Analysis of Anemic Management In End Stage Renal Disease Patients

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Abstract- *End stage renal disease is a condition in which kidney dysfunction prevails. Most of the Indians are not economically sufficient to undergo hemodialysis regularly due to its high cost. Anaemic condition is the common condition that has to managed by the physicians at the time of Dialysis. Erythropoietic agents and vitamin supplements are used in the management therapy of anaemic condition. Injectables such as Inj.Cresp, Inj,Encicarb, Inj.Erypro, Inj.Optineuron are administered to the patients. This study is based on frequency of distribution of both erythropoietic agents and vitamin supplements in ESRD patients.*

Keywords- Chronic Kidney disease, Vitamins, Erythropoietic agents , Hemodialysis.

I. INTRODUCTION

The introduction of the hemopoietic agents into the market has made a tremendous revolution in the treatment of ESRD (End stage renal disease) patients who are also referred as Chronic kidney Disease (CKD) -stage 5 . In India , a study conducted by Harvard university concludes that 17 % of Indians have the advance stage of renal failure i.e,1 in 6 adults have the advance form of kidney failure . Diabetes mellitus , a prevalent condition of most of the kidney failure patients comprises of about 30% which leads to ESRD . Chronic kidney Disease – stage 5 is the final stage where the patient has to undergo either haemodialysis or kidney transplantation[6].2,00,000 new patients have to undergo dialysis treatment but unfortunately, only 10 to 20% of them get proper treatment in India. Majority of the patients with kidney failure diagnose it at their final stage , this can be due lack of knowledge or because of their economic condition . At the time of haemodialysis there is a major risk of anaemic condition . To overcome that at the time of haemodialysis (HD) , Erythropoietic stimulating agents (ESA) and vitamin supplements are administered . In our study the patients are administered with either a short acting ESA agent , a long acting ESA agent and vitamin supplements (B_1,B_6, B_{12}) , depending on the availability and condition of the patient for a better quality of life . Inj.Erypro (Epoetin alpha) is short acting ESA which is used to treat the anaemic condition. Inj. Cresp (Darbepoetin alpha) is a long acting ESA also used to treat the anaemic condition.Inj. Encicarb is used to treat iron deficiency anaemia condition (IDA) to restore the ferritin levels in the body . Inj.Optineuron is a vitamin supplement and a combination of vitamin B_1, B_6, B_{12} .

ESTIMATION OF KIDNEY DISEASE BASED ON eGFR :

eGFR is estimated GFR calculated by the abbreviated MDRD equation : 186 x $(\text{Creatinine}/88.4)^{-1.154}$ x $(\text{Age})^{-0.203}$ x (0.742 if female) x (1.210 if black).For an eGFR level between 16 and 29 ml/min/1.73 m^{2}[16][18-22], the bias compared to mGFR for CKD-EPI and MDRD was similar, 1.9 and 2.0, respectively [1] .

SERUM CREATININE AND CREATININE CLEARANCE:

The Cockcroft–Gault (CG) equation was developed to estimate creatinine clearance, on believing that creatinine clearance is a direct measure of GFR, which actually is not true[14.] This equation uses serum creatinine with respect to age, weight, serum creatinine and gender to derive creatinine clearance. There are many factors which affect the metabolism of creatinine from creatine in the muscles and the rate of secretion of creatinine in the tubules. Creatinine is affected by muscle mass, which changes with respect to old age, between genders and ethnic groups. It includes dietary protein , malnutrition and prescribed medication other factors affect the production and secretion of creatinine and which can also differ in older versus younger patients. Studies have also shown that creatinine clearance overestimates GFR[22,23] due to the secretion of creatinine from the tubules . Complicating factor in using serum creatinine alone is the nonlinear relationship between creatinine and GFR[24,25] . Numerically similar changes in creatinine indicate far greater deterioration in kidney function for patients with better-preserved renal function at baseline, and why eGFR is significantly preferred over creatinine and creatinine clearance.[16]

HAEMOPOIETIC AGENTS :

EPOETIN ALFA (SHORT ACTING ESA) :

Epoetin alfa is a man-made, injectable drug for treating anaemia associated with chronic kidney failure for people who are or will be undergoing dialysis. Erythropoietin is a protein that is produced naturally in the body by kidney by making bone marrow to produce oxygen-carrying red blood cells. When the body fails to activate the compensatory mechanism to restore the red blood cells , bone marrow has to be stimulated through external agent called epoetin alfa .This is a man-made product used to trigger the bone marrow to restore the production of red blood cells in the body . Whereas Darbepoetin alpha is also a man-made protein used to treat the anaemic condition in the patients . The main side effect of this agent is that it causes cardiovascular problems or life-threatening problems[13] . Studies also suggest that short acting ESA are more potent than the long acting ESA in maintaining the mortality rate[9,11-13]. In the interim, strategies targeted at moderating the target Hb level to 10.0 to 12.0 g/dL with the use of moderate ESA doses in conjunction with IV iron therapy seems to be a sensible approach[3]. Hb level of 10–11 g/dL was associated with the lowest mortality among the groups with Hb level <13 g/dL[4].The extensive use of Epoetin and its analogues (erythropoietin- stimulating agents, ESAs) for the purpose of anaemia management had succeeded in reduction of associated morbidity and improvement of functionality, tolerance, cognitive function and overall quality of life. However, over the past few years controversy has been raised about the possible risks of ESA therapy, after the publication of large- scale randomized studies that suggest greater risk with administration of large doses of EPO aiming to higher haemoglobin (Hb) targets. The outcomes of these studies show that ESAs are harmless and that higher Hb levels are beneficial and safe for patients with CKD as investigation of the mechanisms of EPO actions has revealed multiple biologic effects that extend beyond its erythropoietic effect[14] In 2007, the National Kidney Foundation (NKF) & Kidney Disease Outcomes Quality Initiative (KDOQI)[29] Work Group updated its recommended Hb level target between 11.0 and 12.0 g/dL for all patients with CKD and issued a statement warning about greater risk of causing harm when targeting for an Hb level higher than 13.0 g/dL[30].

