Section: General Medicine

Original Research Article

THE IMPACT OF ANEMIA CORRECTION ON CARDIOVASCULAR OUTCOME IN CHRONIC RENAL DISEASE

Amit Kumar[1], Ravi Madhav[1], J K L Das[2]

[1]Junior Resident, Department of General Medicine, PMCH Patna, Bihar, India
[2]Professor & Head, Department of Medicine, PMCH Patna, Bihar, India

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Corresponding Author:
Dr. Amit Kumar,
Email: amit06jlnmcexam@gmail.com

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Abstract

Background: Anemia of chronic renal disease (CRD) is primarily caused by relative erythropoietin (EPO) deficiency and develops in general, as renal function decreases below 50% of the normal. It is impressive how often physicians fail to note the existence and impact of anemia in patients with progressive renal insufficiency. The aim of study is to study the impact of anaemia correction and its cardiovascular outcome in CRD (Chronic Renal disease). **Materials and Methods:** This prospective randomised study was conducted on randomly selected patients of chronic kidney disease (CKD), attending the in-patients and outpatient clinic of general Medicine and nephrology of Patna Medical College & Hospital, from July 2016 to August 2017, Although the proposed sample size was one hundred patients, but due to higher cost of treatment and economic constrains, the study could be conducted on 32 patients and none of these followed up after 6 months and 23 out of these 32 failed to follow up after the first 3 months. In this study the correction of anaemia in chronic kidney disease (CKD) patients was done with recombinant human erythropoietin (r HuEPO) and Ejection Fraction and left ventricular Mass Index (LVMI) were measured by Echocardiography on admission, at 3 month and 6 month follow up to find out the hemodynamic changes that could be achieved by this correction of anaemia. Statistical analysis was done on individual parameters (i.e. Hb%, EF, LVMI) and on their correlation. Statistical significance (P- value) of the parameters was estimated by using the student t- test and correlation between corrected haemoglobin (Hb) levels and subsequent changes in ejection fraction (EF) and left ventricular man index (LVMI) were analyzed Through correlation coefficient ® using Pearson's formula from statistical soft- were. **Result:** Out of these 32 patients 62.5% were male and 37.5% were female. The age group ranged from 30-69 yrs. 59.38% patients had Type 2 Diabetes mellitus, 6.25% had Type 2 Diabetes mellitus along with Hypothyroidism 6.25% had systemic lupus Erythematosus (SLE) and 28.13% patients had chronic kidney disease (CKD) due to chronic glomerulonephritis (CGN). In the study population 31.25% patients had initial creatinine level of <2 mg/dl and 68.75% had initial creatinine level of > 2 mg/dl. Though administration of recombinant human erythropoietin r HuEPO in 34.48% the target Haemoglobin (11gm/dl premenopausal female and 12gm/dl in male) could be achieved and in 50%. **Conclusion:** Correction of anemia, even if partial cases significant improvement in cardiovascular function as evidenced by increased ejection fraction (EF), even at a short term follow up of 6 month in our study.

INTRODUCTION

Anemia of chronic renal disease (CRD) is primarily caused by relative erythropoietin (EPO) deficiency and develops in general, as renal function decreases below 50% of the normal.[1,2] It is impressive how often physicians fail to note the existence and impact of anemia in patients with progressive renal insufficiency.[3] The symptom of anemia vary and some patients may adjust remarkable particularly in the early phase.[4] However, regardless of whether symptoms of anemia are present, the pathophysiological disturbances associated with anemia are set in motion even before CRD is manifested clinically and or biochemically.[5,6] These pathophysiologic disturbances are multiple –

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the most important are left ventricular hypertrophy (LVH), left ventricular dilatation (LVD), congestive cardiac failure (CCF), increasing angina pectoris, impaired immunity, decreasing cognition, increasing bruising, and number of hospitalizations.[7,8] and cardiovascular causes account for almost 60% of all deaths in CRD – LBH/LVD, CCF, coronary artery disease (CAD) are major contributors to overall mortality and morbidity in CRD.[5-10]

Anemia correction even if partial is considered to be the most important and prognostically rewarding intervention in the management of CRD. Of the multiple effects of anemia correction, the most important are reduction in LVH, LVD, number of hospitalization, incidence of infection, improvement in cardiac physiology and performance and renal function.[11-19] the target haemoglobin to be achieved in CRD is 12gm/dl in adult male and post-menopausal women compared to 11 gm/dl in premenopausal women.[20-22]

The correction of anemia is achieved with iron (Parenteral) and recombinant human erythropoietin (rHuEPO) as per prescribed guidelines.[20-22]

Aims and objective

To study the impact of anaemia correction and its cardiovascular outcome in CRD (Chronic Renal disease).

