Treatments and Prophylactics for a Global Emergency Alert: COVID 19 using Allopathic and Indian Phytomedicine

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ABSTRACT

SARS CoV 2 (severe acute respiratory syndrome novel corona virus-2) to which the world paid the complete attention to face the Global Emergency Alert. COVID 19 was first identified in Wuhan, province in China on December, 2020. There are around 12.7 lakhs reported cases and more than 69.4 thousands deaths (06/04/2020) which pave the way for having the health crises in the entire world’s population. Compared to the SARS CoV and MERS CoV, the fatality rate was lower. But it provides the major impacts on elder population (fatality rate more than 40-50 %). Normal/ low white cell counts with elevated CRP (C-reactive protein ) severs as the laboratory findings for the SARS CoV 2 with the symptoms of cough, sneeze, difficulties in breathing and fever followed by ARDS (Acute respiratory distress syndrome) and multi organ dysfunction. By complete understanding of CoV 2 Pathogenesis, presently many drugs are repositioning to completely eradicate the COVID 19. So many drugs are under clinical trials in which the Hydroxychloroquine produces the greater effects on SARS CoV. Likewise many drugs are subjected to this mega clinical trial by repositioning the drugs. AYUSH recommends some of the prophylactics and dietary supplements for the COVID 19. This global emergency was not only for the researchers but also all professionals and their impact to the world’s developed and developing countries still unknown.

INTRODUCTION

COVID 19 (Corona Virus Disease, 2019) also called as severe acute respiratory syndrome novel corona virus which brings the health crises to global emergency alert in more than 200 Countries, areas or territories, which confirmed more than 12 lakhs positive cases around the world wide population with 69 thousand death (fatality:5-6 %). The China National Health commission has reported 17 deaths caused by nCoV on January 22, 2020 initially. WHO declared this situation as global emergency alert and suggest both developed and developing countries
Table 1: Overview on SARS CoV and MERS CoV

| Description * | SARS CoV | MERS CoV | SARS nCoV (Information as per 6th April 2020) |
|---------------|----------|----------|-----------------------------------------------|
| Origin        | Bats     | Bats and camel as an intermediary host | Bats and unknown intermediary animal |
| Originated from | Guangdong province of China | Saudi Arabia | Wuhan, China (capital city of Hubei province) |
| Affected area | China and Hong Kong | Mostly in Saudi Arabia | 202 Countries, areas or territories |
| Year          | 2002-2003 | Later 2012 | Later 2019 |
| Affected      | 8422     | 2494     | More than 12 lakhs people |
| Death         | 916      | 818      | More than 69,400 |
| Mortality     | 11 %     | 34 %     | 5-6 % |

* (Corona Virus Disease, 2019; WHO, 2020; Singhal, 2020; Middle East Respiratory Syndrome Coronavirus, 2020)

COVID 19

WHO categorized COVID 19 as a β genus which belongs to the group 2B that was confirmed by the case report of 9 patients which exhibited 99.98 % similarity in sequence identity and 99.8-99.9 % nucleotide identity through which the new strains of nCoV has been revealed. New Strain is similar 76.5 % to SARS CoV and MERS 50 %. (Ren et al., 2020; Lu et al., 2020; Hui et al., 2020) it is generally believed that the incubation period for COVID 19 is 3 to 7 days (average) with shortest of 1 day and longest of 14 days. These viruses are the enveloped positive sense RNA virus and have the spike like projection (Crown) with the overall size of about 60 to 140 nm. Since it have the crown like projection under electron microscope, it called as the “Corona Virus”. (Singhal, 2020) Basically there are four corona virus (HKU1, NL63, 229E and OC43) which have been circulating in the human and causes mild respiratory syndromes.

