ANEMIA;
TO DETERMINE THE EFFICACY OF ERYTHROPOITEN IN CORRECTION OF HEAMOGLOBIN
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ABSTRACT: Iron, folate and B12 deficiencies are the common throughout in the world. National survey 2011 conducted in Pakistan revealed; nutrition anemia is 50.5% in women of child bearing age and 51% in pregnant women. Iron, folate, and B12 can be corrected by oral/, injectable and dietary supplementation however it takes 3-6 months treatment. The patients are symptomatic in moderate to severe anemia. Erythropoietin injection stimulate erythropoiesis in bone marrow and addition of iron ,folate B12 , improve heamoglobin up to 10g/dl after 04 weeks therapy .There is immediate symptomatic improvement and it avoids multiple blood transfusion. **Objectives:** To determine the efficacy of erythropoietin in correction of heamoglobin along with supplementation of iron, folate, and B12 for a period of 04 weeks. **Period:** January 2015-December 2015. **Study Design:** A prospective descriptive study. **Place of Study**: Mohi-Ud-Din Teaching Hospital Mirpur AJK. **Results:** Among 110 selected male and female patients, (age ranging 20-50 years), after erythropoietin injection plus iron,folateB12 supplementation, the reticulocytes and heamoglobin increased from 1.2 to11% and 4.5 to 10.5 g/dl respectively after 04 weeks therapy. **Conclusion:** Erythropoietin injection plus iron, folate, B12 supplementation is an effective way of erythropoiesis for correction of anemia after 04 weeks therapy. This immediately improved symptoms &sign of anemia thus avoiding the need of repeated blood transfusion.

Key words: anemia, Erythropoietin, reticulocytes count, heamoglobin, iron, folate, B12.

INTRODUCTION

Anemia is defined as a decrease in RBC count, Hb, hematocrit value resulting in a low ability for blood to carry 02 to body. Normal erythropoiesis is regulated by erythropoietin which is released in response to hypoxia.[1] Hypoxia, due to decrease in RBC count, stimulates to release erythropoietin from kidney which in turn stimulate bone marrow and thus enhance erythropoiesis. Normal Hb in men is >13g/dl and women >12g/dl. On the basis of morphology, anemia is classified into Normocytic, microcytic, and macrocytic anemia. Anemia severity according to WHO criteria: is given in Table-III.

Iron deficiency anemia is due to excessive loss of iron. Women are at increased risk for menstrual loss and growing fetus. Risk factors include poor socio-economic class, multiparty and menstrual problems.[2]

Magoblastic anemia is due to less intake of B12and folic acid. Pernicious anemia is inability of stomach to absorb B12 in the small intestine.[3]

Sign of anemia are brittle nails, koilonychias, atrophy of tongue, glossitis. Palpitation, chest pain, and generalized weakness. Investigations include hematocrits, Hb concentration. Hematocrits is the proportion of the volume of blood sample that is occupied by RBCs (Men 42-52% and women36-48%). Iron deficiency anemia is ranked at the top of three anemia.25% of pregnant and 19.95 non-pregnant suffer for anemia.[6]

The use of erythropoietin is expanding rapidly and the new preparations with greater potency and longer half-life are now available. Reticulocytes counts is used for predicting and monitoring

the response to erythropoietin. Response to erythropoietin can be assessed by measuring Hb g/dl.

After 04 weeks therapy a change in Hb>10g/dl and absolute reticulocyte count >40x19.9, identify that the patients is responding to erythropoietin. The purpose of this study is to determine the efficacy of erythropoietin in correction of Hb g/dl along with supplementation of iron, folate and B12.[9]

AIMS&OBJECTIVES
To determine the efficacy of erythropoietin in correction of heamoglobin along with supplementation of iron, folate, and B12 for a period of 04 weeks.

MATERIAL AND METHOTHS
A study was conducted at Mohi-Ud-Teaching Hospital Mirpur AJK from January 2015-december 2015

A total of 110 patients were included in this study. The patients were divided in 02 age groups

Group A-(age-20-40 years) -75patients. Group B-(age-41-50 years) -35patients.
Hb concentration before and after Correction with erythropiten+iron+B12+folate supplement was documented.

INCLUSION CRITERIA
Microcytic hypochromic anemia-
(iron+B12+folate deficiency)

EXCLUSION CRITERIA
1   Sytemic bleeding
2   Thallasemia and trait
3   Hemoyltic anemia
4   Anemia of chronic disease
5   Chronic renal failure
6   Autoimmone disease
7   Patients on immunosuppressive therapy

STUDY DESIGN
A prospective descriptive study.

