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Quercetin Administration in Adult Patients as a Biochemical Potential against Coronavirus Disease 2019 (COVID-19)

Fernando Galeano

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Abstract

To establishing the use of Quercetin as a nutraceutical potential against Coronavirus Disease 2019.Method: This study is a descriptive, prospective longitudinal that included 52 patients treated at the ECOMED-LAMB Clinic from the onset of Covid-19 in our country, March 3, 2020, to January 2021.Results: Were studied 52 patients COVID-19 positive, 20 (38.4

Index terms— clinical benefits, flavonoid, biological therapy.

1 Introduction

t is knows that the COVID-19 is caused by the novel coronavirus SARS-CoV-2, has challenged the health systems and the economy of all countries affected by the pandemic that worldwide until December 2020 has been diagnosed in 93 million individuals and claimed the lives of 2 million people, the most affected countries had been the United States of America, India and at the regional level Brazil (1) with 45% of all cases.

Mortality estimates vary according to the country, and the data reported ranges from less than 0.1% to more than 25% (2); these data have mobilized many researchers in the identification of drugs against this pathology, either as therapeutic or prophylactic for the treatment, or control of viral infection.

In this race against COVID-19, the reuse of numerous drugs has been implemented, with different mechanisms, as well as the use of medication with applications other than antiviral action (3); in this line, some research groups have reported the promising therapeutic effects of hydroxychloroquine or chloroquine, remdesivir (novel antiviral nucleotide analog), lopinavir, and ritonavir against severe COVID-19 (4).

In the fight against diseases and more, when we speak of a pandemic, we have the option of starting a preventive or prophylactic treatment to reduce the incidence or severity of the disease and the public expenditure of the disease (5). However, drug prevention and control are still controversial, without considering the possible adverse effects in some cases, such as hydroxychloroquine or chloroquine (6), then. The use of biochemicals is an alternative that may be imposed in these cases as COVID-19 chemoprophylaxis. Quercetin (3,3?,4?5,7-pentahydroxy flavone) is a plant flavonoid found in various vegetables, leaves, seeds, and grains, where it conjugates with residual sugars to form quercetin glycosides (7) has action known as an antioxidant with anti-inflammatory and antiviral bioactive that acts by inhibiting the entry of viruses and the fusion of viral cells (8) it is know that reduces the pro-inflammatory expression of cytokines and lung inflammation caused by rhinovirus in mouse (9), studies in which Prediction models were applied, it has been seen that quercetin binds to the S protein of SARS-CoV-2 in the host receptor region or to the interface of the human S-ACE2 protein, which interferes with the entrance into the cells of the virus. Cells, this reveals its therapeutic potential (10) and supports the idea that it inhibits infection by the SARS-CoV virus (11). Other authors also found that quercetin combined with vitamin C induces synergistic antiviral and immunomodulatory effects against COVID- **??**9 (12).

The mode of action of vitamin C as an antiviral is supported by the activity of lymphocytes, increasing the production of interferon-?, modulating cytokines, reducing inflammation, improving endothelial dysfunction, and restoring mitochondrial (13) and viricidal function (13)(14).

In this study, we collect scientific evidence of the use of quercetin and vitamin C, vitamin B2B3B5, and ZINC for ATP formation, the use of Copper as an iron stabilizer for the prevention and treatment of the SARS-CoV-2 / COVID-19 Pandemic with the objective of establishing the use of Quercetin as a nutraceutical potential against coronavirus disease 2019 (COVID-19). The association of hospitalization with preventive treatment was not significant (p=0.166); we observed a difference during the hospital stay of the patients (p= 0.084).

2 II.

3 Materials and Methods

A descriptive, prospective work was carried out. Of a total of 75 patients followed up by biweekly or monthly consultation until the disappearance of the clinical and radiological findings in the ECOMED-LAMB Clinic, 52 patients were included in the period from the beginning of Covid-19 in our Country, March 3, 2020, to January 2021.

As inclusion criteria, patients of legal age with a diagnosis confirmed by PCR or symptomatic direct contact with COVID-19 in the period studied was considered, and patients with incomplete data were considered exclusion criteria.

