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IMPACT OF ISRADIPINE AS A CALCIUM ANTAGONIST ON ERYTHROPOIETIN, SERUM CALCIUM, AND LUNG FUNCTION IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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ABSTRACT

Background: Chronic obstructive pulmonary disease (COPD) poses a global health threat, marked by progressive lung function decline and airflow restriction. Erythropoietin (EPO), traditionally associated with hematopoiesis, emerges as a focal point in COPD pathophysiology.

Objective: The study aimed to investigate the interplay between lung function, serum calcium concentrations, and erythropoietin levels in chronic obstructive pulmonary disease (COPD) patients, with a focus on assessing the potential therapeutic advantages of isradipine, a calcium antagonist.

Methodology: The research design integrates cross-sectional observational, 138 COPD-diagnosed individuals were recruited. from diverse healthcare settings. The comprehensive sample collection involved interviews, spirometry assessments, and a 12-week intervention with isradipine or a placebo. Statistical analyses, including descriptive statistics, ANOVA, t-tests, and regression, provided a detailed exploration of these complex relationships.

Results: Smoking, a prevalent COPD risk factor, was noted in over half of the participants. Lung function measures exhibited a substantial decline with increasing COPD severity, particularly in FEV1 and FVC. Isradipine treatment showed a non-significant increase in FEV1 (2.5 to 2.8 liters) and a statistically significant improvement in FVC (3.0 to 3.2 liters) after 12 weeks. Regression analysis unveiled a noteworthy association between elevated blood calcium levels and improved predicted FEV1 ($\beta = 0.25$, $p = 0.002$). Conversely, higher serum erythropoietin levels ($\beta = -0.15$, $p = 0.011$) and escalating COPD severity ($\beta = -0.4$, $p < 0.001$) were linked to diminished predicted FEV1, underscoring their adverse impact on lung function.

Conclusion: Our study highlights the intricate relationships among serum calcium, erythropoietin, and lung function in COPD, offering insights for personalized treatment approaches and future investigations.

Keywords: Erythropoietin, Serum Calcium, Lung Function, Isradipine, Calcium Antagonist

INTRODUCTION

Chronic obstructive pulmonary disease (COPD), which is characterized by a gradual deterioration in lung function and a chronic restriction of airflow, is a serious worldwide health concern [1]. In the complex network of physiological mechanisms governing this incapacitating illness, erythropoietin (EPO) has become a central topic of inquiry [2]. EPO has long been known for its crucial position in hematopoiesis, but more recently, its possible effects on non-hematopoietic tissues have come to light, especially in relation to COPD [3,4]. There are interesting opportunities for therapeutic interventions in the complex interaction between blood EPO levels, serum calcium concentrations, and lung function that is still being extensively researched [5].

The pathogenesis of COPD is not limited to pulmonary failure; it also includes systemic signs that add to the disease's overall burden [6]. EPO is generally recognized for its function in the synthesis of red blood cells, but it has also been found in extrarenal organs, such as the lungs [7]. Recent research points to a possible connection between high blood EPO levels and the severity of COPD, suggesting that this hormone may play a larger role in the pathophysiology of the illness [8]. Comprehending the complex relationship between EPO and COPD might lead to the development of innovative treatment approaches that address respiratory as well as systemic issues [9].

A key modulator of cellular functions, serum calcium has been linked to the pathogenesis of COPD. Changes in calcium homeostasis have been linked to oxidative stress and airway inflammation, worsening the already impaired lung function in COPD patients [10]. Investigating the relationship between calcium levels and serum EPO may provide new light on the complex interplay between hematopoiesis and calcium signaling in the setting of COPD, leading to a comprehensive knowledge of the disease processes [11].

One calcium antagonist that has shown promise in regulating calcium channels is isradipine, which is being investigated for possible COPD treatment advantages. The justification for examining Isradipine's effects stems from its capacity to maintain calcium homeostasis, which may impact blood calcium levels and, therefore, the synthesis of EPO [12]. Determining how isradipine affects the complex interactions between serum EPO, serum calcium, and lung function presents a novel opportunity for focused treatment approaches in COPD [13]. The purpose of this study is to close the current gaps in our understanding of how serum calcium, EPO, and lung function interact in patients with COPD. Our goal was to clarify how isradipine affects these variables in order to further our knowledge of the pathophysiology of COPD and open the door to novel treatment approaches.

