

PAPER DETAILS



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The effect of prophylactic vitamin C use on COVID-19 infection

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ABSTRACT

Aim: In vitamin C deficiency, the immune system deteriorates and the body becomes more susceptible to infections. Since vitamin C levels will decrease significantly in infectious conditions due to increased metabolic requirements, the daily need for vitamin C increases. In our study, it was aimed to investigate the effects of 500 mg and more vitamin C intake on COVID-19 infection during the pandemic process.

Material and Method: A group consisting of 100 participants who received vitamin C supplements at a daily dose of at least 500 mg daily for a minimum of 1-3 months in their diet and a control group of 100 people who did not receive vitamin supplements were included in the study. While determining the amount of Vitamin C intake of the participants; The amount of Vitamin C in oral food supplements or foods containing vitamin C in their diets (orange, tangerine, grapefruit, kiwi, pineapple, strawberry, lemon, red and green peppers, tomatoes, arugula, parsley, greens such as lettuce, fresh rosehip, broccoli, cabbage, spinach) The vitamin level was calculated according to the amount of vegetables (such as vegetables). None of the participants had side effects suggestive of vitamin C toxicity. Besides the height, weight, gender, age, known illness and other demographic data of all participants; COVID-19 disease status, contact with COVID-19 patients, and whether or not they had a COVID infection after contact were examined. In addition, data on the presence of symptoms, severity and duration of the disease were noted in patients with COVID-19 infection, and both groups were compared statistically in terms of results.

Results: In the group receiving less than 500 mg daily; COVID-19 infection symptoms, respiratory distress, disease severity were found to be higher, and the symptoms were found to be more aggressive. While total contact and high-risk contact at all levels was higher in the group that received more than 500 mg of vitamin C daily, the rate of being COVID was lower compared to the other groups.

Conclusion: One of the most effective precautions to be taken to increase body resistance against COVID-19 is adequate vitamin C intake. In the study, it has been shown that adequate vitamin C taken with both food and nutritional supplements reduce the risk of getting COVID-19, reduce the risk of severe respiratory distress on COVID-19, as well as reduce both symptoms and symptom duration.

Keywords: COVID-19, prophylactic vitamin C, COVID-19 violence

INTRODUCTION

Vitamin C (ascorbic acid) is one of the essential water-soluble nutrients. It is synthesized from fructose in plants and glucose in animals. Since it is not synthesized in humans, it must be taken from outside (1). The immune system is a specialized, versatile mechanism developed to protect the body from pathogens. It is divided into congenital immunity and acquired immunity (2). For nearly fifty years, it has been stated that vitamin C has a very important role, especially in the function of immune system cells (3). The recommended daily

intake of vitamin C is 110 mg/day for men and 95 mg/day for women (4). However, in a person exposed to infectious agents and under physical stress, this amount may be insufficient. In order to meet the nutritional needs of the general population and especially adults aged 65 and over, 200 mg of supplements per day is recommended. In addition, it recommends 400 mg per day for individuals 50 years+ of age to strengthen the immune system (5).

To date, 7 corona viruses with respiratory tract involvement have been identified in human beings (HCoVs). Effective in COVID is considered to be beta-CoVs (6). Culture, electron microscopy and serological tests are used for diagnosis. There are four types of proteins called spike (S), envelope (E), membrane (M) and nucleocapsid (N) that participate in the structure of the virus. The S protein enables the viral genome to enter the cell by establishing a connection between the cell it will affect and the virus. E and M proteins participate in the transmembrane structure. Nucleocapsid (N) is used in the cloning and production of recombinant proteins (7).