PHYSIOLOGY:

Erythropoietin which is a glycoprotein hormone stimulates production of erythrocytes in the bone marrow. Circulating levels of erythropoietin rise dramatically, triggering an increase in erythrocyte synthesis in response to anaemia or hypoxia. However, the production of erythrocytes requires iron, vitamin B_{12} and folic acid, the response to erythropoietin is minimal if any of these is deficient.

Erythropoietin has an important physiologic effect outside the hematopoietic system. Animal studies indicate that erythropoietin is produced by cells of the organs like the brain, bone marrow, liver, heart, kidney and blood vessels and that receptors for erythropoietin are present at most of these sites. In the future, these actions may be exploited to treat a variety of disorders, including stroke, diabetic nephropathy, multiple sclerosis, myocardial infarction (MI), and heart failure(HF).Hormonal action includes modulation of angiogenesis and maintenance of cellular integrity by inhibiting apoptotic mechanisms of cell injury.

THERAPEUTIC USES :

ANAEMIA OF CHRONIC RENAL FAILURE :

Epoetin alfa can partially reverse anaemia associated with Chronic Renal Failure thereby reducing but not eliminating the need for transfusions of blood . Initial effects can be seen within 1 to 2 weeks of treatment . Haemoglobin reaches maximal acceptable levels (10 to 11 gm/dL) in 2 to 3 months. Although treatment reduces the need for transfusions, it does not improve quality of life, decrease fatigue, or prevent progressive renal damage .

For therapy to be effective, iron stores must be in required level in the body . Transferrin saturation should be at least 20%, and ferritin concentration should be at least 100 ng/mL. If pre-treatment assessment indicates these values are low, they must be restored with iron supplements.

CHEMOTHERAPY-INDUCED ANAEMIA:

Epoetin alfa is used to treat chemotherapy-induced anaemia in patients with thereby reducing the need for periodic transfusions. Epoetin can be self-administered at home, epoetin therapy can spare patients considerable inconvenience, because epoetin works slowly where the haematocrit may take 2 to 4 weeks to normalise, transfusions are still indicated when rapid replenishment of red blood cells is required. It may stimulate proliferation of these cancers. Furthermore, since ESAs can shorten survival time in all cancer patients , epoetin is indicated only when the goal of cancer therapy is palliation. When the goal is cure, ESAs should not be used as it makes no sense to give a potentially lethal agent toa patient for cure.

DARBEPOETIN ALPHA (LONG ACTING ESA) :

Darbepoetin alfa [Aranesp] is a long-acting analogue of epoetin alfa. Both drugs act on erythroid progenitor cells to stimulate production of erythrocytes. Darbepoetin differs

structurally from epoetin as it has two additional carbohydrate chains and because of these chains, darbepoetin is cleared slower than epoetin, and hence has a longer half-life i.e.,49 hours vs. 18 to 24 hours. As a result, darbepoetin can be administered less frequently than epoetin alpha.

Darbepoetin is indicated for (1) anaemia associated with Chronic Renal Failure and (2) anaemia associated with cancer chemotherapy. In patients with Chronic Renal Failure, darbepoetin can reduce the need for erythrocyte infusions—but will not reduce the incidence of renal events, cardiovascular events, or death nor does it decrease fatigue or improve quality of life. Furthermore, since darbepoetin may increase the risk of cancer-related death, it should be used only when the objective of cancer therapy is palliation, not when the objective is cure.

Table 1: BASIC DEMOGRAPHICS AND LAB PARAMETERS OF ESRD PATIENTS.

S.No	General parameters	Average Values
1.	Age	
	Males	59
	Females	41
2.	Age groups	
	20-30	07
	30-40	08
	40-50	15
	50-60	24
	60-70	37
	70-80	09
3.	BMI	
	under weight	15
	normal	50
	over weight	25
	obese	10
4.	Red Blood Cells	3.604
5.	Glomerular filter rate	7.724
6.	Serum Potassium	5.120
7.	Haemoglobin	10.294

ADVERSE EFFECTS AND WARNINGS:

Darbepoetin is generally well tolerated. The most common problem is hypertension .The risk can be minimized by evaluating that the rate of rise in haemoglobin which does not exceed 1 gm/dL (every 2 weeks). If hypertension is reported, it should be controlled with antihypertensive drugs and if patient is already on antihypertensive therapy, they must increase their dosage. Like epoetin alfa, darbepoetin increases the risk of MI, HF, stroke, cardiac arrest, and other cardiovascular events, especially when the haemoglobin level increases above 11 gm/dL or when the rate of rise in haemoglobin exceeds 1 gm/dL in 2 weeks.

