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Association Between Dietary Nutrient Intake and Chronic Obstructive Pulmonary Disease Severity: A Nationwide Population-Based Representative Sample

Taeyun Kim^a , Hyunji Choi^b , and Jehun Kim^a

^aDepartment of Pulmonology, Kosin University Gospel Hospital, Kosin University College of Medicine, Busan, South Korea; ^bDepartment of Laboratory Medicine, Kosin University Gospel Hospital, Kosin University College of Medicine, Busan, South Korea

ABSTRACT

Several nutrients have been suggested to protect against airway destruction via antioxidant activity. The present study aimed to evaluate the association between disease severity and dietary nutrient intake in chronic obstructive pulmonary disease (COPD) patients using the Korea National Health and Nutrition Examination Survey. Of the 22,948 participants, 702 patients (418 men and 284 women) with COPD, who were defined as the fifth percentile from a reference population were selected. The severity of airflow limitation was measured by the predicted percentage of forced expiratory volume in 1 second (FEV₁%). The Jonckheere–Terpstra test was used to evaluate the dose-dependent association between nutrient intake and disease severity. Multivariate linear regression analysis was used to evaluate the relationship between dietary nutrient intake and predicted FEV₁%. Vitamin A intake showed a positive association with FEV₁% in men in a model adjusted for covariates. Carbohydrate, protein, fiber, thiamin, riboflavin, niacin, and vitamin C intake were significantly associated with decreased disease severity in elderly men (aged ≥60 years). On the contrary, statistical significance was not observed for all the nutrients in women. In conclusion, intake of carbohydrate, protein, fiber, thiamin, riboflavin, niacin, and vitamin C was associated with decreased severity of airway impairment in elderly men with COPD. Our results are in line with those of previous studies into the importance of nutritional status in airway disease. A longitudinal study is required to clarify the mechanisms underlying the association between dietary nutrient intake and COPD severity.

ARTICLE HISTORY

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KEYWORDS

COPD; nutrient; spirometry; KNHANES

Introduction

Chronic obstructive pulmonary disease (COPD) is a complex and heterogeneous condition with many different mechanisms and contributing factors [1]. Both systemic and airway inflammation continuously occur in COPD, and several inflammatory markers such as acute-phase reactant plasma fibrinogen are elevated [2]. Over time, this inflammation results in either chronic bronchitis or emphysema, further increasing the risk of cardiovascular disease [3]. Airway inflammation is thought to be responsible for structural damage and tissue injury which collectively result in airway remodeling [4]. Several techniques and parameters have been developed to evaluate the degree of airway impairment and emphysema. However, observer bias, reproducibility, and the lack of sophisticated software are all limitations associated with these techniques [5]. Indeed, spirometry performed by a trained technician remains important in the diagnosis of airway diseases.

Recently, a number of studies have reported that the anti-inflammatory effect of some micro-nutrients may protect against the worsening of airway disease [6, 7]. Vitamin C is an antioxidant which has been reported to protect against airway inflammation [8]. Furthermore, low dietary

intake of fruit, vitamin E, and beta-carotene has been associated with poor lung function [9]. Although these studies provide evidence that some dietary nutrients play an important role in protecting against airway inflammation in the general population, only a few studies have focused on COPD patients.

Therefore, the present study aimed to evaluate the dose-dependent relationship between dietary nutrient intake and airflow limitation in COPD patients using data from the 6th Korea National Health and Nutrition Examination Survey (KNHANES).

Methods

Study participants

Data from the 6th KNHANES (2013–2015) were used in this study. The KNHANES is a population-based, cross-sectional, nationwide survey conducted annually by the Korea Centers for Disease Control and Prevention. The survey is designed to evaluate the health and nutritional status of nationally representative non-institutionalized Korean citizens. This survey is composed of a health interview, health

CONTACT Jehun Kim libertier@gmail.com Department of Pulmonology, Kosin University College of Medicine, Kosin University Gospel Hospital, 262 Gamcheon-ro, Seo-gu, Busan 49267, South Korea.

