

THE EFFECT OF ERYTHROPOIETIN ON HIGH DENSITY LIPOPROTEIN LEVEL OF CHRONIC KIDNEY DISEASE PATIENTS (STAGE 5)

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Abstract: Erythropoietin is one of the important drugs used in the management of anemia in chronic kidney disease patients. In addition to the induction of erythropoiesis it have several other beneficial effects including anti-inflammatory, antioxidant properties. In CKD patients cardiovascular diseases are the important cause of morbidity and mortality especially in stage 5. Being “good cholesterol” HDL can improve the cardiovascular functioning in kidney disease patients.

Key words: Erythropoietin, Anemia, Cardiovascular, Good Cholesterol, HDL

1. INTRODUCTION

Chronic kidney disease is defined as a progressive loss of kidney function occurring over several months to years, and is characterized by the gradual replacement of normal kidney architecture with interstitial fibrosis. Additionally, kidney failure is associated with a range of metabolic abnormalities due to uraemic toxicity. Large number of population based studies has demonstrated that even slightly reduced renal function can predict cardiovascular diseases and mortality. The cardiovascular mortality rate in stage 5 kidney disease patients is 10–20 times than that in the general population. The increased cardiovascular risk in CKD is multifactorial: advanced kidney failure is associated with a higher prevalence of insulin resistance, high blood pressure, lipid abnormalities, vascular calcification, chronic inflammation, protein-energy wasting, and lack of regular exercise.

Erythropoietin is a sialo – glycoprotein, produced by the peritubular cells of the kidney. In normal individuals, during hypoxia, kidney cells senses and stimulate the hormone erythropoietin. The common side effects of erythropoietin include, fever, swelling, fatigue, pain at the injection site etc. Previous studies clearly demonstrated the beneficial effects of erythropoietin in patients with CKD, in treating anemia. Other beneficial effects are still under study. The reduction in serum levels of HDL cholesterol represents an important lipoprotein abnormality in patients with CKD. The High density lipoprotein (HDL) also called “good cholesterol” has a protective effect on cardiovascular function. Low levels of HDL cholesterol are a risk factor for CAD and premature atherosclerosis, regardless of serum LDL cholesterol and triglyceride levels. HDL reduces the development of atherosclerosis by acceleration of reverse cholesterol transport as well as antioxidant, anti inflammatory activities. So the interventions that increase HDL are anti atherogenic. In CKD, the inflammatory mediators like lipopolysaccharide, cytokines etc inhibit cholesterol efflux from cells. This leads to decrease in reverse cholesterol transport thereby have effect on HDL also. Erythropoietin have an antioxidant and anti inflammatory effect and improves the enzymes involved in metabolism and lipid peroxidation. So any interventions that help in improvement of HDL levels are beneficial in patients with CKD.

AIM AND OBJECTIVES

- To assess the effect of erythropoietin therapy on the high density lipoprotein level in kidney disease patients (stage 5)

OBJECTIVES

- To assess whether erythropoietin itself have a direct influence on HDL level of stage (5) haemodialysis patients.
- To assess the effect of statins on HDL level along with erythropoietin
- To assess the improvement in cardiac profile with the use of erythropoietin.
- To assess the medication adherence.
- To assess the quality of life of patients

➤ STUDY DESIGN

Prospective experimental study

➤ STUDY POPULATION

Patients admitted in the Nephrology ward and dialysis unit.

➤ INCLUSION CRITERIA:

- CKD patients whose GFR <15ml/min and those who are anaemic (Hb <8gm%)
- Those who give consent voluntarily to participate in the study.
- Both male and female.
- Age group of 30-75yrs

➤ **EXCLUSION CRITERIA**

- Patients who are not willing to give consent.
- Patients having other co morbidities (cancer, hepatic failure, autoimmune diseases, heart failure)

II. MATERIALS AND METHODS

A prospective experimental study was conducted in Department of Nephrology in Pushpagiri Medical College Hospital after getting approval from Institutional Ethics Committee. All patients were given a brief introduction regarding the study and the confidentiality of data. A written informed consent was obtained from all the patients. Patients diagnosed with stage 5 chronic kidney disease were enrolled for the study.

