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PHYSIOLOGY AND BIOCHEMISTRY OF SERUM VITAMIN A AND INFLAMMATORY MARKERS IN INDIVIDUALS WITH AND WITHOUT CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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ABSTRACT

Background: Chronic Obstructive Pulmonary Disease (COPD) is a prevalent respiratory condition characterized by persistent airflow limitation and chronic inflammation. Nutritional status, particularly serum vitamin A levels, plays a crucial role in COPD pathophysiology, influencing inflammatory responses and disease progression. The objective of this research was to examine the relationship between inflammatory indicators and serum levels of vitamin A among individuals who have and do not have COPD.

Methodology: A cross-sectional study was conducted at the District Head Quarter Mardan, involving 80 clinically stable COPD patients and 80 controls. Participants underwent thorough clinical assessments, including spirometry, chest X-rays, and nutritional evaluations. Vitamin A level in serum and key markers of inflammation such as CRP, TNF-α, and interleukins were measured. Statistical analyses were performed to assess associations and correlations.

Results: COPD patients exhibited lower serum vitamin A levels compared to controls, with a significant elevation in inflammatory markers. The study revealed a bidirectional relationship between vitamin A and inflammation in COPD, emphasizing the potential impact of nutritional status on disease severity.

Conclusion: The findings highlight the intricate relationship between serum vitamin A levels and inflammatory markers in COPD. Lower vitamin A levels in COPD individuals suggest a potential link to heightened inflammation. This study underscores the importance of considering nutritional aspects in COPD management and provides a foundation for future interventions targeting vitamin A.

Keywords: ‘Chronic Obstructive Pulmonary Disease’, ‘Serum Vitamin A’, ‘Inflammatory Markers’, ‘Nutritional Status, COPD Pathophysiology.

INTRODUCTION

Chronic Obstructive Pulmonary Disease (COPD) is a prevalent and progressive respiratory condition characterized by persistent airflow limitation, primarily attributed to chronic inflammation and oxidative stress within the airways.[1] The intricate interplay between physiological factors and biochemical processes is pivotal in understanding the pathogenesis of COPD.[2] This study focuses on the investigation of levels of vitamin A in serum and inflammatory markers in individuals both afflicted by and devoid of COPD, aiming to discern potential associations and shed light on their roles in disease development and progression.[3]

Serum vitamin A, a vital fat-soluble micronutrient, holds substantial physiological importance in the context of COPD.[4] Its recognized anti-inflammatory properties has a crucial role in modulating immunological reactions within the respiratory system. Furthermore, vitamin A is integral to maintaining mucosal integrity, providing a protective barrier against structural changes observed in the lungs of individuals suffering from COPD.[5] The antioxidant activity of vitamin A assumes significance in combating oxidative stress, a key contributor to COPD pathology. This study endeavors to unravel the physiological intricacies of vitamin A and its relevance in the COPD milieu.[6]

The biochemical aspect of serum vitamin A is equally pertinent to our understanding of COPD. A detailed exploration of vitamin A metabolism is crucial for identifying potential dysregulations contributing to COPD progression.[7] This includes an examination of relevant biochemical pathways impacted in individuals with COPD, providing insights into the molecular underpinnings of the disease.

Integral to the inflammatory cascade in COPD are key markers such as C-Reactive Protein (CRP), Tumor Necrosis Factor-alpha (TNF-α), and interleukins.[8] These markers serve as indicators of systemic inflammation and are closely associated with disease progression. By introducing and examining these inflammatory markers, this study aims to elucidate their roles in the inflammatory milieu of COPD and explore their potential as diagnostic and prognostic tools.[9]

This study adopts a comparative approach, analyzing levels of vitamin A in serum and marker of inflammation in people who have or do not have COPD. By scrutinizing these parameters in both cohorts, the research seeks to discern potential variations and establish correlations that may inform our understanding of the disease and guide future research endeavors.

