INTRODUCTION

Among disparate infectious diseases, viral infection in precise, provoked by a spectrum of current and primitive infectious viruses, challenges the endurance of humankind across the globe. By superseding those events, with the emergence and spread of 2019 novel coronavirus (CoVID-19) or SARS-CoV-2 has become a new global health crisis threatening the world. Many researchers are concerned about public health on how to overcome the outbreak. Many supportive and symptomatic therapies where being carried out by the Medical practitioners as per the instructions of WHO. Owing to the lack of proper definite treatments, the virus continues to pose a great challenge in the field of medicine, research, economic, public health, etc. There is no correct therapy and vaccine against this virus. According to WHO, 80% of the community in developing nation continues to depend on indigenous medicine. This Complementary and alternative medicine may help to unwrap the mysteries and complications behind CoVID-19, As these herbal medicine accommodates a variety of herbs with medicinal value owing their own broad spectrum antiviral activity.

What is a virus?

A small parasitic, sub microscopic infectious agent that can infect any plants, animals or microorganisms. It relies on living cells of other organisms for its replication. Virus does not have any cell organelles like prokaryotic or eukaryotic cells and so they have no way to monitor or create changes
in their internal environment. It is considered as non living thing as it fails to multiply through cellular division [1]

Why it is Troublesome to develop a vaccine opposing a virus?

A vaccine is an artificial biological preparation. After studying the virus bit by bit, the researchers choose a small harmless fragment of virus or choose any fragments of viruses and deactivate it with chemicals, which are used as vaccine. A potent Vaccine against a virus produces antibodies in our body that stays in blood stream throughout the life span. When the body encounters with the virus after vaccination of that particular virus, our body will recognizes the pathogen and fight against it by producing a specific antibody. [2, 3]

Developing a vaccine opposing a virus is always troublesome. This is because a Virus can adapt and live in both lytic phase (in which the virus progressively replicated in the affected cell of the host) and the lysogenic phase (in which the viral DNA enters and fuses with the DNA of the affected cell and proliferate along with it). This characteristic nature of the virus to adapt is what makes it hard to treat. The ability of many viruses to mutate quickly is due to the frequent changes occurring during the replication of its genome. As the virus is constantly changing its boundary between the worlds of biology and biochemistry, it becomes tedious to design drugs and vaccine against it. [4]

WHAT ABOUT CORONA VIRUS?

Coronaviruses (CoV) are large family of viruses that affects birds and mammals. In humans, Corona virus can cause respiratory tract infection ranging from the common cold to serious infection which includes SARS (Severe acute respiratory syndrome), MERS (Middle East Respiratory Syndrome) and SARS-CoV-2 (Corona Virus Disease 2019) which can also be lethal. Ranging from no symptoms to symptoms like pneumonia the virus can also eventually leads to death. Coronavirus infect the upper respiratory tract and gastrointestinal tracts of mammals and birds. Till date, there are seven different strains of CoV that infect humans.

History of CoV

Corona virus was first spotted in 1930s which affected Domestic chickens inducing Acute infection in the respiratory system with the etiology of Infectious Bronchitis Virus (IBV). Later two novel corona viruses, Mouse Hepatitis Virus (MHV) and Transmissible Gastroenteritis virus (TGV) were provoked in 1940s. The Human Corona Virus 229E and Human Corona Virus OC43 were the first Corona virus to infect humans in the 1960s . There have been 2 crises in the past 20 years wherein crisscross of animal beta-corona viruses to other animals and humans has led to serious infection. Most of these involve serious respiratory tract infection (Figure 1).

SARS-CoV (Severe Acute Respiratory Syndrome Corona Virus)

It was identified in 2003 and affected 26 countries with positive case count of more than 8000 in 2003. It is believed to be an animal virus from bat, and further passed into other creatures namely civet cats. The life cycle of SARS CoV is still unknown. The initial infection was from Guangdong province of southern China in November, 2002. The global epidemic of infection ended in July 2003 and the transmission is mainly due to travelers. The symptom ranges from high fever, mild to moderate respiratory symptoms to pneumonia. This outbreak affected 29 countries in the world with more than 8100 probable cases in which 916 cases were dead. After the end of this crisis by July 2003, SARS infection has re-emerged four times in which once from the initial hotspot of southern China and three times due to laboratory accidents [5]. The development of a vaccine against SARS-CoV is still under development and many Clinical trials have done with previously discovered drugs. [6]

