a large number of antibodies against the virus. The transfusion of those antibodies into an ill patient could help their immune system to destroy the virus. Shen et al (2020) reported findings from a preliminary study of five severely ill patients with COVID-19 who were treated in the Shenzhen Third People's Hospital in China, using plasma from recovered individuals. The donor plasma had demonstrable IgG and IgM anti–SARS-CoV-19 antibodies and neutralized the virus in in-vitro cultures. Although these patients continued to receive antiviral treatment with combinations of lopinavir/ritonavir and interferon; the use of convalescent plasma may have contributed to their recovery because the clinical status of all patients had improved approximately 1 week after transfusion. In addition, the patients' neutralizing antibody titers increased and respiratory samples tested negative for SARS-CoV-2 between 1 and 12 days after transfusion.[9]
In addition to above-mentioned medications, there are few other drugs which are under investigation to treat patients with COVID-19, such as oseltamivir (sialidase inhibitor, approved for influenza), azvudine (experimental reverse transcriptase inhibitor against HIV 1), combinations of baloxavir marboxil (cap-dependent endonuclease inhibitor), a combination of darunavir and cobicistat (HIV protease inhibitor and inhibitor of cytochrome p450), thymosin alpha 1 (immune response boosting agent).
"Solidarity" is an international clinical trial to help find an effective treatment for COVID-19, launched by the WHO. The Solidarity Trial will compare four treatment options against the standard of care, to assess their relative effectiveness against COVID-19. By enrolling patients in multiple countries, the Solidarity Trial aims to rapidly discover whether any of the drugs slow disease progression or improve survival.
In order to find appropriate and effective treatments for COVID-19, a wide range of research into several therapies or treatments will need to be looked into including testing out new drugs. As this disease spreads through the continents, it is important that we identify effective treatments as early as possible so that the harm caused by COVID-19 can be considerably lessened.

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Table 1: Selected notifiable diseases reported by Medical Officers of Health 06th– 12th June 2020 (24th Week)

RDHS Division	Dengue Fever		Dysentery		Encephalitis		Enteric Fever		Food Poisoning		Leptospirosis		Typhus Fever		Viral Hepatitis		Human Rabies		Chickenpox		Meningitis		Leishmaniasis		WRCD	
	A	B	A	B	A	B	A	B	A	B	A	B	A	B	A	B	A	B	A	B	A	B	A	B	T*	C**
Colombo	62	3057	0	13	0	5	0	4	0	14	14	131	0	0	0	2	0	0	2	167	0	20	0	1	**58**	**100**
Gampaha	48	1805	0	5	1	1	0	4	0	19	19	99	0	1	0	3	0	0	2	207	0	9	0	17	**45**	**96**
Kalutara	56	1187	0	6	0	4	0	3	0	4	30	365	0	11	0	2	0	0	8	230	4	20	0	0	**51**	**100**
Kandy	113	1522	7	15	0	1	0	7	0	9	20	94	4	58	0	3	0	0	1	123	0	17	0	38	**62**	**100**
Matale	8	475	0	5	1	3	0	1	0	6	4	49	0	3	0	3	0	1	1	45	0	2	6	164	**64**	**99**
NuwaraEliya	2	128	1	15	0	1	0	0	4	4	10	40	2	59	0	3	0	0	2	64	0	9	0	0	**21**	**100**
Galle	3	1086	0	13	0	8	0	2	0	12	5	229	0	24	0	2	0	0	1	210	0	19	0	2	**55**	**68**
Hambantota	4	281	2	6	0	1	0	2	1	38	12	111	5	22	0	2	0	0	0	140	4	18	42	320	**66**	**100**
Matara	0	352	0	9	0	3	0	0	0	0	0	100	0	4	0	6	0	0	0	68	0	5	0	117	**46**	**44**
Jaffna	12	1890	5	51	0	0	0	18	0	19	1	15	3	458	0	0	0	1	4	85	0	6	0	0	**32**	**93**
Kilinochchi	2	110	0	28	0	2	1	9	1	7	2	12	0	23	0	1	0	0	1	11	0	8	0	5	**65**	**100**
Mannar	0	120	0	0	0	0	0	1	0	0	0	5	0	1	0	0	0	0	0	2	0	3	0	0	**38**	**100**
Vavuniya	1	236	2	9	0	0	0	5	0	2	1	36	0	1	0	0	0	0	2	28	0	4	0	1	**64**	**100**
Mullaitivu	0	65	0	5	0	0	0	5	0	1	0	13	0	6	0	1	0	1	1	5	0	4	0	5	**45**	**81**
Batticaloa	12	2155	3	49	1	3	1	1	2	44	2	21	0	0	0	1	0	1	1	73	1	16	0	1	**53**	**100**
Ampara	4	292	0	10	0	2	0	0	0	0	6	74	0	0	0	1	0	0	1	91	0	12	0	4	**65**	**100**
Trincomalee	4	2246	0	8	0	0	0	0	0	2	0	21	1	3	0	0	0	0	1	76	0	8	0	0	**46**	**92**
Kurunegala	14	695	0	9	0	4	0	2	0	29	18	108	2	13	0	2	1	2	2	263	1	12	17	207	**46**	**99**
Puttalam	5	383	0	7	1	3	0	3	0	1	1	29	0	12	0	0	0	1	1	68	4	30	0	2	**56**	**100**
Anuradhapur	8	351	0	15	0	1	0	3	0	22	9	155	1	14	0	4	0	1	5	154	2	25	0	113	**43**	**99**
Polonnaruwa	4	196	0	5	0	0	0	0	0	5	4	98	0	0	1	14	0	1	2	103	0	10	0	119	**66**	**93**
Badulla	8	387	0	10	0	3	0	3	0	3	10	173	2	46	3	10	0	0	1	119	0	23	1	8	**58**	**100**
Monaragala	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0		
Ratnapura	81	1003	1	47	0	14	0	3	0	19	59	825	0	18	0	13	0	0	2	142	4	56	0	44	**48**	**100**
Kegalle	21	491	1	12	0	4	0	2	0	14	32	220	3	26	0	6	0	0	2	127	2	22	2	13	**59**	**100**
Kalmune	2	842	1	33	1	3	0	0	0	1	1	12	0	2	0	1	0	0	3	261	2	29	0	0	**70**	**100**
SRILANKA	**474**	**21355**	**23**	**385**	**5**	**66**	**2**	**78**	**8**	**275**	**26**	**3035**	**23**	**805**	**4**	**80**	**1**	**9**	**46**	**2862**	**24**	**387**	**68**	**1181**	**53**	**91**

