EFFECTS OF VITAMIN C AND D SUPPLEMENTATION ON PULMONARY FUNCTION, SYMPTOMS AND INFLAMMATORY PARAMETERS IN NON-OBSTRUCTIVE CHRONIC BRONCHITIS

ЕФЕКТИ ОД СУПЛЕМЕНТАЦИЈАТА СО ВИТАМИНИ Ц И Д ВРЗ БЕЛОДРОБНАТА ФУНКЦИЈА, СИМПТОМИТЕ И ВОСПАЛИТЕЛНИТЕ ПАРАМЕТРИ КАЈ НЕ-ОПСТРУКТИВЕН ХРОНИЧЕН БРОНХИТИС

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Abstract: *Non-obstructive chronic bronchitis (NCB) is characterized by chronic productive cough without spirometric obstruction ($FEV_1/FVC \geq 0.70$), although patients often experience pronounced symptoms, functional impairment, and signs of systemic inflammation. Oxidative stress and immune dysregulation play an important role in the pathophysiology of the disease, suggesting a potential benefit from antioxidant and immunomodulatory interventions. The aim is to assess the effects of high-dose vitamin C and vitamin D supplementation on pulmonary function, symptoms, functional capacity, and inflammatory status in patients with NCB. Material and Methods: In this cross-sectional observational study, 62 adult patients with non-obstructive chronic bronchitis (NCB) were included and divided into a control group (standard therapy) and an intervention group that additionally received vitamin C (2 g/day) and vitamin D (100,000 IU monthly) for a period of six months. Symptom burden was assessed using the COPD Assessment Test (CAT), functional capacity was evaluated using the six-minute walk test (6MWD), and systemic inflammation was measured through serum C-reactive protein (CRP). Group comparisons were analyzed using independent t-tests or Mann–Whitney U tests, with a level of statistical significance set at $p < 0.05$. Results and discussion: Patients receiving vitamin supplementation showed significantly lower CAT scores ($p = 0.005$), significantly greater 6MWD distance ($p = 0.003$), and lower serum CRP levels ($p = 0.044$) compared to the control group. These results indicate reduced symptom burden, improved functional capacity, and reduced systemic inflammation. Conclusion: Supplementation with high doses of vitamin C and D in patients with non-obstructive chronic bronchitis leads to significant improvement in symptoms, physical endurance, and inflammatory status.*

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Key words: *Chronic bronchitis, pulmonary function, C-reactive protein, vitamin C, vitamin D.*

Апстракт: *Вовед:Не-обструктивниот хроничен бронхитис (NCB) се карактеризира со хронична продуктивна кашлица без докази за спирометриска опструкција, но често е придружен со изразени симптоми, намален функционален капацитет и појава на воспаление. Овие симптоми не се секогаш адекватно објаснети со класичните функционални тестови, што укажува на потреба од проширена системска проценка.Целта е да се проценат ефектите од суплементацијата со високи дози витамин C и витамин D врз симптомскиот товар, функционалниот капацитет и системската инфламација кај пациенти со не-обструктивен хроничен бронхитис. Материјал и методи:Во оваа пресечна опсервациска студија беа вклучени 62 возрасни пациенти со NCB, поделени во контролна група (стандардна терапија) и интервенциска група која дополнително примаше витамин C (2 g/ден) и витамин D (100.000 IU месечно) во период од шест месеци. Симптомскиот товар беше оценет со COPD Assessment Test (CAT), функционалниот капацитет со шестминутниот тест за одење (6MWD), а системската инфламација преку серумски C-реактивен протеин (CRP). Групните споредби беа анализирани со независни t-тестови или Mann–Whitney U тестови, со ниво на статистичка значајност $p < 0.05$. Резултати и дискусија:Пациентите кои примаа витаминска суплементација покажаа значително пониски CAT резултати ($p = 0.005$), значително поголема дистанца на 6MWD ($p = 0.003$) и пониски серумски нивоа на CRP ($p = 0.044$) во споредба со контролната група. Овие резултати укажуваат на намален симптомски товар, подобрен функционален капацитет и редуцирана системска инфламација. Заклучок:Суплементацијата со високи дози витамин C и D кај пациенти со не-обструктивен хроничен бронхитис доведува до значајно подобрување на симптомите, физичката издржливост и воспалителниот статус.*

Клучни зборови: *хроничен брохитис, белодробна функција, Ц реактивен протеин, витамин C, витамин D.*

