

**Research Article**

## **APLASTIC ANEMIA, COMPLETE CURE AYURVEDIC WAY- CASE REPORT (II)**

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### **ABSTRACT**

AA has been recognized and characterized by the science of *Ayurveda*. Numerous formulations have been recommended for the management of this disease condition. The more commonly prescribed drugs are *Tinospora cordifolia*, *Azadirachta indica*, *Emblica officinalis*, *Terminalia chebula* and cow's urine, of them. In our earlier communication we reported the effect of *Terminalia chebula* powder, cow's urine, the juice of *Emblica* fruits and the juice of *Tinospora* + *Azadirachta indica* leaves, advised to the patient suffering from SAA, for which the results have been proved to be significant (Singh *et al.*, 2013). Patient is alive on his own blood (Hb 135 g/L, ANC  $4.10 \times 10^9$ /L and platelets  $3.27 \times 10^9$ /L) with probability to full life survival. The function of bone marrow has been restored and disease eradicated. Treatment was stopped from April 2012. Other parameters of the blood are within normal range. Patient has become the top rank holder among all his fellows in 9<sup>th</sup> standard. His hand writings are matchless. Here we report the outcome of the same therapy given to the 11 number of AA patients. All the patients were diagnosed as AA at various tertiary care hospital/ referral centers in India, and given the treatment on same line at random basis with objective to assess the effect. The duration of therapy was 18 months. Among the cases 6 had very severe (3 non responder to IST, 1 splenomegaly associated, 1 male 58 years and 1 male idiopathic 18 years old), 3 had severe and 1 child was with moderately severe AA. 1 female aged 40 years, who had the diagnosis of MDS (?) her bone marrow cellularity 50% and received 32 units of blood in one year, also advised same treatment. Hematological response to therapy was assessed at 6 months, 12 months and at 18 months. Platelets were transfused prophylactically for levels  $< 0.10 \times 10^9$ /L. Red blood cell transfusions were given for hemoglobin  $< 50$  g/L. Of the 11 cases, 7 achieved complete recovery, 3 died, and 1 patient (splenomegaly associated) developed leukemia at 6<sup>th</sup> month, referred to Hemato Oncologist for further treatment. All the 7 patients who achieved complete recovery have become transfusion free for the last one year and are alive on their own blood. Blood counts are within normal range (platelet count  $> 150.0 \times 10^9$ /L, ANC  $> 1.60 \times 10^9$ /L, Hb  $> 100$ g/L). 3 cases got full recovery in a year without receiving blood transfusion, 2 received one time whole blood transfusion initially and 2 patients shown their requirement of blood transfusion time to time up to the 7<sup>th</sup> month during the treatment. Patient who developed leukemia never received transfusion. Treatment has been stopped in all the 6 patients, one patient under treatment at 4<sup>th</sup> month without receiving blood. The function of bone marrow has been restored. No side effect reported by any of the patients under treatment. The results of the treatment indicate that juice of *Tinospora cordifolia* + *Azadirachta indica* leaves, juice of *Emblica officinalis* fruits and *Terminalia chebula* powder with cow's urine are very much useful in management of AA. Though treatment has been given to a very small number of cases but recovery of patients who respond to therapy is excellent. This combination therapy has better effect than HSCT or IST. It is noninvasive, non hazardous, completely safe and eradicates the disease. Drugs are available everywhere in the world either free or on a very nominal cost. The therapy has given the option for first and foremost choice of treatment to the patient suffering from AA in all age groups. This study confirms our earlier claim for the patient suffering from AA.

**Keywords:** Anti Thymoglobulin (ATG), Bone Marrow Transplantation (BMT), Cyclosporine (CsA), Blood Transfusion (BT), Severe Aplastic Anemia (SAA), Absolute Neutrophil Count (ANC), Hemopoietic Stem Cell Transplantation (HSCT), Immuno Suppressive Therapy (IST), Aplastic Anemia (AA), Graft Versus

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Host Disease (GVHD), *Tinospora Cordifolia* (Giloy), *Azadirachta Indica* (Neem), *Terminalia chebula* (Haritaki), *Embllica Officinalis* (Amalaki), Myelodysplastic Syndrome (MDS)

