

Study the Correlation Between Serum Intact Parathyroid Hormone Levels and Erythropoiesis Resistance Index (ER) in Patients on Maintenance Hemodialysis (MHD)

Parathyroid & Erythropoiesis Levels in Hemodialysis Patients

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ABSTRACT

Objective: To find the correlation between serum intact parathyroid hormone levels and erythropoiesis resistance index (ER) in patients on Maintenance Hemodialysis (MHD)

Study Design: Analytical / Cross-Sectional Study

Place and Duration of Study: This study was conducted at the Dialysis Center and Nephrology OPD of Idris Teaching Hospital, Sialkot Medical College Sialkot from May 2018 to May 2019.

Materials and Methods: About 70 chronic kidney disease patients presenting to the Dialysis Unit and OPD Department and fulfilling the selection criteria were enrolled. Serum iPTH levels were measured by taking a fasting venous sample. Hb was calculated from CBC. ERI was calculated by the formula mentioned earlier. Data were used to calculate the correlation between iPTH levels and ERI using Karl Pearson coefficient with statistically p-value <0.05. Data were stratified for Age, Gender, BMI and Duration of MHD to address effect modifiers. Post stratification Pearson's correlation was applied with p-value < 0.05 was considered as significant.

Results: The mean age of the patients was 43.82±15.89 years. 16(22.9%) of the patients had age 16-35 years, while 32(45.7%) and 22(31.4%) of patients had ages between 36-55 and >55 years respectively. Gender distribution showed that 48(68.6%) were males while 22(31.4%) were females. The mean duration of patients on maintenance hemodialysis was 5.45±1.12 years. The mean BMI of patients on maintenance hemodialysis was 28.3±6.36. The mean iPTH and ERI was 67.54±22.69 and 9.11±4.24 respectively.

Conclusion: It was concluded that intact parathyroid hormone levels (iPTH) is positively correlated with erythropoiesis resistance index (ERI) in patients on Maintenance Hemodialysis (MHD).

Key Words: intact parathyroid hormone levels (iPTH), erythropoiesis resistance index (ERI), Maintenance Hemodialysis (MHD)

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INTRODUCTION

Anemia in chronic kidney disease (CKD) is very common; especially when the effective glomerular filtration rate (eGFR) is less than 35ml/min/1.73m². The main cause of anemia of CKD is decrease Erythropoietin (EPO) production by the kidneys.

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By the invention of Erythropoietin Stimulating Agents (ESAs), there is significant reduction in the requirement of blood transfusions in patients of CKD.^{1,2,3,4,5} Normally the erythropoietin is produced by peritubular interstitial fibroblasts in outer medulla and deep cortex. Hypoxia is a main stimulus for EPO production. EPO is essential for production and maturation of erythrocytes. There are different guidelines for target hemoglobin in ESRD. Generally accepted one is KDIGO. They recommend target Hb level is 10-12g/dl in ESRD. They also recommend the initiation of ESAs if Hb is less than 10g/dl, and can be initiated when Hb is above 10g/dl to improve the quality of life, they don't recommend the use of ESAs to increase Hb above 11.5g/dl due to increase mortality.^{2,6,7,8,9} While some studies suggest the level of 13g/dl is associated with increase in mortality due to thrombosis, hypertension and cardiovascular events.^{3-4,10-14} In spite of extensive use of ESAs, 7-14% of all patients with End Stage Renal Disease (ESRD) show suboptimal or no response to ESAs (i.e. the desired Hemoglobin concentration is not

achieved and remains below 10g/dl).^{5,16-18} There are several factors which can be the cause of ESAs non responsiveness. These include active inflammation, vitamin B12 deficiency,⁶ folate deficiency, malignancies, secondary hyperparathyroidism hyperphosphatemia⁷ and iron deficiency.⁸ However if these conditions are excluded, there is significant proportion of patients who still exhibit Primary ESA-resistant anemia. Intact parathyroid hormone is a marker of bone marrow suppression and previous studies have shown positive correlation between iPTH and erythropoiesis resistance index with a correlation coefficient 0.76 and p-value of < 0.001.⁹ This study is designed to see the correlation between iPTH and primary resistance to ESAs (by measuring ERI) in patients on Maintenance Hemodialysis (MHD) in our population. This will help up to guide management of anemia in patients on maintenance dialysis.

