

COVID-19 Patient with Multifocal Pneumonia and Respiratory Difficulty Resolved Quickly: Possible Antiviral and Anti-Inflammatory Benefits of Quercinex (Nebulized Quercetin-NAC) as Adjuvant

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Abstract

Background: SARS-CoV-2 (COVID-19) is a viral pandemic with no current vaccine or effective treatment. Hydroxychloroquine and azithromycin are not without cardiovascular risk or complications, and these treatments can fail to aid in full recovery from COVID-19. As new treatments become approved for the pandemic, an inexpensive, non-toxic, and safe adjunctive therapy is needed. **Case Presentation:** A 59-year-old male presented with respiratory symptoms. Chest X-ray revealed classic indications of COVID-19 pneumonia. A PCR nasopharyngeal swab test confirmed a COVID-19 infection and hospital doctors prescribed Rocephin, azithromycin, and hydroxychloroquine. The patient was then prescribed Quercinex, a nebulized formula of quercetin-(cyclo-dextrin) (20 mg/mL) and N-acetylcysteine (100 mg/mL) three times daily for 14 days by physicians at Envita Medical Center for continued COVID-19 respiratory symptoms. Following 30 minutes after each nebulization treatment, the patient experienced immediate deep breathing relief that lasted for multiple hours. Within the following 48 hours after the first treatment, respiratory symptoms continued to diminish and resolve quickly. Finally, post-treatment follow-up chest X-rays revealed no pulmonary fibrosis (scarring) and clear lung fields. **Conclusion:** The Quercinex formula appeared to greatly alleviate the unresolved respiratory symptoms rapidly. Several mechanisms of the formula, namely antiviral and anti-inflammatory action, with direct administration via nebulizer to the deep lung tissue, could potentially explain the fast and complete recovery. We recommend that the Quercinex formula

be considered for further clinical study as an adjuvant or on its own for COVID-19 and possibly other viral pulmonary conditions.

Keywords

Quercetin, N-Acetylcysteine (NAC), SARS-CoV-2 (COVID-19), Quercinex, Envita, Zinc, Pneumonia, Case Study, Severe Acute Respiratory Syndrome, Flavonoid, Lung, Antiviral, Human

1. Background

COVID-19 is a viral pandemic that desperately needs effective clinical treatment to confront this global crisis. Currently, no vaccine exists to effectively combat this virus and treatments are widely ineffective with potentially hazardous side effects. The FDA has recommended that hydroxychloroquine only be used in a hospital setting because of potential heart rhythm problems [1]. Also, studies have suggested that azithromycin can increase the risk of cardiovascular death [2]. Furthermore, drugs like Remdesivir may show promise for the treatment of COVID-19, but they are expensive and unavailable to many. Finally, the hopes of a successful vaccination look slim with issues like vaccine immunity, patient reinfection, and the many failed attempts to create vaccines for similar viruses. The unique conditions of this pandemic make finding a cheap, effective, and non-toxic treatment for COVID-19 of high importance.

Quercinex is a nebulizer treatment consisting of a formula with quercetin and NAC as its active ingredients. Quercetin and N-acetylcysteine (NAC) are considered generally safe for human consumption, either as a food ingredient in the case of quercetin or as a medicine [3] [4] [5]. Quercetin also has a dietary monograph and is in category 1 of FDA guidance to 503A compounds [3]. Quercetin is the primary antiviral component of the patented Quercinex formula. Along with antiviral action [6] [7], peer-reviewed research has identified potential anti-inflammatory [8] [9] and antioxidant actions [10] as well. Research studies have observed quercetin to demonstrate activity against herpes simplex virus, polio, respiratory syncytial virus, parainfluenza, MERS, and certain other retroviruses [11]. In cell cultures, quercetin has been shown by research to impede viral replication and reduce the infectivity of viruses, possibly through the mechanism of binding to viral capsid proteins, induction of interferon, or inhibition of DNA gyrase and DNA proteases [11]. Also, quercetin has anti-inflammatory properties that could be relevant in preventing the type of lung scarring seen in severe COVID-19 infections [9]. Potential adverse reactions from quercetin include tingling of extremities and headache for oral use; and flushing, sweating, nausea, vomiting, and injection site pain after infusion for IV [12]. With IV infusions > 945 mg/m² Nephrotoxicity can occur [12]. Caution is advised for patients with renal impairment and liver dysfunction [12]. Due to a

lack of data, quercetin should not be used during lactation or pregnancy [12].

