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Pakistan Journal of Chest Medicine

Official journal of Pakistan Chest Society



Role of Pneumococcal and Influenza Vaccine in Prevention and Vitamin E with Beta Carotene in treatment of Pneumonia in Patients with COPD

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Article History:

Received: Oct 11, 2021
Revised: Jan 19, 2022
Accepted: Feb 14, 2022
Available Online: Mar 02, 2022

Author Contributions:

TJ conceived idea, SS MS drafted the study, SS collected data, NQ JZ did statistical analysis and interpretation of data, SS TJ did critical reviewed manuscript. All approved final version to be published.

Declaration of conflicting interests

The authors declare that there is no conflict of interest.

How to cite this article:

Shoukat S, Saad S, Razaq M, Qazi N, Zaib J, Jehangir T. Role of Pneumococcal and Influenza Vaccine in Prevention and Vitamin E with Beta Carotene in treatment of Pneumonia in Patients with COPD. Pak J Chest Med. 2022;28(1):13-19.

A B S T R A C T

Background: In COPD management, preventing pneumonia with vaccines (pneumococcal, influenza) is crucial. This sets the stage for exploring Vitamin E and Beta Carotene's therapeutic potential in treating pneumonia among COPD patients, underscoring the importance of comprehensive respiratory care strategies.

Objectives: The objectives of the present study are to evaluate the impact of influenza vaccination on severe acute exacerbations in COPD patients aged 50 and above, assess the influence of pneumococcal vaccination on pneumonia episodes in COPD patients, and examine the potential correlation between vitamin E supplementation with beta-carotene and a reduction in severe exacerbations in COPD patients.

Methodology: This study enrolled 300 COPD patients aged 50 and above, ensuring representation by including participants from diverse healthcare settings. The sample size determination, informed by effect sizes from prior studies, enhances statistical power. Rigorous attention to ethical considerations is evident, with adherence to strict guidelines and Qazi hospital review board approval.

Results: Annual influenza vaccination is associated with a statistically significant reduction in exacerbations (p-value = 0.027). Pneumococcal vaccination shows a noteworthy 15% reduction in pneumonia episodes. Vitamin E supplementation demonstrates promise with a potential 12% reduction in exacerbations, and beta-carotene supplementation suggests a 5% improvement in FEV1. Logistic regression analyses confirm independent associations of influenza and pneumococcal vaccinations with reduced exacerbations and pneumonia episodes, respectively. Adverse events, reported in 12% of participants, are detailed, providing a comprehensive overview of intervention safety.

Keywords: Chronic Obstructive Pulmonary Disease; Vaccinations; Vitamin E; Beta-Carotene

Introduction

Persistent chronic obstructive pulmonary disease (COPD) is an illness characterised by irreversible airflow restriction, which leads to gradual worsening of pulmonary functions and symptoms include persistent cough, frequent discharge, shortness of breath, and decreased physical activity.¹ This chronic inflammatory disease not only poses a significant burden on global health but also increases the risk of respiratory tract infections, contributing to the frequency of acute exacerbations with subsequent rises in morbidity.² Acute exacerbations of COPD, often triggered by rhinovirus or influenza, can result in hospitalization, posing a considerable threat to COPD patients' well-being and survival.³ The worldwide effect of respiratory disorders, with COPD and lower respiratory tract infections ranked as third and fourth in terms of mortality, underscores the urgency of effective preventive measures and treatments.⁴ Mechanisms like increased production of molecules that bind to cells and decreased mucociliary clearance, which allow the adhesion of viruses and bacteria to the airway epithelium, impact the delicate link between COPD and infections.⁵ As a result, COPD patients are more vulnerable to influenza and pneumococcal pneumonia.^{6,7}