All the ages are susceptible and can cause the differential clinical features from the asymptomatic state to ARDS (acute respiratory distress syndrome) followed by multi organ dysfunction. The most common clinical features are cough, sore throat and difficulty in breathing which also possess fever (not in all), fatigue and myalgia. This causes the pneumonia in 1st week and causes respiratory failure and death by extreme progression of human immune system response through the cytokines including IL2, IL7, IL10, GCSF, IL10, MCP1, MIP1A, and TNFα. (Chen et al., 2020) Death and adverse outcomes are most common in elder patient (50-70%)

to quarantine the people to eradicate the spreading of Novel Corona Virus (nCoV) through human to human interaction. (Corona Virus Disease, 2019)

Various levels have been evolved in radiating the nCoV (Thacker, 2020).

Stage 1: The person to person,

Stage 2: Person to their crew (local transformation)

Stage 3: Stage of social spreading (very dangerous that might increase the mortality rate) (Community spreading)

Stage 4: Epidemic

Centers for disease prevention and control explained person to person COVID 19 spread were it is thought to spread through the infected person’s respiratory droplet when he starts coughing or sneezing, resembling the spread of influenza. (Centers for Disease Prevention and Control. Available, 2020) nCoV shows the symptoms (fever, cough & shortness of breathing) in the host within the time span of 14 day within which the chance of infection would be possible if a person touches an infected surface and then touches his or her eyes, nose, or mouth. Middle East Respiratory Syndrome Coronavirus (2020) The patients are categorized into symptomatic infection and asymptomatic infection but both the groups will be having the same viral load. (Siddhartha, 2020). Moreover, nCoV 19 was similar to that of their ancestors namely, SARS CoV (severe acute respiratory syndrome coronavirus) and MERS CoV (Middle East respiratory syndrome coronavirus) and their deaths and mortality rate as given in Tables 1, 2, 3, 4, 5 and 6.
Table 2: Present medicines used in the mega clinical trials to accelerate the COVID 19 treatments

| Drug* | Dose | Prior activity | Effectiveness on COVID 19 |
|-------|------|----------------|--------------------------|
| Hydroxy chloroquine | 400 mg per day for 5 days | Antimalarial | Heme polymerase inhibitor and it has the immune modulating activity and it proposed to have a potent antiviral activity. |
| Ganovo + ritonavir +/- Interferon nebulization | Ganovo one tablet (100mg / tablet) at a time, twice a day, up to 14 days. Ritonavir one tablet (100mg / tablet) at a time, twice a day, up to 14 days. With or without spray inhalation of interferon, 50µg / time for adults, twice a day up to 14 days. | Antiretroviral drug | Potential action of COVID 19 |

* (US National Library of Medicine, 2020; Bulloch, 2020; David and Cennimo, 2020)

Table 3: System wise preventive and prophylactic remedies for the COVID 19

| System* | Botanical name | Name of product/ extract | Remedies |
|---------|----------------|--------------------------|----------|
| Ayurveda | Tinospora cordifolia | Samshamani Vati | 500 mg twice a day with warm water for 15 days. |
| | Aegle marmelos, Premna serratfolia, Oroxylum indicum, Mucuna pruriens and others | Agasthya Hareetaki | 05 gm twice a day with warm water |
| Siddha | Andrographis paniculata | NilavembuKudineer decoction | 60 ml twice a day for 14 days. |
| | Zingiber officinale, piper longum, Syzygium aromaticum and others | Kaba Sura Kudineer decoction | 60ml twice a day |
| Unani | Cydonia oblonga, Zizyphus jujube, Cordia myx. | Herbal decoction | Taken twice a day for 14 days. |
| Homeopathy | - | Arsenicum album, Bryonia alba, Rhus toxicodendron, Belladonna Gelsemium Eupatorium perfoliatum. | Daily once in empty stomach for three days. |

