Anemia in Hemodialysis Patients in Gherian Central Hospital.

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Abstract:

Anemia is frequent complication in hemodialysis patients. Compared to conventional hemodialysis (CHD), short daily hemodialysis (sDHD) has been reported to be effective in Gherian central hospital. The aim of the present study was to determine whether (sDHD) could improve anemia and quality of life (QOL) for those patients with end-stage renal disease.
Twenty seven patients (16 males /11 females) were converted from CHD to sDHD in our study.
In this study, In Gherian Central Hospital, all patients undergoing conventional hemodialysis (CHD) have complications including anemia and impaired quality of life (QOL). However, were observed the (CHD) could not improve clinical outcomes in patients with End-stage renal disease (ESRD). According to these studies (CHD) could not improve the state of anemia in males and females N=(27), and also not increase or improvement the quality of life (QOL) scores. However, those results were obtained from hemodialysis patients in our study under good control and follow up in Gherian Central Hospital.
This study shows that action of conventional hemodialysis (CHD) was associated with significantly difference in hemoglobin concentration by erythropoietin treatment in males and females ($P < 0.05$) was considered to be significant.

Introduction:

Anemia has been defined by the World Health Organization (WHO) as a hemoglobin (Hgb) concentration <13.0 g/dL for adult males and postmenopausal women and an Hgb <12.0 g/dL for premenopausal women. (W.H.O, 1968). Based upon these criteria, nearly 90 percent of patients with a glomerular filtration rate (GFR) <25 to 30 mL/min have anemia, many with Hgb level <10 g/dL. (Wh Kazmi, et.al 2001). Ever since the approval of recombinant human Erythropoietin (Epoetin alfa, EPO) by the US Food and Drug Administration (FDA), this and other erythropoiesis- stimulating agents (ESAs) have become the standard of care for the treatment of the anemia that occurs in most patients with advanced chronic kidney disease (CKD) and end-stage renal disease (ESRD). As a result, mean Hgb and hematocrit (Hct) level in

patients with CKD, particularly those on dialysis, rose steadily through 2005. (GT Obrador, et.al, 2001) and (S Hariharan, et.al dialysis in the United State received ESAs, with a mean Hgb level among dialysis patient of 12.0 g/dL. (S Hariharan, et.al, 2006) and (R Kidney. 2005) two -third of all patients had Hgb levels between 11 and 13 g/dL. (S Hariharan, et.al, 2006). Anemia has also been implicated as a contributing factor in many of the symptoms associated with reduced kidney function. these include fatigue, depression, reduced exercise tolerance, dyspnea, and cardiovascular consequences, such as left ventricular hypertrophy (LVH) and left ventricular systolic dysfunction. (A Levin, et.al, 1999) it is also associated with an increased risk of morbidity and mortality, principally due to cardiac disease and stroke (CT Jurkovitz, et.al, 2003, JL Abramson, et.al, 2003, MJ Sarnak, et.al, 2002 and WM McClellan, et.al, 2002) and with an increased risk of hospitalization, hospital length of stay, and mortality in patient with predialysis CKD. (Ma JZ, et.al, 1999, H Xia, et.al, 1999, AJ Collins, et.al, 2001 and AJ Collins, et.al, 2000). Association, however , do not prove causality, thus these associations may reflect underlying co morbid conditions and severity of illness that contribute to both the severity of anemia, reduced responsiveness to ESAs, and poorer outcomes. A review of the data relating to target Hgb or Hct levels for patients with anemia due to renal disease treated with ESAs is presented here. Issues relating to EPO, Darbepoetin and iron administration are presented separately. (See, Erythropoietin for the anemia of chronic kidney disease among 2006). BY 2006, 90 percent of patients maintained on chronic predialysis and peritoneal dialysis patients and Dardepoetin alfa for the management of anemia in chronic kidney disease and Iron balance in nondialysis, peritoneal dialysis, and home hemodialysis patients and use of iron preparations in hemodialysis patients). Anemia and impaired quality of life (QOL) are frequent complications of end-stage renal disease (ESRD) in patients undergoing hemodialysis therapy and are caused by many factors. Hemodialysis patients undergoing hemodialysis therapy and are caused by many factors. Hemodialysis patients often have anemia caused by inadequate synthesis of Erythropoietin (EPO), and require therapy with exogenous recombinant human Eerythropoietin (rHuEPO) to maintain recommended hemoglobin levels. Many treatments to improve the anemia and QOL of patients with ESRD have been investigated (V Panichi, et.al, 2011, J Punal Rioboo, et.al, 2009). Short daily hemodiaysis (sDHD) was first described in 1968 (JR DePalma, et.al, 1968) and has been widely used (N Allen, et.al, 2011). In many countries sDHD has been reported to be effective in hemodialysis patients (J Punal Rioboo, et.al, 2009) but there are few reports on its efficacy in managing anemia and QOL in patients undergoing hemodialysis. The objective of the present study was to determine whether Conventional hemodialysis (CHD) could improve anemia and QOL in patients undergoing hemodialysis in Gherian Central Hospital.

