Convalescent plasma therapy tested on critically ill COVID-19 patients

Patients showed an improvement in clinical symptoms 12–24 hours after plasma infusion

R. PRASAD

In the absence of any preventive vaccine or specific antivirals for treating COVID-19 patients infected with the novel coronavirus SARS-CoV-2, a pharmaceutical company in China has turned to plasma taken from people who have recovered from the infection to treat critically ill patients.

Key indicators: Improvement in clinical symptoms includes blood oxygen saturation and significant reduction in inflammatory indicators. ▪ AFP

Convalescent plasma

Convalescent plasma has been listed as a therapeutic method by China's National Health Commission.

People who have recovered from COVID-19 disease would have antibodies against the virus. Infusing the antibodies to critically ill patients is expected to improve the chances of survival. The plasma that is transfused contains the antibodies.

The company had collected plasma from some recovered patients to prepare therapeutic products including convalescent plasma and immune globulin.Plasma taken from recovered patients in Wuhan since January 20 has been given to more than a dozen patients. Initially, three critically ill patients in a hospital in Wuhan received plasma treatment on February 8. An additional 10 patients have received the treatment since then. According to Xinhua, patients who received plasma therapy showed an improvement in clinical symptoms 12-24 hours after being given the therapy. Improvement in clinical symptoms includes key indicators such as blood oxygen saturation and significant reduction in inflammatory indicators.

This is not the first time that plasma from recovered patients has been used to treat people infected with certain viruses for which drugs are not available. When Ebola struck Guinea, Sierra Leone, and Liberia in 2014, the World Health Organization prioritised the evaluation of treatment with convalescent plasma derived from patients who have recovered from the disease.

Earlier trials

There was hardly any benefit seen in 84 patients treated with convalescent plasma in a trial carried out in Ebola patients in Guinea between mid-February and early August 2015. The results were published in *The New England Journal of Medicine*.

"The transfusion of up to 500 ml of convalescent plasma with unknown levels of neutralizing antibodies was not associated with a significant improvement in survival," the authors write.

Time-tested method

"Treatment with convalescent plasma is a classical, time-tested method. It has been used against measles, chickenpox, and rabies. In the case of rabies, it is acts as passive immunisation after dog bite and before disease develops," says virologist Dr. Jacob John.

Timing is crucial

"Best time to give convalescent plasma containing antibodies is before disease develops. In the case of COVID-19, by the time pneumonia is diagnosed it is too late. That is the reason why therapy using convalescent plasma is not popular for other viral diseases," Dr. John adds.

According to him, as the disease develops, the body has already begun developing antibodies against the virus. Infusing convalescent plasma is essentially like topping with more antibodies hoping that increased amount of antibodies will dampen the disease progression. "Antibodies in the plasma bind to the virus and prevent them from entering the cells. But by the time it is given, many cells have already been infected. Hence, convalescent plasma therapy is not very effective," says Dr. John.

Researchers decode how malaria parasite multiplies

Two large protein complexes help the parasite proliferate

ASWATHI PACHA

With over 4,00,000 deaths in 2018, according to the WHO, malaria still remains one of the biggest killer infections globally, concentrated mainly in Africa and India. The disease is caused by the parasite *Plasmodium* and transmitted by the *Anopheles* mosquito. To understand in detail how this parasite multiplies within a mosquito, an international team of researchers spent years studying different proteins in the parasite. Their study published in *Cell Reports* has found two important proteins essential for proliferation. These finding can help develop new drugs and thus pave way for malaria eradication.

Potent transfer: The parasite is injected into humans at the infective oocyst stage through mosquito bite. ▪ REUTERS

The team found that two large protein complexes (condensins) called SMC2 and SMC4 played essential roles in the parasite proliferation. One of the co-authors Prof. Rita Tewari in an email to *The Hindu* says: "It means that these molecules are required for every stage of parasite multiplication, and even in the cyst-like structure in the mosquito (oocyst) where the infective stage of the parasite develops. It is at this stage that it is injected into humans through mosquito bite." She is from the School of Life Sciences at the University of Nottingham.

The team showed that when genes behind these proteins were deleted, the number of oocysts in the mosquito gut significantly reduced and were smaller in size compared to the normal ones.