* (Government of India, AYUSH, 2020)
### Table 4: Present medicines used in the mega clinical trials to accelerate the COVID 19 treatments

| Drug*                                      | Dose                                      | Prior activity                          | Effectiveness on COVID 19                                      |
|--------------------------------------------|-------------------------------------------|-----------------------------------------|---------------------------------------------------------------|
| Clinical Trial - Under progress (Active)   |                                           |                                         |                                                               |
| Lopinavir/Ritonavir                        | 400/100 mg every 12 h                     | Prevention of HIV/AIDS                  | Currently on Phase 2 Clinical Trial with Hydroxychloroquine   |
| Tolicizumab                                | Tolicizumab 8 mg/kg (up to a maximum of 800mg per dose), with an interval of 12 hours. | Immunosuppressive agents                | Phase 2 Clinical trial                                        |
| Huaier Granule                             | Huaier granule 20g potid for 2 weeks      | Chinese Traditional Medicine            | Currently on Phase 2 and 3 clinical trial                     |
| Remdesivir (RDV) GS-5734                   | Standard of care therapy together with RDV 200 mg on Day 1 followed by RDV 100 mg on Days 2, 3, 4, and 5. | Nucleoside inhibitor                    | Phase 3 Clinical trial                                        |
| Sildenafil citrate                         | 100 mg / day for 14 days                  | Treatment of erectile dysfunction and pulmonary arterial hypertension. | Phase 3 Clinical trial                                        |
| Methyl prednisolone                        | 40-80 mg/ day intravenous drips for 7 days | Used to suppress the immune system and decrease inflammation. | Phase 4 Clinical trial                                        |
| Vitamin C Infusion                         | 12 g infusion – twice a day for 7 days    | Nutrition Supplements                   | Phase 2 clinical trial                                        |

* (US National Library of Medicine, 2020; Bulloch, 2020; David and Cennimo, 2020)

### Table 5: Other potential Agents for the mega clinical trials to accelerate the COVID 19 treatments

| Drug*                                      | Dose                                      | Prior activity                          | Effectiveness on COVID 19                                      |
|--------------------------------------------|-------------------------------------------|-----------------------------------------|---------------------------------------------------------------|
| Other potential Agents for COVID 19        |                                           |                                         |                                                               |
| Umifenovir                                 | 200 mg 3 times a day for up to 10 days.   | Possess antiviral activity against other corona virus | Approved in Russia and China for influenza treatment and prophylaxis |
| Baloxavir                                  | 80 mg given 3 times over a 7-day period   | Antiviral                               | Newer medicine recently approved by the US FDA for influenza  |
| Favipiravir                                 | -                                        | Viral RNA Polymerase inhibitor, more potent than lopinavir/ritonavir against COVID 19 | Approved by other than US FDA for influenza                   |
| Azithromycin with Hydroxychloroquine       | -                                        | Antibacterial with antimalarial drug    | 100 % clearance of SARS CoV 2                                  |

* (US National Library of Medicine, 2020; Bulloch, 2020; David and Cennimo, 2020)
Table 6: System wise preventive and prophylactic remedies for the COVID 19

| System* | Botanical name | Name of product/ extract | Remedies |
|---------|----------------|--------------------------|----------|
| Ayurveda| *Tinospora cordifolia* | Samshamani Vati | 500 mg twice a day with warm water for 15 days. |
| Siddha  | *Aegle marmelos*, *Premna serratifolia*, *Oroxyllum indicum*, *Mucuna pruriens* and others | Agasthya Hareetaki | 05 gm twice a day with warm water |
| Unani   | *Andrographis paniculata* & others. | NilavembuKudineer decoction | 60 ml twice a day for 14 days. |
| Homeopathy | *Zingiber officinale*, *piper longum*, *Syzygium aromaticum* and others | Kaba Sura Kudineer decoction | 60ml twice a day |
|         | *Cydonia oblonga*, *Zizyphus jujube*, *Cordia myx.* | Herbal decoction | Taken twice a day for 14 days. |
|         | - | Arsenicum album, Bryonia alba, Rhus toxicodendron, Belladonna Gelsemium Eupatorium perfoliatum. | Daily once in empty stomach for three days. |

Figure 1: Disorders caused by SERS nCoV
fatal cases) (Coronavirus Outbreak, 2020). Various disorders caused by the COVID 19 was described in Figure 1 (Marco et al., 2020)

