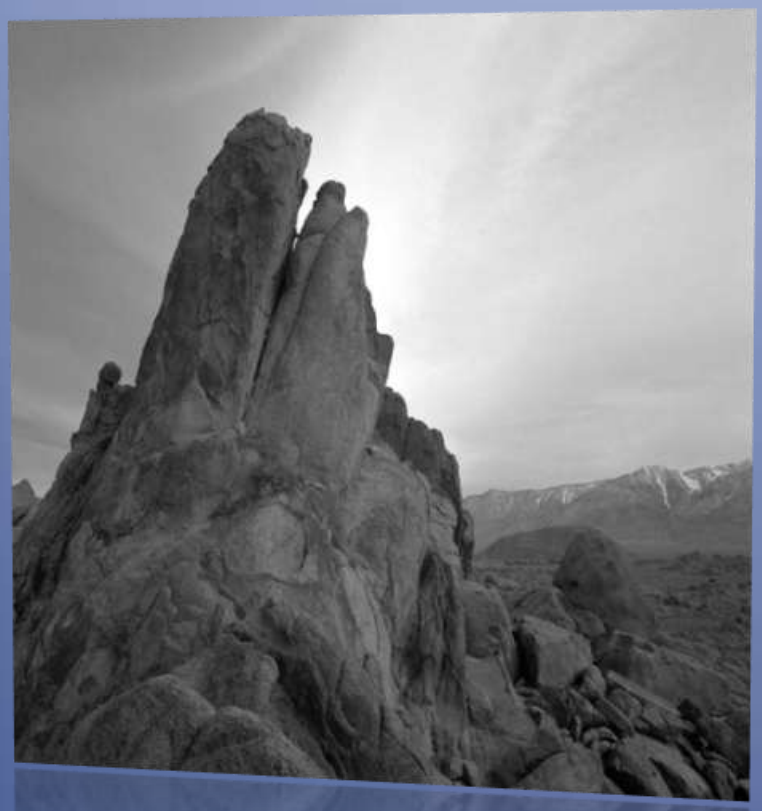

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Ayurvedic Management of Anaemia in Chronic Kidney Diseases- A Clinical Trial

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ABSTRACT

Anemia remains a major challenge in treating cases of Chronic Kidney Disease (CKD), as the pathology is still not fully understood. Anemia in CKD is associated with reduced quality of life, increased risk of cardiovascular disease leading to poor outcomes**.** An open non- randomized clinical trial was conducted on 50 diagnosed Chronic Renal Failure patients. On the basis of CKD-EPI equation,39/50 **(78%) study subjects having CKD stage 5**, 9 (18%) study subjects having CKD stage 4 & 2 (4%) study subjects with CKD stage 3B. There were 47 study subjects (94%) having anemia, out of which 41were having moderate to severe anemia before start of treatment. At the end of study period, there was significant improvement in their status as only 15 remained with moderate anemia& none with severe anemia.Hb % was estimated at 0,28,84,140 & 180 days. The mean Hb% was 8.39 g ±2.10 g on zero day. On 180thday, mean Hb was 11.07g ±1.67.This31.94% rise in Hb % was found to be statistically highly significant(t= 19.50 with p <0.001).Pallor, Oedema, Fatigue, Weakness, Dyspnoeawere the signs and symptoms considered to be associated with anemia and improvement was assessed in reduction of severity. There was statistically significant clinical improvement in respect of signs & symptoms of anemia. This study proved that the Ayurvedic treatment is a suitable alternative treatment of anemia in CKD to modern controversial treatment of parenteral iron therapy &Erythropoietin supplementation.

KEYWORDS

Anemia, CKD, Ayurveda, Management

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INTRODUCTION

Chronic kidney disease (CKD) is increasing in enormous proportions throughout the world. This is a hidden epidemic taking a heavy toll of lives[1]. It is increasing commensurate to the increasing proportion of individuals with hypertension & diabetes; who are at high risk to develop CKD. CKD has 5 stages and Chronic Renal Failure (CRF) corresponds to 3-5 stages of CKD.

Anemia remains a major health problem in CKD. Erythropoietin is the hormone that is produced by mainly kidneys (90%) & liver (10%), which stimulates bone marrow to produce more number of Red Blood cells (RBCs)& initiates the synthesis of hemoglobin inside RBCs. In CKD due to diseased kidney, erythropoietin production is inadequate which causes reduction in RBC production & reduced lifespan of RBCs. Further, this anemia is mostly refractory to oral iron therapy due to poor dietary absorption.

