



## ORIGINAL ARTICLE



# Role of Aerosolized Trichloroisocyanuric acid (TCCA) in the treatment of COVID-19

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## 1 | INTRODUCTION

**HYPOTHESIS:** The nebulization with aerosolized Trichloroisocyanuric acid in COVID-19 patients promotes early recovery and halts the progression of the cytokine storm.

**OVERVIEW** In 2019, novel beta coronavirus, also known as SARS CoV- 2(i), emerged in Wuhan city of China(ii). It is highly contagious and can have profound implications, especially in people with pre-existing co-morbidities. In March 2020, COVID-19 pandemic was declared, and it has affected millions of lives until now. SARS CoV-2 is an RNA virus which enters the human cells through the Angiotensin-converting enzyme two receptors(iii) (ACE 2-Receptor) and multiplies using the RNA dependent RNA polymerase. The mean incubation period is 4-5 days(iv) , and the ones who will become symptomatic will have symptoms by 12 days. However, the majority of patients remain asymptomatic or experience only mild forms of the disease. The infected person

starts shedding the virus one to three days before the onset of symptoms (v), but the duration of the viral shedding remains unclear. The patient presents with a high viral load in the nasopharyngeal swab just before and soon after the onset of symptoms, which fall over the next week. The viral particles are released as droplets when an infected person coughs or sneezes, which spread up to a few meters

and remains viable on the inanimate objects(vi) for variable periods. Therefore, maintaining a distance of at least 2

meters, frequent cleansing of the surfaces and hand sanitization significantly contains the spread of the virus(vii). The detection of viral RNA through the Polymerase Chain Reaction performed on the nasopharyngeal swab confirms the diagnosis(viii). The patient experiencing a mild form of the disease have a fever, sore throat, myalgias and malaise. They can also develop anorexia, nausea, diarrhoea, ageusia and anosmia(ix). Some patients report Shortness of breath 5 to 8 days after the symptom onset, which is a predictor of worsening disease (x). The patients with age > 65, cardiovascular disease, lung disease, diabetes and obesity are at more risk of developing complications. The other potential risk factors are immunodeficiency, infection with HIV, chronic kidney disease and chronic liver disease(xi). The severity of clinical presentation outlines the management. Patients with mild disease generally do not require additional evaluation as infection will spontaneously resolve with minimal supportive care and isolation. However, some of these patients may deteriorate and develop dyspnea, tachypnea, hypoxemia and abnormal lung findings and need hospitalization.

**DISCUSSION** Chlorination has been the conventional method for water and surface disinfection

# ROLE OF AEROSOLIZED TRICHLOROISOCYANURICACID (TCCA) IN THE TREATMENT OF COVID-19

since the 1800s as it is practical, accessible and economical. Despite the use of Trichloroisocyanuric acid (TCCA) as a water disinfectant, there is no study in the literature showing its efficacy against SARSCoV2 using nebulization. Our principal aim is to identify if the benefits of aerosolized TCCA disinfectant can be extrapolated to eradicate the SARS CoV-2 virus from the respiratory tract and if it might help curb the transmission of the virus to other people. We observed in a small group of symptomatic patients if they exhibit faster recovery/resolution of symptoms and decrease in viral load as confirmed with RT-PCR on a nasopharyngeal swab, when commenced on the aerosolized (TCCA) in addition to the recommended standard of care as outlined by 3WHO xii and 4MOHFW, India(xiii) (xiv). These patients were either RT-PCR5 positive for SARS CoV2 or had CT findings highly suggestive of coronavirus disease. Since chlorine inhalation can be toxic at higher concentrations, we administered a minimal concentration of 1-2 ppm to see if the disinfectant properties can be productive while avoiding airway injury. We hypothesize that the nebulization with aerosolized Trichloroisocyanuric acid in COVID-19 patients promotes early resolution of symptoms and prevents or halts the progression of an aggressive cytokine storm, which is the leading cause of complications in these patients. However, this hypothesis needs corroboration with a more intense double-blinded randomized clinical trial.

## 2 | REVIEW OF LITERATURE

### 1. CHLORINATION (XV)

Chlorination is the method of adding chlorine to the drinking water to kill germs and disinfect it. The

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agents used to achieve safe chlorine levels in the water are sodium hypochlorite, calcium hypochlorite, Trichloroisocyanuric acid

(TCCA) and compressed elemental gas. While the higher concentrations of these agents can be harmful, but when they are added to water and diluted to lower concentrations, they are enough to kill germs but safe to drink. According to

Centre of Disease Control and Prevention (CDC) guidelines, the Chlorine levels up to 4 milligrams per litre (mg/L or

four parts per million (ppm) are considered safe in drinking water, and no harmful effects are likely to occur.