1. INTRODUCTION

Non-obstructive chronic bronchitis (NCB) is defined by chronic productive cough and sputum expectoration lasting for at least three months in two consecutive years, in the presence of preserved spirometry, specifically a ratio of forced expiratory volume in the first second to forced vital capacity equal to or greater than 0. 70 ($FEV_1/FVC \geqslant 0.70$) (Global Initiative for Chronic Obstructive Lung Disease–GOLD, 2023). Although these patients do not exhibit fixed airway obstruction, they frequently experience substantial morbidity manifested by persistent cough, increased sputum production, reduced exercise tolerance, recurrent respiratory infections, impaired quality of life, and an increased risk of progression to chronic obstructive pulmonary disease (COPD).

Recent research indicates that, despite normal spirometric findings, patients with NCB demonstrate significant pathophysiological alterations, including chronic airway inflammation, oxidative stress, mucus dysfunction, and immune dysregulation. Such impairments can be objectively assessed using tests such as the six-minute walk distance (6MWD), as well as through elevated scores on symptom assessment instruments such as the COPD Assessment Test (CAT).

Micronutrient supplementation, particularly with vitamin C and vitamin D, has been explored as a potential adjuvant strategy for modulating inflammatory processes, oxidative stress, and impaired immune defense in chronic respiratory diseases.Vitamin C is a water-soluble antioxidant that plays an important role in neutralizing reactive oxygen species (ROS), maintaining epithelial barrier integrity, and supporting both innate and adaptive immune

responses. Although direct clinical evidence regarding its effects in NCB is limited, available data suggest that vitamin C may reduce oxidative stress and enhance respiratory immune defense, which may indirectly contribute to improvement in symptoms and inflammatory status in chronic respiratory conditions (Wu et al. , 2022).

Vitamin D is a fat-soluble secosteroid hormone with well-established immunomodulatory and anti-inflammatory properties. Clinical studies and meta-analyses conducted in patients with COPD have demonstrated that vitamin D supplementation is associated with improvements in lung function (FEV_1), reductions in exacerbation frequency, decreased symptom burden as measured by the CAT score, and enhanced functional capacity, as reflected by increased six-minute walk distance (6MWD) (Zendelel et al. , 2015; Liu et al. , 2019). Furthermore, vitamin D plays a key role in regulating inflammatory responses, which may also be reflected in reductions in systemic inflammatory markers such as C-reactive protein (CRP) (Lehouck et al. , 2012; Domej et al. , 2014; Martineau et al. , 2017).

In this context, combined supplementation with vitamin C and vitamin D represents a biologically plausible strategy for improving pulmonary function, reducing symptom burden, enhancing functional capacity, and modulating the inflammatory response in patients with NCB (Schrumpf et al. , 2020; Sluyter et al. , 2021).

2. MATERIALS AND METHODS

2.1 Study Design and Participants

This cross-sectional observational study was conducted in 2025 and included 62 adult participants diagnosed with non-obstructive chronic bronchitis (NCB). Inclusion criteria were current or former smokers with a smoking history of more than 20 pack-years and age between 32 and 68 years. Participants were recruited through outpatient clinics, physician referrals, and public announcements distributed in clinical and community settings. All participants were fully informed about the purpose and procedures of the study and provided written informed consent prior to enrollment. The study protocol was reviewed and approved by the local ethics committee (Ref. No. 14211).

2.2 Grouping

Participants were divided into two groups based on whether they received vitamin supplementation (vitamin C and/or vitamin D). The control group received standard care for NCB without micronutrient supplementation, whereas the intervention group received high-dose supplementation consisting of vitamin D (100, 000 IU every four weeks) and vitamin C (2 g/day, administered as 500 mg four times daily) for a period of six months, in addition to standard care (Hemilä, 2017).

2.3 Symptom Assessment

Symptom burden and the impact of disease on daily functioning were assessed using the COPD Assessment Test (CAT). CAT is a simple, validated, self-administered questionnaire widely used in clinical practice to evaluate the impact of chronic respiratory diseases on quality of life and to monitor disease progression. The questionnaire consists of eight items,

each scored on a scale from 0 to 5. The items cover various disease-related domains, including respiratory symptoms (such as cough, sputum production, and dyspnea), sleep disturbances, energy levels, and limitations in daily physical and social activities. The total CAT score ranges from 0 to 40, with higher scores indicating greater symptom burden and more pronounced impairment of quality of life (Jones et al. , 2009).