Inflammation is commonly observed in CKD that impairs both the early erythropoietin-dependent period of erythropoiesis and the later iron-dependent period. In addition, inflammatory cytokines stimulate hepatic release of 'hepcidin', produced by the liver; it is the hormone responsible for maintaining systemic iron homeostasis[2],which simultaneously blocks iron absorption in the gut and thereby promoting iron-deficiency erythropoiesis. Thus, the anemia in CKD is hypoproliferative and iron-deficiency erythropoiesis[3].

The current management of treating Anemia in CKD patients is controversial as there are only few clinical trials that reveal that erythropoiesis stimulating agents were associated with increased morbidity & mortality[4].There are reports of serious effects of parenteral iron therapy due to over dosage of iron.

Treating anemia in CKD patients is therefore a challenge. The present clinical trial focuses on a safe and suitable alternative therapy to treat Anemia.

.AIM

To develop a simple & effective line for management of Anemia in CKD with the help of Ayurveda.

Objectives:-1. To assess the efficacy of Ayurvedic therapy for treatment of Anemia in CKD.

2. To study the correlation of Hemoglobin with Serum creatinine& blood urea in CKD.

MATERIALS & METHODS

Study Design: Present study was conducted as –Open labeled systematic non randomized clinical trial- Phase I.

Ethical Committee Approval Number: RSTH/PG/IEC/308/2010 Dated 7/10/2010

Sample size:-In the present study sample size was taken as 50, as approved by the Ethical committee.

Inclusion Criteria:-

1. Any diagnosed CRF patient for last 6 months duration.
2. Age: More than 18 years
3. Sex: Both sexes.
4. Serum Creatinine level: > 1.8 mg, Blood Urea : > 50 mg% for last 6 months
5. Patients put on Dialysis or otherwise
6. Patients willing to participate in the research project.

Exclusion Criteria:-

1. Patient with malignant Hypertension having > 130 mm diastolic B.P.
2. Renal artery stenosis
3. Neoplasm of kidney
4. History of previous kidney transplant
5. Adult polycystic kidney disease.
6. Uncontrolled arrhythmia or severe cardiac disease within the past 6 months

Treatment period- 180 days

Study period:- From July 2012 to Aug 2016

Treatment Procedure:-There was treatment cycle of 28 days to be followed as mentioned below

- Deepan-Pachan- Mrudu virechan-1-5 days
- Shaman chikitsa-6-28 days
- Bastichikitsa- 22-28 days

Such 6 cycles were to be completed in 180 days.

a) Deepan-Pachan&Mrudu-Virechana- Pippali (*Piper longum*) choorna 500 mg with Erandpatra (*Ricinuiscommunis*) swaras/ freshly prepared 50 ml juice is given early morning on empty stomach for 5 days. This was repeated every consecutive month for 6 months.

b) Shaman chikitsa:-In Shaman chikitsa, the doshas are not removed from the body but those are brought down to equilibrium. It is materialized by combined effect of Rasayan, Mutral, shothghna&Raktaprasadakdravyas. In the present study Shaman chikitsa was given in the form of Kasanyadichoorna along with Anupan mentioned below.

Kasnyadiyogchoorna:-	
Kasni (Cichoriumintybus)	500 mg
Sariva (Anantmool/ Hemidesmusindicus)	500 mg
Punarnawa (Boerhaaviadiffusaroxb)	500 mg
Gokshoor (*Tribulusterrestris*)	500 mg
AmraHaridra (*Curcuma aromatica*).	500 mg
Amlaki (*Emblicaofficianalis*)	500 mg
Palash (*ButeafrondosaKoen*)	500 mg

Anupan: Ashmantak (Bauhinia racemosa) and Kasni (*Cichoriumintybus*) 50 ml quath twice daily from 6th to 28th day of every cycle for 6 months

Kasnyadiyogchoorna was mixed with Ashmantak&Kasniquath 50 ml twice daily to be consumed from 6th to 28th day of cycle for 6 months.

c) ***Bastichikitsa:-(Medicated enema)***

*Tiktakshirbasti*contained ingredients asGuduchi (*Tinosporacordifolia*), Punarnawa (*Boerhaaviadiffusa,roxb*), Musta (*Cyperusrotundus*), Pashanbhed (*Coleus aromaticus*). With these ingredients *Siddha kshir* was prepared and100 ml. was administered per rectally daily for 7 days from 22nd to 28th day of cycle, and this was repeated for every consecutive month.