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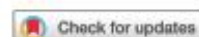
BMJ Open Effects of dietary antioxidant vitamins on lung functions according to gender and smoking status in Korea: a population-based cross-sectional study

Ji Young Hong,^{1,2} Chang Youl Lee,^{1,2} Myung Goo Lee,^{1,2} Young Sam Kim³

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¹Division of Pulmonary and Critical Care Medicine, Department of Medicine, Chuncheon Sacred Heart Hospital, Hallym University Medical Center, Chuncheon, South Korea

²Lung Research Institute of Hallym, University College of Medicine, Chuncheon, South Korea

³Division of Pulmonology, Department of Internal Medicine, Yonsei University College of Medicine, Seoul, Republic of Korea

Correspondence to Professor Young Sam Kim; ysamkim@yuhs.ac

ABSTRACT

Objective Cigarette smoke-induced oxidative stress plays an important role in the pathogenesis of chronic obstructive pulmonary disease (COPD). Dietary antioxidants are thought to prevent smoke-induced oxidative damage. The aim of this study was to investigate associations between lung function and the consumption of antioxidant vitamins in Korean adults.

Methods In total, 21 148 participants from the Korean National Health and Nutrition Examination Survey (2007–2014) were divided into four groups based on smoking history and gender. Multivariate regression models were used to evaluate associations between lung function and intake of dietary antioxidants.

Results Subjects in the highest intake quintile (Q5) of vitamin A, carotene and vitamin C intake had mean forced expiratory volume in 1 s (FEV₁) measurements that were 30 mL, 32 mL and 36 mL higher than those of individuals in the lowest intake quintile (Q1), respectively (p for trend; p=0.008, p=0.010 and p<0.001, respectively). The risks of COPD for male smokers in Q1 increased 7.60-fold (95% CI 5.92 to 9.76), 7.16-fold (95% CI 5.58 to 9.19) and 7.79-fold (95% CI 6.12 to 9.92), for vitamin A, carotene and vitamin C, respectively, compared with those of female non-smokers in Q5. Among patients with COPD, men who smoked >20 pack-years had mean FEV₁ measurements that were 192 mL, 149 mL and 177 mL higher than those of patients in Q1 (p for trend; p=0.018, p=0.024 and p=0.043, for vitamin A, carotene and vitamin C, respectively).

Conclusions These findings indicate that the influence of antioxidant vitamins on lung function depends on gender and smoking status in the Korean COPD population.

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) causes morbidity and mortality.¹ Smoking is a primary risk factor for COPD; however, other factors also contribute as only 10%–20% of smokers develop airflow limitations.²

Dietary antioxidants protect against oxidative stress caused by smoking,³ and multiple studies have revealed associations between the intake of antioxidant vitamins or fibres

Strengths and limitations of this study

- This study revealed that the influence of antioxidant vitamins on lung function depends on gender and smoking status in Korean patients with chronic obstructive pulmonary disease.
- This is a cross-sectional study with a large sample size collected from a national health survey.
- Main limitations include a possible recall bias and no further verification of nutritional intake.

and respiratory diseases.^{4–8} However, evidence supporting the benefits of vitamin supplementation therapy is lacking.^{9,10}

Because micronutrient status is affected by dietary intake and metabolic turnover, which are regulated by oxidative stress, the benefits of antioxidant vitamins may vary by gender and smoking status. Multiple studies have shown that different antioxidants exhibit different effects based on smoking status. Morabia *et al* reported an association between airway obstruction and vitamin A intake in smokers compared with former smokers, whereas Hu *et al* reported that carotene was less strongly associated with FEV₁ in smokers compared with former smokers and non-smokers.^{11,12}

This study used Korean National Health and Nutritional Examination Survey (KNHANES) data to investigate whether dietary antioxidant vitamins were independently associated with pulmonary function and COPD in the Korean population. This study also evaluated whether the effects of antioxidant vitamins on pulmonary function differed based on gender or smoking status.