There is no treatment for COVID-19 yet. Vitamin C has become a potentially helpful *Candidate* for COVID-19 treatment due to its antioxidant, anti-inflammatory and immunomodulatory properties. To date, oral vitamin C has been shown to reduce both the duration and frequency of respiratory infections. In addition, intravenous vitamin C has been shown to reduce hospital stay, stay in mechanical ventilation and intensive care, and reduce mortality. The benefits of using vitamin C in COVID-19 have been shown due to the low cost of vitamin C, the high safety profile, and the increased need for vitamin C during inflammation (5). The need for vitamin C has increased during viral infections such as COVID-19. In these cases, the amount required to keep vitamin C within normal plasma levels has been determined as 2-3 g/day (8). Studies have shown that low vitamin C is associated with high oxidative stress. Since vitamin C is reduced in cases of pneumonia and sepsis, studies have been conducted showing the effectiveness of vitamin C in these groups (9). Our aim in this study; to investigate the effects of the amount of vitamin C taken orally on COVID-19 symptoms, duration and severity of symptoms.

MATERIAL AND METHOD

This study was approved by Yozgat Bozok University Faculty of Medicine Clinical Researches Ethics Committee (Date: 16.12.2020, Decision No: 2017-KAEK-189-2020.12_06). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

Patients over the age of 18 who applied to Yozgat Bozok University Medical Faculty internal medicine outpatient clinics were included in our study. The diet of the patients was questioned and evaluated according to their prophylactic vitamin C content during the pandemic process.

When calculating the amount of vitamin C in the diet of the patients, the foods containing vitamin C in the food

supplement or diet (orange, tangerine, grapefruit, kiwi, pineapple, strawberry, lemon, red and green pepper, tomato, arugula, parsley, lettuce, fresh rosehip, broccoli, cabbage considering the amount of spinach) were included in the study.

Accordingly, the participants were divided into two groups as patients with or without vitamin C at a daily dose of at least 500 mg (10) between 1-3 months on a regular basis. In addition to the height, weight, gender, age, known disease and other demographic data of all participants, COVID-19 disease status and contact with COVID-19 patients were evaluated.

Accordingly, people in intensive contact with COVID-19 patients wearing a Medical (Surgical) mask;

- if all personal protective equipment (PPE) was used properly considered as risk-free,
- if not wearing gloves and gowns or eye protection considered as low risk,
- if not used medical mask or N95 or medical mask in case of N95 indication considered as medium risk.

The data obtained from the questionnaires containing data on the condition of the same participants after contact with COVID-19, and the disease symptoms of patients with COVID-19, the severity and duration of the disease were noted and statistically compared in terms of both groups (11).

RESULTS

Of the two hundred participants in the study, 52.5% (n=105) were female and 47.5% (n=95) were male. The average age was 44.18 years, average height 168.21 cm, average weight 75.83 kg, and body mass index 26.79 kg/cm².

100 (50%) of were using 500 mg or more prophylactic oral vitamin C daily. Among all participants, the rate of getting COVID-19 disease was 52.5%, and the frequency of symptoms in those with COVID was 49.5%.

Any statistically significant difference was found between the groups (receiving 500 mg or more prophylactic oral vitamin C per day (n=100) and less than 500 mg (n=100)) in terms of age, gender, height, weight, BMI, smoking and alcohol use, and being COVID-19 ($p > 0.05$).

When both groups are evaluated in terms of chronic diseases; while there was no significant difference in terms of hypertension, chronic renal failure, chronic heart disease, asthma ($p > 0.05$); those with chronic obstructive pulmonary disease were more in the vitamin C group; and the number of patients with diabetes mellitus was higher in the group not receiving vitamin C supplements ($p < 0.05$) (**Table 1**).

While 46% of the patient group who received 500 mg and more prophylactic oral vitamin C per day became COVID, this rate was 59% in the group receiving less than 500 mg per day. COVID-19 ratio was similar in both groups ($p=0.066$). Disease duration, COVID symptoms, respiratory distress, and disease severity were found to be significantly higher in the group receiving less than 500 mg daily ($p<0.05$). In the group receiving more than 500 mg of vitamin C per day, 86.9% of the patients who had COVID-19, and 100% of the patients in the group receiving less than 500 mg per day showed symptoms. In addition, when the symptomatic ones are evaluated within themselves; while most of the people who take more than 500 mg of vitamin C per day have mild symptoms; those taking vitamin C below 500 mg per day were found to have the majority of moderate symptoms. Education level and income level were similar between the groups ($p>0.05$) (Table 2).