All parenteral iron therapy, folic acid & erythropoietin therapy was stopped and patient was put on Ayurvedic treatment. The particulars of all the 13 herbal drugs used in the clinical trial, are mentioned in Table No. 1.

Table1 Particulars of Ayurvedic drugs used in the clinical trial

Name of Herb	Botanical name	Part used	Form	Proportion
Pippali	Piper longum	Fruit	Choorna (Powdered form)	500 mg
Erandpatra	Ricinuiscommunis	Leaves	Swaras (Juice)	20 ml
Ashmantak	Bauhinia racemosa	Bark	Bharad (Coarse) in Quath	Equal partin Quath500 mg in Kasanyadichoorna
Kasni	Cichoriumintybus	Whole plant	Choorna&Bharad in Quath	
Gokshoor	Tribulusterrestris	Fruit	ChoornaKasanyadiyog	500 mg
Sariva /Anantmool	Hemidesmusindicus	Root	Choorna in Kasanyadiyog	500 mg
AmraHaridra	Curcuma aromatica	Underground stem	Choorna in Kasanyadiyog	500 mg
Amalaki	Emblicaofficianalis	Fruit	Choorna in Kasanyadiyog	500 mg
Palash	Buteamonosperma	Flower	Choorna in Kasanyadiyog	One part
Punarnawa	Boerhaaviadiffusa,roxb	Root	Choorna in Kasanyadiyog &Bharad in Tiktakshirbasti	500 mg One part
Guduchi	Tinosporacordifolium	Stem	Bharad in Tiktakshirbasti	One part
Musta	Cyperusrotundus	Underground stem	Choorna&Bharad in Tiktakshirbasti	One part
Pashanbhed	Coleus aromaticus	Stem	Bharad in Tiktakshirbasti	One part

Assessment criteria:-

Clinical Improvement There are few signs & symptoms of Anemia in CKD viz. Pallor, Oedema,Fatigue,Weakness, Dyspnoea etc. and improvement was assessed in reduction of severity of them.(Table 2)

Laboratory improvement:-

2.1) Reduction in Anemia by estimating Hb%.

2.2) Other parameters of reduction in Serum Creatinine& blood urea value, increase in eGFR, Shifting of CKD stages were discussed by author in the paper published in Ind J Appl Res Aug 2007[5].

Definition of Anemia:-

Table 2 Assessment criteria of symptoms of Anemia as per severity

Symptom	Mild	Moderate	Severe
Pallor	Paleness of conjunctiva & mucus membrane	Paleness of conjunctiva & mucus membrane +Skin	Paleness of conjunctiva and mucus membrane + skin
Oedema	Pitting on both feet below ankle	Pitting on both feet, lower legs, hands or lower arms	Generalized bilateral pitting on feet, legs, arms and face
Fatigue	Feeling of tiredness but carries on routine work with some difficulty	Feeling of tiredness interfering routine work	Feeling of extreme tiredness that is not permitting to work any more
Weakness	Feeling of some reduction in strength	Feeling of considerable reduction in strength	Feeling of extreme reduction in strength
Dyspnoea	Breathlessness on moderate exertion	Breathlessness on mild exertion	Breathlessness at rest

Table 3 Definition of Anemia in terms of Hb%

Normal	Mild	Moderate	Severe
Hemoglobin ≥ 13 g/dl in males and ≥12 g/dl in females.	10 gm /dl to cut off point of normal for male & female	7-10 gm/dl	< 7 gm/dl

Indian CKD guidelines (2014) defined Anemia [in adults with CKD] - The Hb concentration is< 13 g/dl in males and < 12 g/dl in females[6] as mentioned in Table 3.

Follow-up schedule for Biochemical tests:-

1st follow-up 28 days

2nd follow-up - 84days

3rd follow-up - 140 days

4th follow-up - 180 days

RESULTS

Table no. 4 denotes demographical information of study subjects. There were 60% males & 40% females in the study.

Table 4 Age & Sex wise distribution of study subjects

Age group	Male	Female
20-30	4	3
31-40	6	2
41-50	5	2
51-60	6	8
61-70	6	5
> 71	3	0
Total	30	20

Mean age for males- 49.87 ± S.D 15.16 years. Median- 54 years

Mean age for females- 49.69 ± S.D.15.45 years. Median- 54 years

Total- 49.8 ± S.D.15.20 years. Median- 54 years

Socioeconomic status of study subjects:- Table No.5 shows socioeconomic status of study subjects. In the present study majority of study subjects -94% belonged to Upper or upper middle class, only 6% belonged to middle middle class.