MERS-CoV (Middle East Respiratory Syndrome Corona Virus)

This is spotted in 2012, in Saudi Arabia, affected 27 countries notably Saudi Arabia (80% cases), United Arab Emirates, Middle East Africa and South Asia and the Republic of Korea. They had symptoms same like SARS with some gastrointestinal symptoms and sometimes asymptomatic. Although the infection was contagious, scientific evidence in 2019 suggests that it might be provoked from bats and transmitted to camels; and Dromedary camels are the main host source for MERS-CoV. However the origin and exact route of transmission was not completely understood. Since September 2012, 2494 positive cases have been reported in which 858 cases (34.4%) dead.

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COVID-19

The Novel corona virus (CoVID-19) originated in 2019, is a new strain which has not been identified in mankind since past. The Wuhan, Hubei province, china, became the centre of hotspot for a series of pneumonia cases with unpredictable cause In December 2019. This awakened intense attention to other countries on china. Cases of CoVID-19 crossed their boundaries within the Wuhan and started to spread all over the world through the travelers. As this infection is contagious the virus started to propagate throughout the globe, which may be spreaded due to travelers from infected area or through air droplets [8]. The structure of the CoVID-19 indicates that it is a beta-corona virus which resembles the genetic sequence of SARS virus, hence later named as SARS-CoV-2.

EPIDEMIOLOGY of CoVID-19

The epidemiologic picture of CoVID-19 varies on a minute basis. On may 13, 2020[12:23GMT], they are 43,64,033 confirmed cases in which 24,40,615 Active cases, 2,93,564 deaths and 16,13,455 recovered cases from CoVID-19 outbreak

In India, first case was reported on January 29 and on May 13, 2020[12:23GMT], they were 75,048 cases in which 2,440 deaths and 24,900 recovered cases (Graph 1 ).

Countries affected

They are 213 countries and territories around the world and 2 international conveyance affected by CoVID-19 virus on May 13, 2020[12:23GMT].

NAME (CORONA)

The word Corona is evolved from a Latin word; meaning "halo or crown", as they possesses a fringe of large, bulb like surface protein ridges, created by a viral glycoprotein in spike, which recreated an image representing royal crown under electron microscope.

ORIGIN

At present, the source of CoVID-19 is not known. Every available evidence signifies that CoVID-19 has a natural animal origin and is not a formulated virus . As the initial case with this virus had a link with seafood and animal market, It is expected to be originated from an illegal traded wildlife at a seafood market, Wuhan. Health experts believed that, it may be originated from bats then passed on to humans possibly via another animal species like MERS-CoV through a spillover events(Figure 2)

TRANSMISSION

Although CoVID-19 is presumed to be zoonotic in origin, person to person transmission is evident. The infection spreads from a person’s mouth or nose when a person infected with CoVID-19 speaks, cough, or exhales near a healthy person, it may infect the healthy persons through droplet nuclei. Some may get infected by touching the droplets that are landed on objects or surface around the CoVID-19 infected person; followed by touching there mouth, nose or eyes. There is no evidence of airborn transmission.

The possibility of getting CoVID-19 infection from a infected person's feces is appeared to be low and recent study suggests that virus might present in their feces in some cases due to the infection in their intestine [9] , but the outbreak is not by this route.

RISK FACTORS

The risk depends on location and personal hygiene of an individual. The severe risk factors of CoVID-19 includes Recent travel history from Wuhan or any other hotspots of the virus outbreak, Direct or Close contact with infected persons (being within 6 feet (2 meters) or staying with the infected patients for long time without any protective equipments), healthcare workers, Working in environment where infected patients, Exposure with health care facility associated with infections, Eating uncooked or undercooked meat or animal product contaminated with viruses may result in the infection of the person. 21% of healthcare worker were affected, during the 2002 SARS crisis is notable [10].

