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Original Research Article

Comparison of safety and efficacy of desidustat with erythropoietin in newly diagnosed patient of anemia in chronic kidney disease: a prospective, open label, randomized controlled trial

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ABSTRACT

Background: Anemia is a frequent complication of chronic kidney disease (CKD), affecting quality of life and increasing cardiovascular risks. Erythropoiesis-stimulating agents (ESAs) like erythropoietin are standard treatments but raise concerns about safety and long-term outcomes. Hypoxia-inducible factor prolyl hydroxylase inhibitors (HIF-PHIs), such as desidustat, have emerged as potential alternatives. This study compared the safety and efficacy of desidustat with erythropoietin in adults with CKD-associated anemia.
Methods: A randomized controlled trial was conducted in the Departments of Nephrology and Pharmacology at Dr. R.P.G.M.C. Kangra at Tanda. Adult CKD patients (>18 years) with anemia, whether on dialysis or not, were enrolled. Participants received either oral desidustat (50 mg thrice weekly) or subcutaneous erythropoietin alfa (50 IU/kg two to three times weekly). Doses were adjusted to maintain haemoglobin (Hb) between 10-11 g/dl. Hematological and biochemical parameters were assessed at baseline, one month and three months.
Results: A total of 109 patients were randomized: 54 to desidustat and 55 to erythropoietin. Baseline characteristics, including age, weight and BMI, were comparable. Both groups showed a significant increase in haemoglobin from baseline to follow-ups ($p<0.001$). At three months, mean Hb rose by 1.65 g/dl in the desidustat group and by 1.31 g/dl in the erythropoietin group.
Conclusions: Desidustat demonstrated efficacy and safety comparable to erythropoietin in managing CKD-associated anemia. Its oral administration offers practical advantages, supporting its role as a promising alternative pending further large-scale studies.

Keywords: Anemia, Chronic kidney disease, Desidustat, Erythropoietin

INTRODUCTION

Anemia of chronic kidney disease (CKD), is a form of normocytic, normochromic, hypo proliferative anemia. KDIGO 2012 guidelines defines anemia in CKD when Hb falls below 13 g/dl in male and 12 g/dl in female population. Anemia is common complication associated with chronic kidney disease and usually occurs when glomerular filtration rate (GFR) falls below <60 ml/min/1.73 m^2 and present in >90% patients undergoing dialysis.[1] Impact of anemia on CKD patients is via reduced oxygen delivery to organs leading to symptoms like fatigue, shortness of breath, decreased exercise tolerance and overall reduced quality of life. Chronic anemia leads to cardiac remodelling and left ventricular hypertrophy thus leading to cardiovascular morbidity and mortality.[2]

Chronic kidney disease (CKD) is a leading global public health challenge with an estimated prevalence of 13.4% (11.7-15.1%) worldwide. In India, deaths from CKD

increased from 0.59 million in 1990 to 1.18 million in 2016.[3] The National Health and Nutrition Examination Survey (NHANES) analysis pronounced that globally 15.4% (~4.8 million people) had anemia of CKD and prevalence of anemia was 17.4%, 50.3% and 93.4% in CKD Stages 3, 4 and 5, respectively. India has the highest prevalence of anemia globally at 39.86%. and prevalence of anemia increases from 66.6% at Stage 3 to 94.7% at Stage 5.[4]

The causes of anemia in CKD are multifactorial, but traditionally, decreased erythropoietin (EPO) levels have been regarded as a primary contributing factor.[5] EPO gene is hypoxia-sensitive genes when activated, lead to an increased EPO production. The gene for erythropoietin is located on chromosome 7 and is regulated by HIF i.e., Hypoxia-Inducible Factor (HIF). Under anaemic stress or hypoxia, the HIF1 binds to the EPO gene and thus activates its expression. HIF-1 is made up of two subunits: HIF-1α and HIF-1β. HIF1α is virtually absent under normoxic conditions whereas HIF1β is constitutively expressed. However, under low oxygen conditions, HIF-1α accumulates and moves into the nucleus, where it binds to HIF-1β. The HIF-1α/β heterodimer attaches to specific DNA sequences known as hypoxia response elements (HRE), controlling the expression of multiple hypoxia-sensitive genes by either upregulating or downregulating their activity. Among the genes transcriptionally upregulated by the HIF complex are transferrin, the transferrin receptor, vascular endothelial growth factor (VEGF) and endothelin-1.[6]