## INTRODUCTION

The Incidence of aplastic anemia (AA) is on the rise in India. A very high incidence rates are reported from Uttar Pradesh, Bihar, Delhi, NCR and Rajasthan states (Jain *et al.*, 2010). Though, the survival of the patients have been markedly improved because of the advances in haemopoietic stem cell transplantation (HSCT), immunosuppressive drugs and supportive care, however the management of severe aplastic anemia (SAA) remains challenging (Phillip and Neal, 2012). Graft rejection, graft versus host diseases (GVHD) and poor immune reconstitution limit the success of HSCT (Phillip, 2012). Besides, the therapy is so expensive, that a common man in India cannot afford the cost of this treatment. Lakhs of rupees are required for the management of this disease condition in conventional medicine. AA has been recognized by the science of *Ayurveda*. Numerous drugs have been mentioned for the treatment of this disease. The more commonly prescribed drugs are *Tinospora cordifolia* (giloy), *Azadirachta indica* (neem), *Terminalia chebula* (haritaki), *Embllica officinalis* (amalaki) and cow's urine of them (Charaka 2008; Susruta, 1968; Chakrapani, 2007; Gobind, 2006; Yogratnakara, 1955). If evaluated methodically they may generate some curative or supportive remedy for the sufferers of this disease. In our earlier communication we reported the effect of *Azadirachta* leaves + *Tinospora cordifolia* stem juice (neem giloy swaras), the juice of *Embllica* fruits (amalaki swaras) and *Terminalia chebula* powder with cow's urine (gomutra haritaki), in the management of (SAA), for which results have been proved to be significant (Singh *et al.*, 2013). Patient is alive on his own blood (Hb 135 g/L, ANC  $4.10 \times 10^9$ /L and platelets  $3.27 \times 10^9$ /L) with probability of full life survival. Other parameters of the blood count are within normal range. Treatment has been stopped since April 2012. He has become the top rank holder among all his fellows in 9<sup>th</sup> standard. His hand writings are matchless. Here we report the outcome of same therapy given to the 11 number of AA patients.

## CASES

Total 22 patients, all diagnosed cases of AA from various tertiary care hospital/ referral centers in India, visited our institute between Nov. 2010 and Oct. 2014 seeking *Ayurvedic* treatment. But only the guardian of 11 cases agreed to sign the treatment consent form. Treatment was given to them at random basis with the objective to assess the effect of *Ayurvedic* therapy in the management of AA. Among the patients, 3 (1female 24 years, 1 male child 11 year and 1 male 22 years old) were non responder to immunosuppressive therapy (IST), 1 male 15 years old had splenomegaly associated AA, 1 female aged 40 years with the diagnosis of myelodysplastic syndrome (MDS?) and had bone marrow cellularity 50%, 1 male 58 years and other 5 male/female age between 12- 20 years, who received the treatment. The female 24 years old non responder had given the still birth of a child through caesarean at a tertiary care hospital and eventually diagnosed as suffering from AA. She received the complete one course of IST (ATG+CsA) there, but failed to get the response. 22 years male non responder had swollen gums, ulcer and gum bleeding. He had been receiving treatment at a referral centre in India since last one year and advised for bone marrow transplantation (BMT).

He had completed the financial and other formalities for BMT as per the guidelines of referral centre but decided to opt *Ayurvedic* therapy. The female with MDS (?) was suffering from 10- 15 times loose motion per day with mucous and blood, colicky pain and tenderness in abdomen, nausea, vomiting, mild fever and headache. She had been receiving blood transfusion (BT) at every 15- 20 days interval. Till her visit to our institute, she received 32 units blood in a year. The 58 years old male had fever, bleeding from the gums, malena and subcutaneous hemorrhagic patches under the skin. Biopsies of all the patients revealed their bone marrow hypocellular. 5 patients had fever for the last 3-4 months ranging between  $102^{\circ}\text{F}$  –  $105^{\circ}\text{F}$ . Data regarding the therapeutic profile of patient's therapy with antibiotics, transfusion was obtained. All the courses of ATG+CsA were documented and response to therapy at 6 month, 12 month, 18 month and last follow up was recorded.