After obtaining their IP number, name and other demographic details, from the Biochemistry lab residual blood was obtained. Residual blood is the blood remaining after the blood routine analysis in the lab. Blood was not withdrawn directly from the patient and any financial burden was not imposed on the patient.

- The collected residual blood from the lab was analysed for HDL using semi auto analyser in the Pushpagiri College of Pharmacy. Medication adherence of the patients was found out using Morisky Medication Adherence Scale (MMAS 8) questionnaire. Higher scores indicates low adherence. Quality of life was determined using Kidney Disease Quality Of Life Questionnaire (KDQOL).
- Procedure to find out HDL value:
 - Blank: Into the test tube add 10mcL water and 450 mcL R1 reagent.
 - Calibrator: Into the test tube add 450 mcL R1 reagent and 10mcL calibrator.
 - Sample: into the test tube add 10mcL sample and 450mcL R1 reagent.
 - It was then mixed and incubated for 5min at 37C
 - Then 150mcL of R2 reagent was added to blank, calibrator, and sample .
 - It was the mixed and incubated for 5min at 37C.
 - Then it was aspirated into the semiautoanalyser.
 - Read the HDL value using semiautoanalyser.
 - Analysis of data was done using SPSS VERSION 20.00 statistical software. Mean standard deviation of different parameters were compared to determine the changes in HDL value. The significant levels were determined by p value. P value less than 0.05 was considered as significant.

➤ **STUDY SITE**

Tertiary care setting; Department of Nephrology; Pushpagiri Medical college hospital; Thiruvalla. Pushpagiri College of Pharmacy, Thiruvalla

➤ **SAMPLE SIZE OF THE STUDY**

60 patients of stage (5) chronic kidney disease patients

➤ **EQUATION**

$$n_i = 2 (Z\sigma / E)^2$$

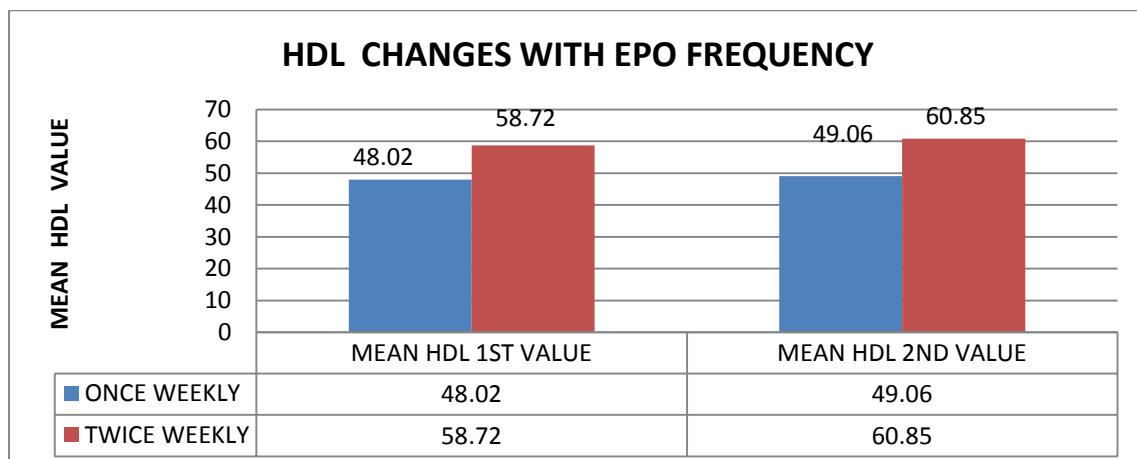
Where Z is the value from the standard normal distribution reflecting the confidence level
 σ is the standard deviation
 E is the desired margin of error