Under nonmonic conditions, HIF1α is degraded. To achieve this, HIF-1α undergoes hydroxylation at two proline residues. This process is catalysed by prolyl hydroxylase domain (PHD) enzymes, a type of HIF-specific prolyl hydroxylases, which require oxygen, iron and 2-oxoglutarate as cofactors.[7] Conversely, when oxygen levels are low, PHD activity is inhibited, leading to the stabilization of HIF-1α and its translocation to the nucleus.[8]

Erythropoietin (EPO) levels are lower than expected in relation to the severity of anemia in patients with chronic kidney disease (CKD). This absolute deficiency of EPO may arise from reduced EPO production and/or impaired EPO sensing. CKD is linked to disrupted oxygen delivery to the kidneys due to decreased blood flow. As a result, renal tissue adapts by reducing oxygen consumption, maintaining a normal tissue oxygen gradient. Consequently, prolyl hydroxylase domain (PHD) enzymes remain active, preventing the formation of the hypoxia-inducible factor (HIF) heterodimer and inhibiting EPO gene activation.[9]

The standard treatment for managing anemia in CKD has been erythropoiesis-stimulating agent (ESA) therapy, which effectively raises haemoglobin levels and minimizes the necessity for blood transfusions.[11] This is associated with increased risk of thrombosis, poor hypertension control, increased chances of stroke and congestive heart failure. About 90% of patients treated with erythropoietin exhibits response in dose related manner but 10% of patients fails to achieve so, leading to use of higher doses of erythropoietin and increasing chances of adverse cardiovascular outcomes.[11]

Recently, a new class of drugs, known as hypoxia-inducible factor prolyl hydroxylase inhibitors (HIF-PHIs), has emerged as a potential alternative treatment for anemia in CKD. HIF-PHIs stimulate the production of erythropoietin and promote erythropoiesis, thereby increasing haemoglobin levels in patients with anemia. Till date six Hypoxia-Inducible Factor Prolyl Hydroxylase Inhibitors has completed phase three clinical trial worldwide are Daprodustat (GSK1278863), Desidustat (ZYAN1), Enarodustat (JTZ-951), Molidustat (BAY 85-3934), Roxadustat (FG-4592, ASP1517, AZD9941), Vadadustat (AKB-6548, MT-6548).[12] Desidustat received its approval from DCGI for anemia associated with CKD in patients either on dialysis or not on dialysis. The recommended starting dosage is 50 mg three times weekly and further dosage should be adjusted based on haemoglobin levels assessment, with a maximum dosage of 150 mg three times weekly.[13]

Despite promising results, further research is needed to compare the safety and efficacy of desidustat with ESA therapy in a randomized control trial. This study aims to evaluate the safety and efficacy of desidustat compared to erythropoietin in the management of anemia in patients with CKD.

METHODS

Study place

The study was carried out in the Department of Nephrology, Department of Pharmacology and Multi-Disciplinary Research Unit at Dr. R.P.G.M.C. Kangra at Tanda, a multispecialty tertiary healthcare facility located in the Kangra valley of Himachal Pradesh in India.

Study design

The study was a randomized (simple randomization technique, coin toss method), prospective, open label, (interventional) controlled trial.

Study duration

The study was conducted over a period of one-year w.e.f. 14/02/2024 to 14/02/2025 (first 9 months for patient recruitment and 3 months for follow up after treatment) after receiving ethical approval.

Inclusion criteria

Patients willing to give written informed consent with age more than 18 years, Male or female patients with a current

clinical diagnosis of anemia due to CKD having baseline haemoglobin concentrations ≤ 10.0 g/dl before enrolment, If patients were on dialysis, they were on adequate dialysis (as prescribed) on either 2 or 3 times per week hemodialysis for at least 12 weeks prior to screening, Patients with no planned renal transplant during the study period, Adequate serum ferritin and/or TSAT as per KDIGO guidelines, No iron, folate or vitamin B12 deficiency.

