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IMPACT OF RAKTABASTI ON SEVERE ANEMIA AND ON REDUCTION OF SERUM CREATININE LEVEL IN CKD STAGE 5: A CLINICAL TRIAL

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ABSTRACT

A clinical trial was undertaken in Ayurvedic Research Department of Sassoon hospital, Pune to evaluate the effect of Raktabasti in 39 patients with severe Anaemia due to End Stage Renal Disease (ESRD).The average age of study subjects was found to be 44.74 years. 60 ml. of blood of a previously screened donor (a close relative) was given to the patient per rectally. The same procedure was repeated after 48 hours. The Haemoglobin rise after two Raktabasti given 48 hours apart was studied after next 48 hours. Raktabasti of total 120 ml blood has showed statistically significant rise in the Haemoglobin level on an average by 1.65 gm/ dL. Further we found inverse/ negative correlation between Haemoglobin and Creatinine that indicated that as Haemoglobin rises, there is reduction in Creatinine value. The mean Creatinine level of the study subjects was 8.63 mg/dL ±3.49 before Raktabasti was administered. The Creatinine value after 48 hours of Raktabasti was noted to be 7.35±2.92 mg/dL- a net reduction of 14.83% which was statistically highly significant. The present study proved that Raktabasti is simple, safe and economical method of treating severe Anaemia in CKD-5 patients with its added advantage of reducing Serum Creatinine level.

KEYWORDS: ESRD, CKD stage 5, Anemia, Ayurved, Raktabasti, Creatinine level.

INTRODUCTION

Chronic Renal Failure is a hidden epidemic and its prevalence is increasing in alarming proportions taking heavy toll of lives.[1] There is progressive and irreversible damage to the nephrons leading to End Stage Renal Disease (CKD stage 5) that warrants possible survival only on Renal Replacement Therapy (RRT).

Anemia remains a major challenge in treating cases of End Stage Renal Disease, 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**.** 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 Haemoglobin 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.

Iron is mainly absorbed from food in the duodenum, recycling of aged erythrocytes by macrophages, and release from hepatocyte stores. Inflammation is commonly observed in CKD that impairs both the early erythropoietin-dependent period of erythropoiesis and the later iron-dependent period. Inflammatory cytokines impair erythropoiesis by inhibiting the production and function of erythropoietin, and by directly inhibiting erythroid progenitor cell proliferation and differentiation. In addition, inflammatory cytokines stimulate hepatic release of 'hepcidin', produced by the liver; it is the peptide hormone that is responsible for maintaining systemic iron homeostasis, suppresses the iron exporter ferroportin to restrict the supply of iron for erythropoiesis. Inflammatory Cytokines further shorten life span of erythrocytes, in part due to macrophage activation, although hemolysis of RBCs may also contribute to anemia.[2,3] In short, anemia in CKD is hypoproliferative and iron deficiency erythropoiesis.[4]

Causes of iron deficiency[5]

1. Blood loss for laboratory tests, aggravated by hospitalizations.
2. Gastrointestinal losses (may be exacerbated by systemic anticoagulation during dialysis, and/or the use of maintenance oral anticoagulants or anti - platelet drugs used for the treatment or prevention of cardiovascular disease).
3. Blood losses associated with the hemodialysis procedure, including dialyzer blood loss and blood loss from the arteriovenous fistula or graft puncture site and from catheters.

4. Reduced intestinal iron absorption, at least in part due to increased hepcidin levels, and medications (e.g., proton pump inhibitors and calcium-containing phosphate binders).
5. Reduced intake due to poor appetite, malnutrition, and dietary advice.(e.g., protein restriction)

Definition of Anemia

Indian CKD guidelines (2014) clearly defined Anemia in Chronic Kidney Disease. The Hb concentration is < 13 g/dl in males and < 12 g/dl in females. The severe anemia is defined as < 7 gm/dl as mentioned below.

Table No. 1: Definition of Anemia in terms of Hb%.[6]

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

It is advocated that in CKD, the aim of maintaining Hb at 11-12 g/dL, as over correction may lead to stroke & thromboembolic phenomenon.[7]

Samprapti:- According to Ayurved, Vrikka is a Matruj organ,it is formed by cream portion of Rakta and Meda dhatu. Vrikka is the moolsthan of Medovahsrotas. Vrikkavikarars have been associated with the cream part of Rakta & Meda from mother, genetically linked and after birth; the host factors also do play a major role. In Chronic Renal Failure - there is depletion of the cream portion the dhatus from which Vrikka has been formed, i.e. Raktadhatu is depleted causing Raktakshaya/ Anaemia. This Anaemia is due to Rakta-dhatvagnimandya.