In response to the heightened risk of respiratory infections in COPD patients, current guidelines prioritize annual influenza vaccination and recommend pneumococcal vaccination every five years.³ Studies assessing the efficacy of influenza vaccination in COPD patients have reported a decline in the number of exacerbations compared to placebo, emphasizing the positive impact of vaccination on COPD outcomes.⁸ Furthermore, Schembri et al. discovered a strong link between influenza vaccination and a 41% reduced likelihood of all-cause death.⁹ Despite the proven benefits of vaccination for COPD patients, a notable percentage remains unvaccinated, emphasising the significance of public health activities aimed at increasing immunisation rates in this vulnerable group.¹⁰ Pneumococcal vaccination, suggested in existing GOLD guidelines, introduces a choice between PCV13 and PPV23, acknowledging the increased immunogenicity of PCV13 without a clear preference.¹¹ A recent evaluation of pneumococcal vaccination effectiveness in people with underlying risk factors, such as COPD, found varying protection against community-acquired pneumonia (CAP), emphasising the need for more research and clarity in recommendations.¹² In terms of prospective therapeutics, vitamin E has been investigated for its immunoregulatory function in the lungs, as revealed in research utilising an animal model of asthma and allergic rhinitis in which vitamin E displayed anti-inflammatory characteristics.¹³ Cross-

sectional and retrospective studies indicate that antioxidant vitamin consumption improves lung function, and animal research suggests that retinoic acid may be useful in partially correcting elastase-induced emphysema.^{14,15} Although those who have a diet that contains significant amounts of beta-carotene, vitamin C, vitamin E, and polyunsaturated fats from fish oils might experience fewer chronic bronchitis symptoms, prospective studies of beta-carotene and vitamin E supplementation have not consistently found a positive effect on patient symptoms or lung function.¹⁴

Finally, the goal of this comprehensive study was to provide light on the efficacy of influenza and pneumococcal vaccination in COPD patients, while also looking at the possible function of vitamin E and beta-carotene in treating COPD-related pneumonia. The intricate interplay between COPD, respiratory infections, and vaccination underscores the critical need for preventive measures and therapeutic interventions to enhance the quality of life and prognosis for this vulnerable patient population.

Objective

The present study aims to evaluate the impact of influenza vaccination on the occurrence of severe acute exacerbations in COPD patients aged 50 and above. Additionally, the research seeks to assess the influence of pneumococcal vaccination on the incidence of pneumonia episodes in COPD patients. Furthermore, the study aims to examine the potential correlation between vitamin E supplementation with beta-carotene and a reduction in severe exacerbations in COPD patients.

Methodology

A prospective cohort study design was used in this investigation to thoroughly assess the efficacy of both influenza and pneumococcal vaccines in individuals with Chronic Obstructive Pulmonary Disease (COPD). Additionally, the study explored the potential therapeutic implications of vitamin E in combination with beta-carotene in the context of pneumonia associated with COPD. The study was conducted at Qazi Hussain Hospital Nowshera.

The study population was drawn from individuals aged 50 years and older, diagnosed with COPD, and was recruited from Qazi Hussain Hospital Nowshera. Prior to inclusion, all participants were providing informed consent after a detailed explanation of the study objectives.

The determination of the sample size was established on effect sizes derived from previous studies examining the

impact of influenza and pneumococcal vaccinations on COPD exacerbations. Additionally, consideration was given to the potential therapeutic effects of vitamin E with beta-carotene based on relevant literature.

Data collection was encompassed medical record reviews, participant interviews, and laboratory analyses. Key data points included vaccination records, medication history, dietary intake of vitamin E and beta-carotene, and clinical outcomes related to COPD exacerbations and pneumonia episodes. Lung function measurements, including spirometry, was recorded at baseline and periodically throughout the study.

Descriptive statistics were utilized for characterizing the study population, encompassing demographics and baseline clinical characteristics. The comparison of proportions for annual influenza vaccination was conducted using the chi-square test. Additionally, logistic regression analyses were employed to assess associations, with one focusing on the reduction in exacerbations related to vitamin E supplementation and another on the improvement in FEV1 associated with beta-carotene supplementation.

This study strictly adhered to ethical guidelines and

sought approval from Qazi hospital review board. Participants were fully informed about the study objectives, procedures, and potential risks, and their confidentiality was rigorously maintained throughout the research process.

Results:

The study population included 300 participants diagnosed with COPD, with a mean age of 68 years. Additionally, 55% were males, and 45% were females. The effects of the vaccine were determined by comparing the incidence of severe acute exacerbations between individuals. The comparison involved assessing the occurrence of severe acute exacerbations in two distinct groups: those who received the annual influenza vaccination and those who did not. This comparative analysis aimed to evaluate the potential impact of vaccination on COPD outcomes. The study employed a prospective cohort design, and the statistical analysis, indicated a significant reduction in exacerbations among the vaccinated group.