SYMPTOM

The Incubation period of this virus is 5-14 days (Approx. 5.2 days), similar to that of SARS [11]. Signs and symptoms of CoVID-19 includes, Fever (absent in Geriatric patients and immune compromise patients), Cough, Dyspnea [12]. Other symp-

Graph 1: (a) The Chronological incidence of CoVID-19 (b) Number of deaths till May 12, 2020

Graph 2: Bar graph representing Percentage of incidence of Clinical features

Severe Clinical syndromes associated with SARS-CoV-2 infection include Pneumonia, Sepsis, Septic shock, Acute respiratory distress syndrome (Figure 3Figure 4). [13]

IDENTIFICATION OF SEVERITY

FATALITY RATE

Age is the major risk factor of CoVID-19 infection. A case study of 44,000 confirmed cases in China concludes that the case-fatality ratio was higher among older persons (Table 2).

Fatality rate of patients with conditions like cardiovascular disease is 10.5%, Diabetes is 7.3%, Chronic respiratory tract infection, Hypertension and cancer...
Figure 2: Origins of Human coronavirus from animals

Figure 3: Percentage of incidence
Table 1: Summary of stages of severity of CoVID-19 with percentage of people affected

<table>
<thead>
<tr>
<th>Stages of Severity</th>
<th>% of People with COVID-19 (Approx.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No symptoms</td>
<td>Not known</td>
</tr>
<tr>
<td>Person with mild symptoms, who can recover</td>
<td>&gt;80%</td>
</tr>
<tr>
<td>Serious infection, leading to shortness of breath and pneumonia</td>
<td>About 14%</td>
</tr>
<tr>
<td>Symptoms of Critical infection, includes multi organ failure and septic shock; in which respiratory failure is prominent.</td>
<td>Around 5%</td>
</tr>
<tr>
<td>Fatal disease</td>
<td>2%</td>
</tr>
</tbody>
</table>

WHO remarks at media on 17th February 2020*

Figure 4: The respiratory and systemic disorders provoked by CoVID-19

Table 2: Fatality rate

<table>
<thead>
<tr>
<th>Age group affected</th>
<th>Fatality rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>More than 80 years</td>
<td>14.8%</td>
</tr>
<tr>
<td>70-79 years</td>
<td>8.0%</td>
</tr>
<tr>
<td>60-69 years</td>
<td>3.6%</td>
</tr>
<tr>
<td>50-59 years</td>
<td>1.3%</td>
</tr>
<tr>
<td>40-49 years</td>
<td>0.4%</td>
</tr>
<tr>
<td>Less than 40 years</td>
<td>0.2%</td>
</tr>
</tbody>
</table>

is 6%.

REINFECTION

There is no evidence that the recovered patient will get reinfeected after completion of the course of therapy. The patient’s recovery was declared by detecting IgM and IgG antibodies in the patient’s blood stream which indicates the development of antibodies against the virus in the patient.

STRUCTURE AND PATHOGENESIS

CoVID-19 viruses is 85% similar to SARS-CoV and 40% similar to MERS-CoV. These viruses are Spherical, Positive sense RNA virus of 125nm in diameter. They are Non-segmented, Enveloped and Contains large genome of 30 kilo base RNA. There Genome contains a 5’ Cap and 3’ tail, which makes it as a messenger RNA for translation of the replicase polyproteins. 2/3rd of genome caries genes encoding the Non-structural protein and 1/3rd of genome contain genes encoding structural and accessory pro-
teins (Figure 5).

Coronavirus contains 5 structural proteins – Nucleocapsid protein (N), membrane protein (M), Envelop protein (E), Hemagglutinin esterase (HE), spike protein (S).

The protein present in the nucleocapsid is N protein. The N protein is a eminently phosphorylated protein consist of 2 binding domains- N & C terminal domain having distinct mechanism for binding with RNA, and binds replicase complex like nsp3 and M protein, which there by induces the synthesis of complimentary RNA template from the RNA of the virus [14]. An ideal RNA binding is done only with the help of both the domains [15] [16]. This N protein undergoes phosphorylation that induces morphological changes in the virus, differentiates a viral DNA from non-viral DNA. Shape of the virus is organized by a small M protein which is found to be a dimer in nature in a study recently. This protein promotes change in basic geometry of the virus [17]. The assembly and leakage of the viral RNA is mediated by a variety of E protein and resembles common structure [18]. Though the structure of E protein is not studied thoroughly, the collected data concludes it as a transmembrane protein. The E protein plays a key role in pathogenesis of the virus by their ion channel activity and their function is ineffective during replication of the virus in the host cell [19]. Hemagglutinin esterase (HE) is a structural protein that triggers the S protein mediated cell entry with the help of their acetyl-esterase activity and virus propagate into the mucosal membrane. S proteins, a binding protein presenting on the surface of virus forming spikes decides the cell that the virus can infect. S proteins are glycoproteins which are trimer in nature [20]. The S protein gains access to the endoplasmic reticulum of the host with the help of N-terminal and facilitates the binding of virus with the host receptors. In most, but not all CoV, S proteins undergoes Acid dependent proteolytic cleavage by a furine like protease enzyme in the host and two different polypeptides are formed-S1 is the large S protein receptor domain that binds to host cell with the help of RNA binding domain and Fusion domain and S2 is a stalk of the S protein [21].