STUDY PERIOD: 6 months

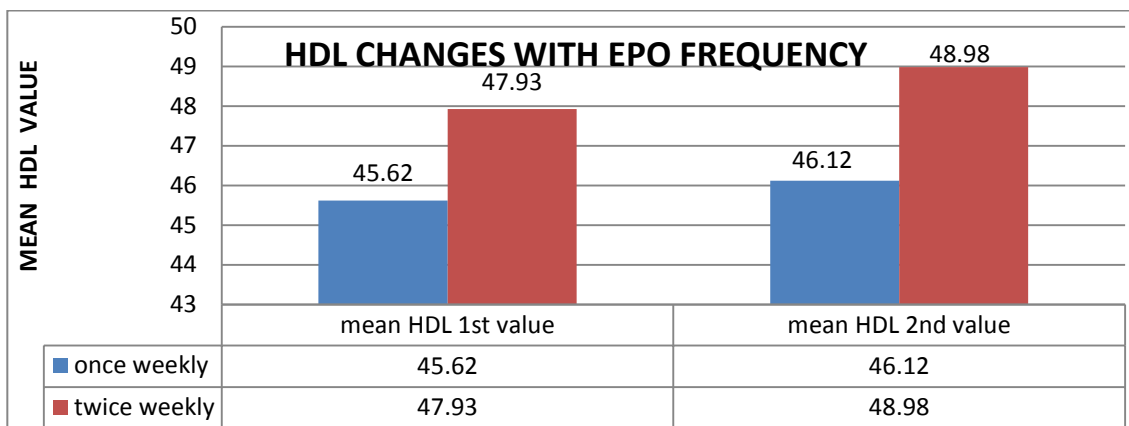
III. RESULTS

In the 6 month study, a total of 60 CKD patients were enrolled as per inclusion and exclusion criteria. All the patients were obtained from IP department of nephrology and from dialysis unit, Pushpagiri Medical College, Thiruvalla. Out of these 60 patients, half of them were having EPO alone without any hypolipidemic agents. The other 30 patients had both EPO and statins in their prescription.