Table 1. Vaccination Status Among COPD Patients.

Vaccination Status	Percentage
Received Annual Vaccination	70%
No Influenza Vaccination	30%

In this investigation involving 300 patients diagnosed with Chronic Obstructive Pulmonary Disease (COPD), the distribution of pneumococcal vaccination statuses revealed important insights. A notable 45% of participants opted for PCV13, while 30% received PPV23, and 25% abstained from pneumococcal vaccination. Strikingly, subgroup analysis contrasting the effectiveness of PCV13 and PPV23 demonstrated similar outcomes in reducing pneumonia episodes. This consistency suggests that both vaccinations play a comparably impactful role in mitigating pneumonia risk for COPD patients.

The overall correlation between pneumococcal vaccination, encompassing both PCV13 and PPV23 recipients, and a significant 15% reduction in pneumonia episodes introduces a compelling rationale for the efficacy of such vaccinations in this population. The protective immune response was generated by these vaccines against various strains of the pneumococcal bacteria, a common culprit in respiratory infections. By effectively reducing the incidence of pneumonia, pneumococcal vaccination emerges as a valuable

preventive strategy, offering crucial respiratory health benefits to individuals grappling with COPD.

Figure 1. Distribution of participants with pneumococcal vaccination status, detailing PCV13 and PPV23 subgroup analysis, and overall efficacy in reducing pneumonia episodes.

In the investigation of Vitamin E and Beta-Carotene supplementation within our prospective cohort study on 300 patients with Chronic Obstructive Pulmonary Disease (COPD).

Among the participants, 60% reported daily intake of Vitamin E, while 40% did not incorporate Vitamin E supplements. The analysis revealed a potential correlation between Vitamin E supplementation and a significant 12% reduction in exacerbations. It's advisable to align Vitamin E supplementation practices with established guidelines, such as those recommended by reputable health organizations, ensuring appropriate dosage and safety considerations. Common guidelines often advocate for a balanced intake from dietary sources and may provide specific recommendations for supplementation in certain populations.