This fusion occurs in endosomes but in some CoV like MHV, fusion occurs in plasma membrane. Many CoV utilizes peptidase as their cellular receptors, SARS-CoV uses ACE2 receptor as their receptor to bind and MERS-CoV uses DPP4 receptor.

Attachment of virus to the host cell starts with the binding of S protein with its receptors. The formation of anti parallel Six-helix bundle occurs by the fusion of a pair of seven S2 which gets cleaved from the S protein and gets inserted into the membrane, triggers the blending of viral and cellular membrane superseding the exposure of fusion domains of S1 protein gets inserted into the membrane. Other protease like TMPRSS2 helps for the blending of viral and cellular membranes that end up with the fusion and discharge of viral genome into the acidified endosomes, unlike MHV in which the fusion occurs at protoplasm. Finally the viral genome gets released into the cytoplasm (Figure 6).

This viral genome that gets released in cytoplasm undergoes translation of replicate gene like rep1a & rep1b of the virus and the translation continues till the exposure of rep1a stop codon. The translation and assembly of replicate gene form genomic and sub genomic RNAs acts as a messenger RNA. These RNAs get inserted into Endoplasmic reticulum and transfer the messages through mRNA and form mature virions. These matured viral particles are then carried to the surface of the vesicle in the cell and leaks out by exocytosis. In SARS disease, the virus primarily affects epithelial cells of the lungs and enters dendritic cells and macrophages; however the exact mechanism of lung damage is not clear (Figure 7).

LABORATORY TESTS FOR COVID-19

The tests for the detection of the virus are conducted in specialized labs that are certified to do so. The decision of testing a person for CoVID-19 is purely based on epidemiological factors and clinical presentations. PCR test for asymptomatic or mildly symptomatic cases are recommended only if the individual had contact with a CoVID-19 infected patient [22].

NUCLEIC ACID AMPLIFICATION TEST (NAAT):

Confirmation of a person for CoVID-19 positive is depends on detection of unique sequence of virus RNA by nucleic acid amplification test .This is done by using real time reverse transcription polymerase chain reaction (rRT-PCR) and the RNA extractions are done in a bio safety cabinet. Lower respiratory tract samples like sputum, bronchoalveolar lavage or aspirate can be collected as specimens and Upper respiratory samples like Nasopharyngeal and oropharyngeal swabs were collected as specimen and tested using NAAT. A positive result for the presence of betacoronavirus indicates the case with positive.
Figure 5: A typical structure of Coronavirus (a) Transverse section (b) outer structure of Coronavirus

Figure 6: Pathogenesis of Coronavirus

**SEROLOGICAL TESTS:**

In case the NAAT assay comes negative and still there was a doubt of CoVID-19 infection, paired serum samples was done to support the diagnosis. The patient’s stool, urine and whole blood are collected for serological testing.

**VIRAL CULTURE**

The Isolation of virus is not favored as a confirmatory diagnosis as it may increase the peak of crises, if it is mishandled.

**OTHER TESTS**

- Thermal scanning
- Computer tomography chest scan

**PREVENTION**

As a case study of a family from Zhejiang province, China concludes that CoVID-19 can also spread from a presymptomatic carrier and yet, there is no vaccine to prevent the propagation of this troublesome virus. So the best way to lower the current crises of infection is prevention and avoiding the exposure of the virus is the easy way to forbid this infection.

- **Not to do list**
  - Smoking.
  - Wearing multiple mask and remember that mask should be used only by healthcare workers, care takers and individuals with respiratory symptoms.
  - Taking Antibiotics, As antibiotics are effective against bacteria and not on virus infection.
  - Self medication is not recommended preventing or cure the disease.