PATIENTS AND METHODS

Study population

Participants were sampled from KNHANES (2007–2014) IV–VI, a nationwide survey

Pengaruh Vitamin C Terhadap Kadar Interleukin-6 Plasma, MDA Plasma dan Lama Rawat Inap Penderita PPOK Eksaserbasi Akut

Fadlia Yulistiana, Suradi, Reviono

Departemen Pulmonologi dan Kedokteran Respirasi
Fakultas Kedokteran Universitas Sebelas Maret - RSUD Dr. Moewardi, Surakarta

Abstrak

Latar Belakang: Eksaserbasi adalah kondisi akut ditandai perburukan gejala yang membutuhkan perubahan terapi. Peningkatan inflamasi saluran napas dan paru saat eksaserbasi menyebabkan peningkatan kadar IL-6 dan MDA plasma serta menyebabkan sebagian besar pasien butuh perawatan di rumah sakit. Vitamin C adalah antioksidan vitamin berefek antiinflamasi dan antioksidan sehingga dapat ditambahkan pada terapi PPOK eksaserbasi. Penelitian ini bertujuan untuk mengetahui pengaruh vitamin C terhadap kadar IL-6, MDA plasma dan lama rawat inap penderita PPOK eksaserbasi akut.

Metode: Penelitian ini adalah uji klinis eksperimental dengan pendekatan pre-test and post-test. Subjek terdiri dari 33 penderita PPOK eksaserbasi yang dirawat di RSUD Soehadi Pridjonegoro Sragen pada Oktober-November 2015 yang dipilih dengan cara purposive sampling. Subjek dibagi dua kelompok yaitu kelompok perlakuan (n=16) mendapatkan terapi tambahan vitamin C 1x1000 mg/hari dan kelompok kontrol (n=17) mendapat terapi tambahan NaCl 0,9% 5mL. Kadar IL-6 dan MDA plasma plasma diukur saat masuk dan saat kriteria pemulangan terpenuhi. Lama rawat inap dihitung berdasarkan jumlah hari perawatan di rumah sakit.

Hasil: Tidak terdapat perbedaan bermakna terhadap penurunan kadar IL-6 plasma ($P=0,379$), kadar MDA plasma ($P=0,27$) dan lama rawat inap ($P=0,24$) kelompok vitamin C dibanding kontrol.

Kesimpulan: Penambahan vitamin C 1x1000 mg/hari selama rawat inap tidak bermanfaat terhadap penurunan kadar IL-6 dan lama rawat inap penelitian ini. (*J Respir Indo 2018; 38(1): 24-32*)

Kata kunci: vitamin C, PPOK eksaserbasi akut, IL-6 plasma, MDA plasma, lama rawat inap.

Effect of Vitamin C to The Plasma Level of Interleukin-6, Plasma MDA and Length of Hospitalization of COPD Exacerbation Patient

Abstract

Background: Exacerbation is an acute condition characterized by worsening of symptoms that require a change in therapy. Increased inflammation of the airways and lungs during exacerbations causes an increase in plasma IL-6 and MDA levels and causes most patients needed treatment at the hospital. Vitamin C is an antioxidant vitamin that has anti-inflammatory and antioxidant effects so that it can be added to COPD exacerbations therapy. This study aims to determine the effect of vitamin C on plasma IL-6, plasma MDA levels and length of hospitalization of acute exacerbation of COPD patients.

Methods: This research is an experimental study with pre-test and post-test design. Subjects consisted of 33 patients with exacerbation of COPD were treated at the Soehadi Pridjonegoro Hospital Sragen in October-November 2015 which were selected by purposive sampling. Subjects were divided into two groups, the treatment group (n=16) received vitamin C therapy 1x1000 mg/day and the control group (n=17) received 5 mL of NaCl 0.9%. Levels of IL-6 plasma and plasma MDA was measured on admission and at discharge criteria are met. Length of hospitalization is calculated based on the number of days' patients in hospital.