As per the principles of 'Samane-samane-vridhhisham,' to save life due to heavy blood loss/ Raktakshaya (Anaemia), either Raktabasti or Rakta-prashan (Drinking blood of goat) may prove to be a wonderful lifesaving tool as prescribed by Charakacharya in Rakta atisar-chikitsa. However Rakta-prashan may not be acceptable to the recipient, in that case to save life due to blood loss/ Anaemia, either blood transfusion or Raktabasti these are the only two options available. Blood transfusion requires govt. accreditated, fully equipped blood bank, blood of correct blood group of donor i.e. typing- cross matching procedure, of donor and recipient blood, to avoid transfusion reactions. However here, the main advantage is that we have liberal option of accepting donor's blood of any blood group in Raktabasti. Further, 60 ml. of blood given by Raktabasti twice, 48 hours apart, is readily acceptable to the donor. It was my personal experience that Raktabasti increases Haemoglobin concentration by 1.5 - 2 gm% within 48 hours. However to establish this fact, it was decided to evaluate role of Raktabasti in treating severe Anaemia in ESRD patients by taking clinical trial.

Aims and objectives

1. To explore role of Raktabasti in treating Anaemia in CKD-5.
2. To find out impact of Raktabasti on reducing serum Creatinine level after 48hours.

MATERIAL AND METHODS

Study design: - A non randomized clinical trial was undertaken in 20 bedded Ayurvedic ward, Sassoon General Hospitals, Pune, the teaching hospital of B.J. Medical College, Pune. Study period:- June 2010 to Dec 2012 Study subjects: - 57 Patients having End stage Renal Disease were admitted to 20 Bedded Ayurvedic ward of Sassoon General Hospitals, Pune in the given study period and out of them 39 patients satisfying the selection criteria were included in the present study.

Selection of patients

1. Patient selected were End stage Renal Failure cases suffering for more than six months, (eGFR- < 15 ml/min/1.73 m2)
2. Haemoglobin level ≤ 6 gm%
3. Patients were not having piles/ hemorrhoids, anal fissure or local lesion in anal canal
4. Written consent was obtained and those who agreed, were included in the study
5. The relative of the patient is preferred as a voluntary donor. He/ she was screened for HIV, Hepatitis B and C, Malaria and Syphilis as done routinely for the blood donors.

Investigations

Renal function tests like Blood urea, serum Creatinine, C.B.C, LFT, Lipid profile , Urine RE estimation of serum electrolytes, Blood sugar - fasting and P.P., USG abdomen were carried out. Haemoglobin level was estimated by Sahli's method. Thus 39 cases were diagnosed as cases of End stage Renal Disease with severe anaemia and those satisfying selection criteria were included in the study. 31 of them had already put on Haemo-dialysis and needed frequent blood transfusions. Haemoglobin level and Serum Creatinine level were monitored after 48 hours of administering Raktabasti. During this period haemodialysis was avoided.

Treatment prescribed:- The ESRD/CKD stage 5, as such was treated by Ayurvedic line of treatment principally by Deepan, Pachan, for treating Agnimandya; Mrudu virechana, Raktashodhan-Prasadhan as done by author for treating Dhatu dusti and Dhatavagnimandya.[8,9] As per Ayurvedic principles "Mutra" is formed in Pakwashaya. Hence Basti chikitsa was given for improving Glomerular Filtration Rate. For treating severe Anaemia.

***Raktabasti* was given with following procedure:-** The patient was asked to take Laghu- supachya aahar / breakfast before undergoing the procedure. It was strictly observed that the stomach of patient was not empty but rectum is empty. The donor and the recipient were kept lying on adjacent beds. The donor was pricked from median cubital vein, taking all the aseptic precautions, and 60 ml. of blood was taken out slowly with 18 no. needle attached to 100 ml. sterilized syringe. The recipient stayed lying on left lateral position. As soon as 60 ml. blood withdrawn from the donor, the needle is removed and a No. 10 sterilized rubber catheter was fixed to the nozzle of the syringe. The catheter was lubricated with sterilized Sahachar oil and immediately introduced per rectum. The syringe was emptied slowly and meanwhile patient was asked to take deep breathing. The same procedure was repeated after 48 hours. Haemoglobin level and Creatinine value were estimated after 48 hours of second Raktabasti procedure.

OBSERVATIONS AND DISCUSSION

Table no. 2: Classification of study subjects as per age.

Age group	No. of patients
25-29	2
30-34	3
35-39	5
40-44	11
45-49	7
50-54	4
55-59	3
60-64	2
65 and above	2
Total	39

Overall there were 31 males and 8 females in the study with mean age of 44.74 years ± S.D 10.64 years (range 25- 73 years).

Table no. 3: Etiology of study subjects.