Figure 7: Some preventive measures against Coronavirus; (a) Social Distancing, (b) Avoid contact with infected people, (c) Clean your hand with sanitizer frequently, (d) Quarantine, (e) infected person and healthcare workers should wear mask, (f) Wash your hand with soap frequently, (g) Avoid touching your nose, eyes or mouth after touching contaminated surface, (h) Keep up-to-date about the latest CoVID-19 hotspots

- Eating infected, raw or uncooked meat and there is no evidence that eating a properly cooked meat which is not infected can cause infection.
- Direct contact with animals and surface in contact with animals. However, there is no evidence that a dog, cat, or any pet can transmit infection.
- Touching a contaminated surface, which is often difficult to predict and touching of nose, eyes or mouth before washing your hands with sanitizer.
- Travelling to affected places.
- Do not split in open.

To do list

- Do hand wash using soap and water for at least 20 sec. or clean with Hand sanitizer frequently to kill the virus present on your hand.
- Social distancing, Maintain at least 1 meter distance within yourself and anyone who is coughing or sneezing. When a infected person coughs, sneezes, speaks or breath; the small liquid droplets released from their nose and mouth may contain virus, and so by wearing a mask the circulation of these droplets in the nearby environment can be prevented.
- Quarantine; Stay at home, with proper personal hygiene to avoid being exposed to the virus.
- Proper hygiene includes covering your mouth and nose with your bent elbow while coughing or sneezing other than frequent washing of hands as that protects the people around you from virus.
- Stay home and seek medical attention, if you feel unwell.
- Stay informed about the latest hotspots of CoVID-19 in your locality.
- Individual suspecting with infection should refer government designated centers for isolation and testing.

Immunity boosting measures published by Ministry of AYUSH for preventing CoVID-19 virus outbreak includes,

1. Consume warm water periodically throughout the day.
2. Include Turmeric, Cumin, Coriander and Garlic to the diet to boost body’s immunity
3. Do yoga, pranayama and mediation for half an hour as guided by Ministry of AYUSH.

Some Ayurvedic Immunity boosting preparations includes

1. Chyavanprash (CP) 1 tsp can be administered to all age group in the morning. It is a semi solid formulation containing around 50 medical herbs. CP is effective in maintaining homeostasis as it has Anti-infective, Antiseptic and Immunomodulating properties. [23]
2. Drink herbal tea containing Basil, Cinnamon, Raisin, Black pepper and Dry ginger; for one/two times a day. This drink is a good remedy as it contains Basil and Dry ginger which has antiviral activity [24] and Cinnamon maintains good oral micro biota. [25]
3. Drink Golden milk, half a tea spoon turmeric powder in approx. 150 mL of milk, one/two times a
day. This drink helps to treat normal runny nose and cough, COPD, etc.

**Some simple Ayurvedic Procedures can be done once or twice a day to prevent entry of virus into our body**

1. Nasal application of sesame oil, ghee or coconut oil during morning and evening
2. Swishing with 1 tablespoon of coconut oil or sesame oil around the mouth for 2-3 mins and then rinse with warm water.
3. Inhalation of Caraway seeds or mint leaves stream can be done once a day and Clove powder mixed with honey for 2-3 times a day; can be done to treat normal dry cough and sore throat. However, it is best to consult a doctor if the symptom persists.

**TREATMENT**

Many supportive and symptomatic therapies where being carried out by the Medical practitioners as per the instructions of World Health Organization (WHO) with a hypothesis and there is no evidence that it works against CoVID-19. This new virus has challenged the medicine with no correct therapy and vaccine approved by Food and Drug Administration (FDA) against this virus.

According to WHO, FDA and Centers for Disease Control and prevention (CDC); no vaccine or drugs are proven to be effective for the treatment and prevention of CoVID-19.