While total contact at all levels was 74% and high-risk contact was 42% in the group receiving more than 500 mg of vitamin C daily, this rate was found to be 52% and 28%, respectively in the group receiving vitamin C below 500 mg per day. In the group that received more than 500 mg of vitamin C daily, the contact rates were found to be significantly higher than the other group ($p<0.05$) (Table 3).

DISCUSSION

In this study, daily prophylactic oral vitamin C intake of 500 mg and above; although there was more contact with COVID and there was a higher risk of contact, the rate of becoming COVID afterwards was found to be significantly lower than the group with a vitamin C intake of less than 500 mg. In addition, it was observed that individuals who took 500 mg and more vitamin C had COVID, their symptoms were milder and the symptom duration was shorter.

The RNA virus called Coronavirus 2 (SARS-CoV-2) causes COVID-19 disease. Coronaviruses take their name from surface proteins called corona (crown) to bind and penetrate host cells (13). It may be asymptomatic or cause serious complications such as flu symptoms, fever, cough, gastrointestinal system symptoms, shortness of breath, pneumonia, respiratory failure and kidney failure. It also has a 3% mortality (14).

Vitamin C has many roles such as energy metabolism, collagen synthesis and repair, adrenal steroid, catecholamine production, iron absorption. In addition, it reduces the risk of infection due to its antimicrobial, immunomodulatory and antioxidant properties (15). Vitamin C protects the mucosal barrier by reducing viral adhesion (16). It has been shown that individuals with

Table 1. Demographic and clinical parameters of groups receiving 500 mg or more daily and less than 500 mg daily oral vitamin C

Properties	Vitamin C		P
	Daily 500 mg and more (n=100)	Daily less than 500 mg (n=100)	
Age	45.37±15.31	43.00±16.01	0.286
Gender (m/f)	51/49	44/56	0.322
Height (cm)	168.68±8.86	167.74±8.77	0.452
Weight (kg)	75.60±13.82	76.07±17.51	0.833
BMI(kg/cm ²)	26.65±5.14	26.92±5.43	0.322
Cigarettes (%)	29	25	0.524
Alcohol (%)	6	4	0.516
COVID-19 (%)	46	59	0.066

BMI: Body mass index

Table 2. Comparison of the effects of oral prophylactic vitamin C supplementation on COVID-19 infection and comparison of education and income levels

COVID-19 Data	Vitamin C		P
	Daily 500 mg and more (n=100)	Daily less than 500 mg (n=100)	
Respiratory distress			0.031
No infection	48	44	
Nasal O ₂ taken	8	2	
CPAP taken	1	0	
Intubated	2	0	
Disease duration			<0.05
<1 day	1	10	
1-3 days	1	16	
3-7 days	15	14	
7-14 days	23	6	
>14 days	19	0	
Disease severity			<0.05
No Infection	0	1	
Mild	7	34	
Medium	27	11	
Severe	25	0	
Disease symptoms			0.012
None	0	6	
Infected	59	40	
Income level			0.55
Low	29	15	
Medium	24	27	
High	47	58	
Education level			0.60
Primary	27	14	
Secondary	11	19	
College	53	61	
Masters	9	6	

CPAP: Continuous positive airway pressure, O₂: Oxygen

Table 3. Effects of prophylactic oral vitamin C supplementation on COVID-19 infection

COVID-19 Vitamin C	Contacted				P
	None	Low	Medium	High	
Infected					<0.05
Daily less than 500 mg	37	2	1	1	
Daily 500 mg and more	19	9	5	21	
Not infected					<0.05
Daily less than 500 mg	11	7	14	27	
Daily 500 mg and more	7	3	12	21	

low dietary intake of vitamin C have a reduced risk of pneumonia with oral vitamin C supplements (17). In our study, the symptoms of those who took 500 mg or more prophylactic vitamin C were mild. This suggests that for those who take higher doses of vitamin C, mucosal viral transmission may be prevented, resulting in less viral load and, consequently, COVID-19 symptoms are milder. In addition, the duration of symptoms was found to be significantly lower in the vitamin C group in our study. It may be due to the antimicrobial, immunomodulatory effects of vitamin C.