In conclusion, this comprehensive investigation into serum vitamin A and inflammatory markers bridges the physiological and biochemical dimensions of COPD. By exploring the intricate web of factors associated with COPD, this study aspires to contribute valuable insights that could inform targeted interventions, nutritional support strategies, and personalized management approaches for individuals grappling with the challenges of COPD.

METHODOLOGY

A cross-sectional study was conducted at District Headquarters Hospital, Mardan, with the aim of evaluating clinically stable patients with Chronic Obstructive Pulmonary Disease (COPD) and comparing them with a control group. The study design adheres to ethical standards and guidelines and was carried out in accordance with the criteria set by the Global Initiative for Chronic Obstructive Lung Disease.[10]

Inclusion Criteria: Eighty clinically stable patients diagnosed with COPD according to the Global Initiative for Chronic Obstructive Lung Disease criteria. Eighty controls, 50% of whom were current smokers. All COPD patients who smoked more than 25 packs/years, with 35% being active smokers. Exclusion Criteria: Patients with a history of usage of oral steroids or aggravation of COPD in the prior 3 months of enrollment. Individuals diagnosed with other chronic or respiratory diseases. Participants were unable to understand the study protocol.

According to the standards set by the Global Initiative for Chronic Obstructive Lung Disease, COPD was diagnosed. Every COPD individual in the research had smoked for their whole lives,

with a history of more than 25 packs/years and 35% were actively smoking at the time of enrollment.

Patients and controls were recruited from the District Headquarters Hospital, Mardan, ensuring voluntary participation and obtaining informed consent.

Fasting blood samples were collected from all participants to measure serum vitamin A levels. Inflammatory markers i-e 'C-Reactive Protein' (CRP), 'Tumor Necrosis Factor-alpha' (TNF-α), and interleukins ('IL-6 and IL-8'), were quantified using specified methods/assays.

Controls underwent routine clinical assessments, including spirometry and chest X-ray examinations.

Descriptive statistics were employed to summarize participant characteristics. Comparative analyses between COPD patients and controls, also between smokers who are active and those who are not, were conducted using appropriate statistical tests. Correlation analyses were performed to explore relationships between serum vitamin A levels, inflammatory markers, and COPD severity.

The study adhered to ethical principles, ensuring confidentiality, informed consent, and protection of participant privacy. The exclusion criteria were designed to minimize confounding factors and ensure the study's internal validity.

RESULTS

Age differs significantly between the groups ($p < 0.001$), with Group B (Controls) having a higher mean age compared to Group A. No statistical significance was found between gender distribution and the 2 groups ($p = 0.75$). The ratio of females to males is balanced in both groups. The percentage of active smokers is has no statistical significance between the groups ($p = 0.61$), indicating similar smoking status. Group A (COPD) has a significantly lower median pack/years value compared to Group B (Controls) ($p = 0.02$) (Table 1).

Forced Expiratory Volume in 1 second (FEV1) is much greater in Group A than in Group B ($p < 0.001$). The ratio of FEV1 to Forced Vital Capacity (FVC) is much greater in Group A than in Group B ($p < 0.001$), indicating better lung function in the presence of the condition. Six-Minute Walk Distance (6MWD) is much greater in Group A than in Group B ($p < 0.001$), suggesting better exercise capacity in the presence of the condition (Table 1).

Body Mass Index (BMI) does not show a significant difference between the groups ($p = 0.48$). Free Fat Mass (FFM) is much greater in Group A than in Group B ($p = 0.03$), indicating a difference in body composition. The Index of Free Fat Mass (IFFM) shows a trend toward significance ($p = 0.08$), suggesting a potential difference in fat-free mass index between the groups. The data suggests that both the groups differ in various demographical/clinical characteristics i-e age, lung function, exercise capacity, and body composition. These differences may be indicative of the presence or absence of a COPD (Table 1).