Table 5 Socioeconomic status of study subjects*

Socioeconomic class	Male	Female	Total	%
Upper	16	2	18	36
Upper middle	13	16	29	58
Middle	1	2	3	6
Lower middle	0	0	0	0
Lower	0	0	0	0
Total	30	20	50	100

*S.E. status is decided as per Modified B.G.Prasad's scale taking in to account current C.P.I. as applicable

There were no study subjects from lower middle or lower class. Majority of women study subjects 16/20 (80%) were in upper middle class, while majority of males 16/30 (53.33%) were from upper class. There were none study subject from lower middle & lower class. These findings substantiate the findings of **Sakhuja & Kohli** who observed

that 90% study subjects with CKD do not report and those include mostly the under privileged & persons below poverty line[7]. This is probably the reason why lower middle & lower class study subjects were not represented.

Duration of CRF:-The mean period of study-subjects suffering from CRF was 1.735 year (20.82 months) with range 6 months to 8 years and median was 1 year. The S.D. was ±1.61. There were 34% of study subjects were suffering from CRF for six months to 1 year, while 58% were suffering from 1-5 years and only 4 subjects (8%) suffering from >5 years.

Dialysis status of study subjects on admission:-There were 24 study subjects undergoing dialysis for a period from minimum 2 weeks to maximum 3 years. The average period on dialysis was 8.54 months. There were 7 study subjects who were advised to start dialysis but did not start it.

Diabetes:- There were 24 study subjects with diabetes; out of them 15 study subjects were having diabetes for a duration less than 10 years of duration, while there were 9 study subjects having diabetes for more than 10 years. The mean duration of diabetes was 10.16 years, having range 1-28 years and median was 9.5 years. S.D. was ±6.64 years.

Hypertension:- There were 32 (64%) study subjects with hypertension out of them26 study subjects were having Hypertension for duration less than or equal to 10 years, while 6 subjects were having that for more than 10 years. The mean duration of hypertension was 4.36 years with range 0 to 28 years and median was 3 years, S.D. ±6.39.

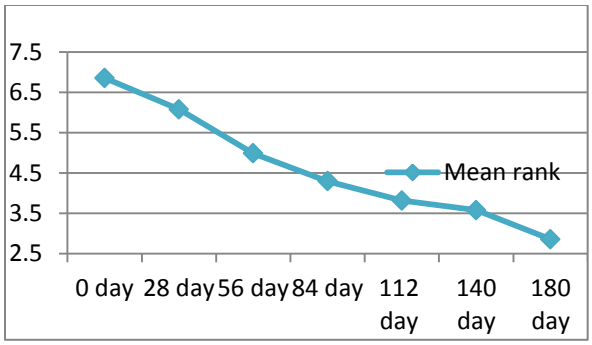
Table 6 Change in grades of Clinical Pallor during Ayurvedic treatment of CKD patients

Grades of Pallor	0th day	28 day	84 day	140 day	180 day
No pallor	3	5	8	9	13
Mild	8	8	16	22	25
Moderate	22	27	25	19	12
Severe	17	10	1	0	0

N=50

CKD stages:-As per EPI equation, there were 39 subjects in CKD stage 5 as, 9 subjects in CKD stage 4 while there 2 subjects in CKD stage 3 Pallor is the main symptom of anemia. Table6 highlights the reduction in severity of pallor during present line of treatment.

There were only 3 (6%) study subjects without pallor before start of treatment, out of them, 39 (78%) were having moderate to severe pallor. At the end of study period, there was highly significant improvement in their status as only 12 (24%) remained with moderate pallor & none with severe pallor. (See Graph No.1)



Graph No. 1 Mean rank of Study subjects having Pallor as per follow up days

Anemia:-There were 47 (94%) study subjects having anemia; 6 with mild, 24 with moderate and 17 with severe anemia. Thus there were 41/47 study subjects having moderate to severe anemia before the start of treatment. At the end of study period, there was significant improvement in their status as only 15/41 remained with moderate anemia& none with severe anemia (Table No.7). We applied Friedman'stest& found that there was statistically significant improvement in the status of study subjects with anemia with p <0.05. (Table No. 8).To test whether there is statistically significant difference in grades of Anaemia at 0, 28th, 84th, 140th &180th day.

