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Review Article

The Effects of Vitamin C in Patients with Chronic Obstructive Pulmonary Disease: A Systematic Review of Clinical Trials

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ABSTRACT

The present systematic review aimed to investigate the effects of vitamin C on the improvement of chronic obstructive pulmonary disease (COPD). Online databases (PubMed, Scopus, Embase, Cochrane Library and Web of Sciences) were systematically searched to find clinical trials evaluating the effects of vitamin C supplementation on COPD up to July 2019. After excluding irrelevant records, 3 studies were included. Two included studies demonstrated significant effect of vitamin C supplementation on COPD improvement, but another study did not. In conclusion, vitamin C might have positive effects on COPD patients. But more future studies are needed to reach a definite conclusion.

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Introduction

Chronic obstructive pulmonary disease (COPD) is a chronic inflammatory disease, which its main feature is the irreversible limitation of airflow. Smoking is the first and most important reason for COPD (1) and becomes a serious health problem worldwide and increases mortality, morbidity and medical costs (2). The prevalence of COPD in Asia, Europe and North America is 4-10% (3). In 2015, three million people died from COPD (4). Several studies showed that COPD will be the third cause of death at 2020 (5, 6).

An important problem in COPD is oxidative stress, which is defined as exposure to some oxidative compounds such as peroxides ion, OH radical, peroxide hydrogen and deficiency of antioxidants (2). Deficiencies of antioxidants are associated with a chronic disease such as COPD (7). Oxidative stress worsens the condition of COPD patients through inactivation of anti-protease and damages the endothelial alveoli (2, 8). Smoking and air pollution worsens oxidative stress and these changes lead to the development of COPD (2). Therefore, controlling oxidative stress through antioxidant administration might help COPD control.

Vitamin C is a water soluble antioxidant that scavenges free radicals and it has a great effect on the metabolic and physical stress (9). Vitamin C supplementation improves either the status of antioxidants and lung function in COPD patients or reduces the symptom of the disease (7). Studies in USA showed that there is a reverse relationship

between consumption of vitamin C and risk of COPD, and also it was documented that high dietary intake of fruits, vegetables and whole grains have positive effects on COPD patients (3). But the clinical trials which evaluated the effects of vitamin C supplementation on COPD patients had inconsistent results (8). Therefore, the present study was designed to assess the trials in a systematic review.

Materials and Methods

We searched PubMed, Scopus, Embase, Cochrane library and Web of Science to identify randomized controlled trials (RCTs) related to "the effect of vitamin C on chronic obstructive pulmonary disease (COPD)" from the first available time up to 31 July 2019 in English language with no other restrictions. We used Endnote X9 computer software to manage the records screening. Human studies with Randomized clinical trials (RCT) design assessing the effects of vitamin C supplementation on COPD patients were included. Combined supplementation of vitamin C along with other nutrients was also enrolled. Eligible studies were abstracted from included articles by two independent investigators including first author's name, publication year, study design, study population, dosage of supplements, duration of study and population age.

Results

The process of data selection was shown in Figure 1. Totally, 227 records were collected through systematic search in online databases (PubMed, Scopus, Embase, Cochrane library and Web of Science). At first, 110 records were deleted as duplicates. In the next step, 140 records were screened in title and abstract. After excluding irrelevant records, 9 articles remained for full text screening. Finally, 3 articles were assessed for eligibility and were included in the study (3, 8, 10). As indicated in Table 1, the studies conducted in Canada, Malaysia and China were enrolled. The range of sample size in intervention groups was between 9 and 13. Two RCTs investigated the effect of vitamin C on respiratory and oxidative factors and one study evaluated the impact of vitamin C on nutritional status.