NAC is an FDA approved agent used for the treatment of acetaminophen overdose and to loosen thick mucus in individuals with cystic fibrosis or chronic obstructive pulmonary disease [4] [5] [13]. It can be taken intravenously, by mouth, or inhaled as a mist [13]. NAC has been correlated with many different anti-inflammatory [14], antioxidant [8] [9] [15], and antiviral properties [16] [17]. Reported side effects from NAC include diarrhea, nausea, vomiting and rash with or without fever [18].

Cyclodextrin is a non-active ingredient in Quercinex. Cyclodextrin is currently used in intravenous drug preparations approved by the FDA, such as Cardio Tec used for Myocardial imaging or Pazeo for ophthalmic applications [19]. Cyclodextrins have been well studied and shown to increase the solubility of poorly soluble drugs as well as to increase their stability and bioavailability [19].

Envita Medical Center has many years of experience using both Quercetin and NAC separately. Quercetin has been compounded for IV use and nebulized for the adjunctive treatment of cancer patients at Envita Medical Center. Envita's doctors have performed thousands of treatments using quercetin with no serious adverse effects. To date, Envita Medical Center has also conducted over 600 nebulized Quercinex treatments safely. Quercinex was prescribed by Envita's doctors (via 503A compounded pharmacy prescriptions) as an adjuvant to the current standard of care recommendations for COVID-19. Quercinex has been observed by Envita's Doctors to be clinically safe and non-toxic with a proposed mechanism that could enhance other drug regimens or to act on its own to improve clinical outcomes significantly.

2. Case History

A 59-year-old male called into Envita Medical Center (Scottsdale, AZ) on 3/23/2020 utilizing our telemedicine system for the reduction of exposure of symptomatic patients. He reported that after returning from New York while on business, he was experiencing symptoms of high fever, chills, cough, general malaise, and fatigue, beginning from six days prior on Tuesday, March 17th. He reported that his symptoms progressively worsened over time, and on 03/23/2020 began to experience shortness of breath and increased fatigue. It is important to note that the patient did not commonly have a medical history of asthma, pneumonia, Chronic obstructive pulmonary disease (COPD), or any other pulmonary conditions. Sociodemographic and clinical characteristics of the patient can be viewed in (Table 1).

He was referred immediately to the emergency department for imaging, evaluation, and COVID-19 screening. Upon arrival at the nearest hospital, Honor Health Shea (Scottsdale, AZ), a full workup was performed, which included chest X-rays (Figure 1), COVID-19 screening, CBC with diff and platelets, and CMP. The patient was admitted to a full contact and droplet isolation room. The chest X-ray (Figure 1) revealed patchy opacities in the periphery of both lungs

Table 1. Patient sociodemographic and clinical characteristics.

Sociodemographic Characteristics	
Age	59
Gender	Male
Marital Status	Married
Occupation	
Education Level	
Income	\$100,000+
Clinical Characteristics	
Intake Vitals	03/23/2020
spO2	~94%
BP	126/76
HR	78 bpm
Temp	99.1°F
Discharge Vitals	03/26/2020
spO2	~95%
BP	109/64
HR	74 bpm
Temp	97.7°F

**Figure 1.** 03/23/2020 Patchy opacities in the periphery of both lungs, diagnosed with multifocal pneumonia.

and the patient was diagnosed with multifocal pneumonia. The patient was positive for COVID-19, which was the attributed cause of the bilateral, multifocal pneumonia. He also was diagnosed with hyponatremia, hypokalemia, shortness

of breath, generalized weakness, and myalgia. Vitals were recorded as follows: spO_2 –94%, Bp 126/76, HR 78 bpm, Temp 99.1°F. He was seen under the care of an ID (infectious diseases) and prescribed 1 g Rocephin IV push, acetaminophen 650 mg tablet, azithromycin 500 mg oral once daily, and hydroxychloroquine 400 mg oral twice on day one and then 200 mg oral twice daily thereafter.