### 2. CHLORINE GAS INHALATION (XVI)

The human exposures to chlorine at toxic levels are generally accidental, short term but high concentration, like in transportation accidents and industrial operations. By contrast, workplace and public exposures are more frequently due to long term exposures with low chlorine concentrations, occasionally associated with transient increases.

#### *Dose-dependent effects of chlorine inhalation(xvii, xviii)*

0.1-0.3 ppm	Chlorine odour detection
1-3 ppm	Mild mucous membrane irritation; tolerable for 1 hour
5-15ppm	Moderate mucus membrane irritation
30 ppm	Substernal chest pain, Shortness of breath and cough
40-60 ppm	Toxic pneumonitis and pulmonary oedema
400 ppm	Fatal over 30 minutes
1000 ppm and above	Fatal within few minutes

\* High-level exposures of chlorine gas can cause asphyxia with respiratory failure, pulmonary oedema, acute pulmonary hypertension, pulmonary vascular congestion, cardiomegaly, burns of upper and lower airways, and death.

### OCCUPATIONAL EXPOSURE LIMITS FOR CHLORINE GAS(xix) :

- Threshold Limit Value – Time-Weighted Average (TLV-TWA): 1 ppm
- Threshold Limit Value – Short-term exposure (TLV-STEL): 3 ppm
- American Industrial Hygiene Association- Emergency Response Planning Guidelines (AIHA ERPG-2) - 3 ppm

**3 | MATERIAL & METHODS:**

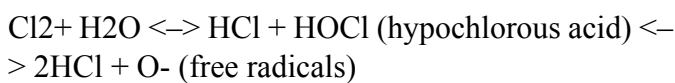
**1. Disinfectant:** Trichloroisocyanuric acid (TCCA) granules(xx).

TCCA is a commonly available commercial agent used in the disinfection of swimming pools, drinking water, industrial

or city sewage, dishware, houses/hotels/ public places, livestock and poultry feeding places, fruits and vegetables

disinfection & preservation and for disease control in hospitals. It is available with 90 per cent chlorine concentration.

The hydrolysis of TCCA leads to the production of hypochlorous acid, which is an oxidizing agent and disrupts the proteins, lipids and DNA framework of the microorganisms and kills them. The chemical reaction is as follows:



The byproduct cyanuric acid is a chlorine stabilizer which binds to chlorine and releases it at a slower rate and

increases the time taken to deplete each dose. The concentration of 1-4 ppm in the water at a pH of 7.2-7.6 is essential for the optimum disinfection of water. The chlorine concentration can be measured using the readily available chlorine testing kits. Some chlorine reacts with impurities and is not available for action against microbes; this is called combined chlorine. The remaining chlorine is called free chlorine and is the active agent against germs.(xxi, xxii)

Total Chlorine = Free Chlorine + Combined Chlorine

**2. Chlorine Testing kit:** Chlorine levels in water can be detected by the commonly available chlorine measuring equipment.

**3. Nebulizer:** The patients were demonstrated with the technique of assembling the parts and using the nebulizer. They were advised to nebulize with the formulation for 5 minutes, four-five times a day, with an interval of 3-4 hours

between doses. This was continued for 4-5 days with a maximum of 7 days.

**4. RT-PCR for SARS CoV2:**Reverse Transcriptase

Polymerase chain reaction (RT-PCR) targets the specific segments of viral genetic material and makes thousands of copies to assess if the virus is present qualitatively. This test only detects active infection and has

low sensitivity, which means it can give high false negatives(xxiii). The possible reasons could be sub-optimal sampling techniques, variations in viral load and manufacturer test kit sensitivity.

**5. CT Scan:**The radiological findings become more confluent and bilateral with the progression of the disease. There is a

preponderance of ground-glass opacity in the early disease, followed by the development of crazy paving and

consolidation later in the disease course.

• COVID-19 Reporting and Data System (CO-RADS ) CLASSIFICATION(xxiv)

It provides a five-point categorical assessment for chest CT in patients under suspicion for COVID-19.

CO-RADS 3 or

more requires confirmatory COVID-19 testing with RT-PCR(xxv).