RESULTS
Among 110 selected male and female patients, age ranging 20-50 years, after erythropoietin injection plus iron, folateB12 supplementation, the reticulocytes and heamoglobin increased from 1.2 to11% and 4.5 to 10.5 g/dl respectively after 04 weeks therapy. The results of a total 110 patients analyzed on SPSS version 20 and tabulated.

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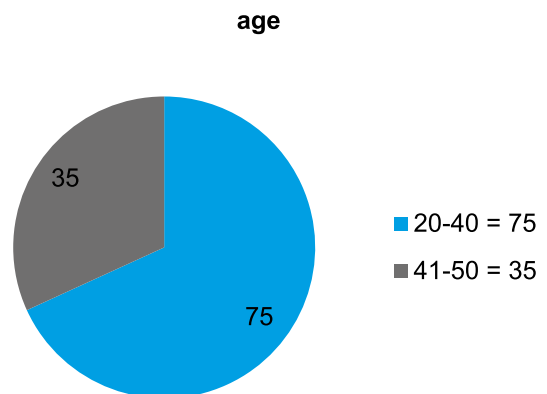

■ 20-40 = 75
■ 41-50 = 35

Table-I shows age group ranging 21-40 years and the type of anemia in male and female patients out of 75 patients. Age group is further subdivided into A and B groups. A group age ranging from 21-30 and B group 31-40 years. Out of 14 male patients, 10 belong to A group 04 to B group.10 male patients has Hb 4.5 and 5.3g/dl of normal Hb15.5 g/dl. Microcytic anemia was found in 10 patients. 03 belong to A group and 07 group B. Macrocytic Anemia was found in 04 patients. 03 (belong to group A and O1 group B.

Out of 61 female patients, 52 belong to A group, 09 to B group. 52 female patients has Hb 4.1in group A and 09 4.2 g/dl group B of normal Hb13.5 g/dl. Microcytic anemia was found in 53 patients. 43 belong to A group and 10 group. Macrocytic anemia was found in 08 patients. 05 belong to group A and 03 group B.

	N	Minimum	Maximum	Mean	Std. Deviation
VAR00001	2	14	16	14.50	1.414
VAR00002	2	4	10	7.00	4.243
Valid N (list wise)	0				
Table-I. Descriptive Statistics					

Total Hb in group A is 13.9 g/dl (89.67% and Group B 14.9g/dl (96.76%).

Table-IA shows age group ranging 21- 40 years and the type of anemia in14 male. Age group is further subdivide into A and B group. A group age ranging from 21-30 and B group 31-40 years. Out of 14 male patients, 10 belong to A group 04 to B group.10 male patients has Hb 4.5 and 04 Hb 5.3 of normal Hb15.5 g/dl. Microcytic anemia was found in 10 patients. 03 belong to A group and 07 group B. Macrocytic anemia was found in 04 patients. 03 (belong to group A and 01 group B. Before injection erythropoietin (4000 IU) reticulocytes count was 1.1% in group A and 1.3% in group B. After injection erythropoietin (4000 IU) reticulocytes count increased to 12.1% in group A and 10.1% in group B. After injection with erythropoietin (4000 IU) iron, B12, folate supplementation, heamoglobin increased from 4.5 to 9.4 g/dl and from 5.3 to 9.6 g/dl in group A and group B respectively.

Total Hb in group A is 8.6 g/dl (59.30% and Group B 9.5 g/dl (65.35%)

Age range(years) -20-40	Male NO-14	Normal Hb-g/dl 15.5	Microcytic anemia N-10	Macrocytic anemia N-4	Female NO-61	Normal Hb-g/dl 13.5	Microcytic anemia N-53	Macrocytic anemia N-8	Total Hb %	Total N0 of patients.
A-21-30	10	4.5	3	3	52	4.1	43	5	8.6(59.30%)	62
B-31-40	4	5.3	7	1	9	4.2	10	3	9.5(65.30%)	13
										75

Table-I. Age group (age-21-40 years) and type of anemia in male and female out of 75 patients.

Age range(years) -20-40	Male NO-14	Normal Hbg/dl-15.5	Microcytic anemia. N0-10	Macrocytic anemia N0-4	Reticulocytes count Without erythropoietin-Normal 0.5%-1.5%	Reticulocytes count With erythropoietin on day 1,10-Normal 0.5%-1.5%	Total Reticulocytes count %	Hb g/dl before Correction with erythropiten + iron + B12 +folate supplement= Normal Hbg/dl-15.5	Hb g/dl 01 month after Correction with erythropiten + iron + B12 + folate supplement Normal Hbg / dl-15.5	TotalHb %	Total=-NO. Of patients.
A-21-30	10	4.5	3	3	1.1%	12.1%	13.2%	4.5	9.4	13.9(89.67%)	10
B=31-40	4	5.3	7	1	1.3%	10.1%	11.40%	5.3	9.6	14.9(96.76%)	4
											14

Table-IA. Reticulocytes counts and Hemoglobin correction before and after injection erythropoietin (4000 IU on day1 and 10 in 14 male patients.