Pirabbasi et al. (3) in 2016 found a significant relationship between taking vitamin C and mean body mass index (BMI) (P=0.046), body fat mass (P<0.001), and the plasma level of vitamin A (P=0.001) in patients with COPD in Malaysia, but there was no significant association between taking vitamin C and lean body mass (P=0.60) and also fat free mass (P=0.64). Wu et al. (8) evaluated COPD patients in Chicago Hospital and did not find any

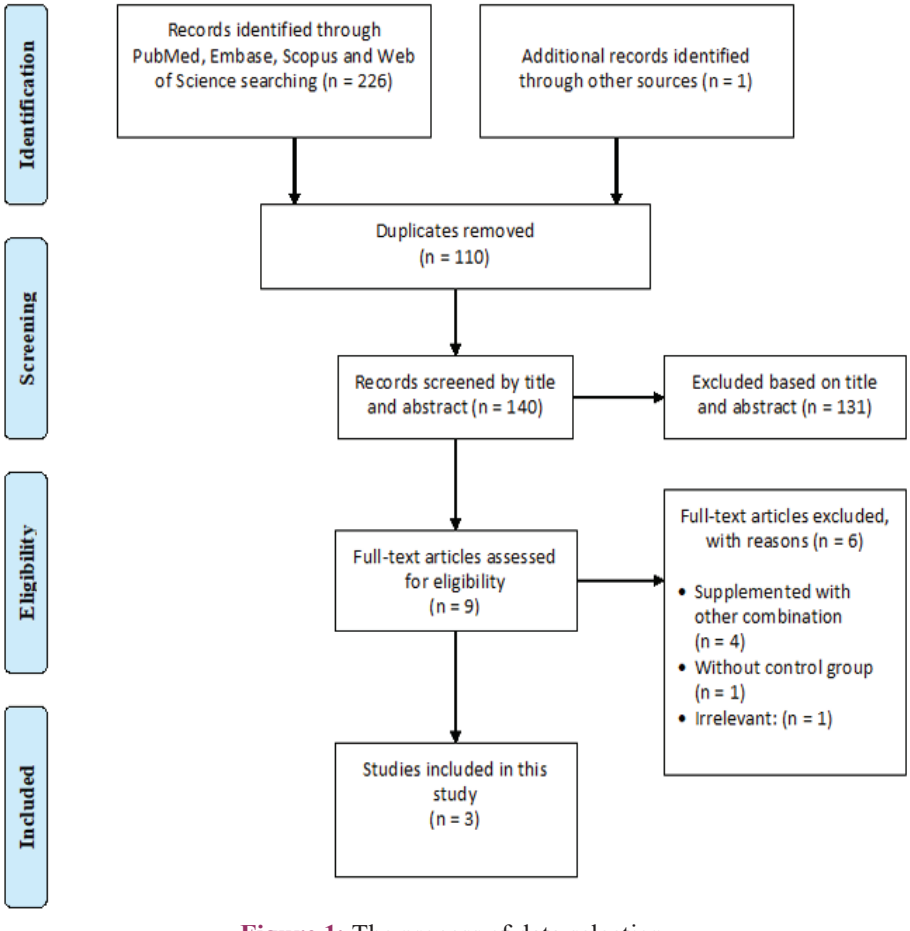

Figure 1: The process of data selection.

Table 1: Characteristics of included studies

Study-year	Region	Study design	Intervention groups sample size	Dosage	Duration	Study population	Age range (mean±SD)	Outcome	Result
Wu et al., (2006)	China	RCT	9	250 mg	3 months	COPD patients	47-89	-TBARS, -FEV1% -FEV1/FVC	There was no significant relationship between taking vitamin C and the level of TBARS, FEV1% and FEV1/FVC (P>0.05)
Hartmann et al., (2015)	Canada	RCT	10	-	-	COPD patients	67±3	FMD NMD MDA SOD catalase	There was no significant association between vitamin C supplementation and the level of NMD (P>0.05). But significant change in FMD (P<0.05)
Pirabbasi et al., (2016)	Malaysia	RCT	13	500 mg vitamin C	3-6 months	COPD patients	64.5±10.2	Nutritional status (primary), antioxidant status (secondary)	There was a significant relationship between mean BMI and taking vitamin C (P=0.046), body fat mass (P<0.001) There was also a significant change for plasma vitamin A (P=0.001). But there was no significant change between taking vitamin C and lean body mass (P=0.60) and fat free mass (P=0.64)