Vitamin C is very important for immunity. The efficacy of chemokines, cytokines, adhesion molecules, inflammatory mediators and apoptosis inhibitors in the immune system has been demonstrated. While inhibiting the production of IL-6 and tumor necrosis factor alpha (TNF- α), GM-CSF may decrease the signal response. Vitamin C helps regulate the proliferation and functioning of T and B cells and natural killer (NK) cells and prevents the cytokine storm from progressing. Oxidative stress has a damaging effect on viral respiratory infections. With vitamin C, the response to oxidative stress increases. The role of oxidative stress in the mechanism of COVID-19 has been emphasized (16). Oxidative stress, immunological damage, endothelial and alveolar membrane damage have been reported in the mechanism of COVID. In the pathophysiology of the progression to Covid19 pneumonia and respiratory failure, the excessive response of the immune system involving IL-6 and endothelin-1 (ET-1) is involved (18). Considering these mechanisms, many treatment regimens that can affect different pathways for Covid19 treatment have been tried. Due to its effect on reducing both COVID and non-COVID hyperinflammation, intravenous vitamin C administration has also taken its place among these regimens. Due to its antioxidant, anti-inflammatory, antithrombotic and immunomodulatory aspects, high amounts of intravenous vitamin C were administered to normalize plasma levels, especially in patients with critically ill sepsis, and it has been shown to reduce mortality (9).

Again in clinical studies; In patients diagnosed with acute respiratory distress syndrome (ARDS) and sepsis, it has been shown that there is a variable degree of effectiveness in cytokine storm with the administration of high doses of intravenous vitamin C. Therefore, it was thought that it could be added to the treatment of ARDS and the treatment of multiorgan dysfunction associated with COVID (16). In our study, respiratory distress was found to be higher in the group that did not take sufficient vitamin C, and the rate of patients who received CPAP and was intubated was higher in this group.

Previous publications on intravenous vitamin C included the results of the application after the diagnosis of COVID-19. Given that vitamin C has substantial evidence on immunity and is also cheap and safe, it was thought that the use of oral prophylactic could be beneficial and the (very) high-dose regimen could be beneficial in severe cases of Covid19, but clinical studies were expected to provide more conclusive evidence (18).

Our study has some limitations. First, the small number of patients, and secondly, the participants were not questioned in terms of other vitamins and minerals that affect immunity. Although the COVID-19 contact of the patients is questioned, the information given about the contact of the patients may not give a definite result due to the asymptomatic COVID-19 cases.

In addition, there might be individuals who stated that they did not have COVID-19 because they were asymptomatic, and those who are misdiagnoses caused by false negative results of the PCR test.

CONCLUSION

In our study, the effects of prophylactic oral use of vitamin C on COVID were investigated. We need to take measures to strengthen the immune system against COVID infection, which has a wide range of symptoms. One of these measures is adequate vitamin C intake. Adequate vitamin C supplements taken with foods and nutritional supplements; has been shown in our study that reduces the risk of getting COVID after contact, reduces severe respiratory distress in those with COVID, and also reduces both symptoms and symptom duration. Previously, publications on intravenous vitamin C included the results of the application after the diagnosis of COVID. Considering that vitamin C has substantial evidence on immunity and is also cheap and safe, oral prophylactic use may be beneficial.

ETHICAL DECLARATIONS

Ethics Committee Approval: This study was approved by Yozgat Bozok University Faculty of Medicine Clinical Researches Ethics Committee (Date: 16.12.2020, Decision No: 2017-KAEK-189-2020.12_06).

Informed Consent: All patients signed the free and informed consent form.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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Author Contributions: All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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