Exclusion criteria

Patients who received red blood cell transfusion within 8 weeks prior to enrolment, Hematological malignancy or primary hematological disease, Malignancy of any organ, Presence or a history of bleeding disorder, Serological status reflecting active hepatitis B or C or Human Immunodeficiency Virus (HIV) infection, History of renal transplant, Unable to swallow tablets or disease significantly affecting gastrointestinal function and/or inhibiting small intestinal absorption such as malabsorption syndrome, resection of small bowel or poorly controlled inflammatory bowel disease affecting the small intestine, History of uncontrolled autoimmune hemolytic anemia, idiopathic thrombocytopenic purpura (ITP) or thalassemia, known hypersensitivity to investigational products or known contraindications to any of the study drugs, Women who were trying to conceive, pregnant and breastfeeding women, History of coronary artery disease or any thromboembolic disorders like PVD, DVT, pulmonary embolism, ischemic stroke etc.

Study intervention

A detailed socio-demographic profile of all the patients with CKD was elicited; clinical examination was performed and hematological and biochemical investigations were carried out. All the information of the participants was recorded/documented in the study proforma.

Patients found to have nutritional deficiencies (iron, B12 and folate) were recruited after supplementation and were enrolled only if they still qualified as per the criteria mentioned above. Once diagnosed, eligible patients who fulfilled the above-mentioned criteria were apprised about the study through the patient information sheet and were thoroughly informed about the study and related aspects. After obtaining written informed consent, the patients were assigned drug therapy on an alternate basis; the first participant was given a drug randomly (coin toss) and subsequently, every next participant was put on an alternate drug regimen.

Treatment regimen

Participants receiving desidustat were given oral tab desidustat 50 mg before breakfast thrice a week, with dose adjustment based on haemoglobin levels to maintain target haemoglobin between 10 and 11 g/dl. On the other hand, participants receiving EPO were given subcutaneous injections of erythropoietin alfa 50 IU/kg as a starting dose twice or thrice per week, with dose adjustment based on haemoglobin levels to maintain target haemoglobin between 10 and 11 g/dl.

If the target haemoglobin level was not achieved with the given drugs, the dose was increased. The tab desidustat dose was increased up to 150 mg thrice a week, while the erythropoietin dose was increased up to 450 IU/kg twice or thrice per week.

These blood biochemical parameters were repeated during follow-ups at the end of the first and third months after initiating treatment. Patients were contacted telephonically the day after initiating therapy and were asked about any discomfort. Any other clinical/laboratory investigation that was required during the study and advised by the physician but not mentioned above was also performed.

A change in haemoglobin level >10 g/dl was taken as an adequate response of the drug for anemia in CKD. On completion of 3 month of intervention the outcome was assessed the efficacy on the basis of Comparison of Haemoglobin, urea and creatinine in between the groups and within each group.

Statistical analysis

The data was collected, cleaned and entered using Microsoft Excel spreadsheet; and was analyzed in Statistical Package for Social Science (SPSS) v 27. Categorical data was expressed as proportions, frequencies and percentages of each, while quantitative data was expressed as mean±SD. Chi square or Fisher's exact probability test was used for comparing the qualitative data between the two groups. Paired t-test was applied for analyzing the change in quantitative parameters at different time intervals as compared to the baseline within each group, whereas independent or unpaired t-test was applied for analyzing the quantitative parameters at respective follow up durations, between the two groups. A two-tailed p value of <0.05 was considered as significant for all analysis.

RESULTS

Total of 116 patients were accessed for eligibility out of which 04 patients were excluded as they did not meet the eligibility criteria. Rest 112 patients were randomized to two groups resulting 56 patients in each Group A and B. Two patients from Group A and One patient from Group B were lost to follow up. Finally, 109 patients were analyzed as shown in CONSORT flowchart Figure 1.

Patients were randomly divided into two groups. The patients in Group A were prescribed with tablet Desidustat 50-150 mg orally before breakfast thrice a week and the patients in group B were prescribed with Injection

Erythropoietin (epoetin alfa) 50–450 IU/kg subcutaneously twice or thrice per week.

The present study found that the mean age of study participants in Desidustat: Mean=59.27±14.32 years and Erythropoietin: Mean=60.02±10.46 years were comparable at the baseline, p value: 0.75. The present study found that the mean heights of study participants in Desidustat: Mean=1.58±0.09 m and Erythropoietin: Mean=1.57±0.08 m were comparable, P-value 0.75. The mean weight of study participants at baseline, first follow-up (FU-1) and 2nd follow-up (FU-2) were comparable. Similarly, the mean BMI of study participants at baseline, first follow-up and 2nd follow-up were also statistically non-significant as presented in Table 1.