Age range(years) - 20-40	Female-NO- 61	Normal Hbg/dl-13.5	Microcytic anemia. NO-53	Macrocytic anemia NO-8	Reticulocytes Without erythropoietin. Normal -0.5%-1.5%	Reticulocytes count With erythropoietin on day1,10 Normal 0.5%-1.5%	Total Reticulocytes count %	Hb g/dl before Correction with erythropiten + iron + B12 + folate supplement Normal Hbg / dl-13.5	Hb g/dl 01month after Correction with erythropiten + iron + B12 + folate supplement. Normal Hbg / dl 13.5	TotalHb %	Total=-No of patients.
A-21-30	52	4.1	43	5	1.3%	10.2%	11.5%	4.1	8.76	12.86(95.25%)	52
B-31-40	9	4.2	10	3	1.2%	10.4%	11.6%	4.2	8.5	12.7(94.07%	9
											61

Table-IB. Reticulocytes counts and Hemoglobin correction before and after injection erythropoietin (4000 iu on day1 and 10 In 61 female patients.

Table-IB shows age group ranging 20- 40 years and the type of anemia in 61 female. Age group is further subdivide into A and B group. A group age ranging from 21-30 and B group 31-40 years. Out of 61 female patients, 52 belong to A group 49 to B group. 52 female patients has Hb 4.1 and 9 4.2 g/dl, of normal Hb 15.5 g/dl. Microcytic anemia was found in 53 patients. 43 belong to A group and 10 group B. Macrocytic Anemia was found in 08 patients. 05 (belong to group A and 03 group B. Before injection erythropoietin (4000 IU) reticulocyte count was 1.3% in group A and 1.2% in group B. After injection erythropoietin (4000 IU) reticulocytes count increased to 10.2% in group A and 10.4% in group B. After Injection with erythropoietin (4000 IU) iron, B12, folate supplementation, heamoglobin increased from 4.1 to 8.76 g/dl and from 4.2 to 8.5 g/dl in group A and group B respectively.

Total Hb in group A is 12.86 g/dl (95.25%) and group B 12.7 g/dl (94.07%).

	N	Minimum	Maximum	Mean	Std. Deviation
VAR00001	2	14	16	14.50	1.414
VAR00002	2	3	9	6.00	4.243
Valid N (list wise)	0				

Table-II. Descriptive Statistics

Age range(years) 40-50	Male NO12	Normal Hb g/dl- 15.5	Microcytic anemia N-4	Macrocytic anemia N-8	Female NO-23	Normal Hb g/dl- 13.5	Microcytic anemia N-15	Macrocytic anemia N-8	Total Hb %	Total=NO. Of patients.
A-41-45	9	5.4	2	5	14	3.4	9	5	8.8(56.77%)	23
B-46-50	3	6.5	2	3	9	6.4	6	3	12.9(83.22%)	12
										35

Table-II. Age group (age-4-50 years) and type of anemia out of 35 patients.

Table-II shows age group ranging 41-50 years and the type of anemia in male and female patients. Out of 35 patients. Age group is further subdivide into A and B group. A group age ranging from 41-45 and B group 46-50 years. Out of 12 male patients, 09 belong to A group 03 to B group. 09 male patients has Hb 5.4 and 03 6.5 g/dl of normal Hb15.5 g/dl. Microcytic anemia was found in 04 patients. 02 belong to A group and 02 group B. Macrocytic anemia was found in 08 patients. 05 (belong to group A and 03 group B.

Out of 23female patients, 14 belong to A group 09 to B group.14 female patients has Hb 3.4g/dl in group A and 09, 6.4g/dl, group B of normal Hb13.5 g/dl. Microcytic anemia was found in 15 patients. 09 belong to A group and 06 in group B. Macrocytic anemia was found in 08 patients.05belong to group A and 03 group B.

Total Hb in group A is8.8 g/dl (56.77%) and Group B 12.9g/dl (83.22%).