Adaptable parasite

Prof. Tewari adds in a release: "This malaria parasite is very adaptable. Even if you kill it in the human bloodstream, some of these sex cells taken in by the mosquito during a bite can develop and multiply further in the mosquito. Over time, it [the parasite] has adapted to survive and multiply using different modes, which is why it is difficult to control the disease."

The malaria parasite has different models of multiplication in different stages of its life cycle, and it is essential to track down all the important proteins behind it for developing a new effective drug. "We are now studying the novel modes of parasite cell division and the crucial regulatory molecules which are involved in the success of the parasite cell division," adds Prof. Tewari.

"With the increase in drug-resident malaria cases, it is essential and urgent to find new drug targets. These two proteins are conserved across all *Plasmodium* species and were found to be important for parasite multiplication. This adds a step towards exploring new drug targets" adds Dinesh Gupta, leader of the Translational Bioinformatics Group from the International Centre for Genetic Engineering and Biotechnology (ICGEB), New Delhi. He is one of the authors of the paper.

How small regulatory molecules are generated in plants

SHUBASHREE DESIKAN

Researchers from National Centre for Biological Sciences, Bengaluru, and SASTRA University, Thanjavur, have discovered how small molecules called microRNAs are made in plants. This finding makes it much easier for studying processes in plants. MicroRNAs are small molecules, about 21 nucleotides long, and help in controlling the levels of proteins in the cell. The research was published in the journal *Nucleic Acids Research*.

All aspects of growth and development of plants, whether it is initiation of flowering or control and distribution of hormones in response to external stress, are regulated at various levels in the cell. Such regulation is always mediated by proteins – the work horses of the cells. At one level, regulation of the processes is about controlling the amount of specific proteins being made in the cells. This is achieved by the microRNAs.

In order to decrease the level of a particular protein in specific cells, the microRNAs destroy the messenger RNA molecules that help with the production of that specific protein in the cell. The microRNA molecules do this by cutting down that particular messenger RNA thereby destroying it. This process is called the silencing of the messenger RNA.

Control centre: Growth and development of plants are regulated at various levels in the cell. ▪ ASHOKE CHAKRABARTY

The microRNA that achieve this silencing are evolutionarily conserved - that is, they are found in all flowering plants, whether they are mosses or roses.

Similarly, the best way to study the effect of a gene in the DNA is to silence or "knockout" the gene. Knocking out a gene does not mean removing the entire gene. In knocking out processes, those RNA that induce the gene to produce proteins are destroyed or their levels are reduced by the microRNA as described earlier.

MicroRNA structure

In this new research, the team has found that microRNAs have a high occurrence of the bases G and C and this helps their formation and abundance in the cells. Further, there is a position-specific bias for these bases in the microRNAs. This is recognised by a specific RNA-binding protein. As N. Anushree of NCBS, who is the first author of the paper clarifies, "We see more G or C in specific positions [across the length of the microRNA consisting of say, 21 nucleotides]. Such a preference is essential to make these molecules at an optimal level in the cells."

The present way to silence genes is by introducing artificial microRNA which binds to the messenger RNA of interest and prevents the production of protein. This is done in a deliberate process of trial and error.

"Researchers try out several artificial microRNAs, introduce them into plants one by one in a cumbersome process and then pick the best one which can remove most messenger RNAs of the gene of interest. Our results can help anyone to choose the one candidate that is sure to work," says P.V. Shivaprasad from NCBS, who led the study.

To avoid panic, WHO will not use SARS in new virus' official name

The Coronavirus Study Group has named the virus SARS-CoV-2 in keeping with conventions

R. PRASAD

Three days after the novel coronavirus got an official name, the World Health Organization has clearly indicated that it will not use the official name in all its public communication while referring to the virus.

On February 11, the WHO announced COVID-19 as the name for the disease caused by the novel coronavirus. The "CO" in COVID stands corona, while "VI" is for virus and "D" for disease. The number 19 stands for the year 2019 when the outbreak was first identified.

The same day, in a preprint posted in the *bioRxiv* repository, the Coronavirus Study Group of the International Committee on Taxonomy of Viruses announced the official name for the virus – "Severe acute respiratory syndrome coronavirus 2" or "SARS-CoV-2".