Age, sex, underlying disease, and hospitalization requirement was studied.

Also, the start of treatment before, at, or after the diagnosis of COVID-19 and the time of improvement was specified.

Was made a descriptive analysis of variables using frequency distribution and percentages. To establish possible associations between evolution and biological treatment was used Chi-Square test.

The research ethics committee of the Institute of Tropical Medicine had approved the study, and the information obtained was kept confidential and used only for scientific purposes.

4 III.

5 Results

In this study, patients with preventive treatment of quercetin, vitamin C, zinc, and Copper were initially included, in addition to a vitamin revitalizer composed of Vitamin B1, B2, B3, B5, B9 and B12, Mg, Zinc, and Copper. Finally, 52 patients diagnosed with COVID-19 have studied, 20 patients (38.4%) was in preventive treatment and 32 patients (61.5%) was administered biological therapy once the diagnosis obtained, the demographic characteristics are demonstrated in Table 1. Regarding comorbidity, which includes: cancer, heart disease, diabetes, obesity, respiratory, puerperal, 24 patients (70.6%) have presented at least one comorbidity and ten patients (29.4%) two of those mentioned, with a total of 34 patients (65%) with some risk factor. About biological treatment, preventive treatment, and the beginning of it, we can see in Table 2 the details of the same, and the observed evolution. The association of hospitalization concerning preventive treatment was not significant ($p = 0.166$). We have observed a difference in terms of the evolution of the patients with a $p = 0.084$ (Table 3). Regarding the evolution of the patients, we have observed that preventive treatment before contracting Covid-19 causes patients to present mild symptoms. Those who started treatment between days 1 to 6 of the confirmation of the Covid-19 diagnosis, had symptoms mild to moderate and improved within 48 hours to mild symptoms.

Patients who had Covid-19 and started treatment on day 7 or 8 of the symptoms improved after 4 to 6 days; two of them was hospitalized.

All received outpatient treatment except for two of them who began treatment with moderate to severe symptoms and required hospitalization.

6 IV.

7 Discussion

Nutraceuticals include any food or part of food that provides health benefits, including the prevention or treatment of disease. Quercetin is a nutraceutical compound with a well-known preventive activity against viral respiratory infections. Quercetin, used orally is considered safe because has low toxicity (15). Also in 1998, was evaluated the carcinogenic effect of quercetin by the International Agency for Research on Cancer, and assigned it to Group 3 mutagenicity, suggesting the absence of carcinogenicity in humans at safe doses (500 mg twice daily for 12 weeks) (16).

Studies have shown that quercetin is active against several viruses, including human immunodeficiency virus (HIV) (17), herpes simplex virus (type 1 and 2) (18), poliovirus (type 1) (19), parainfluenza (type 3) (20), hepatitis C virus (21), respiratory syncytial virus Sindbis virus, vaccinia virus and coronavirus (SARS-CoV) (22). Also, oral quercetin has been described in two studies used as a prophylactic against respiratory viruses, such as avian influenza (H5N1), and rhinovirus (17).

COVID-19 occurs with greater severity in patients with advanced chronological age (5). As reflected in our study where the highest proportion of affected is among those over 60 years of age, in terms of sex, we have not found any relevant difference.

Coronary heart disease and diabetes are common comorbidities in patients with COVID-19, just as SARS and MERS. In SARS, the prevalence of Diabetes mellitus and cardiovascular disease was 11% and 8%, respectively, and the presence of either of the two comorbidities increased the risk of death 12 times (23)(24). Several studies have shown that diabetes mellitus and hypertension were prevalent in approximately 50% of MERS cases (24); on the other hand, cardiovascular disease was present in around 30% of the patients (24). The presence of cardiovascular comorbidities is also valid for COVID-19, especially among those with more major disease. In a cohort study of 191 patients from Wuhan, China, there was at least one comorbidity in 48% (67% of non-

survivors), hypertension in 30% (48% of non-survivors), DM in 19% (31% of non-survivors), and CVD in 8% (13% of nonsurvivors) (25), in our study the presence of at least one comorbidity it was found in 70.6%, well above that reported by Other authors.