MATERIALS AND METHODS

This cross-sectional analytical study with non-probability consecutive sampling was conducted at Dialysis Center and Nephrology OPD of Idris Teaching Hospital, Sialkot Medical College Sialkot during May 2018 to May 2019.

Sample size: Sample size of 70 cases was calculated with 5% type I error and 10% type II error and taking expected correlation of 0.76 between intact PTH and ERI in patients on maintenance hemodialysis.⁹

RESULTS

A total of 70 patients fulfilling the inclusion/exclusion criteria were enrolled in the study to calculate the correlation between iPTH and ERI in patients on maintenance hemodialysis. The mean age of the patients was 43.82±15.89 years. 16(22.9%) of the patients had age 16-35 years, while 32(45.7%) and 22(31.4%) of patients had ages between 36-55 and >55 years respectively. Gender distribution showed that 48(68.6%) were males while 22(31.4%) were females. The mean duration of patients on maintenance hemodialysis was 5.45±1.12 years. The mean BMI of patients on maintenance hemodialysis was 28.3±6.36. The mean iPTH and ERI was 67.54±22.69 and 9.11±4.24 respectively. There was a positive correlation between iPTH levels and ERI with a Karl Pearson correlation coefficient of 0.370 with p-value 0.02. When stratified for age, the correlation coefficient between iPTH levels and ERI was 0.078 (p=0.77), 0.026 (p=0.92) and 0.930 (p=0.0001) in patients aged 16-35, 36-55 years and >55 years respectively. After stratifying the data for gender the correlation coefficient between iPTH levels and ERI was 0.650 (p=0.001) in males and 0.020(p=0.92) in females. When stratified with respect to duration of MHD, the correlation coefficient between iPTH levels and ERI was 0.294(p=0.03) in patients having MHD for >2 years, while the coefficient was 0.036 (p=0.88) and 0.204

(p=0.32) in patients having MHD for 2-4 years and >4 years respectively. When stratified with respect to BMI, the correlation coefficient between iPTH levels and ERI was 0.096(p=0.67) in patients having BMI 19-24, while the coefficient was 0.743 (p=0.002) and 0.687 (p=0.2) in patients having BMI for 25-29 and 30-39 respectively.

Table No.1: Frequency distribution of Gender

Gender	Frequency	Percent
Male	48	68.6
Female	22	31.4
Total	70	100.0

Table No.2: Frequency distribution of Age groups

Age Groups	Frequency	Percent
16-35	16	22.9
36-55	32	45.7
>55	22	31.4
Total	70	100.0

Table No.3: Frequency distribution of BMI

BMI	Frequency	Percent
19-24	31	44.3
25-29	34	48.6
30-39	5	7.1
Total	70	100.0

Table No.4: Frequency distribution of Duration of MHD

Duration of MHD	Frequency	Percent
<2 years	25	35.7
2-4 years	20	28.6
>4 years	25	35.7
Total	70	100.0

Table No.5: Mean±S.D of different variables

Statistics	Age	BMI	iPTH	ERI
Mean	43.83	28.30	67.54	9.11
Std. Deviation	15.90	6.37	22.70	4.24
Minimum	16.00	19.00	31.00	2.00
Maximum	70.00	39.00	112.00	15.00

Table No.6: Correlation Between iPTH levels and ERI

Correlation Between iPTH levels and ERI	n	70
	r	0.370
	p-value	0.02

n= number of patients r = correlation co-efficient

Table No.7: Stratification with respect to Gender of Correlation Between iPTH levels and ERI

Correlation Between iPTH levels and ERI in Males	n	48
	r	0.650
	p-value	0.001
Correlation Between iPTH levels and ERI in Females	n	22
	r	0.020
	p-value	0.92

n= number of patients r= correlation co-efficient

Table No.8: Stratification with respect to Age groups of Correlation Between iPTH levels and ERI