RCT: Randomized clinical trials, TBARS: Thiobarbituric acid reactive substances, FEV: Forced expiratory volume, FEV1/FVC: Forced expiratory volume 1/forced vital capacity, COPD: Chronic obstructive pulmonary disease, FMD: Flow-mediated dilation, NMD: Nitroglycerine mediated dilation, MDA: Malondialdehyde, SOD: Superoxide dismutase, BMI: Body mass index

significant effect from vitamin C on the level of thiobarbituric acid reactive substances (TBARS), forced expiratory volume (FEV) % and FEV1/forced vital capacity (FVC) ratio (P>0.05). The last study was by Hartmann et al. (10) in Calgary, Canada. In this paper, there was a significant relationship between taking vitamin C and flow-mediated dilation (FMD) (P<0.05), but there was no significant difference between nitroglycerine mediated dilation (NMD) level and vitamin C (P>0.05).

Discussion

The aim of this study was to investigate the effects of vitamin C on COPD. Due to the small number of RCTs, it was not possible to conduct a meta-analysis. Vitamin C is a water-soluble vitamin that has many functions such as wound healing, improving the function of lymphocytes and leucocytes and decreasing inflammation and oxidative stress. Oxidative stress is involved in the pathology of many diseases like COPD. Some of

the compounds that arise under these conditions are malondialdehyde (MDA) and advanced oxidation protein products (AOPP), but the level of antioxidants such as glutathione, vitamin C, vitamin E, catalase and superoxide dismutase (SOD) decreased (4, 8).

SODs constitute a very important antioxidant defense against oxidative stress in the body, but MDA is one of the most popular and reliable markers that reveal oxidative stress in clinical situations. AOPP is a uremic toxin emerged during oxidative stress through the reaction of plasma proteins with chlorinated oxidants. The level of MDA and AOPP are increased in COPD patients. Oxidative stress affect nutritional status, muscle function and serum level of vitamins. Vitamin C is a kind of antioxidant that protects tissues against oxidative compounds. On the other hand, vitamin C plays an important role in regulating pulmonary function through regulating collagen production. We need vitamin C as a lysyl and prolyl-hydroxylase cofactor to stabilize the collagen third structure and distribution of collagen in our body dependent on the serum level of vitamin C (3, 11-14).

Taking antioxidants supplements modulate the synthesis of collagen and improve lung function, FEV, FVC and FEV/FVC ratio as important indices of lung function (3, 11, 15). Improving lung function and reducing symptoms in these patients also have a significant effect on their nutritional status, such as body mass index (BMI), body fat mass and some of serum vitamins. Also, vitamin C was shown to improve the function of immune cells and decrease the risk of respiratory infection (12).

First study was conducted in 2006 on Chinese patients with COPD and did not show any significant effect between vitamin C supplementation and respiratory factors. This study indicated that some situation like exercise and smoking increased oxidative stress in this patients and worsened their symptoms so anti-oxidants supplementation protected DNA against oxidants compounds such as H2O2 but did not decrease the level of TBARS or improve FEV1%, and FEV1/FVC ratio. The reason for not being significant may be because of short-term duration or low dosage of vitamin C used (13).

Another study was done at 2015 on outpatients in Canada showed different results, vitamin C had a significant effect on FMD, because patients in this study did exercise and this situation caused hyperoxia and limited the air flow; so anti-oxidants supplementation improved the factor of air-flow (FMD), but no significant effect was seen on NMD (10). The last study was done in 2016 on COPD patients in Malaysia showed that vitamin C supplementation affected nutritional status in addition to respiratory markers (3). We could see a significant correlation between taking vitamin C supplement and mean BMI, body fat mass and plasma vitamin A. In COPD patients, we could observe malnutrition, because they consumed much of their energy in breathing mechanism and most of these patients were underweight, but vitamin C improved their appetite and BMI.

Conclusion

Vitamin C might have positive effects on COPD patients, but more future studies are needed to reach a definite conclusion.

Conflict of Interest

None declared.

References

1 Bigna JJ, Kenne AM, Asangbeh SL, et al. Prevalence of chronic obstructive pulmonary disease in the global population with HIV: a systematic review and meta-analysis. *Lancet Glob Health*. 2018;6:e193-e202. DOI:10.1016/S2214-109X(17)30451-5. PMID:29254748.