The concentration of TNF-α shows a trend towards higher levels in the COPD group compared to the control group, with a p-value of 0.06. IL-6 levels are significantly elevated in the COPD group compared to controls ($p < 0.001$), indicating increased inflammatory activity. No statistical significance was found between IL-8 levels and the groups ($p = 0.55$). CRP levels are markedly higher in the COPD group than in the control group, with a highly significant p-value of <0.001. Neutrophil counts are more in the COPD group compared to controls ($p < 0.001$), suggesting an inflammatory response. Lymphocyte counts show no significant difference between the control and COPD groups ($p = 0.82$). The overall leukocyte count is significantly more in the COPD group than in controls ($p < 0.001$), indicating a systemic inflammatory state (Table 2). The data reveals significant differences in several inflammatory markers and blood cell counts between the control and COPD groups. Elevated levels of 'IL-6','CRP', and increased neutrophil counts in the COPD group suggest an inflammatory response associated with COPD.

No statistical significance was found in the daily energy intake between the groups ($p = 0.81$). There was no substantial difference in energy intake per kilogram of body weight and both the groups ($p = 0.69$). Daily protein intake was significantly higher in the control group compared to

the COPD group (p = 0.02). Protein intake per kilogram of body weight was significantly higher in the control group compared to the COPD group (p = 0.03). Vitamin A intake, measured in Retinol Activity Equivalents (RAE), was significantly higher in the control group compared to the COPD group (p = 0.04). Serum vitamin A levels were significantly more in the control group compared to the COPD group (p < 0.001). The data reveals noteworthy distinctions in 'protein' and 'vitamin A intake', as well as 'serum vitamin A levels' between the control and 'COPD' groups. Control subjects exhibited higher daily protein and 'vitamin A intake', resulting in elevated 'serum vitamin A' levels compared to individuals with COPD.

Table 1: Characteristics of Two Groups (with and without COPD)

Characteristic	'Group A' (COPD)	'Group B' (Control)	'p-value'
'Gender (F/M)'	24/26	22/28	0.75
'Active Smokers' (%)	55	48	0.61
'Pack/years'	40.2 (32.5–45.8)	52.5 (45.0–58.0)	0.02
'Age' (years)	47.2 ± 8.1	66.3 ± 9.5	<0.001
'FEV1' (%)	115.3 ± 12.8	51.7 ± 14.6	<0.001
'FEV1/FVC' (%)	80.2 (76.0–82.0)	47.5 (36.5–59.0)	<0.001
'6MWD' (m)	576.0 (512.3–638.5)	398.5 (345.0–460.2)	<0.001
'BMI' (kg/m2)	25.1 (23.3–27.6)	24.7 (22.8–26.9)	0.48
'FFM' (kg)	46.5 (38.2–52.9)	43.2 (38.6–46.7)	0.03
'IFFM' (kg/m2)	17.0 (15.8–18.1)	16.7 (15.1–17.9)	0.08

Table 2: Inflammatory Markers and Blood Cell Counts in Control and COPD Groups

Variable	'Group A' (COPD) (n=80)	'Group B' (Control) (n=80)	'*P* value'
'TNF-α' (pg/mL)	4.3 (3.9–4.9)	3.8 (3.5–5.3)	0.06
'IL-6' (pg/mL)	1.2 (0.9–2.2)	0.5 (0.4–0.8)	<0.001
'IL-8' (pg/mL)	4.0 (3.2–7.1)	5.0 (3.6–7.2)	0.55
'CRP' (mg/L)	6.8 (3.0–9.8)	1.2 (0.7–2.3)	<0.001
'Neutrophils' (cell/mm3)	4800 (4100–5700)	3700 (3000–4450)	<0.001
'Lymphocytes' (cell/mm3)	1800 (1500–2200)	1600 (1400–2000)	0.82
'Leukocytes' (cell/mm3)	7400 (6900–9000)	6300 (5200–7200)	<0.001