MATERIALS AND METHODS

This prospective randomised study was conducted on randomly selected patients of chronic kidney disease (CKD), attending the in-patients and outpatient clinic of general Medicine and nephrology of Patna Medical College & Hospital, from July 2016 to August 2017, Although the proposed sample size was one hundred patients, but due to higher cost of treatment and economic constrains, the study could be conducted on 32 patients and none of these followed up after 6 months and 23 out of these 32 failed to follow up after the first 3 months. In this study the correction of anaemia in chronic kidney disease (CKD) patients was done with recombinant human erythropoietin (r HuEPO) and Ejection Fraction and left ventricular Mass Index (LVMI) were measured by Echocardiography on admission, at 3 month and 6 month follow up to find out the hemodynamic changes that could be achieved by this correction of anaemia.

Statistical analysis was done on individual parameters (i.e. Hb%, EF, LVMI) and on their correlation. Statistical significance (P- value) of the parameters was estimated by using the student t- test and correlation between corrected haemoglobin (Hb) levels and subsequent changes in ejection fraction (EF) and left ventricular man index (LVMI) were analyzed Through correlation coefficient ® using Pearson's formula from statistical soft- were.

RESULTS

Out of these 32 patients 62.5% were male and 37.5% were female. The age group ranged from 30-69 yrs. and in this group 9.37% were male and 15.63% were female. 21.87% patients were in the age group of 40-49 years and in this age group 18.75% were male and 3.12% were female. 28.13% patients were in the age group of 50-59 yr and in this age group 21.87% were male and 6.25% were female. 25% patients were in the age group of 60-69 yr and in this age group 12.50% were male and 12.50% were female. 59.38% patients had Type 2 Diabetes mellitus, 6.25% had Type 2 Diabetes mellitus along with Hypothyroidism 6.25% had systemic lupus Erythematosus (SLE) and 28.13% patients had chronic kidney disease (CKD) due to chronic glomerulonephritis (CGN). Among the Type 2 Diabetes mellitus patients 94.74% were male and 5.25% were female. Among the patients with chronic glomerulonephritis 88.89% were female and 11.11 were male. Among the patients with systemic lupus Erythematosus (SLE) 50% was male and 50% were female, and among the patients with Type 2 Diabetes mellitus and Hypothyroidism 50% were male and 50% were female.

In the study population 31.25% patients had initial creatinine level of <2 mg/dl and 68.75% had initial creatinine level of > 2 mg/dl.

Though administration of recombinant human erythropoietin r HuEPO in 34.48% the target Haemoglobin (11gm/dl premenopausal female and 12gm/dl in male) could be achieved and in 50%. The Haemoglobin could be corrected up to the range of 9-11 gm/dl and in 15.62% in improvement in the Haemoglobin level could be achieved.

Table 1:

Sl. No	Population	On Admission	3month Follow Up	6 month Follow Up
01.	Total Population	7.97 (+ 1.54)	9.76 (+ 12.13)	10.86 (+ 2.22)
02.	Total Male Population	8.29 (+ 1.43)	10.09 (+ 2.23)	10.99 (+ 2.38)
03.	Total Female Population	7.47 (+ 1.79)	9.22 (+ 2.12)	10.63 (+ 2.01)

Mean and standard deviation of Haemoglobin % in study population matched according to total population, Total male population & Total female population in different times of parameter studies.

Table 2.

Sl. No	Population	On Admission	3month Follow Up	6 month Follow Up
01	Total Population	59.31 (+8.52)	62.37 (+ 8.92)	64.56 (+9.11)
02	Total Male Population	58.95 (+8.96)	62.0 (+9.31)	64.33 (+10.64)
03.	Total Female Population	59.92 (+ 8.14)	63 (+8.6)	65 (+6.5)

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Mean and standard deviation of Ejection fraction (%) in the study population matched according to Total population, Total Male population & Total female population in different time of parametric studies.