	Level of Suspicion	CT Findings
CO-RADS 1	No	Normal/ Non- infectious
CO-RADS 2	Low	Infections other than COVID-19
CO-RADS 3	Intermediate	Unclear whether COVID-19 Is present
CO-RADS 4	High	Suspicious for COVID-19
CO-RADS 5	Very High	Typical for COVID-19

• Chest CT Score- This score uses opacification of the lung as a surrogate for the extension of lung disease. Score >18 is highly predictive of patient mortality in short term follow-up.(xxvi, xxvii)

**PREPARATION of Aerosolized Trichloroisocyanuric acid:**The solution is prepared by mixing TCCA granules in water and titrated to formulate the concentration of 1 – 2 PPM, which is measured by a chlorine Testing kits.

**ADMINISTRATION**Aerosolized TCCA is administered through a nebulizer for 5 minutes, four-five times a day, with an interval of 3-

4 hours between doses. It should be given for 4-5 days for the successful eradication of the virus from the airways,

with a maximum duration of 7 days to avoid any irreversible mucosal damage.

## ROLE OF AEROSOLIZED TRICHLOROISOCYANURICACID (TCCA) IN THE TREATMENT OF COVID-19

**CASES:** This is a pilot study conducted on ten COVID-19 subjects, to determine the efficacy and safety profile of aerosolized TCCA in treatment of COVID-19. The therapy with aerosolized TCCA was initiated after taking informed consents from the participants. The patients were administered aerosolized Trichloroisocyanuric acid along with the recommended standard of care as outlined by the World Health Organization and Ministry of Health and Family Welfare (xxviii). The details are as follows:

### CHEST CT FINDINGS

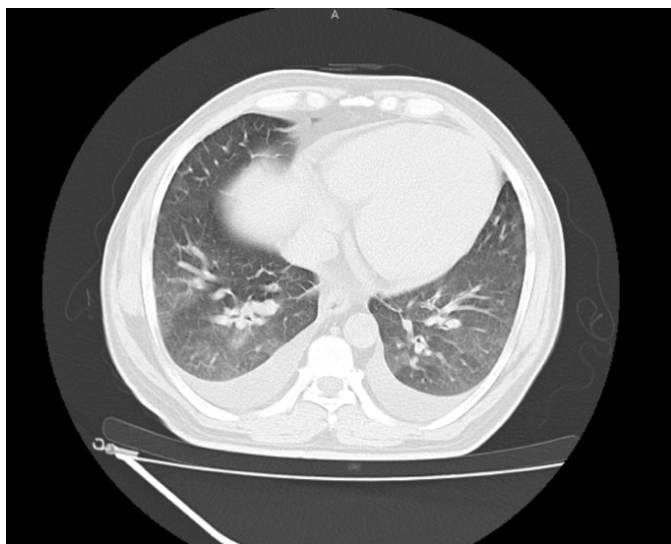


Image Courtesy: 5c Network | Vardhman CT Scan Center

**CASE ID #7A** 52-year-old male presents with complaints of fever, cough, chest pain and Shortness of breath two days and loss of taste for one day.

**CT FINDINGS:** Mild bilateral pleural effusion seen. Multiple patchy ground-glass areas are seen in both lower lobe and both upper lobe of lungs with septal thickening in bilateral lungs.

CO-RADS 3

CT Score- 13/40

**CASE ID #9A** 50-year-old male presents with complaints of fever, cough for ten days. He developed chest pain and Shortness of breath one day back despite his ongoing treatment at the district hospital, because of which he came to our facility.

**CT FINDINGS:** Peripheral subpleural Patchy areas

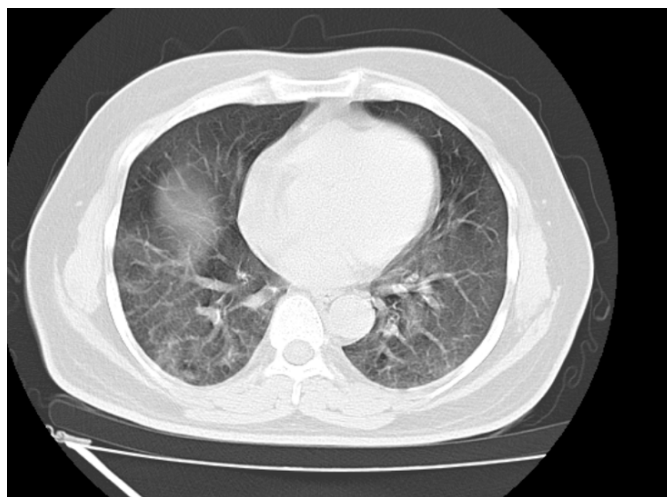


Image Courtesy: 5c Network | Vardhman CT Scan Center

of Ground

Glass opacifications involving multiple segments of bilateral lung fields. - Viral Pneumonia