CAT is a practical tool for routine clinical monitoring, as it is easy to complete, requires minimal time, and allows early identification of changes in clinical status. In this study, a CAT score $\geqslant$ 10 was considered indicative of clinically significant symptom burden and was used as a threshold to identify patients with pronounced symptoms. The entire procedure was conducted under the supervision of qualified healthcare personnel, in accordance with ethical principles ensuring participant safety and respect (Lee et al. , 2021).

2.4 Assessment of Functional Exercise Capacity (6MWT)

Functional exercise capacity was assessed using the Six-Minute Walk Test (6MWT), with the six-minute walk distance (6MWD) taken as the primary outcome measure. The test was performed in accordance with the recommendations of the American Thoracic Society (ATS) and represents a simple, validated, and widely used functional test for evaluating cardiorespiratory capacity and exercise tolerance, particularly in patients with chronic pulmonary and cardiovascular diseases.

The 6MWT was conducted in an indoor, flat, straight corridor with a standard length of 30 meters. Participants were instructed to walk at a self-selected pace that they could maintain for six minutes, aiming to achieve the maximum possible distance. During the test, short rest periods were allowed if necessary; however, participants were encouraged to resume walking as soon as they felt able, without stopping the timing of the test. Subjective symptoms such as fatigue, dyspnea, or other discomforts were recorded if they occurred during the test.
The 6MWT provides an objective assessment of patients' ability to perform daily physical activities and represents a clinically relevant indicator of functional status. In addition, the test is used to monitor disease progression and to evaluate the effectiveness of therapeutic interventions, including pharmacological and adjunctive strategies, in patients with chronic respiratory diseases (Jones et al. , 2013).

2.5 Assessment of Inflammatory Status

Systemic inflammation was assessed by measuring serum levels of C-reactive protein (CRP), a sensitive and widely used biochemical marker of acute and chronic inflammatory activity. CRP is synthesized in the liver in response to pro-inflammatory cytokines and is commonly used in clinical practice to assess the intensity of inflammatory responses in chronic respiratory diseases.

Blood samples were obtained from peripheral venous blood under routine laboratory conditions using standard aseptic techniques. Collected samples were analyzed in serum using a validated biochemical method, in accordance with laboratory protocols. CRP values were expressed in milligrams per liter (mg/L) and used as an indicator of the presence and degree of systemic inflammation.

To minimize the influence of acute inflammatory conditions, no active infection or acute respiratory exacerbation was documented in participants at the time of blood sampling. The obtained CRP values were included in the analysis as a continuous variable and compared between the vitamin and control groups in order to evaluate the potential effect of vitamin C and vitamin D supplementation on systemic inflammatory activity in patients with non-obstructive chronic bronchitis.

2.6 Statistical Analysis

All statistical analyses were performed using IBM SPSS Statistics for Windows, version 27. Descriptive statistics were presented as means and standard deviations (SD) for continuous variables and as frequencies (%) for categorical data. Data distribution was assessed using the Shapiro–Wilk test.
Depending on data normality, independent t-tests or Mann–Whitney U tests were used to compare pulmonary function parameters between the vitamin and control groups. Statistical significance was set at $p < 0.\ 05$.

3. RESULTS AND DISCUSSION

This study investigated the effects of combined supplementation with high-dose vitamin C (2 g/day) and monthly high-dose vitamin D (100,000 IU) on symptom burden, functional exercise capacity, and systemic inflammation in patients with non-obstructive chronic bronchitis (NCB) over a six-month period.

3.1 Assessment of Symptom Burden (CAT)

Symptom burden, assessed using the COPD Assessment Test (CAT), was significantly lower among participants receiving vitamin supplementation (Table 2). The mean CAT score was 11.29 ± 2.25 in the vitamin supplementation group compared with 13.77 ± 4.06 in the control group, with median values of 11 and 13, respectively. CAT scores ranged from 5 to 23 in the control group and from 6 to 18 in the vitamin group. The difference between the groups was statistically significant (independent t-test, $P = 0.005$), indicating a significantly reduced symptom burden among participants receiving vitamin supplementation.

Table 1. Comparison of CAT scores between the group without vitamins and the vitamin supplementation group.