**Significant receptor for SARS CoV binding and potential approaches to address COVID 19**

Crown proteins of the SARS CoV-2 possess the similar receptor binding domain to the SARS CoV in the ACE II Receptor which was explained by the Xu et al. (2020) through the computer modeling. More over the ACE II receptor are widely spread in the epithelial cells of the lungs, that makes the lungs to become most susceptible organ in the human body. Hence to treat or prevent COVID 19, the following potential approaches can be given to manage the same. (Xu et al., 2020)

**Approaches in the SARS Cov-2**

**Development of TMPRSS2 inhibitor**

Hoffmann et al. (2020) demonstrated the spike protein which was prepared by the TMPRSS2 (Trans membrane Protease Serine 2) is needed for it’s entry and their spread in the host by the interaction with ACE II receptor. Hence the development of the TMPRSS2 inhibitors will be the promising role to the complete eradication of SARS CoV-2. (Hoffmann et al., 2020; Glowacka et al., 2011; Iwata-Yoshikawa et al., 2019; Kawase et al., 2012; Zhou et al., 2015)

**Soluble form of ACE II**

By administering the excessive soluble form of ACE II will interact with the CoV 2 and may aid the down regulation of ACE II and protect the lungs from the injury and may slow down the entry of virus (Kuba et al., 2005; Imai et al., 2005).

**Crown vaccine/ Spike Vaccine**

By complete understanding of the various sub units in the Spike/ crown parts in the virus may help to produce the appropriate vaccine and will pave the way for demolishing it (Zhang et al., 2020).

**Approaches in the ACE II Receptor**

**ACE II Inhibitors**

An atomic level understanding of the SARS CoV 2 to the ACE II has been performed recently, they postulated ACE receptor blocker or other vacsins can be developed to manage this global emergency. Antihypertensive agents that regulate the blood pressure by inhibiting the ACE receptors are readily existing in the market. So these medicines are hypothesized to repurpose the restriction in viral entry and prevent the infection. But in other hand due to its up regulation of ACE II receptor that will produce more reception to nCoV, no cases has been reported to continue the treatment with this medication which was reported by European society of cardiology. (De and Simone, 2020)

**Current Treatments for this Global Emergency**

Besides identification of so many treatments and intervention, no medication has been approved, represents the reposition of other therapeutic agents to treat this emergency alert and to decrease the mortality caused by COVID 19.

**Antiviral activity of Indian natural herbs**

They are many natural herbs and their respective active substance that can be used to treat the viral disease. The following Indian Traditional medicinal herbs can be used to treat COVID 19.

**Gymnemasylvestre**

Gymnemic Acid is the potent antiviral compound with sufficient scientific studies has been reported since 1968 against influenza (Sinsheimer et al., 1968). Recently, Vimalanathan et al studied the same compound against Human Corona virus, which showed greater activity against the SARS CoV with the concentration of 0.5 µg/ml (Vimalanathan et al., 2009). Hence using this herbal extracts will play a promising role in controlling COVID 19.

**Achyranthesaspera**

Leaves extract of the L. aspera revealed the anti-viral activity against the Epstein-Barr virus in in vitro studies (Radha and Vijayaraj&amp;vidhya, 2016) and their anticoronal activity was recently evaluated. Since the SARS CoV 1 & 2 are similar in their characteristics, the L. aspera can be used to treat the COVID 19. (Vimalanathan et al., 2009)

**Other medicine plants**

Clerodendruminerme, Pergulariadaemia,Sphaeranthusindicus, Crescentiaalata are the indirational plants with the recent studies reported positive against the activity Human Corona virus hence this medicinal plants can be used for the COVID 19 treatment (Vimalanathan et al., 2009).