The patient was discharged from the hospital 3/26/20 and given home quarantine instructions as per CDC guidelines. He was asked to continue azithromycin 500 mg and Hydroxychloroquine 200 mg twice a day. The patient began to stabilize (the patient reported that he experienced an improvement in the hospital but maintained a sensation of drowning when breathing and continued shortness of breath). Discharge vitals: spO_2 -95%, Bp 109/64, HR 74 bpm, Temp. 97.7°F. At home, he explained that he felt as though he was only able to use about 60% of his breathing capacity and difficulty taking deep breaths. Discharge X-rays (**Figure 2**) showed continued evidence of patchy opacities in the periphery of both lungs and the persistence of multifocal pneumonia. He was prescribed and began the Envita Medical Center COVID-19 adjuvant protocol, Quercinex. The patient began nebulizing the quercetin and N-acetylcysteine formula in an open-air space.

3. Case Management and Protocols

The patient was prescribed Quercinex: 1 mL of quercetin (20 mg/mL) and 1 mL NAC (100 mg/mL), 3 times daily via nebulization by Envita Medical Center. The prescription was prepared by a 503A custom compounding pharmacy that has extensive experience with this formula. The patient completed a hospital prescribed protocol of Azithromycin and Hydroxychloroquine while undergoing

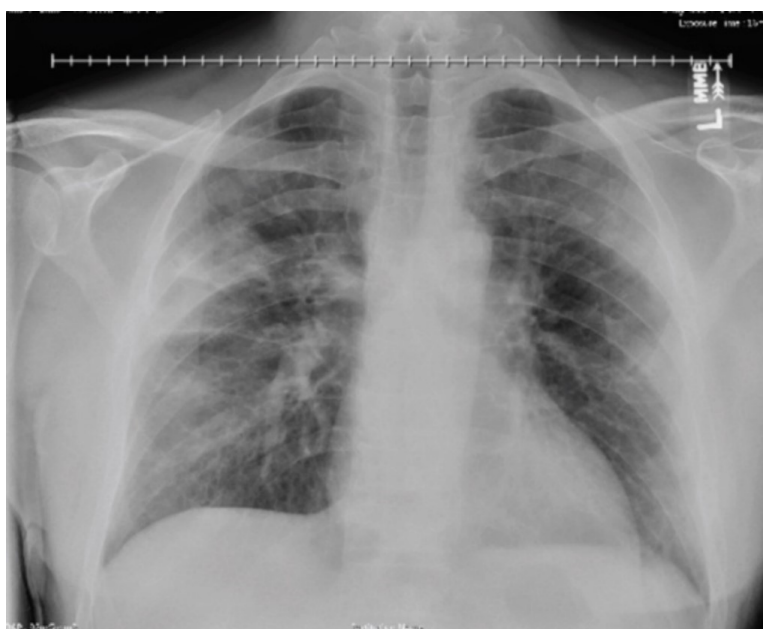


Figure 2. 03/26/2020 Unresolved patchy opacities in the periphery of both lungs, multifocal pneumonia persists after leaving the hospital.

nebulized Quercenix treatment three times a day for 14 days as adjuvant therapy.

Nebulizer: Quercinex Adjuvant Protocol

Quercetin (20 mg/mL), NAC (100 mg/mL) formula

Sig: Nebulize 1 mL Quercetin (200 mg/mL) and 1 mL NAC (100 mg/mL) to be combined in a nebulizer reservoir and breathing treatment done in full mask nebulization three times per day. To be nebulized in open-air three times daily, morning, noon, and evening.

Courier to home for drop off: 1 nebulizer, 4 vial Quercetin 20 mg/mL, 1 vial NAC 100 mg/mL. ***Provide enough needles, syringes, and alcohol swabs for a 14-day supply. ***

Oral Adjuvant:

Quercetin

Quercetin 400 mg per capsule

Sig: 3 caps twice daily by mouth

Zinc

30 - 50 mg of any form of zinc once daily by mouth to prevent from Zinc deficiency. Both hydroxychloroquine and quercetin utilize zinc as a possible mechanism of action against viral invasion.

