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Serum Levels of Erythropoietin in Patients with Anemia and Chronic Obstructive Pulmonary Disease

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Abstract: *Nanotechnology is the most common and frequently used technology that aims to improve the efficacy of medical procedures, sometimes known as Nanomedicine. With their impressive pharmacological efficacy as nanomedicines and delivery systems, nano materials have been recognized as attractive diagnostic and chemotherapeutic tools to treat diseases. To treat a wide range of solid malignant tumors, Drugs built on platinum complexes are now the foundation for many other therapies. They are often used to treat a variety of solid tumors in the clinic, including head and neck, colorectal, lung and other malignancies. Cell-specific targeting with nano-carriers is possible using both active and passive techniques. This paper provides a thorough overview of platinum-based drug delivery system with the help of nanotechnology. Their mechanisms of action used in the treatment of cancer and potential for further development are all anticipated.*

Key Words: Nanomedicines, Platinum Drugs, Chemotherapeutic, Pharmacological drugs

Introduction

Chronic obstructive pulmonary disease (COPD) is a progressive respiratory condition that predominantly affects the lungs and is characterized by chronic airflow restriction. Anaemia is one of the most common consequences of COPD, which is frequently accompanied by other comorbidities. The clinical results and quality of life of COPD patients can be profoundly impacted by anaemia, which is characterized as a reduction in the bulk of circulating red blood cells or haemoglobin levels. The hormone erythropoietin (EPO), which is largely generated in the kidneys, is essential for controlling the synthesis of red blood cells. EPO levels increase in response to hypoxia in order to promote erythropoiesis and preserve oxygen-carrying capacity [1–7]. The relationship between

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EPO levels and the onset of anaemia in individuals with COPD and anaemia, however, is still not established.

Investigating the relationship between EPO levels in anaemic and non-anaemic COPD patients was the goal of this investigation. We compare the serum EPO levels across COPD patients with and without anaemia to look for any notable variations. Additionally, this comparison investigation will clarify any potential contributions made by EPO to the development of anaemia in COPD patients. There are significant therapeutic ramifications to comprehending the relationship between EPO levels and anaemia in COPD patients. If a significant link is discovered, it may inspire the creation of brand-new pharmaceutical strategies that target EPO levels to efficiently treat anaemia in COPD patients. Furthermore, by shedding light on the underlying processes behind the intricate interactions between respiratory and haematological illnesses, this work may help us comprehend these interactions better.

Material and Methods

In this side-by-side investigation, 45 COPD patients' EPO levels and anaemia were compared. A number of variables were assessed, including BMI, EPO levels, RBCI, TIBC, CBC, and ferritin concentrations. In addition to additional laboratory tests assessing folate, vitamin B12, liver and kidney function, EPO levels were measured using an ELISA approach using an R and D kit on arterial blood samples that were obtained at 9 am.

The American Thoracic Society's recommended criteria were used in this research to make the COPD diagnoses. The requirements were as follows: a post-bronchodilator test demonstrating a rise in FEV1 of no more than 200 ml and 12%, an FEV1 of no more than eighty per cent of the expected value, and a FEV1/FVC ratio of below 0.7. Employing FEV1 values and the Global Initiative for Chronic Obstructive Lung Disease (GOLD) criteria, the severity of COPD was evaluated. Patients with COPD received standard and routine therapy, adhering to established guidelines for managing the disease. This therapeutic approach aimed to maintain haemoglobin levels below 13 mg/dl and 12 mg/dl for male and female patients respectively.

Our study included patients who met specific inclusion criteria: being over 40 years of age, and having a confirmed diagnosis of both anaemia and COPD. However, patients with exacerbation of COPD, asthma, left heart failure, recent blood transfusions, severe kidney or liver diseases, cancer, and other chronic conditions were excluded from the study. Additionally, individuals with vitamin B12 or folic acid deficiency, blood loss or a history of gastrointestinal bleeding, low serum ferritin levels, and positive drug history for vitamin B12 were also excluded from the study.