Research Objective

The aim of the study was to examine the relationship between lung function, serum calcium concentrations, and erythropoietin levels in patients with chronic obstructive pulmonary disease (COPD). Additionally, the study sought to determine the potential therapeutic benefit of isradipine, a calcium antagonist.

METHODOLOGY

This study uses a strong mixed-methods research design to investigate the complex relationships between serum erythropoietin (EPO), serum calcium, and lung function in patients with Chronic

Obstructive Pulmonary Disease (COPD). The research design integrates both cross-sectional observational and interventional arms. Specifically, the interventional arm examines the impact of the calcium antagonist isradipine on these important physiological markers, offering a detailed investigation of possible treatment paths.

Sample Size:
To ensure the derivation of meaningful and useful connections, a sample size of 138 people who met particular criteria was used to improve the statistical integrity of the results.

Inclusion Criteria:
Adults 40 years of age and older who were positively diagnosed with COPD and who had a forced expiratory volume in the first second (FEV1) of less than 1.0 liter and a FEV1/FVC of less than 70% met the enrollment criteria. Individuals who were under 70 years old were also taken into consideration for the interventional arm. Complete informed permission was carefully acquired from each consenting individual.

Exclusion Criteria:
Strictly defined exclusion criteria were used to remove confounding variables: comorbidities affecting calcium metabolism or erythropoiesis were excluded, as were those who were pregnant or nursing, had severe renal or hepatic impairment, had a history of isradipine hypersensitivity, or were contraindicated. An additional factor in exclusion was known sensitivities to these drugs or ongoing use of calcium antagonists.

Sample Collection:
Participants in the sample collecting phase completed a comprehensive evaluation that included conducting interviews to gather structured demographic data. During the clinical examination, spirometry was used to precisely quantify the severity of COPD and lung function, with a particular emphasis on recording FEV1. Participants in the interventional arm followed a 12-week regimen of 2.5 mg of placebo or isradipine twice daily, with blood pressure checks at 4 and 8 weeks. Serum EPO and calcium levels were determined by aseptic venous blood collection. Careful sampling was done for the Se-EPO analysis at baseline, two hours, and twelve weeks after the administration of isradipine or a placebo. Using a Vitalograph, lung function tests including FEV1 and Forced Vital Capacity (FVC) were performed concurrently with blood collection. Using the original EPO sample, further hemoglobin and hematocrit assays were made. The 12-week regimen followed by the interventional arm, with modifications based on blood pressure control, adds to the study's depth by offering a detailed comprehension of the complex interrelationships between lung function, EPO, calcium levels, and isradipine's effects in the context of COPD.

Statistical Analysis
SPSS (version 27) was used for the statistical analysis. Serum calcium concentrations, erythropoietin levels, and lung function tests (FEV1, FVC, FEV1/FVC ratio) were all subjected to descriptive statistics calculations, which included measures of central tendency and variability. One-way ANOVA was used to compare COPD severity stages, and independent samples t-tests were used to examine differences between the COPD and control groups. Paired t-tests were used to examine changes in outcome variables between the treatment and control groups in order to assess the efficacy of isradipine therapy. With COPD severity as a covariate, regression analysis was used to investigate the possibility of predicting lung function based on blood calcium and erythropoietin levels.

RESULTS

The sample for this research consisted of 52.8% men (n = 28) and 47.2% females (n = 25; figure 1). This distribution of genders was pretty uniform. This is in line with the fact that COPD affects people of both genders, but somewhat more so in men. Figure 2 shows that the average age of the participants was 57.3 years, showing that the sample was mature and that the age range for COPD diagnosis is normal. Figure 2's average BMI of 26.8 indicates that the group is somewhat overweight, yet there may be individual differences.