4. Results & Responses to Treatment

Patient Response: COVID-19 positive Multifocal Pneumonia

It was not until the patient began the nebulizer protocol of Quercinex that he reports he was able to breathe far deeper and overall better. The shortness of breath and drowning sensation greatly improved within 30 min of each treatment, and the recovery would last for three or more hours; we consider this to be a notable and beneficial response. After each therapeutic nebulizer treatment, within 30 min of finishing the treatment, the patient reported that his breathing was much deeper and improved directly related to treatment. After starting the protocol, the patient felt that his recovery was much faster and directly attributed his recovery to breathing nebulized Quercinex. The protocol was associated with a self-reported significant improvement in breathing, and this improvement was noticeable after each subsequent nebulization treatment. After two days of Quercinex treatment, the patient reported that his lung function continued to significantly improve.

As an additional detail, within the first two days of the nebulizer treatment, the patient had improved so greatly that he reported being able and inclined to build a gym in his garage. At this time, the patient started moving about with more energy and improved breathing. After finishing the protocol, the patient has not reported any sensation of shortness of breath since. All symptoms appear to be entirely resolved, and the patient has resumed his cardiovascular exercise with no complaints. No adverse event was reported, but the patient stated that he had increased expectorant of mucus and sneezing after the first two treatments. The patient follow-up included a chest X-rays completed on 4/24/20

(**Figure 3**) revealed the following evidence of recovery from the infection: Clear lung fields bilaterally, no effusions, normal heart size, and no skeletal abnormalities. No active cardiopulmonary abnormalities. It is important to note that no pulmonary fibrosis was seen in the patient's lungs post COVID-19 bilateral pneumonia treatment with Quercinex when compared with pre-Quercinex treatment (**Figure 4**).

5. Discussion

This case history is representative of the current clinical environment and the



Figure 3. 04/24/2020 Post Quercinex Treatment Follow up Imaging—Clear lung fields bilaterally, no effusions, normal heart size, and no skeletal abnormalities. no pulmonary fibrosis (scarring).

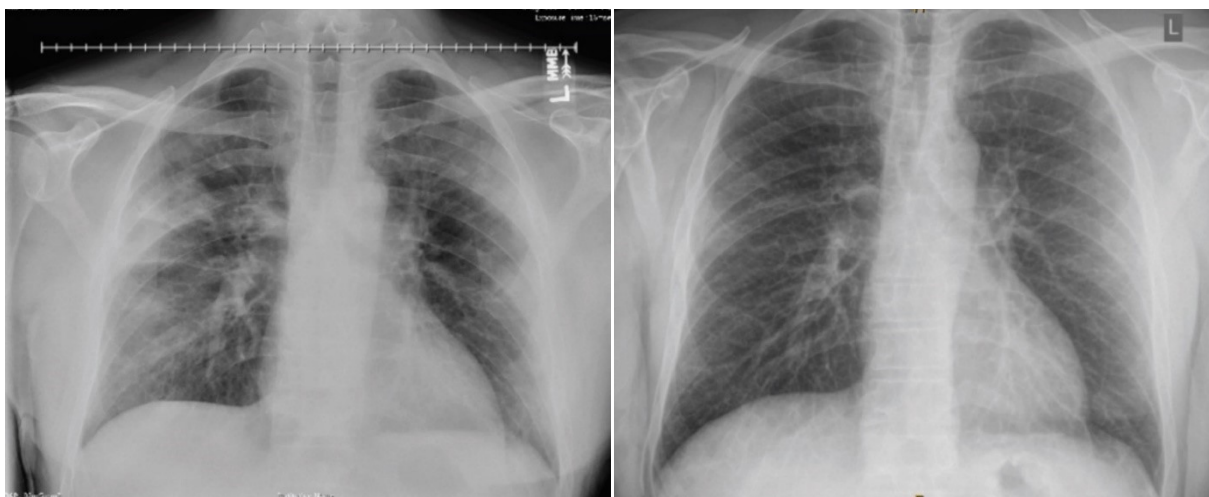


Figure 4. Side-by-side comparison of before and after chest x-rays following Quercinex protocol. 03/26/2020 on Left, 04/24/2020 on Right.

medical cases that are likely to be seen going forward with COVID-19. We wanted to share this important clinical outcome with nebulized Quercinex. The current pandemic requires bold action and the rapid implementation of practical clinical solutions, including those of symptom management in lieu of a vaccine which will not likely be available until near the end of 2021 at the earliest. Managing symptoms of upper respiratory viral infections early is critical, both for patient outcomes and sparing healthcare resources for sicker patients. Quercinex is an inexpensive, safe, and non-toxic nebulization formula that has shown promise from our clinical experience and warrants further investigation.