Quality of life:

An improved quality of life and functional status is associated with the attainment of a near -normal Hgb concentration in some but not all, studies (MA Pfeffer, et.al, 2009): 1- Two 2010 systemic reviews found that the administration of Erythropoietic agents to increase Hgb levels improved exercise tolerance, energy, and physical function among patients with CKD (SR Gandra, et.al, 2010). 2- Benefits with a normal Hgb concentration in terms of quality of life were shown in the CREATE study (TB Drueke, et.al, 2006). Compared with those in the 10.5 to 11.5 g/dL group, patients assigned to the 13.0 to 15.0 g/dL Hgb level had at the end of year 1, significantly better quality of life, general and mental health, physical function and role, social function, and vitality (TB Drueke, et.al, 2006). Benefits in general health and vitality were maintained over the second year of the study. 3- Improvements in quality of life, neuroconginitive function,

and exercise performance have been noted in additional Hgb near- normal or observed in patients with malignancy who have received erythropoietic agents.

4- In the TREAT study, fatigue, energy, and physical functioning were assessed at 25 weeks using the functional Assessment of Cancer Therapy- fatigue (FACT-fatigue) and the Short Form-36 (SF-36) (MA Pfeffer, et.al, 2009). A modest improvement in fatigue was noted in those assigned to Darbepoetin, but there was no change in energy or physical function. The normalization studies (PS Parfrey, et.al, 2005). A similar benefit has also been improvement in fatigue was also noted at 97 weeks among a subset of 2295 patients (EF Lewis, et.al, 2011). In this subset, overall quality of life, as assessed by the self-administered assessment measure, EuroQol (EQ-5D), was also mostly improved in the Darbepoetin group.

No quality of life benefits were observed in the CHOIR study, although this may have been due to the large dropout rate (AK Singh, et.al, 2006).

Overview of treatment options:

The anemia of chronic kidney disease (CKD) if left untreated can result in deterioration in cardiac function and decreased cognition and mental acuity. It can also be accompanied by debilitating symptoms such as fatigue, weakness, lethargy, anorexia, and sleep disturbances. In addition, anemia patients commonly lack the stamina needed to perform normal daily activities or work.

furthermore, anemia in patient with CKD is also associated with an increased risk of morbidity and mortality, principally due to cardiac disease and stroke, and with an increased risk of hospitalization, hospital length of stay, and mortality in patients with predialysis CKD. Associations, however do not prove causality. (See Anemia of chronic kidney disease: Target hemoglobin /hematocrit for patients treated with Erythropoietic agents). The primary therapeutic options for the anemia of CKD include red blood cell transfusions, erythropoietin-stimulating agents (ESAs) and to a much lesser degree androgens. (JW Eschbach, et.al, 1991).

Erythropoietin stimulating agents (ESAs)

The clinical availability of ESAs subsequently provided an additional treatment option. There have been no prospective randomized studies that directly compared outcome with Erythropoietic agents versus red blood cell transfusions in patients with anemia and CKD. Instead the best data in support of Erythropoietic agents versus transfusions were provided by the initial phase III clinical trial showing that recombinant human EPO was effective and eliminated the need for continued transfusions. In this study 333 dialysis patients with hemoglobin levels < 10 g/dL received recombinant human EPO to maintain the hematocrit at 35 percent. (JW Eschbach, et.al, 1989). Within two months of initiation of therapy, the need for transfusions (1030 within the six months prior to beginning treatment) was eliminated. In addition there was a 40 percent reduction in ferritin levels after six months among the 68 patients with iron overload. Thus, the administration of these agents was particularly attractive because they substantially reduced the need for red

cell transfusions, with an attendant decrease in and/or risk for transfusion-related complications (eg. transfusion-transmitted infection, transfusion reactions, with CKD and iron overload due to previous transfusions. However, the safety of ESAs in treating sever anemia has not been evaluated in large placebo- controlled trials. We agree with the 2012 Kidney Disease: Improving Global Outcomes (KDIGO) guidelines that the potential benefits of reducing blood transfusions and anemia related symptoms should be balanced against the harm in immunologic sensitization, iron overload syndromes, and/or volume overload). They also help mobilize iron stores, which is particularly beneficial in patients individual patients (such as stroke, vascular access loss, and hypertension). (Kidney Int. Suppl, 2012).