Age range (years) NO - 40-50	Male NO - 12	Nor- mal Hbg / dl- 15.5	Mi- cro- cytic ane- mia N0-5	Mac- ro- cytic ane- mia N0-7	Reticu- locytes count Without eryth- ropoie- tin-Nor- mal 0.5%- 1.5%	Reticu- locytes count With eryth- ropoietin on day 1,10 - Normal 0.5%- 1.5%	Total Reticu- locytes count%	Hb g/dl before Correction with erythro- piten + iron + B12 + folate supplement = Normal Hb g/dl- 15.5	Hb g/dl 01 month after Correction with eryth- ropiten + iron + B12 + folate supple- ment Nor- mal Hb g/dl- 15.5	Total-Hb %	Total=NO. Patients.
A-41-45	9	5.4	2	5	1.3%	9.4%	10.7%	5.4	8.4	13.70(88.38%)	9
B-46-50	3	6.5	3	2	1.4%	10.4%	11.8%	6.5	8.3	14.8(95.48%)	3
											12

Table-IIA. Reticulocytes counts and Hemoglobin correction before and after injection erythropoietin (4000 iu on day1 and 10 male patients out of 35 patients.

Table-IIA shows age group ranging 41-50 years and the type of anemia in 12 male. Age group is further subdivide into A and B group. A group age ranging from 41-45 and B group 46-50 years. Out of 12male patients, 09 belong to A group 03 to B group. 09 male patients has Hb 5.4 and 03 6.5 g/dl of normal Hb15.5 g/dl. Microcytic anemia was found in 05 patients. 02 belong to A group and 03 group B. Macrocytic anemia was found in 07 patients. 05 (belong to group A and 02 group B. Before injection erythropoietin (4000 IU) reticulocytes count was 1.3% in group A and 1.4% in group B. After injection erythropoietin (4000 IU) reticulocytes count increased to9.4% in group A and 10.4% in group B. After injection with erythropoietin (4000 IU) iron, B12, folate supplementation, heamoglobin increased from 5.4 to 8.4 g/dl and from 6.5 to 8.3 g/dl in group A and group B respectively.

Total Hb in group A is13.70 g/dl (88.38%) and Group B14.8 g/dl (95.48%).

Age range (years) NO=40-50	Fe-male NO - 23	Nor-mal Hbg/dl-13.5	Micro-cytic anemia NO-15	Mac-rocytic anemia NO-8	Reticulo-cytes count Without erythropoi-etin. Normal -0.5%-1.5%	Reticu-locytes count With eryth-ropoietin on day1,10 Normal 0.5%-1.5%	Total Reticu-locytes count%	Hb g/dl before Cor-rection with erythro-piten+iron+B12+-folate supplement Normal Hbg/dl-13.5.	Hb g/dl 01 month after Correction with erythropiten + iron + B12 + folate supple-ment. Normal Hbg / dl-13.5	TotalHb %	Total=-NO. Of pa-tients.
A-41-45	14	3.4	9	5	1.6%	7.3%	8.9%	3.4	7.8	11.2(82.96%)	14
B-46-50	9	6.4	6	3	1.5%	9.6%	11.1%	6.5	6.6	13.1(97.030%	9
											23

Table-IIB. Reticulocytes counts and Hemoglobin correction before and after injection erythropoietin (4000 IU on day1 and 23 female patients.

Table-II B shows age group ranging 41-50 years and the type of anemia in 23 female. Age group is further subdivide into A and B group. A group age ranging from 41-45 and B group 46-50 years. Out of 23 female patients, 14 belong to A group 09 to B group.14 female patients has Hb 3.4g/dl in group A and 6.4 g/dl in group B of normal Hb13.5 g/dl. Microcytic anemia was found in 15 patients. 09 belong to A group and 06 group B. Macrocytic anemia was found in 08 patients. 05 (belong to A group and 03 group B. Before injection erythropoietin (4000 IU) reticulocytes count was 1.6% in group A and 1.5% in group B. After injection erythropoietin (4000 IU) reticulocyte count increased to 7.3% in group A and 9.5% in group B. After Injection with erythropoietin (4000 IU) iron, B12, folate supplementation, heamoglobin increased from 3.4 to 7.8 g/dl in group A and from 6.5 to 6.6 g/dl. In group B respectively.

Total Hb In group A11.2 g/dl (82.96%) is and group B 13.1g/dl (97.30%).

	Mild	Moderate	Severe
Non –pregnant women(above 15)	11.-11.9	8.-10.9	<8g/dl
Pregnant women	10-10.9	7-9.9	<7g/dl
Men (above 15	11-12.9	8-10.9	<8 g/dl

Table-III. Assessment of anemia severity

DISCUSSION

Anemia is most common particular microcytic and megaloblastic anemia which is quite manageable. Iron and folate, B12 deficiencies are the main causative factors. Iron and folate in frequently common women.[14] The global prevalence of anemia for general population is 24%. Pregnant women 51% & and women of child bearing age 50.5%. The most frequent causes include lack of required nutrients, loss of blood, chronic disease, genetic abnormalities and inadequate production of RBC.