**AYUSH recommendations in the race of this Global emergency alert**

(Government of India, AYUSH, 2020) Press Information Bureau, Government of India, AYUSH has conducted meeting on 7th March, 2020. In the various vision of AYUSH, few medications and approaches has been suggested from the individual holistic Indian traditional medicinal systems. The various medications, dietary management and prophylactic intervention were recommended for the treatment of COVID 19. Tulsijuice or infusion (Ocimum sanctum), Guduchi juice/decoction with honey
(Tinosporacordifolia). Ginger juice/decoction with honey (Zingiberofficinale) and Turmeric powder in honey or warm milk (Curcuma longa) can be used as the prophylactics. Causative factors and their respective symptoms can be avoided by the boosting the immune system through the treatment of Ayurveda.

With the above mentioned recommendations, some of the general preventive measures has to be taken for the health crises. (Government of India, AYUSH, 2020)

1. Observation of Best and better personal Hygiene.
2. Practice frequent hand wash with soap which prevent the entry of SARS CoV 2 or any other disease causing agent by touching eyes, nose or mouth.
3. Wear face mask or cover the mouth when coughing or sneezing.
4. Avoid the close conduct with the people who are feeling sick, difficulty in breathing.
5. Avoid the conduct with pets or any other animals.
6. Avoid travel to the farms or garden, animal slaughter house or markets.
7. Use the hand sanitizer with Alcohol.

Other hypothetical approaches to aid this race to manage COVID 19

Aerosol related formulation approaches

Since Lungs are the most vulnerable organ for SARS CoV 2, the administration of drug by the aerosol through oral route may produce the immediate therapeutic actions. Moreover the Nitric oxide gas inhalation for the patient suffered by SARS CoV 2 can be given, which showed the greater antiviral activity against the SARS CoV in 2003. Hence the same treatment was referred by the health professionals and the respective clinical trials were also in progress for the treatment of COVID 19. (US National Library of Medicine, 2020)

Approaches associated with natural herbs

Preferable remedies that can be used against COVID 19 are ACE inhibitors, TMRASS 2 inhibitors and CD 13 inhibitors of the Indian herbs can be selected and can be takenin the form of steam. Steam will produce immediate on set of action once it reaches the mucosal layer of the epithelial tissues in the lungs. Nicotinamine (Vitamin B3) is effectively preventing the tissue damage in the Lungs (Shi et al., 2020)

Mycleyecordata (plume poppy) is used in the Chinese traditional medicine, which inhibit the CD 13 receptors that pave the reception to the CoV. The pathogenesis of the CD 13 receptor associated SARS CoV 2 was not explored. But by inhibiting this receptors we can provide the prophylactic action for the COVID 19.

Curcumin polyphenols has been reported as the potent HIV 1 and HIV 2 protease inhibitor. Since it has proven antiviral activity in the many viruses, it can be utilized for the SARS CoV 2 treatment. (Verma, 2019)

Nicotinamine (Vitamin B3) is effectively preventing the tissue damage in the Lungs (Shi et al., 2020)

Glycyrrhizin an active constituent of liquorice root and considered to be a potent antiviral agent that was prior used to treat the Influenza virus that can be used for treating COVID 19 too. (Wang et al., 2015)

Recently using Molecular docking and Computer modelling, Chen and Du (2020) suggested some of the compounds which have shown greater affinity towards ACE II receptors by the vander waal forces. baicalin, Scutellarin, Hesperetin, glycyrrhizin and Nicotianamine will play the promising role for the complete eradication of COVID 19. (Chen and Du, 2020)

CONCLUSIONS

Epidemic of the 2020 causes huge impact throughout the world. In developed countries particularly in US more than 3.3 lakhs cases were reported on 6th April, 2020. In other hand, Wuhan in china was slowly recovered by quarantining their people and taking timely action by their respective governing bodies. This virus is not new for this world, the same strains SARS CoV was reported in 2003 followed by MERS CoV in 2012. But due to lack of prediction on the CoV, we paid more than 50 thousand deaths and it may increase the count in the upcoming days. Therefore, the more research on these types of viruses should happen in future to predict and focus the upcoming health crises. Thereby controlling the disease and repositioning of the Pharmaceuticals can be done in the shorter span of time.

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