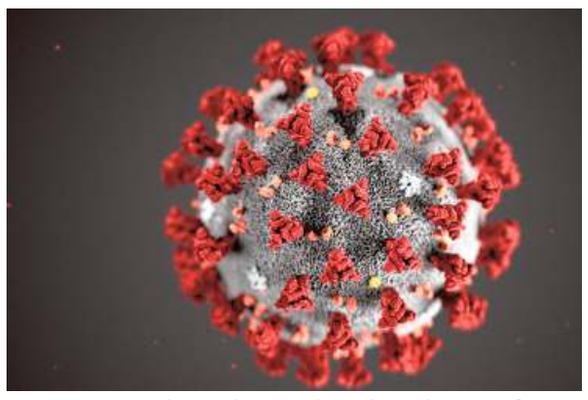
Official classification

The Study Group had assessed the novelty of the virus to arrive at the name. The Coronavirus Study Group is responsible for developing the official classification of viruses and taxa naming of the Coronaviridae family to which the novel coronavirus belongs.

A news item published in the journal *Science* mentions that WHO is "not happy" with the name given to the virus and hence is not planning to adopt it. It will instead call the pathogen "virus responsible for COVID-19" or the "COVID-19 virus", a WHO spokesperson told *Science*.

The WHO has clarified that neither of the two names that it plans to use to refer to the novel coronavirus are "intended as replacements for the official name of the virus" that the Study Group has chosen.

The reason why the WHO is not happy with the name and its refusal to use it while referring to the virus stems from the fact that the official name given to the virus has SARS (Severe acute respiratory syndrome) mentioned in it. The SARS coronavirus, which was identified in 2003, first infected humans in the Guangdong province of southern China in 2002. The SARS epidemic spread to 29 countries and resulted in 8,096 cases and 774 deaths before it was contained in July 2003.



Naming a virus: The Study Group has adopted a scientific approach while naming the new coronavirus. ▪ AP

So, from a "risk communications perspective, using the name SARS can have unintended consequences in terms of creating unnecessary fear for some populations, especially in Asia, which was worst affected by the SARS outbreak in 2003", the spokesperson told *Science*.

Different criteria

The WHO and the Study Group use two very different criteria and approaches while deciding the names. The WHO arrives at the name of a new disease by following the May 2015 guidelines. According to the guidelines, the disease name should not include geographic locations and people's names as this can be stigmatising. Also, names of animals such as swine flu should be avoided as this leads to confusion. The guidelines also say that it should avoid "terms that incite undue fear" while choosing a name.

The Study Group adopts a "scientific approach" while naming a new coronavirus. Based on whole genome sequence shared by China and other countries, scientists have confirmed that the novel virus belongs to the same species as the one that caused the SARS epidemic, which is called SARS-related coronavirus.

"The virus may be novel to the rest of the world, but it isn't really to taxonomists. So it's not getting its own name. Instead, the committee appended a '2' for viruses isolated from patients in Wuhan and elsewhere," the chair of the Study Group John Ziebuhr of Justus Liebig University Giessen told *Science*.

According to the journal, the paper was sent to *bioRxiv* repository on February 7, four days before it was posted on the repository. The authors had also sent the paper to a scientific journal for publication. After the outbreak, the WHO had requested all scientific journals to first share with it any paper that they receive before publishing.

"Research findings relevant to the outbreak are shared immediately with the World Health Organization (WHO) upon journal submission, by the journal and with author knowledge," notes a February 4 editorial in *Nature*.

So, the WHO was aware of the official name given by the Study Group well before it announced the name of the disease. "The timing of WHO's announcement was not influenced by the arrival of the manuscript," the WHO spokesperson told *Science*.

Warming terrain: The temperature in a densely populated city is as much as 2 degrees higher than suburban or rural areas. ▪ V SREENIVASA MURTHY

Urban heat islands in India

Why are our cities warmer than their suburbs and rural areas?

SPEAKING OF SCIENCE

D. BALASUBRAMANIAN

A recent study from IIT Kharagpur called "Anthropogenic forcing exacerbating the urban heat islands in India" noted that the relatively warmer temperature in urban areas, compared to suburbs, may contain potential health hazards due to heat waves apart from pollution. Arun Chakraborty an author of the study said, "Our research is a detailed and careful analysis of urban heat islands in India. We study the difference between urban and surrounding rural land surface temperatures, across all seasons in 44 major cities from 2001 to 2017." He further said, "For the first time, we have found evidence of mean daytime temperature of surface urban heat island (UHI Intensity) going up to 2 degrees C for most cities, as analysed from satellite temperature measurements in monsoon and post monsoon periods." Other researchers from elsewhere have also noticed similar rise in daytime temperatures in Delhi, Mumbai, Bengaluru, Hyderabad and Chennai.