Cause	No. of patients	%
Diabetes	13	33.3%
Hypertension	12	30.76%
Repeated U.T.I	3	7.69%
Polycystic disease	3	7.69%
Drug induced	3	7.69%
Urinary tract blockages and reflux	2	5.1%
Other causes	3	7.69%
Total	39	100%

In majority of study subjects the cause of CRF/ESRD was Diabetes and Hypertension, followed by Repeated U.T.I, Polycystic disease of kidney, drug induced nephritis (H/O use of Steroids, antibiotics and analgesics). Other causes were related to faulty life style. As per Ayurved, it takes around 48 hours for formation of Rakta dhatu hence it was decided to study the Haemoglobin rise after 48 hours of giving the 2nd Raktabasti. It was observed that treatment with Raktabasti showed significant raise in level of Haemoglobin by1.65 (±0.08) gm/dL.

Table no. 4: Rise in haemoglobin level observed after *raktabasti*.

Baseline Hb (Mean±SD) (N= 39)	Post Interventional Hb(Mean±SD)(N= 39)	Difference (Mean ±SD)	p value
5.43(±0.2) gm/dl	7.07(±0.5)gm/dl	1.65 (±0.08)gm/dl	<0.001

(df-38, t= 20.07, p<0.001) p value calculated using paired sample 't' test.

Table no. 5: Classification of patients based on increase in Haemoglobin.

Rise in Haemoglobin gm/dL	No. of patients
1-1.4 gm	12
1.5 - 1.9gm	19
2-2.5gm	8

It was observed that those subjects having <4 gm Hb had maximum rise in Hb up to 2.5 gm.

Table no. 6: Impact of *raktabasti* on serum creatinine.

Mean S.Creatinine level before Raktabasti SD±	Mean S.Creatinine level after Raktabasti SD±	t value	p value (2-tailed)
8.63 ±3.49	**7.35 ± 2.92**	**8.2**	**0.000**

n=39

The mean Creatinine level of the study subjects was 8.63 mg/dL ±3.49 before Raktabasti was administered. The Creatinine value after 48 hours of Raktabasti was noted to be 7.35±2.92 mg/dL- a net reduction of 14.83% which was statistically highly significant.

Table no. 7: Correlation between Hb% and Serum Creatinine.

Correlation between Hb% & serum Creatinine	r value	p value (2 tailed)
	-0.346	0.000
Correlation was statistically significant at the 0.05 level (2-tailed).		

There was statistically significant negative association found between Hb% & Creatinine. The negative correlation coefficient -0.346 suggested that as Hb% increases, creatinine decreases.

Charakacharya has enumerated various types of Basti and one of them is *Raktabasti*.

Rakte rakten pitte tu kashayswadu tiktakaihei I Charak Sidhhisthan Chapter 8 verse 25 Rakte rakteneti sarakte-atisaryamane Rakta bastirdeyah II Chakrapani Wherever there is blood loss in large quantity, then Rakta-basti has to be given. Tadev darbha mruditam raktam bastim pradapyeta I Shyama kashmarya badri durvoushirehe shrutam payaha II Charak Sidhhisthan Chapter 6 verse 83. Charaka advocated that before Raktabasti is given, the blood is to be mixed with Darbha, which acts as an anticoagulant. Charaka has further stated that fresh blood extracted from living deer, rabbit, ox, male buffalo, male goat etc. may be given orally (Rakta- prashan), to treat the conditions caused due to blood loss. Though Charaka prescribed Raktabasti for treating conditions occurring due to blood loss, we decided to explore treating severe Anaemia in CKD stage 5 by use of human blood through Raktabasti which was rarely used in clinical practice and to study impact of Raktabasti on Serum Creatinine level. Sarvada sarvabhavanam samanyam vridhhikaranam I Rhashetu visheshashchya, pravrittir-ubhayasya tu II Charak Sutrasthan Chapter 1 verse 44 As per the principles of Samane samane vridhhi sham, to save life due to heavy blood loss/ Raktakshaya (Anaemia), either Raktabasti or Raktaprashan may prove to be a wonderful lifesaving tool as prescribed by Charakacharya in Rakta-atisar chikitsa. However Raktaprashan may not be acceptable to the recipient, in that case to save life due to blood loss/ Anaemia, either blood transfusion or Raktabasti these are the only two options available. Blood transfusion requires well accreditated, fully equipped blood bank, blood of correct blood group of donor, matching- cross matching procedure, of donor and recipient blood, to avoid reactions. However here, the main advantage is that we can use donor's blood of any blood group in Raktabasti. Further, 60 ml. of blood given by Raktabasti twice, (48 hours apart) is not a difficult task for a donor and it was found quite acceptable. The total blood introduced by Raktabasti through rectum, raises Haemoglobin concentration by 1.5 - 2 gm% within 48 hours. Anaemia in C.R.F. patients is refractory to oral iron therapy. Anemia in ESRD subjects are treated either by ESA (Erythropoiesis Stimulating Agents) or by Intravenous Iron therapy. ESA have potential risk of stroke and thromboembolic phenomenon7. Many clinical studies in CKD subjects demonstrated that I/V Iron therapy promote oxidative damage to peripheral blood lymphocyte DNA.[10] We are treating CRF with ESRD by Ayurvedic line of management since long, however we encountered Rakatakshaya that was not responding to the desired extent by Ayurvedic line of treatment, hence it was decided to explore the use of the Raktabasti in treating Anaemia in these patients.