At the beginning of the infection, quercetin inhibits the entrance of SARS-CoV-2 into the host cell, what makes it a promising drug for COVID-19 chemoprophylaxis (17). In the recent study by **??**ang D et al. (26), they showed that the concentration required to suppress at least 50% of SARS-CoV-2 is 83.4 ?M, this concentration is considerably lower than the concentration achieved in human blood. (418 ?M for a daily dose of 500 mg for 12 weeks) (21), the biological treatment administered to our patients consists of 300 mg of quercetin, 300 mg of vitamin C, 5 mg of zinc and 0.2 mg copper (Immunocu ©), 53.8% of the patients received this biological compound at the time of confirmation of the diagnosis of COVID-19, without preventive treatment. In 75% of the patients has been seen an improvement, only 3 (5.7%) manifested some respiratory symptoms such as asthma (1 patient) and pneumonia, and 4 (7.7%) required oxygen only for 24 hours and therefore hospitalization, the other patients was treated on an outpatient basis.

No deaths have been recorded in our study group, and the time to improve once the treatment has started and the manifestation of symptoms is three days.

These Reverse Transcriptase Enzymes and 3CL are essential for viral replication and have become a molecular target in the development of anti-SARS-CoV-2 drugs (quercetin blocks two enzymes that are involved in viral replication, one of the reverse transcriptase and 3CLpro which is a protease). Also, because glycosylated quercetin is more soluble and highly bioavailable in the lumen of the intestine (23), its use could be more beneficial than using of the aglycone form, the best intestinal absorption of Quercetin was obtained if it was combined with Vitamin C or Bromelain. There is actually a clinical trial in Turkey, named NCT04377789, titled "Quercetin for the prophylaxis and treatment of COVID-19". This study says that quercetin's strong antioxidant and anti-inflammatory activity accompanies an excessive immune reaction in severe cases, making it effective in both to prevent and treat of COVID-19.

V.

8 Conclusions

Due to the results obtained, we can say that quercetin could prevent and decrease the duration of SARS-CoV-2 infections, so it is plausible to propose the prophylactic use of this flavonoid to achieve clinical benefits. Although these tests are preliminary due to the sample's size, it would be interesting to confirm them through in vitro tests and subsequently in a randomized clinical trial.

Despite this, given the clinical evidence of this study and the improvement results of patients with positive Covid-19, treated early or at the time of acquiring the disease, initial positive Covid-19 symptomatic patients without symptoms of severe hypoxia, we see that quercetin therapy and revitalizing vitamin compounds could be used on an outpatient basis.

Severe symptoms shorten the use of oxygen and, in 24 to 72 hours, improve its saturation.

This form of treatment can be of preventive and coadjuvant use in severe cases, reducing hospital stay.

9 Financial support

None.

1

Demographic characteristics	N= 52	%
Gender		
Female	24	46.15
Male	28	53.85
Grouped age		
20 -29 years	4	7.69
30 -39 years	9	17.31
40 -49 years	12	23.08
50 -59 years	9	17.31
> 60 years	18	34.62

Figure 1: Table 1 :

2

Variables	N= 52	%
Biological treatment		
Immunocu	43	84.69
Immunocu + Revitalizer	4	7.69
Immunocu + Revitalizadorcu	3	5.77
Revitalizing	1	1.92
Vitamin C, Zinc and D3		
Start of treatment	20	38,4
Before the diagnosis of COVID-19	32	61,5

Figure 2: Table 2 :

3

Variables	Previous biological treatment No n=32 (61.5%)	Yes n=20 (38.4%)	p
Internment			
Yes No	4 (12.5) 28 (87.5)	6 (30) 14 (70)	0.156
Evolution			
Improved	24 (75)	15 (75)	
Oxygen requirement	4 (12.5)	0	
Pneumonia	2 (6.25)	0	0.035
Asymptomatic	1 (3.1)	5 (25)	
Asthma	1 (3.1)	0	

Figure 3: Table 3 :

.1 Conflict of interests

The authors declare that they have no competing economic interests or personal relationships that could influence the work reported in this article.

.2 Author contributions

All listed authors have made a substantial, direct, and intellectual contribution to the work and have approved it for publication.

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