Results: There was no statistically significant difference to decreased of IL-6 plasma level ($P=0,379$), MDA plasma level ($P=0,27$) and length of hospitalization ($P=0,24$) between treatment and control group.

Conclusions: The addition of vitamin C 1x1000 mg/day during hospitalization is not helpful to decreased in levels of plasma IL-6, plasma MDA and length of hospitalization in this study. (*J Respir Indo 2018; 38(1): 24-32*)

Keywords: vitamin C, acute exacerbation of COPD, plasma IL-6, plasma MDA, length of hospitalization.

Korespondensi: Fadlia Yulistiana
Email: fadlia.yulistiana@gmail.com

Article

The Impact of Changes in the Intake of Fiber and Antioxidants on the Development of Chronic Obstructive Pulmonary Disease

Young Ju Jung ^{1,2}, Se Hee Lee ³, Ji Ho Chang ², Hye Seung Lee ², Eun Hee Kang ² and Sei Won Lee ^{1,*}

¹ Department of Pulmonology and Critical Care Medicine, Asan Medical Center, University of Ulsan College of Medicine, Seoul 05505, Korea; tazo76@amc.seoul.kr

² Health Screening and Promotion Center, Asan Medical Center, Seoul 05505, Korea; jhchang@amc.seoul.kr (J.H.C.); grayhs@nate.com (H.S.L.); ehkang@amc.seoul.kr (E.H.K.)

³ Department of Pulmonology, Allergy and Critical Care Medicine, CHA Bundang Medical Center, CHA University, Seongnam 13496, Korea; celestia7@gmail.com

* Correspondence: seiwon@amc.seoul.kr; Tel: +82-2-3010-3990; Fax: +82-2-3010-6968



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Abstract: Diet is a health-related factor that can modify lung function. This study hypothesized that the change in age-related dietary intake affects lung function. The subjects who undertook a dietary assessment and spirometry in 2012 and 2017, were retrospectively collected in a health screening center. Dietary intakes were directly evaluated using food frequency questionnaires (FFQ) administered by trained dietitians and were compared at the baseline (2012) and 5-year follow-up (2017). A forced expiratory volume in one second (FEV₁)/forced vital capacity (FVC) value below 0.70 was defined as airflow limitation. Logistic regression models were used to estimate the odds ratio (ORs) adjusted for potential confounders. A total of 1439 subjects with normal spirometry were enrolled. New airflow limitations were detected in 48 subjects (3.3%) at the 5-year follow-up, including 41 (85.4%) men and 11 (22.9%) current smokers. After adjusting for age, sex, smoking history, and baseline FEV₁/FVC, the odd ratios (OR) for new airflow limitation in fiber, vitamin C, and folic acid per 10% decrease in daily recommended requirement were 2.714 (95% confidence interval (CI), 1.538–4.807; *p* = 0.001), 1.083 (95% CI: 1.020–1.149; *p* = 0.007), and 1.495 (95% CI: 1.172–1.913; *p* = 0.001), respectively. A decreased intake of dietary fiber, vitamin C, and folic acid is associated with a newly developed airflow limitation.

Keywords: dietary fiber; antioxidants; diet; lung function; chronic obstructive pulmonary disease

1. Introduction

Chronic obstructive pulmonary disease (COPD), characterized as persistent airflow limitation, is a major global health concern with a prevalence of 5–25% in adults and the fourth leading cause of death worldwide [1,2]. COPD is treatable but is a progressive disease that generally cannot be cured. Smoking is the most important risk factor for COPD development and progression but it is well-established that its effect is individually different. Clinically significant airflow limitations never develop in 50–85% of smokers [3,4]. This indicates that there are ‘susceptible’ and ‘non-susceptible’ phenotypes among smokers [5] and the factors that decide this are of considerable interest. In terms of innate factors that contribute to COPD, multiple loci have been identified in genome-wide association studies [6] and these cannot be modified. In relation to acquired factors, physical activity is suggested to prevent COPD development [7]. However, COPD still progresses in some cases even after smoking cessation and appropriate physical activity. Hence, additional modifiable factors are likely to contribute to COPD and need to be identified to improve patient management.