Table 3:

Sl. No	Ejection Fraction (EF %)	P – Value
01.	Between EF0 & EF3	.1567
02	Between EF0 & EF6	.1012
03.	Between EF3 & EF6	.7905

Test of Significance between EF0, EF3 & EF6 in total population (EF0 = EF on admission) (EF3 = EF at 3 month follow up) Hb6 = Hb at 6 month follow up)

Table 4:

Sl. No	Left Ventricular (LVMI)gm/m^2 Mass Index	P – Value
01.	Between LVME0 & LVMI3	1.0
02.	Between LVMI0 & LVMI6	.8271
03.	Between LVMI3 & LVMI6	.8271

Test of Significance between $LVMI_0$, $LVMI_3$, $LVMI_6$ in total population ($LVMI_0$ = LVMI on admission $LVMI_3$ = at 3 month follow up) $LVMI_6$= LVMI at 6 month follow up).

Table 5:

Sl. No.	Correction between Hb, EF and LVMI an admission	Correction between Hb, EF, LVMI at 3 month follow up	Correction between Hb, EF & LVMI at 6 month follow up
01	Between Hb_0 & EF_0 =.411	Between Hb_3 & EF_3=.519	Between Hb_6 & EF_6=.619
02	Between Hb_0 & LVM_0=.228	Between Hb_3 & $LVMI_3$=.059	Between Hb_6 & $LVMI_6$= .0329

Correction Coefficient ® between (Hb_0, EF_0, $LVMI_0$), and Hb_3, EF_3, $LVMI_3$) and (Hb_6, EF_6, $LVMI_6$) in the total population.

DISCUSSION

It is an established fact that anemia in Chronic kidney disease (CKD) is primarily caused by relative Erythropoietin deficiency,[1,2] Anemia generally develop when renal function decreases below 50% of the normal.[1,2] Among the multiple pathophysilogic disturbances of chronic kidney disease (CKD) the most important are the cardiovascular effects which includes left ventricular hypertrophy (LVH), left ventricular dilatation (LVD), Congestive Cardiac failure (CCF) and there are the main cause of mortality in chronic kidney disease (CKD).[5-10] Numerous small studies have shown that even partial correction of anemia with r Hu EPO has resulted in a decrease of left ventricular mass and volume in the range of 15% to 30%.[25] On this prospective this study was conceived to show the impact of anemia correction and its cardiovascular outcome in chronic kidney disease (CKD). In our study, in contrast to the studies carried out in the western world, 68.75% of the patients had a creatinine level of >2 mg/dl. But even then a complete correction of anemia could be achieved in 34.38% of patients and partial correction of anemia in 50% of patients. Statistically significant improvement of anemia was achieved and 3 month follow up (P=.00047) and at 6 month follow up (P=.0000004). Along with this improvement of anemia there was statistically significant improvement of ejection fraction (EF) at 6 month follow up (P=.03747) but not at 3 month follow up. (P=.16598). But for left ventricular Mass Index (LVMI) there was no significant change, even at 6 month follow up. There was strong positive correlation between improvement of anemia with improvement of ejection fraction (EF) both at 3 month (r = .519) and 6 month (e=.619) follow up. Although there was no significant change in left ventricular mass index (LVMI) even at 6 month follow up, but improvement of anaemia (in haemoglobin level) had a weak negative correlation with Left ventricular mass index (LVMI) only at 6 month follow up (r= -.0329) but not at 3 month follow up.

All the major clinical levels done previously by Foley RN, Parfrey PS, Harnett JD, et al, Levin A, Thompron CR, Ethier J, et al, Schuartz AB, Prior JE, Mintz GS et al, Echardt KU, London GM, Parmier B, Guerin AP et al, Silber berg J, Remin N, Borre P, Sriderman AD, and many other have shown statistically significant decrease in left ventricular dilatation, increase in ejection fraction(EF) and decrease in left ventricular mass index LVMI but in most of them they had a successful follow up of around five to ten years.

CONCLUSION

The cardiovascular disturbances associated anemia in chronic kidney disease (CKD) are set in motion even before chronic kidney disease (CKD) is manifested clinically and/or biochemically 5,6 Thus anemia is an important independent risk factor for surrogates of cardiovascular disease (CVD), such as left ventricular hypertrophy, left ventricular

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dilatation, congestive cardiac failure (LVH), (LVD) and (CCF). Correction of anemia, even if partial cases significant improvement in cardiovascular function as evidenced by increased ejection fraction (EF), even at a short term follow up of 6 month in our study. But to observe a statistically significant decrease in left ventricular Mass Index (LVMI) would require a long term follow up although a weak negative correlation between Hb and LVMI is observed at 6 month follow up in our study.

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