Envita Medical Center put together the Quercinex formula after many years of observing the effects of nebulized and intravenous quercetin and NAC separately. Quercetin is non-toxic and has well defined antiviral properties [11] [20]. In the case of the patient mentioned in this study, the decision was made to administer treatment at home because of ease of use and conscious decision not to expose any of our high-risk cancer and chronic disease patients to possible COVID-19 contagion in clinic.

In this case study, we have seen an unusual and unexpected benefit from the patient infected with COVID-19. The patient appeared to recover rapidly from respiratory symptoms (difficult/painful breathing, drowning sensation, shards of glass sensation in the lungs while breathing, shortness of breath, tightness in the lungs and restricted breathing) within the first two treatments. The symptoms rapidly decreased until most of the breathing problems had been greatly resolved within the first 48 hours after beginning the Quercinex protocol. The rapid clinical improvement in this case may suggest a helpful clinical adjuvant via nebulization if the treatment is performed in an open-air environment, conscious of the risk of corona virus spreading through nebulized particles.

Noteworthy to reiterate is that symptom improvement was reported 30 minutes directly after each nebulizer treatment, further signifying Quercinex's potential adjuvant benefits. The treatment is directly administered to the lungs where the ACE2 receptors on Type II pneumocytes are located and the Coronavirus spike proteins favor infiltration, invasion and, replication within the respiratory system [21]. The nebulized mist of the Quercinex potentially blocks the invasion of the virus with a non-toxic and safe adjuvant antiviral therapy directly to the respiratory tissue under attack, and for this reason we feel it to be clinically relevant for care during this crisis, and more importantly, for future research. It is promising that the formula appears to be effective and that the reported fast symptomatic relief is linked directly to nebulization of Quercinex.

Potential complications from this Quercinex protocol include copper deficiency via zinc supplementation [22] [23], and safety precautions involving patients with liver dysfunction and renal impairment from quercetin [12]. All other possible side effects are considered mild. Despite these precautions, peer-reviewed literature considers quercetin to be generally well-tolerated [12]. In human studies, no adverse effects on blood parameters of liver and kidney function, hema-

tology, or serum electrolytes were found in doses up to 1000 mg/day for several months [20]. Also, the levels of zinc used in this protocol are not high enough to suspect copper deficiency [23]. All the agents in this protocol are substances that are considered generally safe at these doses. He leads us to believe that for doses used in this protocol, the potential for complications is extremely low, and no further complications are anticipated.

Both Quercetin and NAC have been nebulized separately and administered to patients at Envita Medical Center over several years. We are publishing this case study now to illuminate the effect the combined formula has had on a confirmed case of COVID-19. After the notable reversal of symptoms soon after administration and the fact that the patient fully recovered from respiratory symptoms quickly and without any lung scarring, we believe that this Quercinex formula warrants further investigation for its potential benefits in symptom management for the current health crisis and potentially other viral lung infections as well. The inexpensiveness and ease of production of both quercetin and NAC lends itself to potential widescale distribution if the formula is found to be effective in other large-scale studies. Currently the formula can be ordered by prescription via compounding pharmacies. The non-toxic, inexpensive and safe nature of the agent warrants its consideration as adjuvant treatment for COVID-19 respiratory symptoms.

Availability of Data and Material

All available information is contained within the manuscript.

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Author Contributions

DP and JO have full access to all the patient's records and data for these case histories and accept full responsibility for the integrity and accuracy of the data as presented.

Consent for Publication

Written informed consent was obtained for the treatment and the right to publish the data in accordance with patient protection and HIPPA of this case studies and any accompanying images. A copy of the written consent is available for review by the Editor of this journal.

Conflict of Interest

On behalf of all authors, Dino Prato NMD is founder and CEO of Envita Medical Centers and Developer of Quercinex formulation.

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