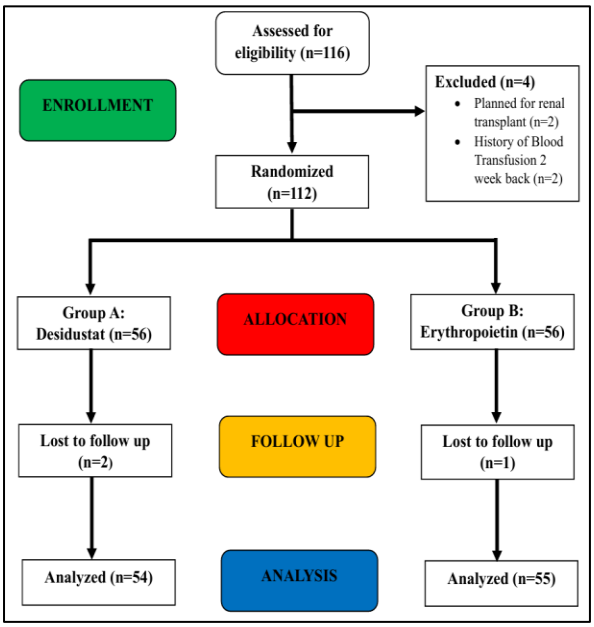

Figure 1: Consort flowchart diagram.

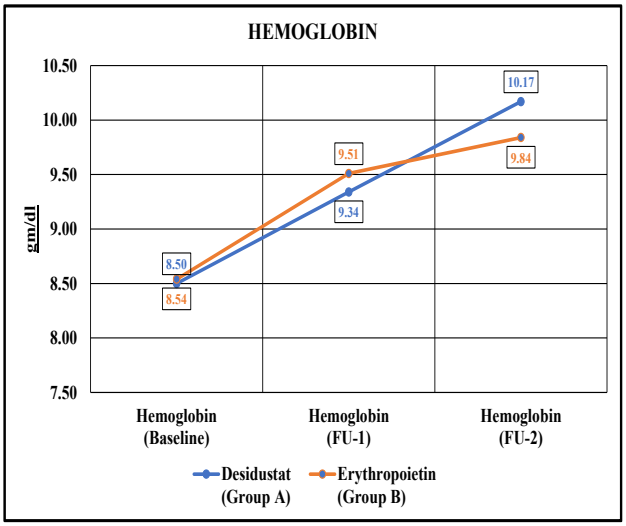

Figure 2: Line plot showing comparison of mean value of haemoglobin between the two groups at different follow ups.

The present study found that there was statistically non-significant distribution of gender within the groups. However, females were more on both Desidustat (62.5%) and Erythropoietin (66.1%) groups than males as presented in Table 2.

The present study found that out of 54 participants in Desidustat group 9 were on dialysis and 45 were not on dialysis whereas out of 55 participants in Erythropoietin group 11 were on dialysis and 44 were not and there was statistically non-significant (p=0.653) difference in distribution of participants based on dialysis between the groups.

This study compared the mean value in Desidustat group and found that there was statistically significant mean difference for Haemoglobin between Baseline to FU-1 (MD: 0.82, p value <0.001), FU-1 and FU-2 (MD:0.83, p value<0.001) and between Baseline to FU-2 (MD: 1.65, P value<0.001). This study also found that there was statistically significant mean difference between FU-1 and FU-2 for serum urea (MD: -10.81 mg/dl, p value 0.01); between baseline and FU-1, baseline and FU-2 for total bilirubin (MD: 0.11 mg/dl, p value 0.02), (MD: 0.22 mg/dl, p value <0.001); between FU-1 and FU-2 for globulin (MD: 0.16 gm/dl, p value 0.03) and between FU-1 and FU-2 and baseline and FU-2 for total protein (MD: -0.19 mg/dl, p value 0.02), (MD: -0.18 mg/dl, p value 0.02). There were no statistically significant changes in TLC, Platelet, Serum Creatinine, SGOT, SGPT, ALP and serum albumin in Desidustat Group between Baseline and FU-1, FU-1 and FU-2 and between Baseline and FU-2 as presented in table 3.