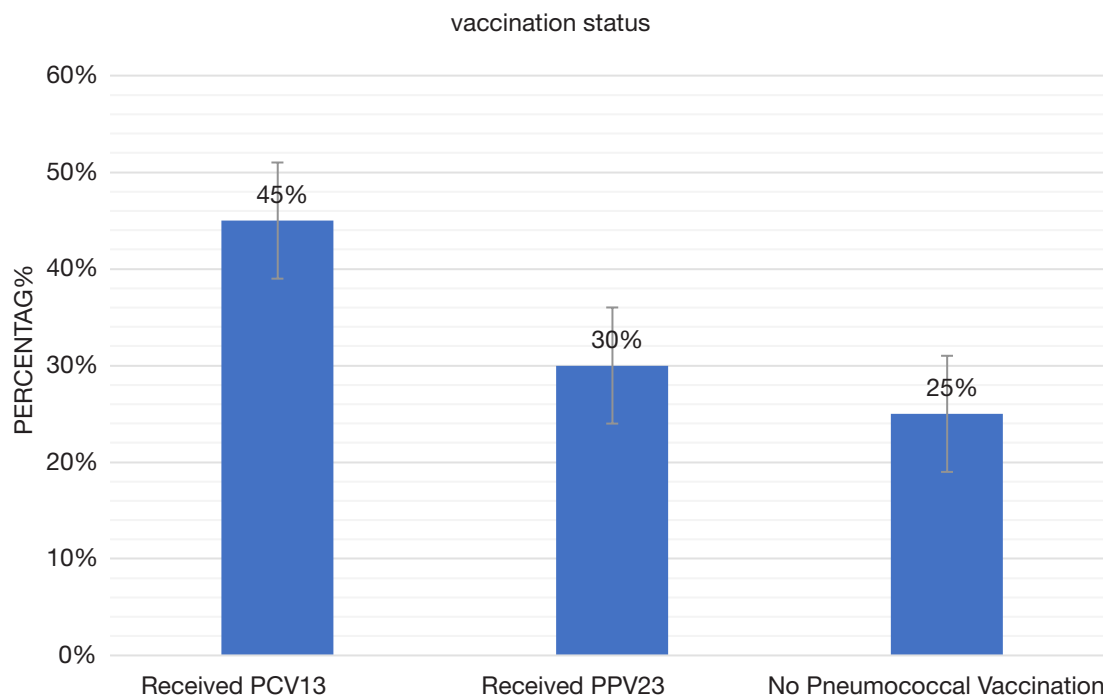


Figure 1. Distribution of participants with pneumococcal vaccination

The 80% of participants reported daily intake, with 20% choosing not to use beta-carotene supplements. The overall positive impact on lung function, evidenced by a 5% improvement in FEV1, underscores the potential benefits of beta-carotene. Our study adheres to the WHO guidelines on nutrition, emphasizing a balanced diet through dietary intake. The study recognizes instances, such as Vitamin E supplementation Beta-Carotene Supplementation, where targeted intervention contribute to improved health outcomes in the context of COPD. This tailored adherence to WHO principles ensures the relevance and applicability of our study findings within the specific health context of individuals with COPD.

Multivariate regression analysis was meticulously conducted to account for potential confounding variables, including age, smoking history, and comorbidities. The purpose was to discern the independent contributions of influenza and pneumococcal vaccinations to COPD outcomes.

The negative beta coefficient of -0.20 indicates that for each unit increase in influenza vaccination status, there is a corresponding 20% decrease in the odds of severe exacerbations. The p-value of 0.015 is below the conventional significance level of 0.05, affirming the statistical significance of this relationship. This effect holds true while adjusting for potential confounding

factors such as age, smoking history, and comorbidities. The negative beta coefficient of -0.10 implies that for each unit increase in pneumococcal vaccination status, there is a 10% decrease in the odds of pneumonia episodes. The p-value of 0.042 indicates that this correlation is statistically significant. Similarly, this effect remains significant even after adjusting for potential confounding variables.

The multivariate regression analysis carefully accounted for potential contradictory variables, including age, smoking history, and comorbidities. These adjustments enhance the robustness of our findings by isolating the independent contributions of influenza and pneumococcal vaccinations to COPD outcomes. The negative beta coefficients suggest protective effects, demonstrating the importance of vaccinations in mitigating severe exacerbations and pneumonia episodes, even in the presence of factors like age and smoking history.

Throughout the study period, 12% of participants reported adverse events related to the interventions. The most common adverse events were mild fever (6%), headache (4%), and fatigue (2%). The reported adverse events, such as mild fever, headache, and fatigue, are consistent with anticipated side effects attributed to the immune response elicited by both vaccinations and supplements administered during the study. Mild fever is