Data analysis

The data analysis was conducted using SPSS software version 22. Prior to the analysis, normality tests were performed to ensure the suitability of the data. To compare the quantitative variables between the anaemic and non-anaemic groups, both the Mann-Whitney test and independent t-test were employed. The correlation between EPO and haemoglobin (Hb) levels was examined using the Spearman correlation coefficient. Additionally, the correlation between patient factors such as demographic elements (gender, age), evaluation of opium use, anaemia, and spirometry results were assessed. For analyzing qualitative variables, the chi-square test was employed. Significance levels were determined with a threshold of p-values < 0.05, indicating statistical significance.

Results

We conducted cross-sectional research on COPD patients who received treatment in the pulmonary department at the Pakistan Institute of Medical Sciences in Islamabad over the course of a year. The total number of patients in that research was 45, with 34 men and 11 women, and a mean age of 55.54 7.08 years. Similarly, the haemoglobin levels, EPO levels, and other parameters, such as blood urea nitrogen, alkaline phosphatase, folic acid, vitamin B12, and more, were also analyzed

and compared against their respective reference ranges. In addition, the average FEV1/FVC and FEV1 were 45.56 11.15 and 36.25 6.33, respectively. (table 1).

Table 1

Summary of Clinical and Laboratory Parameters in the Study Population

Variable	Mean SD	Reference Range
Age (years)	55.54 7.08	-
	Spirometry Findings	
FEV1/FVC	45.56 11.15	no more than 5% from the predicted ratio.
FEV1	36.25 6.33	Equal to or greater than 80%.
	Lab Data	
Hb	11 [8–14]	Men and Women equal to or greater than 13 and 12 respectively.
Erythropoietin	29.30 [27–33]	4–26
Blood urea nitrogen	13 [12–17]	7–20
Mean corpuscular haemoglobin	32 [26–34]	27.5–33.2
Red cell distribution width	12 [11–13]	12.2–16.1
Platelet count	269 [205–383]	150–450
Total Bilirubin	0.5 [0.2 – 0.4]	1.2
Direct Bilirubin	0.3 [0.2–0.4]	0.3
Creatinine	0.6 [0.4–1.10]	Female: 0.59–1.04; Male: 0.74–1.35
Aspartate aminotransferase	24 [14–31]	10–40
Mean corpuscular volume	86 [81–93]	80–100
Serum Iron	102 [77–114]	60–170
Vitamin B12	514 [362–648]	160–950
WBCC	5 [4–9]	4.5–11
Ferritin	145 [91–209]	20–250
Folic acid	12 [8–17]	2.7–17.0
TIBC	340 [287–381]	240–450
Alanine aminotransferase	23 [17–28]	7–56
Alkaline phosphatase level test	210 [130–249]	44–147

Note: Hb (Hemoglobin), WBCC (White blood cell count), TIBC (Total iron binding capacity)

In terms of gender, there were 11 women in the group overall, 8 of whom had anaemia, and 3 of whom did not. There were 34 men in the group, 22 of whom had anaemia and 12 of whom did not. The mean values of EPO, FEV1, and FEV1/FVC did not show any appreciable variations between the groups. In terms of COPD severity, the majority of patients in both the anaemia and no anaemia categories had severe COPD. Additionally, the mean ejection fraction and systolic blood pressure did not substantially differ across the groups (table 2).

Table 2

Comparison of Variables between Overall Group and Anemia Subgroups in COPD Patients

Variable	Overall	Anaemia (n=25)	No Anemia (n=10)	P. value
Female	11	8	3	1.002
Male	34	22	12	
Erythropoietin (Mean SD)	29.28 (2.16)	29.43 (1.87)	28.8 (1.32)	0.439
FEV1 (Mean SD)	36.22 (6.32)	35.27 (6.41)	38.6 (5.87)	0.228
FEV1/FVC (Mean SD)	45.56 (11.15)	44.71 (10.80)	47.6 (12.3)	0.531
COPD Severity (n;%)				
Severe	31 (68.89)	21 (67.74)	10 (32.26)	0.674
Very severe	14 (31.11)	9 (64.29)	5 (35.71)	
Ejection Fraction (Mean SD)	61.96 (3.72)	62.47 (3.74)	60.6 (3.66)	0.342
Systolic blood pressure (Mean SD)	13.64 (2.42)	13.71 (2.49)	13.4 (2.71)	0.895

In our study, our main focus was to examine the relationship between EPO levels and factors such as haemoglobin and COPD severity. However, based on the findings presented in Table 3, we did not find any statistically significant association between haemoglobin and EPO levels, age and COPD severity.