This study compared the mean value in erythropoietin group and found that there was statistically significant mean difference for haemoglobin between baseline and first follow up (FU-1) (MD: 0.98 gm/dl, P value<0.001), FU-1 and second follow up (FU-2) (MD: 0.33 gm/dl, P value=0.01) and between baseline and FU-2 (MD: 1.31 gm/dl, p value<0.001). This study also found statistically significant mean difference between baseline and FU-2 for SGOT, SGPT and Albumin, (MD: 0.06, p value<0.001), (MD: 10.44, p value<0.001), (MD: 12.84, p value<0.001) and (MD: 0.19, p value=0.03). The study found statistically significant mean difference between baseline and FU-1, baseline and FU-2 for total bilirubin; ALP and total protein; (MD: 0.18, p value<0.001), (MD: 0.19, p value<0.001); (MD: 0.14, p value<0.001), (MD: 0.14, p value<0.001); (MD: -15.22, p value<0.001), (MD: -20.67, p value:0.02); and (MD: 0.24, p value 0.04), (MD: 0.33, p value 0.01). There was no statistically significant mean difference for TLC, platelet, serum urea and serum creatinine as presented in Table 4.

This study found that there was statistically non-significant difference in mean haemoglobin, TLC, platelet count, serum urea, serum creatinine, liver function test and serum protein at baseline, first follow up and 2nd follow in between both groups as presented in Table 5, Figure 2.

Table 1: Comparison of means of demographics variables among two groups.

Variables	Desidustat (Group A)		Erythropoietin (Group B)		P value*
	Mean	SD	Mean	SD	
Age	59.27	14.32	60.02	10.46	0.75
Height (Mt.)	1.58	0.09	1.57	0.08	0.75
Weight (Kg) (Baseline)	56.96	10.86	55.20	9.12	0.35
Weight (Kg) (FU-1)	57.09	10.86	55.18	9.18	0.32
Weight (Kg) (FU-2)	57.37	10.51	55.02	8.56	0.20
BMI (Baseline)	22.90	3.98	22.38	3.66	0.47
BMI (FU-1)	23.01	3.93	22.37	3.69	0.38
BMI (FU-2)	23.12	3.83	22.30	3.47	0.25

*Independent t-test.

Table 2: Gender wise distribution of study participants between two groups.

Gender	Desidustat (Group A)	Erythropoietin (Group B)	P value*
Female n=70 (64.2%)	34 (62.9%)	36 (65.5%)	0.693
Male n=39 (35.8%)	20 (37.1%)	19 (34.5%)	

Data expressed as frequency (percentage), *Chi-square test.

Table 3: Comparison of mean values at admission, first follow up and second follow up for CBC, RFT and LFT variables in Desidustat group.

Variables	Time	Mean	SD	Mean	SD	Mean Diff.	P value*
Hb (gm/dl)	Baseline - FU 1	8.52	0.69	9.34	1.25	0.82	<0.001
	FU 1- FU 2	9.34	1.25	10.17	1.19	0.83	<0.001
	Baseline-FU 2	8.52	0.69	10.17	1.19	1.65	<0.001
TLC (cells/mcl)	Baseline - FU 1	7474.26	2623.19	7710.00	2613.35	235.74	0.50
	FU 1- FU 2	7710.00	2613.35	7704.81	2490.75	-5.19	0.99
	Baseline-FU 2	7474.26	2623.19	7704.81	2490.75	230.56	0.58
Platelet	Baseline - FU 1	168074.07	55059.44	174314.81	68511.07	6240.74	0.50
	FU 1- FU 2	174314.81	68511.07	174537.04	60800.54	222.22	0.98
	Baseline-FU 2	168074.07	55059.44	174537.04	60800.54	6462.96	0.49
Serum urea (mg/dl)	Baseline - FU 1	101.43	37.69	107.41	42.73	5.98	0.19
	FU 1- FU 2	107.41	42.73	96.59	35.71	-10.81	0.01
	Baseline-FU 2	101.43	37.69	96.59	35.71	-4.83	0.31
Serum creatinine (mg/dl)	Baseline - FU 1	4.73	2.46	5.01	2.92	0.28	0.22
	FU 1- FU 2	5.01	2.92	4.96	2.54	-0.05	0.84
	Baseline-FU 2	4.73	2.46	4.96	2.54	0.24	0.39
Total bilirubin (mg/dl)	Baseline - FU 1	0.41	0.32	0.52	0.56	0.11	0.02
	FU 1- FU 2	0.52	0.56	0.63	0.58	0.11	0.15
	Baseline-FU 2	0.41	0.32	0.63	0.58	0.22	<0.001
SGOT (IU/l)	Baseline - FU 1	27.56	39.96	24.83	32.73	-2.72	0.21
	FU 1- FU 2	24.83	32.73	26.56	12.54	1.72	0.65
	Baseline-FU 2	27.56	39.96	26.56	12.54	-1.00	0.83
SGPT (IU/l)	Baseline - FU 1	21.07	37.60	19.91	35.03	-1.17	0.61
	FU 1- FU 2	19.91	35.03	23.91	19.17	4.00	0.36
	Baseline-FU 2	21.07	37.60	23.91	19.17	2.83	0.52
ALP (IU/l)	Baseline - FU 1	144.59	67.26	130.87	78.06	-13.72	0.10
	FU 1- FU 2	130.87	78.06	146.26	128.47	15.39	0.28
	Baseline-FU 2	144.59	67.26	146.26	128.47	1.67	0.92
Total protein (gm/dl)	Baseline - FU 1	7.24	0.58	7.23	0.59	-0.01	0.88
	FU 1- FU 2	7.23	0.59	7.42	0.64	0.19	0.02
	Baseline-FU 2	7.24	0.58	7.42	0.64	0.18	0.02
Albumin (gm/dl)	Baseline - FU 1	3.96	0.40	3.99	0.47	0.03	0.54
	FU 1- FU 2	3.99	0.47	4.04	0.44	0.06	0.34
	Baseline-FU 2	3.96	0.40	4.04	0.44	0.09	0.10