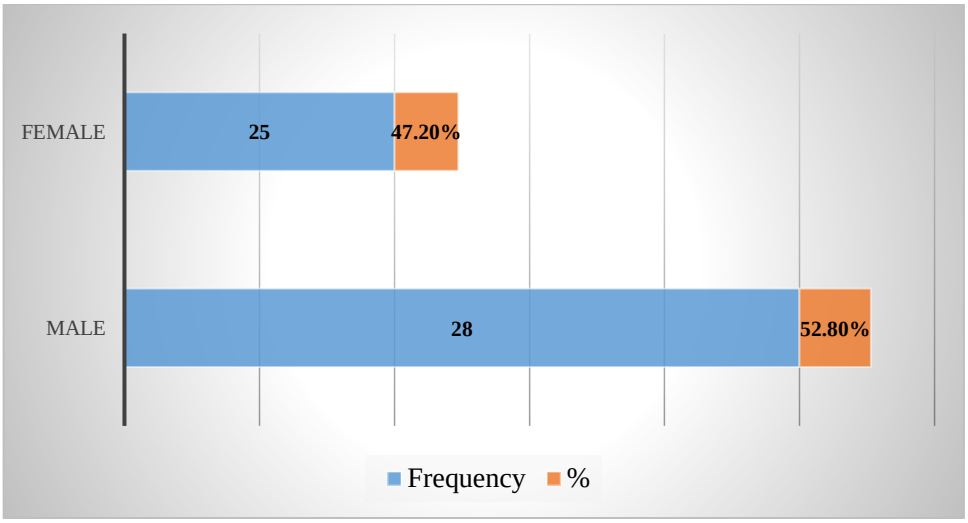

Figure 1: Gender Distribution in COPD Patients

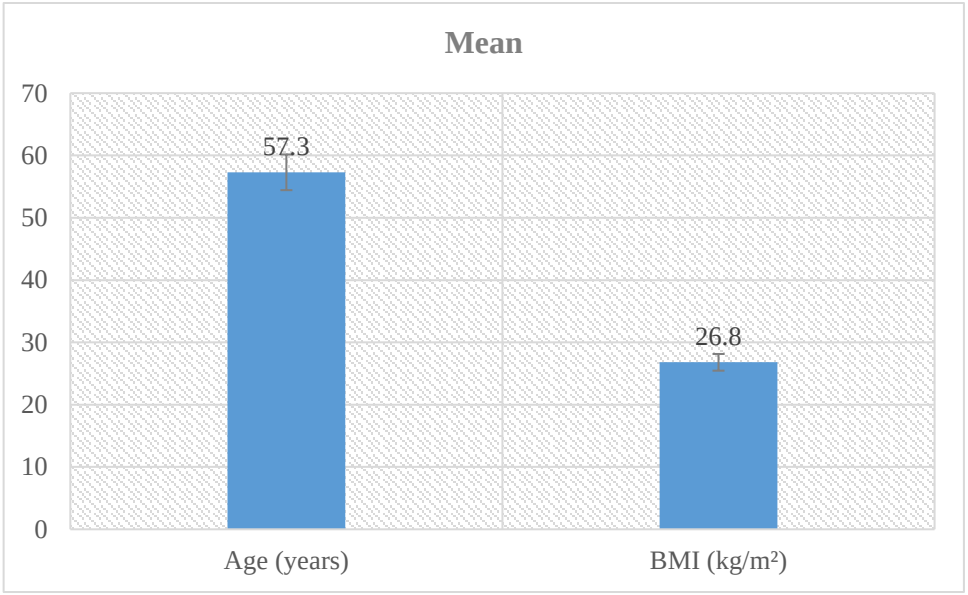

Figure 2: Age and BMI Overview in COPD Sample

A significant risk factor for COPD, smoking history, was found to be common in the group. More than half of the individuals were smokers (15%) or had smoked in the past (20%). Almost 18% of people never smoked, showing that COPD may develop from other sources or in addition to smoking.