Correlation Between iPTH levels and ERI in 16-35 age group	n	16
	r	0.078
	p-value	0.77
Correlation Between iPTH levels and ERI in 36-55 age group	n	32
	r	0.026
	p-value	0.92
Correlation Between iPTH levels and ERI in >55 age group	n	22
	r	0.930
	p-value	0.0001

n= number of patients r= correlation co-efficient

Table No.9: Stratification with respect to BMI groups of Correlation Between iPTH levels and ERI

Correlation Between iPTH levels and ERI in 19-24 BMI group	n	31
	r	0.096
	p-value	0.67
Correlation Between iPTH levels and ERI in 25-29 BMI group	n	34
	r	0.743
	p-value	0.002
Correlation Between iPTH levels and ERI in 30-39 BMI group	n	5
	r	0.687
	p-value	0.200

n= number of patients r= correlation co-efficient

Table No.10: Stratification with respect to Duration of MHD of Correlation Between iPTH levels and ERI

Correlation Between iPTH levels and ERI in <2 years duration of MHD	n	25
	r	0.294
	p-value	0.03
Correlation Between iPTH levels and ERI in 2-4 years duration of MHD	n	20
	r	0.036
	p-value	0.880
Correlation Between iPTH levels and ERI in >4 years duration of MHD	n	25
	r	0.020
	p-value	0.328

n= number of patients r= correlation co-efficient

Inclusion Criteria: (1)Age >16 years and < 70 years (2) ESRD patients with Hemodialysis thrice a week for more than 3 months(3)Patients on weight based erythropoietin for at least 8 weeks(4)Hemoglobin <12 g/dl

Exclusion Criteria: (1)Patients having transferrin saturation < 30%.(2)Patients having vitamin B12 levels < 200 pg/ml(3)Patients having plasma folate levels < 4.5 ng/ml(4)Patients with history of myocardial infarction in the previous 3 months.(5)Patients with history of malignancy and active infection.

DISCUSSION

Anemia of ESRD is a multi-factorial disorder.^{19,20} There is some evidence suggesting that elevated levels of parathyroid hormone may inhibit the endogenous production of erythropoietin or the responsiveness to

erythropoietin.^{21,22} In our present study, we found that patients on MHD had positive correlation between iPTH value and ERI. Meyseset al²³ stated that iPTH directly inhibits human peripheral blood erythroid colony formation. Furthermore, ERI levels and blood reticulocytes were noted to be dramatically increased one to two weeks after parathyroidectomy in some HD patients.^{24,25} These results were matched with the results from Shih et al,²⁶ who found that the iPTH levels in MHD patients had the better responsiveness to ERI. Age >55 years had any influence on the responsiveness to ERI in our study. This is in agreement with the results from Jinn et al,¹⁰⁵ who found an influence of age >60 years, and Ishimura et al²⁷ suggested that Obesity is a risk factor for the severity of anemia in patients with renal failure not yet receiving dialysis. Power et al^{5,6} stated that the ERI response to anemia in the elderly is not similar to that in the young. In contrast, Yun et al^{6,7} found that a reduced ERI response to anemia could explain the anemia present in diabetics having no advanced diabetic nephropathy. Karioet al^{1,2} suggested that a decreased ERI responsiveness to low iPTH in the elderly. A higher percentage of male gender was found in this study; however, a direct causal relation or association between male gender and hyperparathyroidism needs further clarification.

CONCLUSION

It was concluded that intact parathyroid hormone levels (iPTH) is positively correlated with erythropoiesis resistance index (ERI) in patients on Maintenance Hemodialysis (MHD).

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- Concept & Design of Study: Ahmed Ammar
- Drafting: Saleh Muhammad, Amir Waheed
- Data Analysis: Maqsood Ahmed Khan, Muhammad Haris, Muaaz, Kamran Hamid
- Revisiting Critically: Ahmed Ammar
- Final Approval of version: Ahmed Ammar

Conflict of Interest: The study has no conflict of interest to declare by any author.

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