Sections provide additional detail to the use and specific indications for EPO. The use of Darbepoetin, a different Erythropoietic agent, is presented separately. (See Darbepoetin alfa for the management of anemia in chronic kidney disease).

Anemia in patients on chronic hemodialysis

The anemia of chronic renal failure is in most patients, normocytic and normochromic and is due to reduced renal erythropoietin (EPO) production (a presumed reflection of the reduction in functioning renal mass) and to a lesser degree, to shortened red cell survival. (N Muirhead, et.al, 1995). Other forms of anemia can occur, including blood loss from the gastrointestinal tract or via the technique of hemodialysis, as well as folate and B12 deficiency. In addition to recombinant human EPO, Darbepoetin alfa is another Erythropoietin stimulating agent (ESA) that can be used for the treatment of anemia of chronic renal failure. Darbepoetin is a molecule with 165 amino acids that differs from recombinant human EPO in that it contains five N-linked oligosaccharide chains, whereas EPO has only three. The additional N-glycosylation sites result from five amino acid substitutions on the EPO peptide backbone. The additional carbohydrate chains result in a half-life that is longer than that for EPO. A detailed discussion of Darbepoetin is presented separately. Several general principles govern the administration of recombinant human ESAs (JW Eschach, et.al, 1991 and N Muirhead, et.al, 1995): 1- The response to EPO is dose-dependent, but varies greatly among patients. 2- The response is dependent on the route of administration (intravenous (IV) versus subcutaneous (SC) and the frequency of administration. With subcutaneous administration, frequency is not as important as with the IV route. Response is less dependent on route of administration for Darbepoetin alfa than for Epoetin. 3- The response may be limited by low iron stores, bone marrow fibrosis, infection, inflammation, inadequate dialysis, and other conditions. (O Ifudu, et.al, 2000). 4- Stroke, mortality, and hypertension may complicated therapy.

This is primarily limited to patients undergoing dialysis.

Patients and Methods:

The subjects were stable outpatients with ESRD undergoing Conventional hemodialysis (CHD) in Gherian Central Hospital Hemodialysis Unit. They undergoing CHD using a native arteriovenous fistula for 8 months or longer. (27) patients (16males / 11 females), 46.8 ± 13.4 years of age (mean ± SD, range: 26-70

years) were enrolled. They were treated with CHD for 54.7 ± 32.9 months (8–133 months) for 4 hours, 3 times per week. The causes of ESRD were glomerulonephritis (n = 13), diabetes mellitus(n = 6), hypertension(n = 4) table 1.

Baseline Characteristics	
Patients (male/female)	27 (16/11)
Age (years, mean ± SD)	46.8 ± 13.4
Duration of CHD (months, mean ± SD)	54.7 ± 32.9
Etiology of ESRD	
Glomerulonephritis	13
Diabetes mellitus	6
hypertension	4

Table 1. Baseline characteristics of Patients.

There were no specific patient selection criteria. All patients underwent CHD period. All hematological parameters were measured during CHD.

Calcium carbonate, Ferrous Sulfate, Folic acid, Epirex and Enalapril drugs were administered either orally or intravenously. Information on dosage and administration of other drugs used concomitantly throughout the study was recorded.

Serum albumin concentration and serum C-creative protein (CRP) were measured throughout the study.

Statistical Analysis:

All data are reported as means ± SD. statistical analysis was performed using the student one sample test (t-test) for data analysis and the (Smirnov Kolmogorov test) as hypothesis test summary to detect the type of distribution either (Parametric analysis) or (non-Parametric analysis) because, the size of test N= (27) for male and female.

($P < 0.05$) was considered to be significant.

Results:

Test	Mean ± SD	Normal Values
Hgb (g/dL)	9.39 ± 2.25	*14 - 18*
Hct	26.38 ± 8.52	*42 - 52*
MCV	88.50 ± 9.40	*80 - 94*
MCH	29.89 ± 3.00	*27 - 31*
WBC	6.25 ± 2.52	*4.8 - 10.8*
PLT	190. 3 ± 79.4	*130 - 400*

Table 2. Changes in Laboratory Values during the conventional hemodialysis in Males Patients (n= 16).