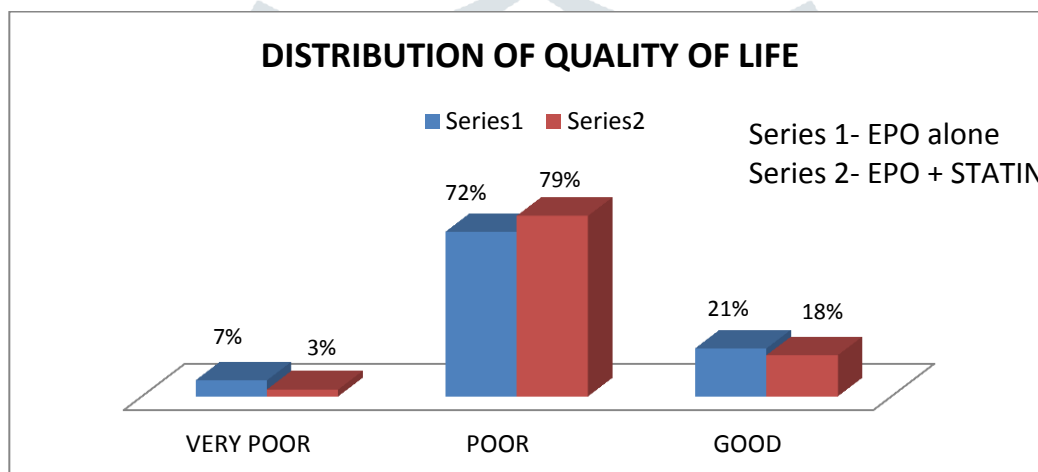
1. HDL CHANGES BASED ON ERYTHROPOEITIN FREQUENCY IN EPO + STATIN GROUP



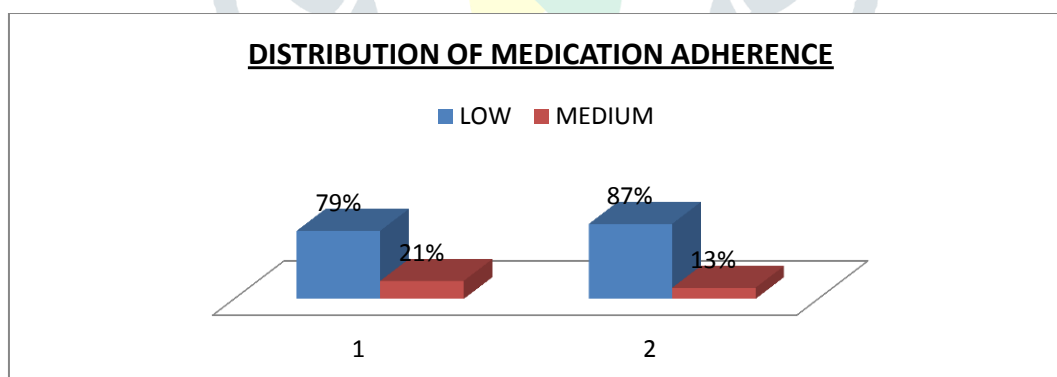
2 HDL CHANGES BASED ON ERYTHROPOEITIN FREQUENCY IN EPO ALONE



3. DISTRIBUTION PATIENTS BASED ON QUALITY OF LIFE

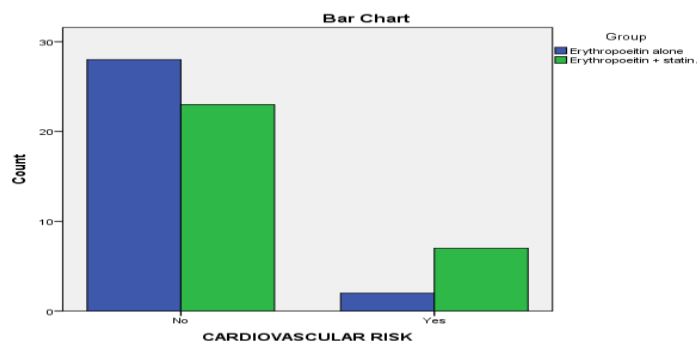


1. DISTRIBUTION OF PATIENTS BASED ON MEDICATION ADHERENCE

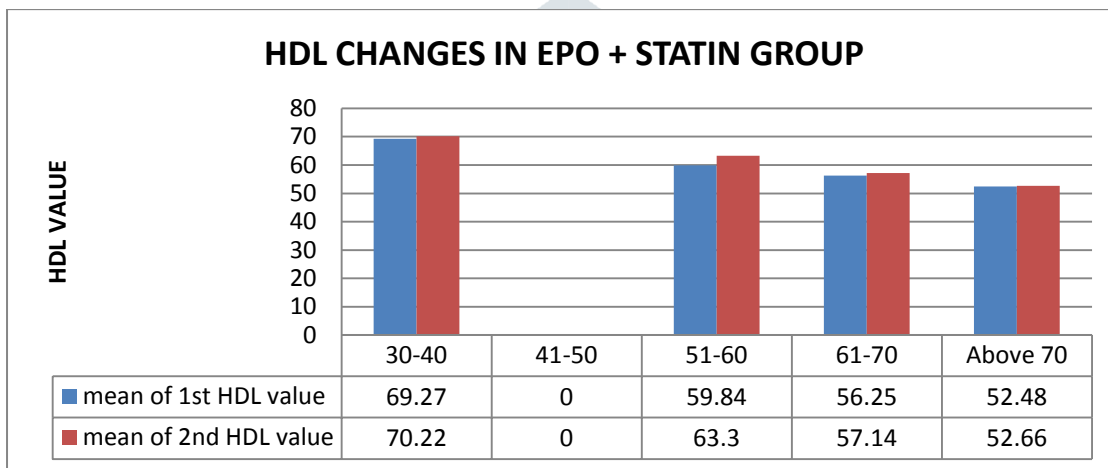
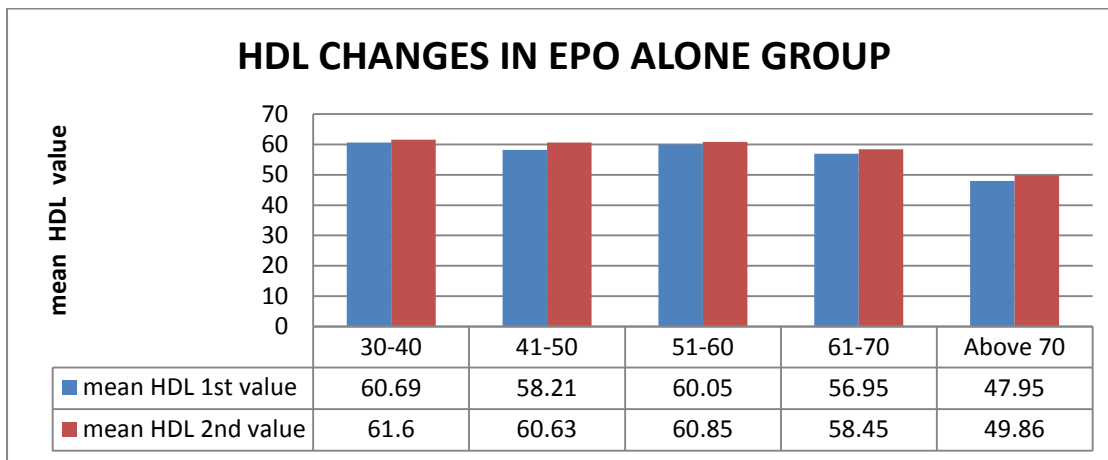