To test the hypothesis,

Table 7 Change in grades of Anemia during Ayurvedic treatment of CKD patients

Grades of Anemia	0 day	28 day	84 day	140 day	180 day
No	3	5	7	8	11
Mild	6	8	11	18	24
Moderate	24	25	30	24	15
Severe	17	12	2	0	0

Separate criteria as per Indian CKD guidelines (2014) were applied for deciding status of anemia in males & females[5].

Table 8 Mean rank of severity of Anemia according to follow up days

Severity of Anaemia	Follow up days					
	0 day	28 day	84 day	140 day	180 day	Chi Sq.
Mean rank	4.21	3.71	2.90	2.35	1.83	123.190 Sig

n=50; d.f.=4

The null hypothesis, H_0: There is no statistically significant difference in grades of Anemia at 0, 28th, 84th, 140th&180th day.

Vs.The alternative hypothesis, H_1: There is statistically significant difference in grades of Anaemia at 0 day, 28th, 84th, 140th&180th day.Table no.8 shows the status of Anemia in study subjects. The test used is Friedman's test. Since p value < 0.001, there was strong evidence to reject the null hypothesis.

The mean ranks of study subjects according to grades of Anemia at 0 day, 28th, 84th, 140th& at 180th day are shown in Graph no. 2 with line graph.

The mean Hb was 8.39 g ±2.10 g with range from 5 g to 14.2 g/dl on zero day. There was highly significant rise in Hb % on 28th day, 84th day, 140th day & 180th day. The mean Hb% on 180th day was 11.07± 1.67 gm %. There was 31.94% increase noted in mean

Hb%. This increase in Hb% was statistically highly significant ($p < 0.001$). (See Table No. 9 and Graph No. 3).

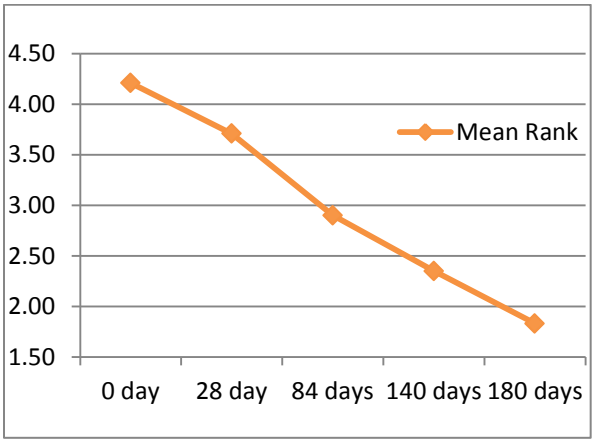
Table 9 Hemoglobin status during various stages of follow up.

Item	0 day	28 day	84 day	140 day	180 day
Mean	8.39	8.96	9.69	10.37	11.07
Range	5-14.2	5.6-14.2	6.7-14.7	7.7-14.8	8.2- 15.4
Standard deviation	±2.10	±2.05	±1.89	±1.77	±1.67
Paired 't' test value	N.A.	9.018	13.008	15.233	19.502
Statistical Significance		P <0.001 highly significant	P <0.001 highly significant	p < 0.001 highly significant	p < 0.001 highly significant

Table 10 Reduction in severity of symptoms of study subjects for Anemia in CKD

	0 day				84 day				180 day			
Sign	No	Mild	Mod	Severe	No	Mild	Mod	Severe	No	Mild	Mod	Severe
Pallor	3	8	22	17	8	16	25	1	13	25	12	0
Oedema	1	8	39	2	43	7	0	0	50	0	0	0
Fatigue	3	11	34	2	39	11	0	0	48	2	0	0
Weakness	0	4	43	3	40	10	0	0	50	0	0	0
Dyspnoea	2	18	29	1	43	7	0	0	50	0	0	0

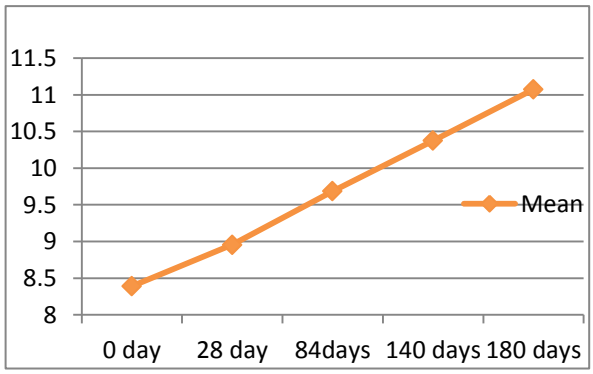
Note: Due to shortage of space data of all the follow ups is not shown.