Data are reported as means ± SD, SD: Standard Deviation, Hgb: Hemoglobin, Hct: Hematocrit, MCV: Mean cell volume, MCH: Mean cell , WBC: White blood cells count, PLT: Platelet count.

Test	Mean ± SD	Normal Values
Hgb (g/dL)	8.44 ± 1.32	*12 - 16*
Hct	24.49 ± 4.82	*37 - 47*
MCV	83.42 ± 21.70	*81 - 99*
MCH	29.73 ± 1.28	*27 - 31*
WBC	5.67 ± 1.56	*4.8 - 10.8*
PLT	169.4 ± 75.2	*130 - 400*

Table 3. Changes in Laboratory Values during the conventional hemodialysis in Females Patients (n= 11).

Test	Mean ± SD
Hgb (g/dL)	9.03 ± 1.98
Hct	25.64 ± 7.22
MCV	86.51 ± 15.16
MCH	29.83 ± 2.40
WBC	6.03 ± 2.19
PLT	182.5 ± 76.9

Table 4. Changes in Laboratory Values during the conventional hemodialysis in Males and Females Patients (n= 27).

after applied of (Smirnov Kolmogorov test), was resulted the type of distribution Statistically is (Parametric analysis).

In all laboratory values during the conventional hemodialysis in both males and females patients are summarized respectively in table 1 and table 2. Hemoglobin concentration not increased significantly by treatment. However the Erythropoietin (EPO) not cause statistically significant differences in hemoglobin concentration during conventional hemodialysis.

After applied statistical analysis (t-test) as Parametric analysis for Males and Females was resulted:

P value = (0.000) for male and female, therefore

*Significant deference in comparing with positive control at ($p < 0.05$).

Discussion:

Currently, the major hemodialysis technique in many countries is conventional hemodialysis (CHD). in Gherian Central Hospital, all patients undergoing CHD have complications including anemia and impaired quality of life QOL. In this study were observed the CHD could not improve clinical outcomes in patients with End-stage renal disease (ESRD). According to these studies CHD could not improve the state of anemia in males and females, and also not increase the (QOL) scores. However, those results were obtained from hemodialysis patients in our study under good control and follow up in Gherian Central Hospital. This study shows that action of CHD was

associated with significantly difference in hemoglobin concentration by erythropoietin treatment, may be due to present many factors affecting negative on treatment as smoking behavior, coronary artery disease, administration of certain drug, drug-drug interaction, nature of diet, body weight or other causes. (J Punal Rioboo, et.al, 2009).

Summary and recommendations:

1- Anemia has been implicated as a contributing factor in many of the symptoms associated with reduced kidney function. The partial correction of anemia in chronic kidney disease (CKD) patients with end-stage renal disease (ESRD) and CKD improves physiologic and clinical parameters and quality of life, compared with the severely low hemoglobin(Hgb) levels that were common prior to the availability of erythropoiesis stimulating agents (ESAs).

2- The treatment of anemia during dialysis should be individualized. We suggest targeting Hgb levels in the range of (10.0) to (11.5) g/dL in most dialysis (Hemodialysis and peritoneal) patients who are treated with ESAs. In such patients with Hgb levels >11.5 g/dL, appropriate measures should be instituted, such as decreasing the dose of the ESA or increasing the dosing interval to maintain Hgb levels in the range of (10.0 - 11.5 g/dL).

3- Among dialysis patients with CKD who are treated with ESAs, we recommend not targeting Hgb levels >13 g/dL. Hgb targets >13 g/dL are associated with adverse outcomes.

4- the treatment of anemia among nondialysis patients with CKD should be individualized. For most nondialysis patients with CKD who have symptoms attributable to anemia, we suggest initiating ESAs when the Hgb level is < 10 g/dL. However, we attentive to possible symptoms of anemia in younger patients who have CKD with few co morbidities, whose symptoms of anemia occur at higher Hgb levels, for such patients, we may initiate ESAs at Hgb levels of 10 g/dL or even higher after discussing potential risks and benefits with each patient.

5- For most patients with CKD who are not on dialysis are on ESAs, we suggest maintaining Hgb levels between 10.0 and 11.5 g/dL. Some clinicians would allow an Hgb level > 11.5 g/dL for younger patients with CKD who have few co morbidities and who have persistent, severe symptoms of anemia. There are no data on the benefits of Hgb concentrations between (11.5 - 13.0 g/dL).

6- Among predialysis patients with CKD who are treated with Erythropoitic agents, we recommend not targeting Hgb levels > 13 g/dL. Hgb targets > 13 g/dL are associated with adverse outcomes.

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