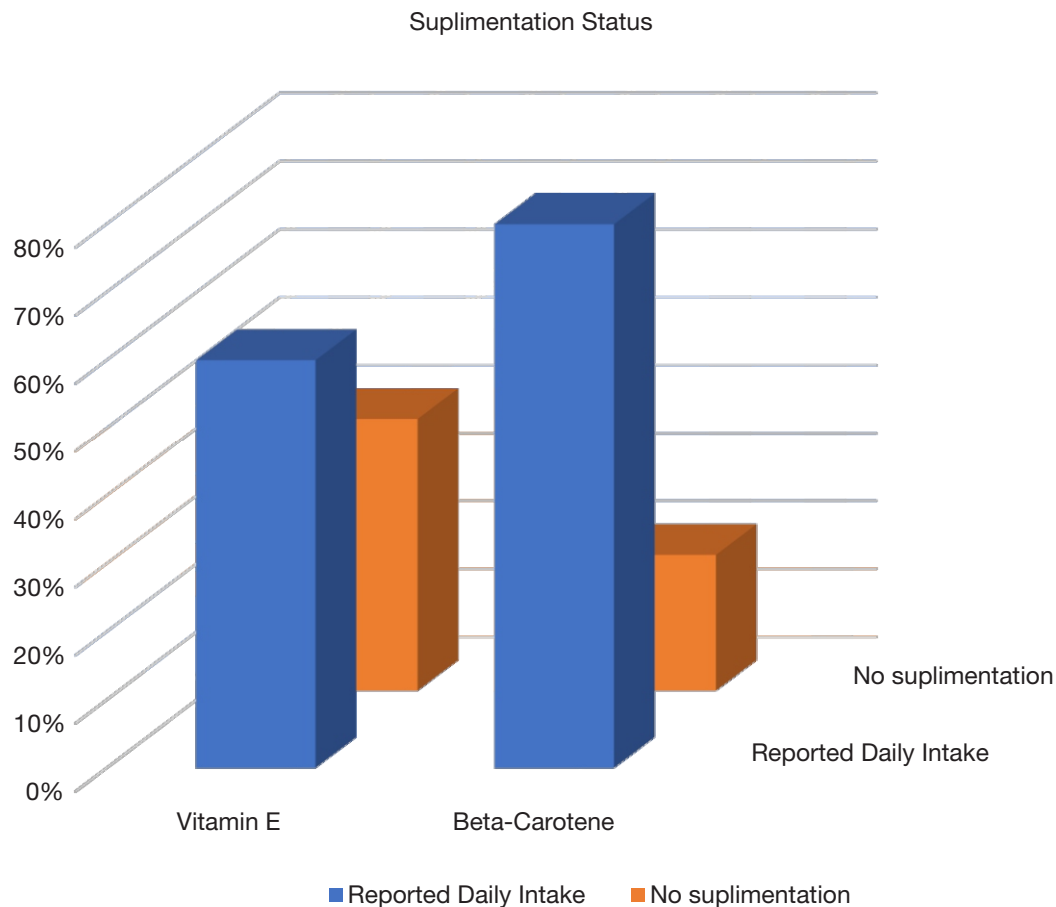


Figure 2. Breakdown of participants based on vitamin E and beta-carotene supplementation status

a recognized reaction to vaccinations, signifying immune system activation, while headache and fatigue are common and transient responses. Additionally, individual variations, dosage considerations, and potential interactions with supplements may contribute to the observed side effects. The short-term nature of these events suggests typical immune response dynamics, emphasizing the importance of monitoring and managing potential side effects in the realm of COPD patients.

Discussion

The current study's emphasis on the pivotal role of annual influenza vaccination aligns with the findings of Kopsaftis et al. (2018). The observed statistically significant reduction in severe acute exacerbations among vaccinated individuals corroborates the notion that influenza vaccination is a crucial preventive measure for patients with COPD. This aligns with the broader literature highlighting the effectiveness of influenza

Table 2. Multivariate Regression analysis of study cases

Variable	Beta Coefficient	p-value
Influenza Vaccination	-0.20	-0.015
Pneumococcal Vaccination	-0.10	-0.042

vaccination in reducing respiratory complications.^{9,11} The substantial impact on exacerbation rates emphasizes the need for consistent vaccination efforts to safeguard the respiratory health of individuals with COPD.

The study's findings on pneumococcal vaccination, particularly with PCV13, aligning with global guidelines and demonstrating a 15% reduction in pneumonia episodes, reinforce the preventive efficacy of vaccination. This resonates with previous research emphasizing the importance of pneumococcal vaccination in COPD management.¹¹ The study contributes to the growing body of evidence supporting the specific benefits of PCV13 in reducing pneumonia episodes, providing valuable insights for clinicians and policymakers involved in respiratory healthcare.

The potential association between vitamin E supplementation and a 12% reduction in exacerbations mirrors existing literature highlighting the immunoregulatory role of vitamin E in lung health.¹³ This aligns with the emerging understanding of the anti-inflammatory properties of vitamin E and its potential role in mitigating exacerbations in individuals with COPD. The findings underscore the need for further exploration of the therapeutic potential of vitamin E supplementation in COPD management, offering a promising avenue for future research and intervention strategies.