Diet is one of the most important lifestyle determinants of health but is relatively ignored in relation to lung disorders. Current dietary guidelines do not provide enough

Clinical Study

Additional Effects of Nutritional Antioxidant Supplementation on Peripheral Muscle during Pulmonary Rehabilitation in COPD Patients: A Randomized Controlled Trial

Fares Gouzi¹, Jonathan Maury^{2,3}, Nelly Héraud³, Nicolas Molinari⁴, Hélène Bertet⁴, Bronia Ayoub¹, Marine Blaquièrre¹, François Bughin¹, Philippe De Rigal³, Magali Poulain³, Joël Pincemail⁵, Jean-Paul Cristol¹, Dalila Laoudj-Chenivresse², Jacques Mercier¹, Christian Préfaut⁶, Pascal Pomiès², and Maurice Hayot¹

¹PhyMedExp, Montpellier University, INSERM U1046, CNRS UMR 9214, Montpellier University Hospital, France

²PhyMedExp, Montpellier University, INSERM U1046, CNRS UMR 9214, France

³Pulmonary Rehabilitation Centers Les Cliniques du Souffle®, 5 Santé/Fontalvie Corporation, 66350 Toulouges, France

⁴IMAG, CNRS, Montpellier University, Montpellier University Hospital, Montpellier, France

⁵Department of Cardiovascular Surgery and CREDEC, University of Liège, Sart Tilman University Hospital, 4000 Liège, Belgium

⁶Montpellier University, France

Correspondence should be addressed to Fares Gouzi; f-gouzi@chu-montpellier.fr

Fares Gouzi and Jonathan Maury contributed equally to this work.

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Background. Skeletal muscle dysfunction in patients with chronic obstructive pulmonary disease (COPD) is not fully reversed by exercise training. Antioxidants are critical for muscle homeostasis and adaptation to training. However, COPD patients experience antioxidant deficits that worsen after training and might impact their muscle response to training. Nutritional antioxidant supplementation in combination with pulmonary rehabilitation (PR) would further improve muscle function, oxidative stress, and PR outcomes in COPD patients. **Methods.** Sixty-four COPD patients admitted to inpatient PR were randomized to receive 28 days of oral antioxidant supplementation targeting the previously observed deficits (PR antioxidant group; α -tocopherol: 30 mg/day, ascorbate: 180 mg/day, zinc gluconate: 15 mg/day, selenomethionine: 50 μ g/day) or placebo (PR placebo group). PR consisted of 24 sessions of moderate-intensity exercise training. Changes in muscle endurance (primary outcome), oxidative stress, and PR outcomes were assessed. **Results.** Eighty-one percent of the patients ($FEV_1 = 58.9 \pm 20.0$ %pred) showed at least one nutritional antioxidant deficit. Training improved muscle endurance in the PR placebo group ($+37.4 \pm 45.1\%$, $p < 0.001$), without additional increase in the PR antioxidant group ($-6.6 \pm 11.3\%$; $p = 0.56$). Nevertheless, supplementation increased the α -tocopherol/ γ -tocopherol ratio and selenium ($+58 \pm 20\%$, $p < 0.001$, and $+16 \pm 5\%$, $p < 0.01$, respectively), muscle strength ($+11 \pm 3\%$, $p < 0.001$), and serum total proteins ($+7 \pm 2\%$, $p < 0.001$), and it tended to increase the type I fiber proportion ($+32 \pm 17\%$, $p = 0.07$). The prevalence of muscle weakness decreased in the PR antioxidant group only, from 30.0 to 10.7% ($p < 0.05$). **Conclusions.** While the primary outcome was not significantly improved, COPD patients demonstrate significant improvements of secondary outcomes (muscle strength and other training-refractory outcomes), suggesting a potential "add-on" effect of the nutritional antioxidant supplementation (vitamins C and E, zinc, and selenium) during PR. This trial is registered with NCT01942889.