2. DISTRIBUTION OF CARDIOVASCULAR RISK.

3.



4. HDL LEVEL CHANGES IN DIFFERENT AGE GROUP OF PATIENTS



DISCUSSION

- Our primary objective was to assess whether erythropoietin itself have a direct influence on HDL level of stage (5) haemodialysis patients.
- ❖ Based on the EPO frequency the following results were obtained.
 - i. In EPO + STATIN group, while considering once weekly therapy, there is a mean increase of 1.04 mg/dl, whereas in twice weekly therapy, the increase was about 2.13mg/dl.
 - ii. In EPO alone group, once weekly therapy has a mean increase of 0.5 mg/dl and with twice weekly therapy it is about 1.05 mg/dl.

From this, we can summarize that EPO itself can produce an improvement in HDL level (p value <0.05) near to that of the changes produced by EPO + STATIN coadministration (P value < 0.05).

- ❖ While considering age as a parameter, the EPO alone group, showed a significant improvement of HDL values in almost all age groups,ie, irrespective of age EPO can produce a direct effect on HDL value.
- ❖ Our second objective was to determine the effect on cardiac profile with EPO therapy.

In both groups, EPO therapy produced a significant reduction in cardiovascular risk. More proportion of patients with improved cardiac profile was seen in EPO alone group. It suggests the cardioprotective effects of EPO.

- ❖ Our third objective was to assess the medication adherence using MMAS – 8. In both groups, majority of the patients had a low medication adherence. It is because of the presence of multiple comorbidities and complicated medication regimen, so the patients may have an intention to skip the medication which they considered less important. It points out the requirement of pharmacist intervention
- ❖ Our final objective was to assess the quality of life using KDQOL scale. Based on that, the patients were divided in to 3 groups: very poor, poor and good. A significant proportion of patients have a poor quality of life. This is because of the disease and treatment related undesirable outcomes . As a result, there was a significant reduction in quality of daily activities. Both socio-economic factors play a key role in this. So any interventions that improve quality of life are important

CONCLUSION

Alterations in serum lipid profiles observed in patients with CKD may significantly contribute to high incidence of cardiovascular diseases that complicates CKD. From the study it can be concluded that in addition to improvement in anemia, erythropoietin have an additional beneficial effect on HDL levels. The improvement in HDL values of EPO alone group suggests that this improvement is not only due to statins but also the direct effect of erythropoietin therapy. Several studies suggest that HDL is a promising target of therapeutic intervention to achieve cardiac protection, so interventions that improve HDL are essential. So EPO is one of the best advisable therapy. The results provide optimism that the high incidence of morbidity and mortality due to cardiac events in patients with CKD may be reduced with erythropoietin treatment.

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