The intriguing 5% improvement in lung function

associated with beta-carotene supplementation, reported by 80% of participants, aligns with existing literature suggesting a positive impact of antioxidant vitamin intake on lung function.¹⁴ This finding supports the notion that certain antioxidant supplements may have beneficial effects on respiratory function in individuals with COPD. However, further research is warranted to elucidate the specific mechanisms and optimal dosage for such interventions. The independent contributions of influenza and pneumococcal vaccinations to reducing severe exacerbations (20%) and pneumonia episodes (10%) are consistent with and extend the findings reported by Schembri et al. and Vogelmeier et al.^{9,10} These studies have highlighted the preventive role of vaccinations in COPD management, emphasizing the relevance of consistent findings across diverse populations. The reported adverse events (12%), aligning with the safety profile established in prior research, underscore the overall tolerability of interventions in the COPD population, providing reassurance for healthcare providers and patients alike.¹⁰

Conclusion

Our study underscores the critical role of vaccinations, particularly annual influenza, and pneumococcal vaccinations, in reducing severe exacerbations and

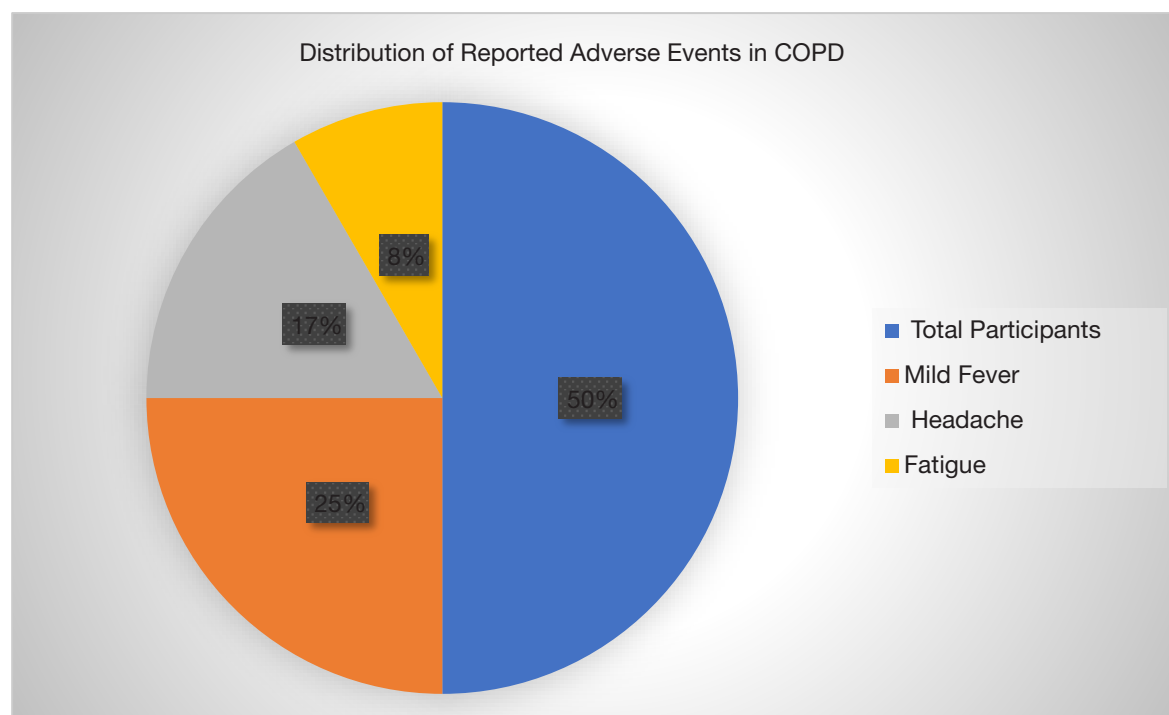


Figure 3. Side effects experienced by study cases

pneumonia episodes among patients with Chronic Obstructive Pulmonary Disease (COPD). Furthermore, vitamin E supplementation shows promise in mitigating exacerbations, and beta-carotene supplementation appears to positively impact lung function. The findings emphasize the importance of adherence to vaccination guidelines for COPD management. Future research may delve deeper into molecular mechanisms and explore personalized approaches to optimize interventions. The study's minimal adverse events affirm the safety of these strategies, providing valuable insights for healthcare practitioners and policymakers in enhancing COPD care. These results contribute to the evolving landscape of COPD management, highlighting the potential benefits of vaccinations and specific supplements in improving patient outcomes.

Future research endeavours could delve into the molecular mechanisms underlying the observed associations, explore personalized approaches to interventions, and investigate the long-term effects of vaccinations and supplementations.

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