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### Disease Severity

Patients were classified according to published severity criteria. AA was considered severe if the marrow cellularity was  $<25\%$  and at least 2 of the following criteria were met: neutrophil count  $<0.5 \times 10^9/L$ , platelet count  $<20 \times 10^9/L$  or reticulocyte count  $<20 \times 10^9/L$ . It was considered very severe if the above criteria were fulfilled, and the neutrophil count was  $<0.2 \times 10^9/L$ . Moderate AA was defined as hypocellular bone marrow with at least two of the following hematological values: neutrophil count  $<1 \times 10^9/L$ , platelet count  $<50 \times 10^9/L$  or reticulocyte count  $<60 \times 10^9/L$ , but not sufficient for severe category (Nair et al., 2011).

### Treatment Protocol

- I. Juice of *Azadirachta* leaves + *Tinospora cordifolia*: 40-50 ml. in the morning and in the evening (between 6 and 7 o'clock) an empty stomach twice daily for 18 months or till the desired results obtained.
- II. Juice of *Emblica officinalis* fruits: 50- 60 ml. in the morning and in the evening twice daily 30 minutes later to the first juice.
- III. *Terminalia chebula* powder: 2-3 g. early in the morning (5 o'clock) with 100 ml. cow's urine initially for one and a half month.

### Method of Preparation

- I. *Terminalia chebula* powder: Purchased *Terminalia chebula* fruits (small variety) from the market, shed dried, and powdered it with the help of iron pestle and mortar.
- II. Juice of *Azadirachta* leaves + *Tinospora cordifolia*: Collected matured stem of *Tinospora cordifolia* 200 g. approx. sized 1.5 -2cm. diameter, cut into small pieces, added 10- 15g. soft *Azadirachta indica* leaves and cleansed with water. Made the pulp using iron pestle and mortar (*imamdasta*) pouring little water. Put the pulp into cloth and squeezed to obtain the juice.
- III. Juice of *Emblica officinalis* fruits: Collected 200 g approx. *Emblica officinalis* fruits cut its small pieces separating the seeds. Put the pieces into stone mortar and pestle (*khalva*) and ground into pulp. The pulp is put into the cloth and squeezed to get the juice.



**Figure 1:** Plants used in the treatment- *Tinospora cordifolia*; *Azadirachta indica* and *Emblica officinalis*

### Response Criteria

A complete recovery was defined as transfusion free patient (having minimum gap of 6 months from last transfusion) with absolute neutrophil count (ANC)  $>2.0 \times 10^9/L$ , platelet  $>150 \times 10^9/L$  and hemoglobin value  $>80g/L$ . Partial recovery was defined when the counts were not sufficient for a complete recovery and the ANC was  $>0.5 \times 10^9/L$ , platelets  $>20 \times 10^9/L$  and hemoglobin  $>80g/L$  in patients with severe, and ANC  $>1.0 \times 10^9/L$ , and platelets  $>30 \times 10^9/L$  and hemoglobin  $>80 g/L$  in patients with moderate AA. The response was assessed 6 months after the initiation of Ayurvedic therapy. Relapse was indicated by a decline in peripheral blood cell counts to levels meeting the definition of severe or moderate AA.

### Results

Among the patients 6 had very severe (3 non responder to IST, 1 splenomegaly associated, 1 male idiopathic age 58 years, and 1 male 18 years old), 3 had severe, 1 female had MDS (?) and 1 child had moderately severe AA. In total, 11 patients were registered for Ayurvedic management. Of the 11 case 7 achieved complete recovery, 3 died, 1 (splenomegaly associated) developed leukemia at the end of 5<sup>th</sup> month referred to the hemato oncologist for further management. All the 7 patients who achieved