CAT	Without vitamins	With vitamins	Total
N	31	31	62
Mean	13.77	11.29	12.53
Median	13	11	12
SD	4.06	2.25	3.49
Min-Max	5 – 23	6 – 18	5 – 23
Range	18	12	18
Independent samples t-test	P = 0.005		

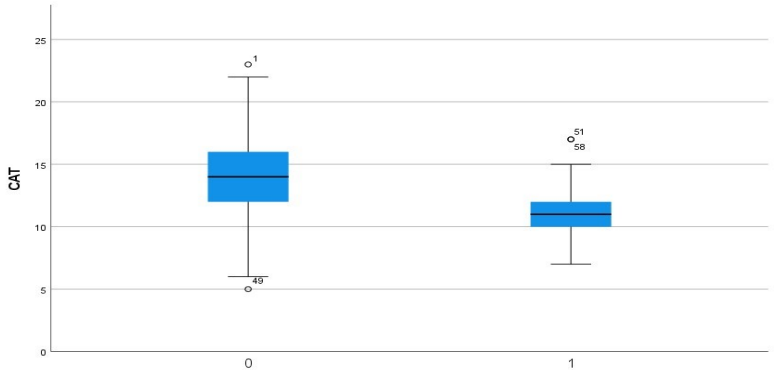

Figure 1. Comparison of CAT scores between the non-vitamin group and the vitamin-supplemented group (independent samples t-test: p = 0.005)

One of the main findings of this study is the significant reduction in symptom burden among patients who received vitamin supplementation, as evidenced by lower CAT scores. This indicates an improvement in subjective symptoms and quality of life, which represents a key clinical goal in patients with non-obstructive chronic bronchitis (NCB), as symptoms in these patients are often persistent and substantially affect daily functioning. The reduction in CAT scores suggests that vitamin supplementation may have a positive effect on the overall clinical burden of the disease, independent of traditional functional parameters.

3.2 Functional Exercise Capacity (6MWD)

Functional exercise capacity, assessed using the six-minute walk distance (6MWD), was significantly better in the vitamin-supplemented group (Table 4). The mean walking distance over six minutes was 407.61 ± 47.61 m in the supplemented group, compared with 362.77 ± 66.16 m in the control group. Median values were 407 m and 383 m, respectively. Walking distance ranged from 195 to 535 m in the control group and from 320 to 487 m in the vitamin group. This difference was statistically significant (independent t-test, p = 0.003), indicating a significantly improved functional exercise capacity among participants receiving vitamin supplementation.

Table 2. Six-minute walk distance (6MWD) by group

6MWD	**Without vitamins**	**With vitamins**	**Total**
N	31	31	62
Mean	362.77	407.61	385.19
Median	383	407	385
SD	66.16	47.61	61.47
Min–Max	195 – 535	320 – 487	195 – 535
Range	340	167	340
Independent samples t-test	P = 0.003		

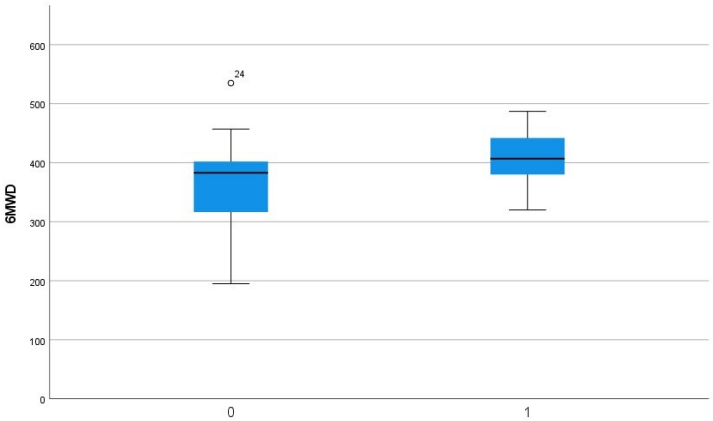

Figure 2. Comparison of 6MWD between the non-vitamin group and the vitamin-supplemented group (independent samples t-test: p = 0.003)

Functional exercise capacity, assessed using the six-minute walk test, was significantly improved in the vitamin supplementation group. The increase in 6MWD indicates improved exercise tolerance and more efficient cardiorespiratory adaptation, which has direct clinical relevance for patients' ability to perform daily activities.

This finding is particularly important in non-obstructive chronic bronchitis (NCB), where reduced functional capacity is often present despite the absence of spirometric obstruction and may be associated with chronic inflammation, reduced physical activity, and the occurrence of fatigue.