Graph No. 2 Mean Rank of subjects having Anemia as per follow up days

Table No. 10 highlights the degree of reduction of signs and symptoms of anemia. It is evident from the table that severity of most of the symptoms reduced considerably on 84th day. Table No. 11 highlights the statistically significant reduction in severity of signs & symptoms by Friedman's test.

Table No. 12 denotes the Correlation between Hb% and Serum Creatinine. Since p value = 0.00 < level of significance = 0.05, there is strong evidence to reject the null hypothesis.



Graph No.3 Hb gm % Mean Values according to follow up days

The negative correlation coefficient -0.346 suggests that as Hb% increases, Creatinine decreases.

Table 11 Mean rank of signs/ symptoms of Anemia according to follow up days

Mean rank	0 day	28 day	56 day	84 day	112 day	140 day	180 day	Chi Sq. value & Significance	Remarks
Pallor	6.86	6.08	4.99	4.30	3.82	3.58	2.86	204.724 Sig..000	Highly Significant
Oedema	7.86	6.43	5.31	3.62	3.30	3.16	3.16	288.630 Sig..000	Highly Significant
Fatigue	7.64	6.38	5.12	3.91	3.20	3.35	3.20	264.031 Sig..000	Highly Significant
Weakness	7.93	6.71	5.31	3.71	3.13	3.07	3.07	304.367 Sig..000	Highly Significant
Dyspnoea	7.74	6.07	4.91	3.79	3.39	3.46	3.32	257.729 .Sig..000	Highly Significant

n=50; d.f.=6. Friedman's test used

Table 12 Correlation between Hb% & Serum Creatinine

Correlation between Hb% & serum Creatinine	r value	p value (2 tailed)
	-0.346	0.000

Correlation is statistically significant at the 0.05 level (2-tailed) by Pearson's correlation coefficient test

Table 13 Correlation between Hb% & Blood urea

Correlation between Hb% & Blood urea	Correlation coefficient r value	p value (2 tailed)
	-0.392	0.014

Correlation is statistically significant at the 0.05 level (2-tailed) by Pearson's correlation coefficient test

Table No. 13 denotes the Correlation between Hb% and Blood urea. Since p value = 0.00 < level of significance = 0.05, there is strong evidence to reject the null hypothesis. There is statistically significant association between Hb% & blood urea.The negative correlation coefficient -0.392 suggests that as Hb% increases, Blood urea decreases.

DISCUSSION

Anemia is the cardinal feature of advanced CKD. Nina Tolkoff-Rubin[7], contemplated that Anemia parallels the progression of CKD[7].

Acharya Charak & **Vagbhat** have mentioned that Pandu (Anemia) as the vyadhi of Rasavahstrotas while **Sushrutacharya** described Pandu as Raktavahstrotas-dushtijanya vyadhi. In CKD the Kaphadosha is increased and Pitta dosha has become kshin/ weak that is why Rasa-Raktadusti, Raktalpata, Alpamedaskata and Ojakshay occurs[8].

According to Ayurved, Yakrut/ Liver & Spleen are the moolsthan of Raktavahstrotas. Yakrut is primarily organ of Tejtatva (Tejmahabhut) & is main center of Dhatvagni. Further Yakrut is the main centre of Pitta dosha& one of the utpattisthan of

Raktadhatu. Therefore for taking into account RasRaktastrotasvikruti, we have to understand the physiology & pathology of Yakrut/ Liver. *Vrikka*is made up of *Prasad ansh* of *Rakta&Medadhatu*, therefore, dysfunction of liver plays important role in *Vrikkarog*(CRF). As per modern science liver is an organ responsible for metabolic processes &haemopoietic activity. Iron is stored in liver and Hb is produced as per body requirement. Liver is an extra renal source of Erythropoietin[9]. It is documented that 10% Erythropoietin is produced by liver. It is postulated that the present line of treatment stimulated liver to produce more amount of erythropoietin which would have helped in correcting Anemia. There is a need to pursue research how the Ayurvedic treatment maintained erythropoietin level in CRF. Erandpatra also works as *Vata-Kaphanashak* but *Pitta wardhak* by its *Ushnaveerya&pitta shamak*by its *Madhurras*&*Vipak*. In *Paitikvikar* it is used as *Virechak*. Erandpatra controls infection. It cures *Mutrakrichha&Kamala*. It reduces 7 types of *Vriddhi* including Splenomegaly.

