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Diabetes & its Complications

Quercetin for COVID19?

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ABSTRACT

An 18-year-old male asthmatic had symptoms of COVID19, not his usual asthma, although PCR and antibody testing were negative. He responded dramatically to quercetin. Quercetin may be useful for treatment of COVID19, and perhaps even prophylaxis.

Keywords

COVID19, Asthma, Prednisone.

Case Report

An 18 yr old white male asthmatic presented with 2 weeks of diarrhea, crampy abdominal pain, and anterior chest pain on 10 April 2020. His asthma began at age 4. Until the age of 10, it had been controlled with inhalers only. At the age of 10, he required oral Prednisone for the next two years.

He was begun on 60 mg/day Prednisone but developed nausea and a severe cough on 12 April. He began using his albuterol rescue inhaler. On 13 April, his Prednisone was tapered to 40 mg/day according to a standard protocol. On 14 April, he experienced acute shortness of breath, and Prednisone was raised to 60 mg/day. On 15 April, the Prednisone dose was raised again to 80 mg/day for increased dyspnea, inability to sleep, and worse cough. On 16 April, the patient felt worse, with new burning and pressure in his chest which he had never experienced before. He described the pressure and chest heaviness as feeling squeezed between two walls. His breathing felt labored. Prednisone was raised to 120 mg/day. Around this time he had decreased taste; he had to add more seasoning to his food. This had never happened before.

On 17 April, the patient continued to have severe chest pain, and was taking acetaminophen every 3 hrs for fever, chills, and nausea, up from every 4 hrs the day before. He never experienced fever with any asthma attack before.

He finally felt better on 18 April. On Sunday, 19 April, his Prednisone dose was divided in thirds (40 mg every 8 hours) unbeknownst to his physician (DWM). The patient's breathing deteriorated that day, 19 April, requiring nebulizer treatments every 4 hours. He felt better on the morning of Monday 20 April, but during the day, while still taking Prednisone 40 mg three times a day, his breathing significantly worsened between 2 pm and 11 pm. His chest burned intensely with each breath. His parents took him to the ER, but because he was afebrile, he was refused admission. Pulse oximetry at a nearby fire station showed 100% oxygen saturation; his BP was 150/96. He took 9 breathing treatments during the afternoon and evening of 20 April, more than twice his usual number.

He took his first dose of quercetin (1 g orally) on the afternoon of 20 April. On 21 April, he resumed 120 mg Prednisone all at once in the morning, and his quercetin dose was increased to 1 gram twice a day. His breathing improved as the day progressed, for the first time since 10 April. Until then, his breathing had only worsened in the evening. His Prednisone was halved on successive days and he was weaned off completely on 27 April. His only side effect was acne on his face and back. He continues to feel 100% back to normal as of 9 May. His quercetin dose was kept at 1 g twice a day for an extra week (27 April- 3 May). On 4 May he decreased his quercetin dose to to 1 g/day.

On 27 April his COVID19 nasal swab test was negative by PCR, as expected a month after symptoms began. Surprisingly, the patient's Abbott serology test, drawn 30 April and performed by

LabCorp, was negative for IgM, IgG, and IgA.

Discussion

The patient's gastrointestinal symptoms (diarrhea, nausea, crampy abdominal pain), fever, dysgeusia, and unusual chest pain (heaviness, pressure, and burning) have been described with COVID19 but had never occurred during the patient's previous 14 years' of asthma. His poor response to Prednisone was also novel. After 8 days, his breathing finally stabilized on high dose Prednisone (120 mg/day). But the effect was precarious, since he rapidly deteriorated when the dose was divided in thirds for the next two days. Only two doses of quercetin, 16 hours apart, improved his breathing for the first time in a month. He recovered fully over the next 48 hours despite rapid tapering of Prednisone, and remains completely asymptomatic on 1 g/d quercetin as of 8 May.

Severe COVID19 symptoms resemble an asthma attack, yet no asthmatics were affected in an early case series from Wuhan, China [1] suggesting that standard asthma treatment can usually prevent worsening of COVID19.

When this patient worsened despite high dose Prednisone, which had managed his asthma before, quercetin was chosen because it is a high affinity (micromolar) inhibitor of the MRGPRX2 receptor [2]. MRGPRX2 is a recently described receptor located uniquely on the mast cell [3-5]. Mast cells are present in the lung and gut. The MRGPRX2 receptor is promiscuous. It is activated by basic secretagogues [6], molecules that combine a strong positive charge with a hydrophobic portion. Viral nucleocapsid proteins contain a strongly positive charge to bind the negatively charged phosphate backbone of the viral nucleic acid, while a hydrophobic segment of amino acids attaches to the viral membrane [7]. Specifically, COVID19 nucleocapsid contains an unusually basic region at amino acid #369-KKDKKKK-#375. SARS-1 contains the same segment at amino acids #370-376.

MRGPRX2 can activate the high affinity IgE receptor, Fc-epsilon-RI, in the absence of pre-formed IgE. IgE signaling in the absence of IgE ensues, with mast cell degranulation and anaphylaxis. The over 200 bioactive molecules released by the mast cell could easily account for the pathology seen in COVID19.

This patient had COVID19 symptoms without seroconverting, like 5-10% of COVID19 patients, especially his age [8,9].

Quercetin, the most common plant flavonoid, is inexpensive and readily available, present in onions, capers, tea, cilantro, apples, etc. It makes flowers yellow. This patient was doing poorly but responded dramatically to quercetin. In the absence of any treatment for COVID19, quercetin should certainly be considered. It may even serve as prophylaxis. In addition, quercetin should be considered for additional viruses whose nucleocapsid proteins are basic secretagogues that could activate the mast cell MRGPRX2 receptor, such as Ebola and dengue, etc.

From the public health point of view, quercetin is ideal. It is safe: the average diet already consists of quercetin 10-15 mg/day, and large doses are well tolerated [10]. It may be the yellow lining in the COVID19 pandemic.

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