However this excellent Panchkarma procedure is hardly used by the modern Ayurvedic experts. It may be due to undue phobia of introducing HIV infection/ Hepatitis B and C. Certainly; we have to take all the required universal precautions to avoid transmission of blood transmissible diseases. If these precautions are followed, ***Raktabasti* does not have any extra risk than that of Blood transfusion**.

It is experimentally proved that the material introduced by basti is detected in ileum and even up to duodenum and stomach. Therefore blood introduced via rectum (Rakta basti) reaches 'Grahini' where Agni acts and forms the Rakta dhatu. Further the absorption potential of rectum is much more potent and the blood introduced by Raktabasti is readily absorbed. There is no urge to pass stools after giving Raktabasti. Even if the patient given Raktabasti passes stools, there is no trace of blood found in the stool. In ESRD there is insufficiency of Erythropoetin hormone and patients put on Dialysis are given Inj. Erythropoietin on regular basis but still the Haemoglobin is not stabilized and such patients do require whole blood transfusion frequently. If we transfuse a unit of whole blood (350 ml), it raises Haemoglobin level by nearly 1 gm/ dl.

Advantages of raktabasti over blood transfusion[11]

Point No.	Blood transfusion	*Raktabasti*
1.	Strict matching and cross matching of donor's blood and recipient blood is mandatory.	Matching and cross matching of donor's blood and recipient blood is not at all required.
2.	It may cause severe transfusion reactions.	Totally safe and simple procedure.
3.	Requires accreditated blood-bank, sterilized container, anti coagulants, cold chain, trained technician, physician etc.	No need of a blood bank. No anticoagulant, no cold chain required. An Ayurvedic physician or assistant/ nurse can perform it.
4.	Large quantity of blood is required to cover up the blood loss and to raise the Haemoglobin concentration.	Small quantity of blood is sufficient to raise the Haemoglobin concentration.
5.	Costly.	Economical.

In the present study Raktabasti of only 120 ml blood there was mean rise in Haemoglobin level by 1.65gm / dl. Ayurvedic management of CRF/ESRD takes some more time to raise the Haemoglobin level but here Raktabasti increased the Haemoglobin within 48 hours, giving opportunity to increase the efficacy of the Ayurvedic management to a great extent. Why Creatinine level was reduced? The Raktabasti increased Raktagni, reducing Samata and Raktagnimandya. That increased Raktaprasadan; that was able to remove the Vishaktata (toxic elements in the blood) like Creatinine. Hence Serum Creatinine level was reduced.

There were no adverse reactions or pyrexia and it went on very well in all the patients. This procedure was well accepted and tolerated by all the patients. Further, patients having earlier symptoms of lethargy, tiredness, breathlessness, loss of appetite etc., were relieved of these symptoms and felt sense of well being.

Follow up: - Haemoglobin was estimated every month for 6 months for each and every patient and it was found that the Haemoglobin level was stable in all the patients. Raktabasti stabilized the Haemoglobin and this was noteworthy accomplishment of the study. The study subjects were treated by Ayurvedic line of treatment; it might be a combined effect of Raktabasti and Ayurvedic treatment. Does Raktabasti triggers the production of Erythropoetin, is a question that needs to be addressed by a separate clinical research.

As already discussed above, these patients were on similar Ayurvedic line of treatment, (the details were published in International J Ayu Pharm Chem[8] and Indian Journal of Applied Research[9]) and all were maintained on Ayurvedic treatment without dialysis.

Raktabasti is the simple route of administration and has exceptional results due to excellent absorption capacity of rectum but modern science has yet to take note of this wonderful route of administration. Though it was not part of this study, it is expressed that thousands of victims of road traffic accidents die due to haemorrhage for timely not getting the right type of blood, by blood transfusion. ***Raktabasti*** **can be a excellent option to these victims as any type of blood timely given by** ***Raktabasti*** **will cover up the blood loss and may save thousands of lives.**

CONCLUSION

The present study proved that ***Raktabasti*** **is an alternative, simple, safe and economical method of treating severe Anaemia in CKD stage 5 patients with its added advantage of reducing Serum Creatinine level.**

Fig. no.1: Donor's blood withdrawn.

Figure no.2: Author administering raktabasti to CKD-5 recipient.

Figure no.3: sister administering raktabasti.

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