*Paired t-test.

Table 4: Comparison of mean values at admission (Baseline), First follow up (FU-1) and second follow up (FU-2) for CBC, RFT and LFT variables in Erythropoietin group.

Variables	Time	Mean	SD	Mean	SD	Mean Diff.	P value*
Hb (gm/dl)	Baseline - FU 1	8.54	0.81	9.51	1.40	0.98	<0.001
	FU 1- FU 2	9.51	1.40	9.84	1.32	0.33	0.01
	Baseline-FU 2	8.54	0.81	9.84	1.32	1.31	<0.001
TLC (cells/mcl)	Baseline - FU 1	7352.18	2444.83	7379.25	2040.28	27.07	0.93
	FU 1- FU 2	7379.25	2040.28	7322.36	2031.04	-56.89	0.83
	Baseline-FU 2	7352.18	2444.83	7322.36	2031.04	-29.82	0.93
Platelet	Baseline - FU 1	172818.18	61204.60	182836.36	51579.41	10018.18	0.12
	FU 1- FU 2	182836.36	51579.41	176054.55	54136.80	-6781.82	0.34
	Baseline-FU 2	172818.18	61204.60	176054.55	54136.80	3236.36	0.65
Serum urea (mg/dl)	Baseline - FU 1	103.27	46.05	96.53	49.04	-6.74	0.20
	FU 1- FU 2	96.53	49.04	96.45	36.98	-0.08	0.99
	Baseline-FU 2	103.27	46.05	96.45	36.98	-6.82	0.13
Serum creatinine (mg/dl)	Baseline - FU 1	5.31	3.09	5.30	3.17	-0.01	0.97
	FU 1- FU 2	5.30	3.17	5.48	3.18	0.18	0.49
	Baseline-FU 2	5.31	3.09	5.48	3.18	0.17	0.38
Total Bilirubin (mg/dl)	Baseline - FU 1	0.31	0.15	0.49	0.28	0.18	<0.001
	FU 1- FU 2	0.49	0.28	0.51	0.20	0.01	0.73
	Baseline-FU 2	0.31	0.15	0.51	0.20	0.19	<0.001
SGOT (IU/l)	Baseline - FU 1	20.56	8.26	74.35	370.57	53.78	0.29
	FU 1- FU 2	74.35	370.57	31.00	18.31	-43.35	0.39
	Baseline-FU 2	20.56	8.26	31.00	18.31	10.44	<0.001
SGPT (IU/l)	Baseline - FU 1	14.38	7.49	74.96	400.21	60.58	0.27
	FU 1- FU 2	74.96	400.21	27.22	25.20	-47.75	0.38
	Baseline-FU 2	14.38	7.49	27.22	25.20	12.84	<0.001
ALP (IU/l)	Baseline - FU 1	141.62	71.17	126.40	57.98	-15.22	<0.001
	FU 1- FU 2	126.40	57.98	120.95	60.22	-5.45	0.47
	Baseline-FU 2	141.62	71.17	120.95	60.22	-20.67	0.02
Total protein (gm/dl)	Baseline - FU 1	7.18	0.76	7.42	0.65	0.24	0.04
	FU 1- FU 2	7.42	0.65	7.50	0.60	0.08	0.36
	Baseline-FU 2	7.18	0.76	7.50	0.60	0.33	0.01
Albumin (gm/dl)	Baseline - FU 1	3.80	0.71	3.93	0.50	0.12	0.18
	FU 1- FU 2	3.93	0.50	3.99	0.56	0.07	0.32
	Baseline-FU 2	3.80	0.71	3.99	0.56	0.19	0.03