2 Agacdiken A, Basyigit I, Özden M, et al. The effects of antioxidants on exercise-induced lipid peroxidation in patients with COPD. *Respirology*. 2004;9:38-42. DOI:10.1111/j.1440-1843.2003.00526.x. PMID:14982600.

3 Pirabbasi E, Shahar S, Manaf ZA, et al. Efficacy of Ascorbic Acid (Vitamin C) and/N-Acetylcysteine (NAC) Supplementation on Nutritional and Antioxidant Status of Male Chronic Obstructive Pulmonary Disease (COPD) Patients. *J Nutr Sci Vitaminol (Tokyo)*. 2016;62:54-61. DOI:10.3177/jnsv.62.54. PMID:27117852.

4 Carr AC, Maggini SJN. Vitamin C and immune function. *Nutrients*. 2017;9:1211. DOI:10.3390/nu9111211. PMID:29099763.

5 Minov J, Bislimovska-Karadzhinska J, Petrova T, et al. Effects of Pleuran (Beta-Glucan from Pleurotus Ostreatus) Supplementation on Incidence and Duration of COPD Exacerbations. *Open Access Maced J Med Sci*. 2017;5:893-8. DOI:10.3889/oamjms.2017.198. PMID:29362614.

6 Gupta I, Ganguly S, Rozanas CR, et al. Ascorbate attenuates pulmonary emphysema by inhibiting tobacco smoke and Rtp801-triggered lung protein modification and proteolysis. *Proc Natl Acad Sci U S A*. 2016;113:E4208-17. DOI:10.1073/pnas.1600056113. PMID:27382160.

7 Park HJ, Byun MK, Kim HJ, et al. Dietary vitamin C intake protects against COPD: the Korea National Health and Nutrition Examination

Survey in 2012. *Int J Chron Obstruct Pulmon Dis*. 2016;11:2721-8. DOI:10.2147/COPD.S119448. PMID:27843308.

8 Wu TC, Huang YC, Hsu SY, et al. Vitamin E and vitamin C supplementation in patients with chronic obstructive pulmonary disease. *Int J Vitam Nutr Res*. 2007;77:272-9. DOI:10.1024/0300-9831.77.4.272. PMID:18271282.

9 Hemila H. Vitamin C and Infections. *Nutrients*. 2017;9:E339. DOI:10.3390/nu9040339. PMID:28353648.

10 Hartmann SE, Waltz X, Leigh R, et al. Blood Flow during Handgrip Exercise in COPD: Effect of Vitamin C. *Med Sci Sports Exerc*. 2016;48:200-9. DOI:10.1249/MSS.0000000000000766. PMID:26339724.

11 Dhakal N, Lamsal M, Baral N, et al. Oxidative stress and nutritional status in chronic obstructive pulmonary disease. *J Clin Diagn Res*. 2015;9:BC01-4. DOI:10.7860/JCDR/2015/9426.5511. PMID:25859442.

12 Paschalis V, Theodorou AA, Kyparos A, et al. Low vitamin C values are linked with decreased physical performance and increased oxidative stress: reversal by vitamin C supplementation. *Eur J Nutr*. 2016;55:45-53. DOI:10.1007/s00394-014-0821-x. PMID:25526969.

13 Joshi P, Kim WJ, Lee SA. The effect of dietary antioxidant on the COPD risk: the community-based KoGES (Ansan-Anseong) cohort. *Int J Chron Obstruct Pulmon Dis*. 2015;10:2159-68. DOI:10.2147/COPD.S91877. PMID:26504380.

14 Padayatty SJ, Levine MJOd. Vitamin C: the known and the unknown and Goldilocks. *Oral Dis*. 2016;22:463-93. DOI:10.1111/odi.12446. PMID:26808119.

15 Findik R, Ilkaya F, Guresci S, et al. Effect of vitamin C on collagen structure of cardinal and uterosacral ligaments during pregnancy. *Eur J Obstet Gynecol Reprod Biol*. 2016;201:31-5. DOI:10.1016/j.ejogrb.2016.03.022. PMID:27042769.