3.3 Inflammatory Status (CRP)

Serum levels of C-reactive protein (CRP) were significantly lower in the vitamin-supplemented group compared with the control group (Table 5). The mean CRP value was 2.51 ± 2.43 mg/L in the supplemented group versus 3.92 ± 2.92 mg/L in the non-vitamin group, with median values of 1.8 mg/L and 3.9 mg/L, respectively. CRP values ranged from 0 to 11.5 mg/L in the control group and from 0 to 9.3 mg/L in the vitamin group. The difference between groups was statistically significant (independent t-test, p = 0.044), indicating a significantly lower systemic inflammatory burden among participants receiving vitamin supplementation.

Table 3. Comparison of serum CRP values between groups

CRP	Without vitamins	With vitamins	Total
N	31	31	62
Mean	3.92	2.51	3.21
Median	3.9	1.8	2.6
SD	2.92	2.43	2.75
Min–Max	0 – 11.5	0 – 9.3	0 – 11.5
Range	11.5	9.3	11.5
Independent samples t-test	P = 0.044		

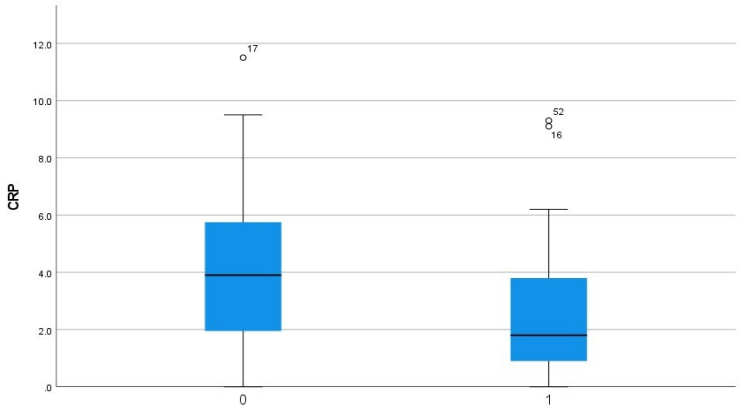

Figure 3. Comparison of CRP values between the non-vitamin group and the vitamin-supplemented group (independent samples t-test: p = 0.044).

Regarding systemic inflammation, patients in the vitamin supplementation group exhibited significantly lower serum levels of C-reactive protein (CRP) compared with the control group. This finding suggests a potential anti-inflammatory effect of combined vitamin C and vitamin D supplementation. The reduction in CRP provides biological support for the observed clinical improvements and indicates that part of the positive effects may be attributable to a decrease in chronic low-grade systemic inflammation, which is characteristic of chronic bronchitis.
The combined administration of vitamin C and vitamin D is biologically justified, given their complementary mechanisms of action. Vitamin C contributes to the reduction of oxidative stress, which is pronounced in smokers and in patients with chronic airway inflammation, while vitamin D has well-documented immunomodulatory and anti-inflammatory effects. These mechanisms may result in improved symptoms, enhanced physical endurance, and reduced systemic inflammation, without necessarily affecting classical parameters of pulmonary function.

4. CONCLUSION

The results of this study demonstrated that supplementation with high-dose vitamin C (2 g/day) and monthly high-dose vitamin D (100,000 IU) was associated with significant clinical improvements in patients with non-obstructive chronic bronchitis (NCB).
Patients receiving vitamin supplementation showed a significant reduction in symptom burden, assessed using the COPD Assessment Test (CAT), indicating an improvement in subjective clinical status and quality of life.

Functional exercise capacity, evaluated using the six-minute walk test (6MWD), was significantly improved in the vitamin supplementation group. The increased walking distance indicates enhanced physical endurance and better tolerance of daily activities, which has a direct positive impact on functional independence and overall patient well-being.
Regarding inflammatory status, the supplemented group exhibited significantly lower serum levels of C-reactive protein (CRP), suggesting a reduction in systemic low-grade inflammation. This finding provides biological support for the observed clinical

improvements and indicates that part of the positive effects may be attributable to the anti-inflammatory and immunomodulatory actions of combined vitamin supplementation.

These results have important clinical implications. Although patients with NCB have preserved spirometric measurements without airway obstruction, they often experience substantial symptom burden, reduced physical endurance, and impaired daily functioning. Introducing a low-cost, easily accessible, and relatively safe intervention, such as vitamin C and D supplementation, may represent an effective strategy to improve clinical and functional outcomes in this population.

In conclusion, the findings suggest that vitamins C and D may play a significant therapeutic role in patients with NCB, contributing to symptom reduction, improved functional capacity, and decreased systemic inflammation through mechanisms that extend beyond conventional spirometric assessment.

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