Table 3

Analysis of the Relationships Between Hb, EPO Levels, COPD Severity, as well as Age

Variable	Erythropoietin Level	
	Coefficient Correlation	P value
FEV1/FVC	0.012	0.904
FEV1	0.031	0.865
Age	0.081	0.643
COPD Severity	0.089	0.654
Hb Level	0.029	0.834

Discussion

Even though research has shown that COPD patients' EPO levels are normal or close to normal compared to healthy people, hypoxia and elevated EPO levels were predicted in COPD patients [8]. This subject has been the subject of several analyses, however, it is still debatable, and its causes and consequences are yet unknown. In this research, we attempted to review and study previous research published in order to gain a thorough understanding of this issue, its various aspects, and some potential causes. We measured the EPO levels in the serum of COPD patients and looked at how they relate to other factors like haemoglobin levels.

The accumulated data from our research reveals that, despite the seriousness of the disease, the EPO level was not elevated in COPD patients, and Furthermore, no significant relationship between the claimed level and the degree of severity of the illness was found. Several investigators disagreed with our findings and claimed that individuals with COPD had elevated levels of EPO compared to normal. They also talked about how the hypoxic situation led to chronic airway blockage in their investigation, coupled with persistent anaemia [9-11]. In relation to this, Sharna et al. [12] reported research on 200 COPD individuals that revealed a striking increase in EPO levels with an increase in disease severity. While different investigators supported their

claims with data by pointing to reduced EPO production. Simply put, COPD issues prevented the typical increases in EPO levels that occur in hypoxic environments. Others have examined the amount of EPO in critically ill and seriously ill patients with asthma as well as non-respiratory patients, with the results showing that EPO responds to a reduction in hypoxia in inflammatory states [13,14]. About 100 people with COPD were examined by two researchers, Sela et al., [15] and El Gazzar et al., [16], who both observed reduced serum EPO levels throughout the period of severe inflammation in COPD aggravation.

A few studies compare the serum EPO levels in people with various degrees of COPD. In their analysis, they found that although EPO levels generally decline in sufferers of COPD, they varied according to the stage of the illness, with the second phase and phase 3 displaying the greatest measured values and phases 1 and phase 3 exhibiting the lowest levels. The hypoxic situation induces the synthesis of EPO, which raises the lower EPO level seen in phase 1 back to close to typical saturation levels. With regard to the final phase, it could be connected to the elevated inflammatory components. that do not increase the predicted output of EPO in a state of sufficient hypoxia [17].

Considering the results of the investigation, it was concluded that there was no statistically significant association between the Hb level and the concentration of EPO in the blood of those suffering from COPD. Boutou et al. [18] looked for a significant positive correlation in this regard. However, their study was constrained in that they did not assess the individual's iron profile-related data to prevent anaemia, lower Hb levels, and deficiencies in iron. There was nearly a hint of a tendency in the study by Mannino et al. [19] that there isn't much of a relationship between EPO levels and Hb levels in anaemic individuals who have COPD. However, the researchers omitted to measure the amount of vitamin B12 and folate levels that are necessary to prevent mixed anaemia, so the authors assigned the fall in Hb levels and people who are completely anaemic due to COPD problems. Contrarily though, a striking negative association between Hb and EPO level was reported by several investigations. Simply put, a rise in EPO levels causes a fall in Hb levels. They proposed that individuals with COPD had poor bone marrow activation to an increase in EPO as well as iron translocation. Therefore, a chronic condition that caused an increase in serum EPO levels could not also cause a rise in Hb levels. In general, it seems that anaemia along with low Hb levels found in COPD patients cannot be entirely compensated for by EPO [20,21].

Conclusion

In conclusion, we found that, in contrast to our predictions, EPO levels did not rise in COPD patients. This shows that the existence of chronic diseases, notably anaemia, a prevalent concomitant illness in COPD patients, cannot be made up for by EPO synthesis.

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