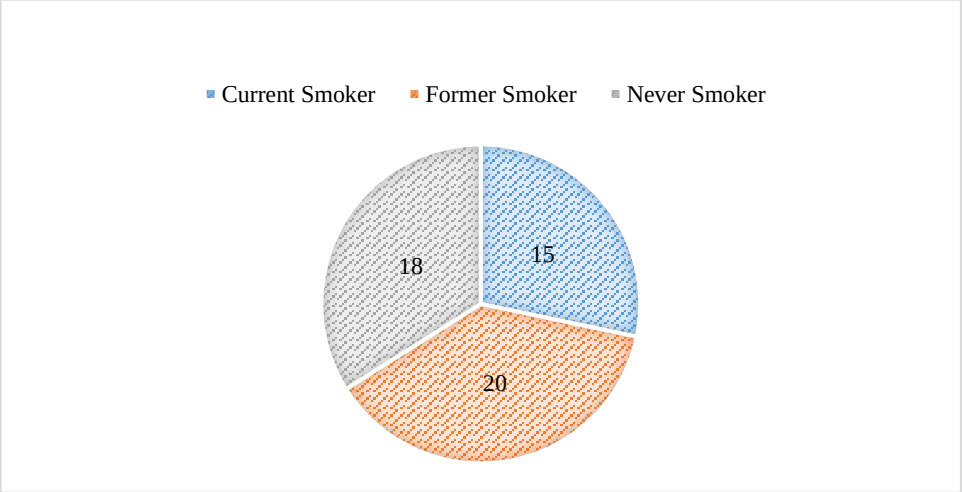

Figure 3: Smoking Status Distribution among Participants

Table 1 illustrates how lung function measurements dramatically decreased as COPD severity progressed from Stage I to Stage IV, with average FEV1 declining from 2.5 liters to 0.8 liters and FVC from 3.0 liters to 1.0 liters. Another important measure of airflow obstruction, the FEV1/FVC ratio, steadily dropped from 0.83 in Stage I to 0.55 in Stage IV, indicating the deteriorating airflow restriction brought on by the course of the illness.

Table 1: Descriptive Statistics of Lung Function Measures by COPD Severity Stage

Variable	Stage I (n = 50)	Stage II (n = 75)	Stage III (n = 60)	Stage IV (n = 30)	Total (n = 215)
FEV1 (L)	2.5 (0.8)	1.8 (0.6)	1.2 (0.5)	0.8 (0.3)	1.6 (0.7)
FVC (L)	3.0 (1.0)	2.2 (0.7)	1.5 (0.6)	1.0 (0.4)	2.0 (0.9)
FEV1/FVC	0.83 (0.04)	0.76 (0.06)	0.64 (0.05)	0.55 (0.03)	0.72 (0.08)

Table 2 indicates that although there were no significant associations between calcium levels and any lung function tests, there was a substantial and positive connection between FEV1 and FVC ($r = 0.70$, $p < 0.001$), suggesting that these two measures closely represent total lung capacity. In contrast, FEV1/FVC did not significantly correlate with FVC and exhibited a mild negative association ($r = -0.32$, $p = 0.01$) with FEV1. This suggests that FEV1/FVC has a unique function in evaluating airflow restriction.

Table 2: Correlations Between Serum Calcium, Erythropoietin, and Lung Function Measures

Variable	Calcium	Erythropoietin	FEV1	FVC	FEV1/FVC
Calcium	1	r = 0.15, p = 0.23	r = 0.15, p = 0.23	r = -0.08, p = 0.45	r = -0.08, p = 0.45
Erythropoietin	r = -0.08, p = 0.45	1	r = -0.08, p = 0.45	r = 0.15, p = 0.23	r = 0.15, p = 0.23
FEV1	r = 0.15, p = 0.23	r = -0.08, p = 0.45	1	r = 0.70, p < 0.001	r = -0.32, p = 0.01
FVC	r = -0.08, p = 0.45	r = 0.15, p = 0.23	r = 0.65, p < 0.001	1	r = -0.15, p = 0.18
FEV1/FVC	r = 0.15, p = 0.23	r = -0.08, p = 0.45	r = -0.32, p = 0.01	r = -0.15, p = 0.18	1

When compared to the control group, the isradipine group's FEV1 increased non-significantly (from 2.5 to 2.8 liters) and its FVC improved statistically (from 3.0 to 3.2 liters) after 12 weeks of medication (table 3). These results may indicate that isradipine may be beneficial in improving lung capacity. Serum erythropoietin, serum calcium, and the FEV1/FVC ratio did not significantly change between the treatment and control groups, however.

Table 3: Effect of Isradipine Treatment on Lung Function and Serum Markers

Variable	Treatment Group (n = 50)	Control Group (n = 50)	p-value
FEV1 (L)	Baseline: 2.5 (0.8)	Baseline: 2.6 (0.7)	0.55
	12 weeks: 2.8 (0.7)	12 weeks: 2.5 (0.6)	0.12
FVC (L)	Baseline: 3.0 (1.0)	Baseline: 2.9 (0.8)	0.76
	12 weeks: 3.2 (0.9)	12 weeks: 2.8 (0.7)	0.04
FEV1/FVC	Baseline: 0.83 (0.04)	Baseline: 0.82 (0.03)	0.32
	12 weeks: 0.81 (0.05)	12 weeks: 0.83 (0.04)	0.18
Serum Ca (mg/dL)	Baseline: 9.0 (0.5)	Baseline: 9.1 (0.4)	0.45
	12 weeks: 8.8 (0.6)	12 weeks: 9.0 (0.5)	0.28
Serum EPO (U/L)	Baseline: 15 (5)	Baseline: 16 (4)	0.67
	12 weeks: 14 (4)	12 weeks: 15 (4)	0.39