II. METHODOLOGY

An overall study was conducted on different age group of patients > 25 ±5 to >75±5 years in a period of 6 months. Both male and female patients were considered . Pregnant women and lactating females were not taken into consideration . Hemodialyzer machine used for the dialysis where the patients undergo the process thrice a week and twice a week based upon their availability. These patients were undergoing Haemodialysis for a minimum period of 6 months.

III. DISCUSSION

100 samples were collected in which 59 patients are males and 41 patients are females , all were previously diagnosed with CKD – 5th stage also called as ESRD (End Stage Renal Disease) .

From the Table 1, age when calculated as percentages (%) 20-30yrs -7%, 30-40yrs -8% , 40-50yrs -15% ,50-60yrs -24% , 60-70yrs – 37% , 70-80yrs – 8% .The RBC (Red blood cells) values are decreased to an average value of 3.604 (1.34-4.66) million of cells / microlitre . This decrease of value is because of the nephron failure which lessen the release of erythropoietin hormone.In these patients 40% of them undergo dialysis for twice a week and the rest 60 % of them undergo thrice a week. The eGFR (Glomerular Filtrate Rate) is always calculated to check the kidney function . On an average we had observed that eGFR value is 7.724 mL/min/1.73m^2 (5.00- 13.00) which clearly demonstrates that all the patients fall into the category ESRD (End Stage Renal Disease). Another key factor that confirms kidney failure is serum potassium level , this study reveals that on an average the serum potassium level is 5.120 (3.9 – 5.9) mEq/L. Haemoglobin average levels are 10.294(7.7-12.7)gm/Dl

Table 2: TREATMENT OF ANEMIA IN END STAGE RENAL DISEASE PATIENTS:

S.no	Name of medication	Category of Drug	0-2nd month	2nd-4th month	4th-6th month	Average of Usage (%)
1.	Inj. Cresp	Long acting ESA	21%	24%	27%	**27%**
2.	Inj. Encicarb	Iron supplement	60%	80%	80%	**70%**
3.	Inj. Erypro	Short acting ESA	55%	42%	49%	**48.6%**
4.	Inj. Optineuron	Vitamin B1.B6,B12 supplement	11%	10%	15%	**12%**

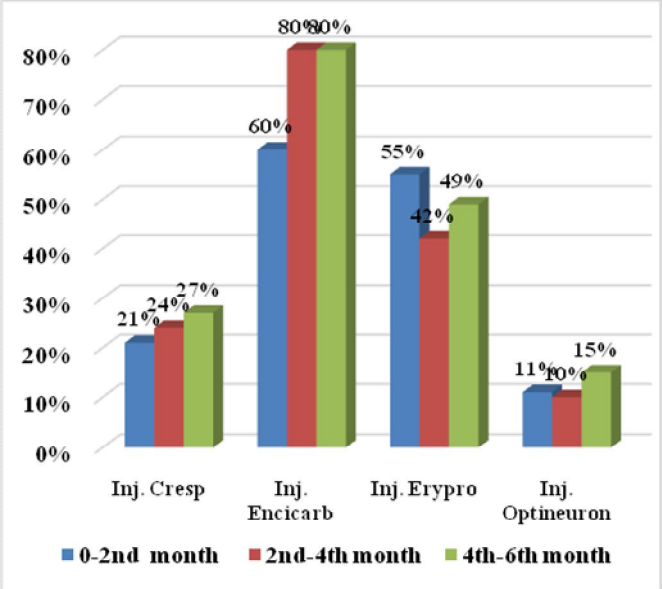

Figure1 : Illustrates that Inj.Encicarb is more frequently used with a dosage of 20,000 units per dialysis , parallelly Inj. Erypro is also administered (Epoetin alpha) to the patients observed in the period of 6 months .Compared to the Inj.cresp {Darbepoetin alpha (LHA)}, Inj.Erypro {Epoetin alpha (SHA)} is preferred at a higher rate.

Likewise, Table 1 shows that 50 % of them have normal BMI and remaining 50% [25%+10%+15%] are abnormal as they are either underweight, overweight or obese patients. From Figure1, and Table 2, Inj.Encicarb was the highest administered (70%) followed by Inj.Erypro (48.6%), Inj.Cresp (27%), Inj.Optineuron (12%). This concludes that Inj.Erypro was a potent agent in the management of anaemic condition in ESRD patients under concerned physician observation. There are no cases of death are reported during our study period.

IV. CONCLUSION

When compared with the vitamin supplements, haemopoietic agent – short acting ESA was most frequently used to treat the anaemic condition in ESRD patients . Iron supplements are being administered very often which has minimal side effects.

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