Source: Weekly Returns of Communicable Diseases (WRCD).

*T=Timeliness refers to returns received on or before 12 th June , 2020 Total number of reporting units 356 Number of reporting units data provided for the current week: 300 C**-Completeness

Table 2: Vaccine-Preventable Diseases & AFP

06th– 12th June 2020 (24th Week)

Disease	No. of Cases by Province									Number of cases during current week in 2020	Number of cases during same week in 2019	Total number of cases to date in 2020	Total number of cases to date in 2019	Difference between the number of cases to date in 2020 & 2019
	W	C	S	N	E	NW	NC	U	Sab					
AFP*	01	00	01	00	00	00	00	00	00	02	01	17	39	- 56.4 %
Diphtheria	00	00	00	00	00	00	00	00	00	00	00	00	00	0 %
Mumps	00	02	00	00	00	00	01	00	00	03	05	85	175	- 51.4 %
Measles	00	01	00	01	00	00	00	00	00	02	09	30	162	- 81.4 %
Rubella	00	00	00	00	00	00	00	00	00	00	00	00	00	0 %
CRS**	00	00	00	00	00	00	00	00	00	00	00	00	00	0 %
Tetanus	00	00	00	00	00	00	00	00	00	00	00	03	08	- 50 %
Neonatal Tetanus	00	00	00	00	00	00	00	00	00	00	00	00	00	0 %
Japanese Encephalitis	01	00	00	01	00	00	01	00	00	00	00	16	09	77.8 %
Whooping Cough	00	00	00	00	00	00	00	00	00	00	02	05	33	- 83.8 %
Tuberculosis	41	14	00	07	10	66	00	08	03	149	141	2006	3897	- 43.3 %

Key to Table 1 & 2

Provinces: **W**: Western, **C**: Central, **S**: Southern, **N**: North, **E**: East, **NC**: North Central, **NW**: North Western, **U**: Uva, **Sab**: Sabaragamuwa.

RDHS Divisions: **CB**: Colombo, **GM**: Gampaha, **KL**: Kalutara, **KD**: Kandy, **ML**: Matale, **NE**: Nuwara Eliya, **GL**: Galle, **HB**: Hambantota, **MT**: Matara, **JF**: Jaffna, **KN**: Killinochchi, **MN**: Mannar, **VA**: Vavuniya, **MU**: Mullaitivu, **BT**: Batticaloa, **AM**: Ampara, **TR**: Trincomalee, **KM**: Kalmunai, **KR**: Kurunegala, **PU**: Puttalam, **AP**: Anuradhapura, **PO**: Polonnaruwa, **BD**: Badulla, **MO**: Moneragala, **RP**: Ratnapura, **KG**: Kegalle.

Data Sources:

Weekly Return of Communicable Diseases: Diphtheria, Measles, Tetanus, Neonatal Tetanus, Whooping Cough, Chickenpox, Meningitis, Mumps., Rubella, CRS,

Special Surveillance: AFP* (Acute Flaccid Paralysis), Japanese Encephalitis

CRS =**Congenital Rubella Syndrome

Dengue Prevention and Control Health Messages

Look for plants such as bamboo, bohemia, rampe and banana in your surroundings and maintain them free of water collection.

Comments and contributions for publication in the WER Sri Lanka are welcome. However, the editor reserves the right to accept or reject items for publication. All correspondence should be mailed to The Editor, WER Sri Lanka, Epidemiological Unit, P.O. Box 1567, Colombo or sent by E-mail to **chepid@sltnet.lk. Prior approval should be obtained from the Epidemiology Unit before publishing data in this publication**

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