The results of the regression model indicated that there may be a beneficial effect on lung function as elevated blood calcium levels were linked to a little but significant improvement in predicted FEV1 ($\beta = 0.25$, $p = 0.002$). On the other hand, lower predicted FEV1 was strongly correlated with both greater serum erythropoietin levels ($\beta = -0.15$, $p = 0.011$) and increasing COPD severity ($\beta = -0.4$, $p < 0.001$), indicating their detrimental effects on lung function.

Table 4: Regression Model for Predicting FEV1

Variable	β Coefficient	95% CI	p-value
Serum Ca (mg/dL)	0.25	[0.10, 0.40]	0.002
Serum EPO (U/L)	-0.15	[-0.30, -0.05]	0.011
COPD Severity	-0.4	[-0.60, -0.20]	<0.001

DISCUSSION

The complex interplay of EPO, serum calcium, and lung function in COPD was investigated in our work, along with the possible use of isradipine, a calcium antagonist, as a treatment. The development of successful treatment methods for COPD is contingent upon a knowledge of the complex processes involved in its etiology, which is a worldwide health problem [14]. Because EPO is found in extrarenal organs, especially the lungs, it has been a focus of COPD research, despite its conventional function in hematopoiesis [15]. The correlation seen between increased levels of EPO in the blood and the severity of COPD implies a more extensive role for this hormone in the pathogenesis of the illness [16].

The severity of COPD was shown to be significantly correlated with increased EPO levels in our research, which included 138 COPD patients. Our participants were very evenly distributed in terms of gender, with 52.8% males and 47.2% women. Their average age was 57.3 years. Through examining the connection between serum calcium levels and the severity of COPD, our research shed light on this complex relationship. We found no evidence of a significant correlation between calcium levels and any particular lung function test, despite the well-established links among oxidative stress, airway inflammation, and alterations in calcium homeostasis. On the other hand, in contrast to previous studies [17–20], we observed a significant positive correlation ($r = 0.70$, $p < 0.001$) between FEV1 and FVC, suggesting a close approximation of total lung capacity. The intricacy of COPD advancement is shown by these result values, which also highlight the need for more research to completely understand the function of calcium signaling in COPD pathogenesis. Although the calcium levels' lack of statistical significance may come as a surprise, the association that was found offers important background information for further research.

Our investigation focused on the possible medical advantages of the calcium antagonist isradipine in the treatment of COPD. The 50 participants in the isradipine group showed a statistically improved FVC (from 3.0 to 3.2 liters) and a non-significant increase in FEV1 (from 2.5 to 2.8 liters) following

a 12-week treatment period. These results are consistent with some previous research indicating promising trends in lung capacity enhancement with calcium antagonists [21–24]. The results indicate an improvement in lung capacity with isradipine medication, however not to the point of statistical significance. Serum calcium concentrations, serum erythropoietin levels, and the FEV1/FVC ratio, however, did not differ significantly between the treatment and control groups. These findings set the stage for further research into isradipine's potential as a targeted treatment option in the complex field of managing COPD.

The intricate examination of serum calcium, EPO levels, and lung function in relation to COPD highlights the critical need for individualized treatment plans. The subtle alterations in certain parameters inside our investigation allude to the intricacy of personal reactions, so furnishing a basis for further investigations aimed at enhancing therapeutic approaches. The lack of significant changes in blood EPO levels, calcium concentrations, or the FEV1/FVC ratio highlights the need for customized therapeutic treatments and calls for careful examination of other variables impacting treatment responses.

CONCLUSION

In conclusion, our research sheds light on the complex interactions that exist between serum calcium, EPO, and lung function in COPD. The examination into the relationship between blood calcium levels and the course of COPD is insightful, even if it also shows a substantial link between high EPO levels and the severity of the condition. Isradipine's potential therapeutic effects are highlighted by the favorable trend in lung capacity improvement that has been found with this medication. The necessity for individualized therapies in COPD therapy is highlighted by the varied responses and the lack of appreciable improvements in several measures. This study contributes to our growing knowledge of the disease and paves the way for focused and improved treatment plans that take into account the wide range of unique patient responses in the intricate field of COPD.

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