*Paired t-test.

Table 5: Comparison of means of hemogram (CBC), RFT and LFT variables among two groups.

Variables	Time	Desidustat		Erythropoietin		P value*
		Mean	SD	Mean	SD	
Hb (gm/dl)	Baseline	8.50	0.69	8.54	0.81	0.73
	FU-1	9.34	1.25	9.51	1.40	0.50
	FU-2	10.17	1.19	9.84	1.32	0.17
TLC (cells/mcl)	Baseline	7356.00	2710.00	7339.00	2425.00	0.97
	FU-1	7710.00	2613.00	7379.00	2040.00	0.46
	FU-2	7705.00	2491.00	7322.00	2031.00	0.38
Platelet	Baseline	168232.00	54108.00	173500.00	60860.00	0.63
	FU-1	174315.00	68511.00	182836.00	51579.00	0.46
	FU-2	174537.00	60801.00	176055.00	54137.00	0.89
Serum urea (mg/dl)	Baseline	102.96	38.77	103.02	45.67	1.00
	FU-1	107.41	42.73	96.53	49.04	0.22
	FU-2	96.59	35.71	96.45	36.98	0.98
Serum creatinine (mg/dl)	Baseline	4.85	2.58	5.32	3.07	0.38
	FU-1	5.01	2.92	5.30	3.17	0.62
	FU-2	4.96	2.54	5.48	3.18	0.35
Total bilirubin (mg/dl)	Baseline	0.41	0.32	0.32	0.15	0.06
	FU-1	0.52	0.56	0.49	0.28	0.75
	FU-2	0.63	0.58	0.51	0.20	0.14

Continued.

Variables	Time	Desidustat		Erythropoietin		P value*
		Mean	SD	Mean	SD	
SGOT (IU/l)	Baseline	28.09	39.34	20.41	8.26	0.16
	FU-1	24.83	32.73	74.35	370.57	0.33
	FU-2	26.56	12.54	31.00	18.31	0.14
SGPT (IU/l)	Baseline	21.75	37.15	14.30	7.44	0.14
	FU-1	19.91	35.03	74.96	400.21	0.32
	FU-2	23.91	19.17	27.22	25.20	0.44
ALP (IU/l)	Baseline	145.11	66.80	140.57	70.96	0.73
	FU-1	130.87	78.06	126.40	57.98	0.74
	FU-2	146.26	128.47	120.95	60.22	0.19
Total protein (gm/dl)	Baseline	7.27	0.59	7.17	0.76	0.44
	FU-1	7.23	0.59	7.42	0.65	0.12
	FU-2	7.42	0.64	7.50	0.60	0.49
Albumin (gm/dl)	Baseline	3.96	0.41	3.79	0.70	0.13
	FU-1	3.99	0.47	3.93	0.50	0.52
	FU-2	4.04	0.44	4.00	0.56	0.61

*Independent t-test.

DISCUSSION

The present study was carried out in the Department of Nephrology, Department of Pharmacology and Multi-Disciplinary Research Unit at Dr. R.P.G.M.C. Kangra at Tanda, a multispecialty tertiary healthcare facility located in the Kangra valley of Himachal Pradesh. The study aimed to compare the effectiveness of desidustat against erythropoietin in newly diagnosed adult patient of anemia in chronic kidney disease. The study also assessed the treatment effectiveness of desidustat against erythropoietin, safety profile of Desidustat against erythropoietin and compared the hematological and biochemical parameters in study participants receiving different drugs.