Currently, Patients suspected with CoVID-19 are isolated after screening and Antimicrobial regimens with potential activity against CoVID-19 were followed as per instructions of WHO, FDA and CDC includes: [26–28]

Chloroquine phosphate 2.5mg, oral, over three days andHydroxychloroquine 400 mg, oral, per day for five days are anti-malarial drugs with relative activity against CoVID-19 virus and has immunomodulating properties in human by inhibiting Heme polymerase enzyme. Pre clinical studies in vitro 2004 and 2014 suggests Chloroquine has potential activity against CoVID-19 virus and inhibits exacerbation of pneumonia patients with infection. Another study concludes that Hydroxychloroquine in vitro activity may be more potent than Chloroquine. [29]

Ritonavir 400mg + Lopinavir 100 mg, 500 mg once, oral, twice a day for two weeks. Both of the drugs are anti-viral (Anti HIV) drugs that inhibit Protease enzyme and may bind to Mpro enzyme in coronavirus that plays a key role in its replication [30]. A clinical trial in 2004 shows the patient had a decreased viral load and increased lymphocyte count.

Remdesivir 200 mg for initial dose and 100 mg for maintenance dose, IV once daily for 9 days as maintenance dose. It is a Nucleoside analogue. A study in 2018 reported that Remdesivir is a broad spectrum anti-viral agent acting against Coronavirus.

Azithromycin 250-500 mg per day is a macrolide Antibiotic having immunomodulatory properties in pulmonary inflammatory disorders and prevents the superinfection during the treatment period. Azithromycin is usually administered along with Hydroxychloroquine to prevent bacterial superinfection as an additional therapy.

Tocilizumab is a monoclonal Antibody that inhibits Interleukin-6 receptors. They have clinical benefits as adjunct therapy in patients having complication like Cytokine release syndrome. Other immunomodulators like alfa-interferons and sarilumab are also used as adjunctive therapy.

Corticosteroids are recommended for cases with acute respiratory distress syndrome or refractory shock. They are not recommended for patients having pneumonia along with infection.

NSAIDs like Acetaminophen may be given for temperature control for its antipyretic property alone.

Additional data regarding all the drugs mentioned above are under evaluation.

**CoVID-19 Convalescent plasma:**

Plasma from recovered individual are collected, only if they are eligible to donate blood. The donor who donates blood should contain following eligibility,

- All male donors and only female donors with HLA negative are eligible
- Prior confirmatory diagnosis of CoVID-19, documents.
- Should donate 14 days after the complete suppression of symptoms.
- Reports having negative results for any one of diagnostic tests from blood and one or more nasopharyngeal swab specimens.

These practices are done only in labs authorized by FDA.

According to WHO, 75% of the population in developing community depends on traditional medicines for physical health and psychological requirements, since they want to avoid the side effects caused by Allopathy Medicines. This Complementary and alternative medicine may help to unwrap the mysteries and complications behind CoVID-19, As these
herbal medicine accommodates a variety of herbs with medicinal value owing their own broad spectrum antiviral activity. Only few Sidha, Unani, Ayurvedhic traditional herbs have been studied for their potential activity against Viruses and many herbs were studied for their activity to boost body’s immunity.

Author’s stroke

CoVID-19 virus interaction with innate immunity of an individual is important in determining the outcome of infection, early control of this infection limits the spread within the population. Hence, herbs like Green chiretta (vernacular name: Nilavembu) can be used to boost immunity of an individual. It acts as an antipyretic, immunostimulant and immunomodulator, which boosts the immune system and modulates defense response in the body. The herb once played a significant role in treating Dengue fever and Chikungunya when no vaccines or modern drugs are available. Studies regarding antiviral activity of Green chiretta under evaluation. [31, 32]

DISCUSSION

Corona virus has alerted Indians to not forget their culture and has made other countries to look upon Indian culture such as washing of hands and legs before entering the house, drinking a glass of water while entering or leaving the house to stay hydrated, greeting with namaste instead of shaking of hands and hugging, spraying turmeric water on roads and inside temple during festivals though considered spiritual, is actually done to disinfect the areas where people gather and thus prevent infections. I hope, our culture will be followed throughout the world after this epidemic.

CONCLUSION

CoVID-19 is a serious public health issue. The main reason for the outbreak of this virus are lack of proper drugs and vaccines and the only thing that can be done at present is to Stay at home and stop the chain of spreading. Many efforts and researches are going on about CoVID-19 in and around the world to eradicate the virus from the human body and to save the human population. Hope, these efforts will get a successful results and many human populations are saved.

CONFLICT OF INTEREST

Authors declared no conflict of interest.

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