Similarly *Agnyashay* (Pancreas) is *poorakshan*of*Yakrut* for *Pitta dosha*. Therefore the *vikruti*/ pathology of Pancreas may affect functioning of *Yakrut*. In Diabetes there is dysfunction of Pancreas, which affects functioning of Liver.We reduced *Agnimandya*that helped *Yakrut*and Pancreas to regain its function. In the present study there were 24 diabetic study subjects. There was statistically significant reduction in Fasting & P.P. blood sugar levels. This was an indication of improved functioning of pancreas which also helped to improve functions of liver.

In the present study we used Pippali with Erandpatraswaras early in the morning for 5 days at the beginning of each cycle. Pippali increases '*Kshin*' *Pitta*/bile secretion to the *Prakrut*/normal levels, which improves functioning of *Ranjak Pitta*& that leads to *Raktotpatti/* haemopoiesis. Further Pippali increases production of *RaktaposhakSar-bhag&Raktadhatwagni*. Therefore *Pandu*(Anemia), *Shoth*(Oedema) and *Pleehavruddhi*(Splenomegaly) gets cured. Spleen vruddhi occurs due to *Rakta&Medadhatu- dushti*. *Pitta &Kapha* vitiates *Raktadhatu*. That gives rise to Splenomegaly/ *Pleehavruddhi*. *Medakshay*is also cause of Spleen vruddhi. Pippali exhibits *Deepan&Pachan* effect that acts as *Vat-Kaphanashak, Aam-pachak*; corrects *Vishamagni*& removes the *Stroto-vibhandh*. Due to *Agni - vardhan* property of Pippali, *Dhatubala* is increased that strengthened *Rakta, Meda, Majja&Shukradhatu,*

particularly Pippali removed extra *Pitta* by *Virechan*owing to its *'Sar-guna'* property. The discoloration to the stool is due to this excreted *Pitta.* Modern science believes it due to bile pigment Stercobilinogen.

In the present study we used Hepatoprotective drugs like Punarnava reported to be as Hepatoprotective as well as Hepato- antitoxic while Gokshur as Hepatoprotective. Further there were drugs like *Pippali, Erandpatra, Palash* used in the present study having proven Hepatoprotective activity. Most of the drugs used in *Kasanyadichoorna*were *Tikta rasa pradhan* which has *Vayu&Akash* as *Mahabhootpradhan.* Here *Akashmahabhut* creates space for flaming *Agni* while *Vayumahabhut* kindles it[8,10].Tikta rasa increases *Agni by its Deepaniya*properties, reduces Mala form of excessive *Kapha& Pitta.* In CRF, the *Dhatubala*is very low &*Dosh bala* is very strong. It is advocated by Granthkaras for controlling such diseases, we have to use *Rasayandravyas* which increases *Dhatubala*. In the present study we used Rasayandravyas like Guduchi, Gokshur, Amalaki, Pippali, Punarnava and Kasni. Gokshur helps to increase *Poshan of saptadhatu*. Pippali increases *Agni &improves Dhatu- Pariposhankriya*. Guduchi&Punarnava digest the *Sanchi / accumulated Aam*and *Mala*. That is instrumental in its Rasayan function. Amalki&Pippali bring out the *Vardhan of DwadashPranas* in the body. *Kshir*/ Milk used in the present study in the form of Tiktakshir- Bastiis also termed as *Rasayan.*

In the present study, 47/50 subjects were Anemic- 6 subjects having Mild, 24 subjects having Moderate while 17 subjects were having Severe anemia.

The study subjects were brought in the desired Hb target level between 11-12 g/dl as advised by NKF[7]. **Prashanth GS** et al, observed reduction in Hb% in all the 3 groups in a comparative clinical trial on CRF patients with Ayurvedic drugs & conventional allopathic drugs, conducted in Jamnagar, Gujarat[11].The CKD subjects put on dialysis are prone to develop Anemia and there is reduction in Hb% noted after dialysis. In the present study *Raktaprasadakdravyas*/ herbal drugs like *Sariva, Punarnawa, Guduchi, Kasni, AmraHaridra, Palash, Ashmantak* were used, that might have stimulated erythropoiesis, reducing anemia. It is pertinent to note that in CRF, the anemia is refractory to oral hematinics, and CRF patients are required to take frequent injections of costly drug, i.e. Erythropoietin, Iron Sucrose parenterally as well as frequent