CO-RADS-5

CT Score- 20/40

**RT-PCR for SARS CoV 2 -POSITIVE**

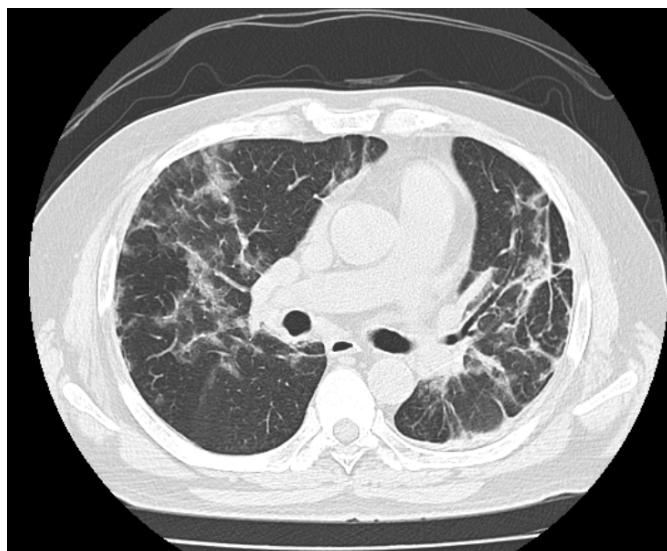


Image Courtesy: 5c Network | Vardhman CT Scan Center

**CASE ID #10A** 62-year-old male presents with complaints of fever for ten days and chest pain and Shortness of breath for two days. The patient was diagnosed with low platelets -92,000, 7days back, which was managed at a different facility. Sp02



CASE ID	Age/sex	Chief complaint	Antigen Positive date	Tt Onset Date	Adverse events	Antigen negative date	CT Scan
#1	28Y/M	Fatigue fever and cough on 10th Sep Symptoms relieved within three days of Tt	12 <sup>th</sup> Sep	12 <sup>th</sup> Sep	none	15 <sup>th</sup> Sep	-
#2	26 Y/ F	Body ache and fever on 11th Sep Symptoms relieved within three days of Tt	12 <sup>th</sup> Sep	12 <sup>th</sup> Sep	none	19 <sup>th</sup> Sep	-
#3	7 Y/ F	Asymptomatic; DX through contact tracing	12 <sup>th</sup> Sep	12 <sup>th</sup> Sep	none	15 <sup>th</sup> Sep	-
#4	5 Y/ M	Asymptomatic; DX through contact tracing. The child developed chest pain on 16 <sup>th</sup> Sep when a CT scan was done.	15 <sup>th</sup> Sep	15 <sup>th</sup> Sep	none	19 <sup>th</sup> Sep	WNL (16 <sup>th</sup> Sep)
#5	50 Y/ M	Fever- 1 <sup>st</sup> Sep Weakness/body ache/chest pain- 7 <sup>th</sup> Sep Symptoms relieved within four days of Tt	10 <sup>th</sup> Sep	10 <sup>th</sup> Sep	none	16 <sup>th</sup> Sep	
#6	52 Y/M	Fever and Shortness of breath- 8 <sup>th</sup> Sep Loss of taste – 10 <sup>th</sup> Sep Diagnosis based on symptoms and high suspicion for COVID 19 and CT Scan findings. Symptoms resolved within four days of treatment.	-	10 <sup>th</sup> Sep	none	-	10 <sup>sep</sup> CO-RADS 3 CT Score- 13/40
#7	61 / M	Fever and loss of taste-11th sep Shortness of breath- 14 <sup>th</sup> sep Diagnosis based on symptoms and high suspicion for COVID	-	14 <sup>th</sup> Sep	none	-	14 <sup>th</sup> Sep CO-RADS 5 CT Score- 12/25

measured at presentation = 92 %.

**PMH-** Coronary artery disease

**CT FINDINGS:** Diffuse ground-glass opacities with Patchy fibrosis with traction bronchiectasis is seen in the right middle lobe and the posterobasal segment of the left lower lobe. Fibrotic patches are also seen in the left upper lobe, lingular segments, right middle lobe and right lower lobe.