Laboratory tests include CBC, Hb level, Red blood cell count, hematocrit, platelets and reticulocyte count. Diagnostic criteria in non-

pregnant women is <12g/dl and in pregnant women<11g/dl.[16] Anemia assessment of severity is divided into mild, moderate and severe. In non –pregnant women (above 15) mild, moderate, anemia is11-11.9g/dl, 8-10.9g/dl and <8g/dl respectively. In pregnant women mild, moderate, severe anemia is 10-10.9g/dl, 7-9.9g/dl and <7g/dl respectively. In men (above 15) mild, moderate, severe anemia11-12.9g/dl, 8-10.9 g/dl, and <8 g/dl respectively. Blood smear in microcytic <80fl, HB Contents are indicated by mean corpuscular heamoglobin MCH.

Blood smear in normocytic is indicated MCV 82-92 and MCHC>30. MCHC the mean cell hemoglobin concentration is the measure of (MCHC) is of concentration of Hb in average RBC. Macrocytic is when MCV >91 fl.[18]

In microcytic aneamia, serum iron is decreased and total iron binding capacity (TIBC) is increased. The serum ferritin level indicates iron stores in the body.

Macrocytic anemia (megaloblastic anemia) is due to deficiency of serum folate acid and vitamin B12.

Types of nutritional anemia include, iron deficiency anemia (maternal), pernicious anemia (B12 deficiency), and folic acid deficiency. Persons at greater risk of maternal anemia are due to inadequate intake, inadequate absorption, increased requirements; pregnancy and lactation. The most common type anemia is iron deficiency anemia. It is due to increased excretion-excessive menstrual loss.[21] Nutritional survey of Pakistan in 2011 shows that microcytic anemia in pregnant women 25%and non-pregnant 19.9%.Maternal anemia has inadequate effect on infant health and development and maternal iron deficiency also increases the risk of preterm delivery and subsequent low birth weight.

Regarding the mechanism of iron, Hepcidine is the main master regulator of iron heamosidrin. Expression is induced in the liver. Hepcidine inhibits duodenal iron absorption and macrophages iron release. Hepcidine interfere with ferropotin thereby leading to ferropotin degradation and blockage of iron absorption.[24]

In healthy individuals, the amount of iron store (estimated from serum ferritin) is powerful determine of erythropotic response to erythropoietin.

Several reports have been published on the use of reticulocyte for predicting and monitoring response toerythropoiten.[26] Response to erythropoietin can be associated by measuring Hb and reticulocytes count after 04 weeks of therapy. A change in Hb>10g/dl and change in absolute count, 40x10 9 identify the patients as responder to erythropoietin. Above correction of anemia >12 g/dl in not indicated.

Erythropoietin is mainly indicated in chronic renal failure .Its role in erythropoiesis has been studied in pre-op patients and maternal anemia with encouraging results. The main contra-indications of its use is hypertension, coagulopathy, pulmonary embolism, myocardial infarction and malignancy.[35]

The purpose of our study was to build up heamoglobin in iron deficiency anemia in the shortest time with reducing the need of multiple transfusion.

In our study among 110 selected male and female patients, age ranging 20-50 years ,after erythropoietin injection plus iron, folateB12 supplementation, the reticulocytes and heamoglobin increased from 1.2 to11% and 4.5 to 10.5 g/dl respectively after 04 weeks therapy.

CONCLUSION
Erythropoietin injection plus iron, folate, B12 supplementation is an effective way of erythropoiesis for correction of anemia after 04 weeks therapy. This immediately improved symptoms &sign of anemia thus avoiding the need of repeated blood transfusion
**Copyright© 25 Oct, 2016.**

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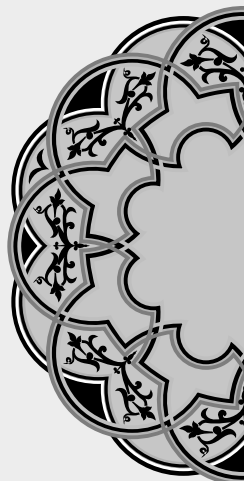
"Difficult roads often lead to beautiful destinations."

Unknown

AUTHORSHIP AND CONTRIBUTION DECLARATION

Sr. #	Author-s Full Name	Contribution to the paper	Author=s Signature
1	Dr. Abid Naeem	Idea, Analysis, Write-up	
2	Dr. Robina Kouser	Data Collection	
3	Dr. Arshid Mahmood	Data Collection	