Understanding urban heat island effect

We know of urban water lakes (as in Bhopal, Hyderabad, Bengaluru or Srinagar) which add pleasure and coolness, but an urban heat island? An urban heat island (abbreviated as UHI) is where the temperature in a densely populated city is as much as 2 degrees higher than suburban or rural areas. Why? This happens because of the materials used for pavements, roads and roofs, such as concrete, asphalt (tar) and bricks, which are opaque, do not transmit light, but have higher heat capacity and thermal conductivity than rural areas, which have more open space, trees and grass. Trees and plants are characterised by their 'evapotranspiration'– a combination of words wherein evaporation involves the movement of water to the surrounding air, and transpiration refers to the movement of water within a plant and the subsequent lot of water through the stomata (pores found on the leaf surface) in its leaves. Grass, plants and trees in the suburbs and rural areas do this. The lack of such evapotranspiration in the city leads to the city experiencing higher temperature than its surroundings.

UHI s also decrease air quality in the cities, thanks to pollution generated by industrial and automobile exhaust, higher extent of particulate matter and greater amounts of dust than in rural areas. Due to this higher temperature in urban areas, the UHI increases the colonisation of species that like warm temperatures, such as lizards and geckos. Insects such as ants are more abundant here than in rural areas; these are referred to as ectotherms. In addition, cities tend to experience heat waves which affect human and animal health, leading to heat cramps, sleep deprivation and increased mortality rates. UHIs also impact nearby water bodies, as warmer water (thanks to the pavements, rooftops and so on) is transferred from the city to drains in sewers, and released into nearby lakes and creeks, thus impairing their water quality.

It is painful to realize that Bengaluru, once known for its salubrious climate, now has UHIs, even in places like Koramandala and Jayanagar. The rapid expansion of buildings, industrial parks and associated high-rise apartments in suburbs, such as Electronic City and Whitefield, has made the city insalubrious (read: <urba-heat-island-effect-report>, prepared by The Energy and Resources Institute, India). Some of its praiseworthy lakes are dirty and diseased. Likewise, when my family and I moved to Hyderabad in 1977, we were told that we do not need air conditioning or even ceiling fans at night. Now, we have UHIs, again due to reckless expansion of industrial parks, factories and associated buildings in what was once a vast suburb, which has now become the third city called Cyberabad. These have not only led to formation of UHI but also the associated pollution due to a drastic reduction in the Air Quality Index (AQI), thanks to the exhausts from industries and automobiles. The 'safe' AQI is thought to be between 61-90 units (when particles from the air enter the human and animal bodies causing discomfort and illness), but in places like Delhi it has gone to very poor-to-dangerous levels of about 323. Fortunately, it is still on the safe side in Hyderabad and Bengaluru, but it is time to take steps to keep it low.

Control of UHIs and mitigation

Industrialisation and economic development are vital to the country, but the control of UHIs and their fallouts are equally vital. Towards this, several methods are being, and can be, tried. One of them is to use greener rooftops, using light-coloured concrete (using limestone aggregates along with asphalt (or tar) making the road surface greyish or even pinkish (as some places in the US have done); these are 50% better than black, since they absorb less heat and reflect more sunlight. Likewise, we should paint rooftops green, and install solar panels there amidst a green background.

The other is to plant as many trees and plants as possible. It is interesting to realise how beneficial trees are to us. The organisation Treepeople lists as many as 22 benefits from trees and plants (see <Tree people .org/tree-benefits>). Relevant to the present context are: they combat climate change; clean the surrounding air by absorbing pollutant gases (N_xO_y, O_3, NH_3, SO_2, and others) and trapping particulates on their leaves and bark; cool the city and the streets; conserve energy (cutting air-conditioning costs by 50%); save water and help prevent water pollution; help prevent soil erosion; protect people and children from UV light; offer economic opportunities; bring diverse group of people together; encourage civic pride by giving neighbourhoods a new identity; mask concrete walls, thus muffling sounds from streets and highways, and eye-soothing canopy of green; and the more a business district has trees, more business follows. So, plant as many trees and plants as you can around and between your buildings, schools, houses and apartment complexes. But, 'token' planting will not do, nurturing them year after year is vital!

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