blood transfusions when the Hb is < 6gm%. It is worth mentioning here that GaikwadSarita (author) conducted one clinical trial on 39 study subjects of ESRD having Hb< 6 gm % and infused 60 ml of (previously screened) fresh blood from near relative to the study subject per rectally. This procedure was repeated after 48 hours. This procedure is called as *Raktabasti*mentioned by *Granthkaras* but human blood is rarely used. She observed that *Raktabasti* of total 120 ml Human blood showed rise of mean Hb% of 1.65 gm/dl ±SE 0.08& this rise in Hb was found to be statistically highly significant. She also found that *Raktabasti*helped to stabilize Hb[12].

Anemia is one of the accompaniments of CKD. The treatment was not specific for treating Anemia alone but the total *samprapti*of CKD is taken in to account while treating CKD. That corrected the *samprapti*and kidney started resuming its function.

All the 13 drugs used in the study were herbal drugs and did not show any adverse effect. Thus serious side effects of EPO/ESAs like hypertension & thrombosis were automatically prevented. This is an undisputed evidence of efficacy of Ayurvedic treatment on Anemia in CKD.

Correlation of Anemia in terms of Hb% & Serum Creatinine value:-In CRF, the level of Creatinine goes up than the normal value, i.e. > 1.4 mg/dL in males &>1.2 mg/ dL in females. In the present study the minimum value of Creatinine was taken as 1.8 mg/dL to label a case as CRF. In CRF, as the kidney function is reduced to a great extent around 10%. Erythropoietin is produced by kidneys to the extent of 90% while the remaining 10% is produced by liver. Thus due to loss of kidney function Erythropoietin production is greatly reduced. Further, the Life span of RBCs is also reduced; causing increased haemolysis, hematuria and gastrointestinal blood loss that may play a role in decrease of red blood cell count as well as hemoglobin%. In the present study, the mean Serum Creatinine value was 7.37 mg/dl on zero day that was reduced to 3.93 mg/dl; further the Hb % was 8.39 gm % on 0 day while on 180th day Hb % increased to 11.07 gm%. Thus there was statistically significant negative correlation observed between Hb% & Serum Creatinine as ($r = - 0.346$, $p < 0.05$), visible from Table No. 13. As Hb% is increased, Serum Creatinine value is reduced. Suresh M et al[13], also observed similar findings that the concentration of Serum Creatinine shows negative correlation with all the hematological parameters.

Chronic renal failure patients have lower haematological indices and the degree of changes depends on the severity of chronic renal failure.

Correlation of Anemia in terms of Hb% &Blood urea value:-Blood urea is the second most important indicator of CKD. The normal blood urea level is 15-40 mg/dl. In the present study, criterion of CRF was taken as any blood urea value ≥ 50 mg/dl. CRF affects all the hematological parameters as mentioned above. This finding was confirmed with rise in Blood urea & decline in Hb%. Table No. 13 shows statistically significant negative correlation found between Hb% & Blood urea ($r = - 0.392$, $p < 0.05$); that indicated, as Hb% is increased, blood urea value is reduced. It is postulated that by correcting Anemia in CKD, kidney function improved and thereby blood urea is reduced.

Thus clinically as well as biochemically there was ample evidence that Ayurvedic treatment was effective in treating anemia in CKD patients. This treatment has proved that patients could be treated without Erythropoietin supplementation and with present Ayurvedic treatment kidney started functioning & probably also producing erythropoietin. It is postulated that this Ayurvedic line of treatment stimulated and improved the metabolism in liver that regulated hormone hepcidin, with the result that anemia was corrected. More research has to be carried out on this aspect.

CONCLUSIONS

- Ayurvedic treatment was successful in treating anemia in CKD. The rise in Hb % was highly significant statistically with $p < 0.001$.
- There was statistically significant clinical improvement observed in respect of symptoms of anemia viz. Pallor, Oedema, Fatigue, Weakness & Dyspnoea. There was statistically significant negative correlation found between Hb% & S. Creatinine/ Blood urea.
- The anemia in CKD could be corrected without conventional modern treatment with parenteral iron therapy, Folic acid & EPO supplementation that spared patients from the harmful side effects of that therapy.
- This line of treatment not only treated Anemia in CKD successfully but was successful in improving kidney function too.

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