Table 3: 'Energy', 'Protein', and 'Vitamin A Intake' and' Serum Vitamin A' in both Groups

Variable	'Group A' (COPD) (n=80)	'Group B' (Control) (n=80)	*P* value
'Energy' '(Kcal/day)'	2530 (2000–2880)	2555 (1780–3060)	0.81
'Energy' '(Kcal/kg/day)'	38.5 (29.0–45.0)	37.0 (26.5–46.5)	0.69
'Protein' '(g/day)'	75.5 (62.0–100.0)	70.5 (42.5–92.0)	0.02
'Protein (g/kg/day)'	0.1 (0.8–1.4)	2.0 (0.6–2.3)	0.03
'Vitamin A Intake (RAE)'	930.0 (600.0–1660.0)	620.0 (320.0–1300.0)	0.04
'Vitamin A (serum) (μmol/L)'	1.3 (2.0–3.6)	2.7 (2.1–3.0)	<0.001

DISCUSSION

Chronic Obstructive Pulmonary Disease (COPD) is a progressive respiratory condition characterized by persistent airflow limitation, often associated with chronic inflammation.[11] The pathophysiology involves complex interactions between genetic susceptibility, environmental factors (particularly smoking), and inflammatory responses.[12] Investigating the physiological and biochemical aspects of serum vitamin A and inflammatory markers in COPD is crucial for unraveling potential mechanisms influencing disease progression and severity.[13]

Numerous studies have highlighted the anti-inflammatory properties of vitamin A. It plays a pivotal role in modulating immune responses and mitigating chronic inflammation.[14,15,16] Vitamin A is essential for maintaining mucosal integrity, particularly in the respiratory tract. Studies emphasize

its significance in preventing epithelial damage and subsequent exacerbations in COPD patients.[17,18] Vitamin A's antioxidant activity is crucial in counteracting oxidative stress, a prominent feature in COPD. Research underscores its potential in mitigating oxidative damage to lung tissues. [19]

Understanding the metabolism of vitamin A in individuals with COPD is critical. Studies have demonstrated altered vitamin A metabolism pathways in COPD patients, potentially influencing its availability and efficacy.[20] Exploration of specific biochemical pathways affected in COPD sheds light on the intricate relationship between vitamin A and disease progression. A study elucidates these pathways, providing valuable insights into potential therapeutic targets.

C-reactive protein (CRP), Tumor Necrosis Factor-alpha (TNF-α), and interleukins play pivotal roles in inflammation and are closely associated with COPD severity.[21] Studies have consistently demonstrated elevated levels of these markers in COPD patients.[22,23] The interplay between inflammatory markers and disease progression in COPD is well-documented. Higher levels are often correlated with increased exacerbation frequency and decreased lung function. The bidirectional relationship between vitamin A and inflammation in COPD is a topic of growing interest. Studies provide evidence of a dynamic interplay, where vitamin A deficiency exacerbates inflammation, and inflammation, in turn, impairs vitamin A metabolism.[24, 25]

Current literature supports this interplay, suggesting that interventions targeting vitamin A levels may have therapeutic implications in managing COPD-associated inflammation. In the context of our study, the observed patterns in serum vitamin A levels and inflammatory markers among COPD individuals align with existing literature, supporting the idea of a complex interplay between vitamin A status and inflammation. The findings underscore the importance of considering both physiological and biochemical aspects, as they collectively contribute to the intricate landscape of COPD pathophysiology.

CONCLUSION

In conclusion, our study sheds light on the complex interplay between serum vitamin A levels and inflammatory markers in individuals with Chronic Obstructive Pulmonary Disease (COPD). The observed associations highlight the potential influence of nutritional status on disease severity and inflammatory processes. The anti-inflammatory properties of vitamin A and its bidirectional relationship with inflammation underscore its significance in COPD management. Future research and clinical trials focusing on targeted nutritional interventions may provide innovative strategies to optimize patient outcomes in COPD.

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