CO-RADS-5

CT Score- 20/40

#### RT-PCR for SARS CoV 2 - POSITIVE

The above three CT Scans demonstrate diffuse lung involvement in patients with COVID-19. The most common pattern identified is the presence of ground-glass opacities. A CT Score can be established based on the percentage of lung involvement, and higher CT Scores are associated with increased mortality in the short-term follow-up. RT-PCR of the nasopharyngeal swab can diagnose most patients with

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		19 and CT Scan findings. Symptoms relieved with three days of Tt					
#8	44Y / M	Fever and body ache Sep5 <sup>th</sup> Loss of taste and smell on Sep8 <sup>th</sup> Symptoms relieved within two days of Tt	14 <sup>th</sup> Sep	14 <sup>th</sup> Sep	none	21st Sep	14 <sup>th</sup> Sep CO-RADS 5 CT Score- 9/25
#9	50Y/ M	Fever [103-104]- 4 <sup>th</sup> Sep Chest pain and Shortness of breath- 9 <sup>th</sup> Sep Symptoms resolved by four days of treatment.	7 <sup>TH</sup> SEP	10 <sup>th</sup> SEP	none	19 <sup>TH</sup> SEP	10 <sup>SEP</sup> sep CO-RADS-5 CT Score- 20/40
#10	62Y/ M	Fever and fatigue -10 days Shortness of breath for two days with SpO2- 92% Symptoms resolved four days of treatment	3rd Oct	5 <sup>th</sup> oct	none	8 <sup>th</sup> Oct	5 <sup>th</sup> Oct CO-RADS-5 CT Score- 20/40

COVID-19, but it has a high false-negative rate due to the test’s low sensitivity. In that case, diagnosis can be made by repeat testing or based on CT findings in patients with high suspicion for coronavirus disease(xxix).

**MANAGEMENT**

Five patients presented with mild symptoms of fever, cough, fatigue and loss of taste, while five had more severe symptoms of chest pain and Shortness of breath. With the present circumstances, we kept a low threshold for suspecting COVID-19. At all times, an appropriate distance was maintained, and the use of personal protective equipment was employed while evaluating these patients. The patients underwent RT-PCR testing at District Hospital, Etah, and those with dyspnea also underwent a CT Scan to assess the degree of lung involvement. The disease severity was evaluated on the parameters outlined by the National Institute of Health(xxx) Mild cases of COVID-19 were advised strict home isolation(xxxi) along with aerosolized TCCA6 and supportive care(xxxii). Moderate to severe cases of COVID-19 who pre-

sented with chest pain and Shortness of breath underwent CT Scan imaging of the chest in addition to RT-PCR and other necessary investigations(xxxiii). They were initially stabilized with supplemental oxygen as needed and provided the standard of care(xxxiv) followed by discharge with instructions on home isolation, nebulization with aerosolized TCCA and supportive care. The follow up was determined based on disease severity, where mild cases were followed up after a week, and moderate-severe cases were followed up after three days and seven days. The patients underwent repeat RT-PCR testing at the district hospital7 and the reports evaluated on the next visit. In addition to the administration of aerosolized TCCA, patients were advised to use the incentive spirometer for improvement in lung compliance(xxxv), especially in patients with diffuse lung parenchymal involvement.

**RECOVERY:**

The patients reported relief in symptoms within 24-48 hours, and complete resolution within three to four days of

commencement of aerosolized TCCA; however, most patients still reported fatigue even in the absence of other symptoms like fever, cough, Shortness of breath and chest pain. The patients with severe symptoms like chest pain and Shortness of breath did not progress into complications like Acute Respiratory Distress Syndrome/ Acute Respiratory failure/ Septic shock during this treatment. None of the patients developed any adverse effects which could be attributed to mucosal irritation expected during chlorine inhalation like runny nose and sore throat. The patients who had progressed to later stages with diffuse lung parenchymal involvement do not show an immediate reversal in the CT scan findings, especially the ones with fibrosis and calcifications.

#### 4 | CONCLUSION:

The COVID-19 patients nebulized with Trichloroiso-cyanuric acid at a minimal concentration of 1-2 ppm along with the standard treatment as outlined by WHO and MOHFW, demonstrated faster recovery as compared to the global and national standard and did not suffer from complications due to the cytokine storm. The hypothesis is a potential domain for research and needs further corroboration, substantiation, and establishment by standardized randomized, double-blinded clinical trials. (1–35)

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