Efficacy

The present study found that there was statistically significantly rise in haemoglobin levels among study participants who were treated with Desidustat as well as with erythropoietin however there was statistically no significant difference when both the groups were compared together, although the rise was more in Desidustat group. A study by Jin et al, found that the median haemoglobin rise at 12 weeks was 10.5g/l and change from baseline was 15 g/l in the roxadustat group and 9.94 g/l and 11g/l in the EPO group respectively and Roxadustat group had higher maximum Hb levels at same time points than those in EPO group.[14]

A study by Gang et al, found that the least mean square change in haemoglobin from the baseline to 16-24 weeks was 0.95 (0.09) gm/dl in Desidustat group and 0.80 (0.09) gm/dl in the epoetin alfa group (difference 0.14 gm/dl) confirming substantially more haemoglobin responders in the Desidustat group.[15] A study by Agarwal et al, found that desidustat group's haemoglobin change from baseline to Weeks 16–24 was 1.95 g/dl, while the darbepoetin group's was 1.83 g/dl (difference: 0.11 g/dl; 95% CI: -0.12, 0.34).[16] A study by Joharapurkar et al, found that the subjects who received Desidustat showed a haemoglobin increase of more than 0.5 g/dl at any time compared to placebo and Hb increase of >1.0 g/dl was seen more in subjects treated with Desidustat when compared to those who received placebo.[17] A metanalysis by Zheng et al, found a significant difference in the efficacy of Desidustat (mean difference: 2.46; 95% CI 0.93-3.99) in increasing Hb when compared to placebo.[18]

The present study observed that there was statistically significantly rise in RBC levels among study participants who were treated with Desidustat as well as with erythropoietin (except for 1st follow up) however, there was statistically no significant difference when both the group were compared together. In the current study, there was a rise in serum urea levels from baseline to 1st follow up of patients who were treated with Desidustat and then a significant decline in the serum urea level was found between 1st and 2nd follow up. A study by Joharapurkar et al, found that Desidustat prevented elevation of serum creatinine, urea, IL1B, IL-6 and kidney injury molecule and elevated erythropoietin levels in rats that were subjected to acute kidney injury.[17]

Safety

The safety profile of the desidustat oral tablet was comparable with the erythropoietin injection. There were no new risks or no increased risks seen with the use of desidustat compared to erythropoietin. In our current study the majority of treatment emergent adverse event (TEAEs) were mild, unrelated and resolved without any action with the change of drug in both the treatment groups. No deaths due to any adverse events occurred during the trial. Safety outcomes from this study showed no trends of electrocardiography (ECG) abnormalities in any patients receiving both the treatment. No significant change in systolic/ diastolic blood pressure and pulse rate from baseline to FU-1 and FU-2 were seen following 3 months of desidustat and erythropoietin administration.

This study has some limitations, like short study duration and small sample size, but due to time-bound nature of

dissertation study only 112 patients were enrolled to the study. In Current study route of administration of both the drugs were different and secondly universal sampling technique was used in enrolling the study participants which may affect the generalizability of the result.

CONCLUSION

The findings of this study indicate that desidustat is a promising alternative to erythropoietin in the management of anemia associated with chronic kidney disease (CKD). Both treatment groups demonstrated significant improvements in haemoglobin levels over the study period, with desidustat showing a comparable rise in haemoglobin to erythropoietin. Furthermore, desidustat maintained a similar safety profile with no significant adverse events reported during the study duration.

One of the key advantages of desidustat is its oral administration, offering greater convenience compared to the subcutaneous route of erythropoietin. This could potentially improve patient adherence and quality of life, particularly for non-dialysis-dependent CKD patients. Additionally, the ability of desidustat to effectively stimulate erythropoiesis while avoiding some of the risks associated with erythropoietin therapy, such as thromboembolic events and blood pressure fluctuations, makes it a valuable therapeutic alternative. Although this study provides valuable insights into the efficacy and safety of desidustat, further large-scale, long-term clinical trials are required to validate these findings across diverse patient populations. Future research should also focus on evaluating the cardiovascular outcomes, long-term safety and cost-effectiveness of desidustat compared to traditional erythropoiesis-stimulating agents.

In conclusion, desidustat represents an effective and well-tolerated alternative to erythropoietin in treating CKD-associated anemia, warranting further investigation and potential incorporation into routine clinical practice.

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