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complete recovery have become transfusion free for the last one year and are alive on their own blood. Blood counts are within normal range (platelet count  $> 150.0 \times 10^9/L$ , ANC  $> 2.5 \times 10^9/L$ , Hb  $> 100g/L$ ). 3 cases got complete recovery in a year without receiving blood transfusion, 2 received one time whole blood transfusion initially and 2 patients shown their requirement of blood transfusion time to time up to the 7<sup>th</sup> month during the treatment. Patient who developed leukemia never received transfusion. Treatment of the 6 patients has been stopped and one is continuing. The function of bone marrow has been restored. Of The 3 non responders, 2 cases (11 years child and 22 years old male patient) have been recovered fully from the disease. The 40 years old female with MDS (?) got full recovery within 6 months (ANC  $2.6 \times 10^9/L$ , hemoglobin 100.5 g/L and platelet  $286.0 \times 10^9/L$ ). She had got BT 3 days prior to visit our institute. Cases who succumbed to the disease, 1 female non responder to IST got *Plasmodium vivax* infection at 7<sup>th</sup> month and died of malaria. 1 male 20 years old died from recurrent infection at 5<sup>th</sup> month. The 58 years old male, who had the partial response (ANC  $1.4 \times 10^9/L$ , platelet  $50.0 \times 10^9/L$ , hemoglobin 84 g/L), got the disease relapsed at end of 13<sup>th</sup> month and died from hematemesis. The patient with splenomegaly, when visited initially, had fever for the last three and a half months, become a febrile within 13 days of treatment and continued the treatment without receiving blood up to 5<sup>th</sup> month. At the end of 5<sup>th</sup> month he got fever again, investigated thoroughly and found to be sufferer as a patient of leukemia. No side effect reported by any of the patients under treatment.

## DISCUSSION

The treatment of anemia (*Pandu*) in *Ayurveda* is based on a set of principles involving life supporting measures, palliative care and detoxification therapy. Detoxification, in which oleation (use of medicated *ghrit*), emesis and purgation included, has been found most effective in the management of this ailment. The main objective behind this procedure is to eliminate the factors causing disease from body preserving the immunity of the patient. Oleation is considered the most effective remedy in the treatment of *vata* diseases (Singh, 2004). Use of cow's *grith* in the patients of AA induces the secretion of enzymes within the alimentary canal. It corrects digestion and improves appetite. The accumulated waste materials/toxins that obstruct the channels causing disease are expelled from body either by the process of emesis or by the down flow action of purgation. In fact detoxification is the pre therapy in the actual line of management. It cleanses the channel, improves absorption and ensures smooth conduction of nutritive substances in the body. Palliative treatment given after detoxification (*shodhan*) therapy is believed to act more effectively and disease not relapsed once cured. Since patients having poor strength in the body in case of AA, mild emetics recommended. The powder of *Piper longum* in 500 mg quantity, acted as a mild emetics. When given to the patient an empty stomach with honey desired response of one or two vomit obtained within half an hour. *Terminalia chebula* responded as a soft bowel evacuator, when given to the patient with 100 ml. cow's urine an empty stomach in the morning ensured 1-2 times clear motion. The role of detoxification therapy has been studied in various diseases. Study showed that these procedures increased body weight, improved serum immunoglobulins, increased hemoglobin levels and normalized liver functions (Sahu and Mishra, 2004). There has been a strong suspicion that insecticides such as DDT and organochloride compounds, number of drugs and chemicals, wide variety of infections and immunologic diseases are responsible for cases of AA. *Tinospora cordifolia* is reported to act as antipyretics (Ikram *et al.*, 1987), immunomodulator (Atal *et al.*, 1986), immunosuppressive (Dhawale, 1984), corrects the liver function (Singh *et al.*, 1981) and eradicates the various types of infections from the body. It has an anti endotoxic property (Sharma *et al.*, 2001). Drug possibly prevents stem cell destruction and induces the formation of new hemopoietic cells in the bone marrow. *Azadirachta indica* showed a potent anti viral, anti bacterial, anti fungal, nematocidal (Akhtar and Mahmood, 1983), pesticidal (Chom, 1996), anthelmintic (Bhatnagar and Nama, 1990), and immunomodulatory (Kores *et al.* 1993) properties in various studies. The drug is useful as liver tonic. *Azadirachta* neutralizes the effect of endotoxin in the body. *Emblica officinalis* arrests the bleeding (Tawde, 1980), heals the ulcer and act as digestive, stomachic, immunomodulator (Mitra *et al.*, 1999) and laxative. Thereby control over the disease. When patient visited initially to the institute 5 had fever few of them were with widal positive. All the cases



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become afebrile within a month of treatment and test reports were found negative. Oozing blood from gums checked spontaneously within a month. Increased level of serum iron gradually normalized during the treatment in cases having raised serum iron. No adverse effect reported by any of the patients under study. The major risk factors during immunosuppressive/BMT therapy in conventional system are repeated infection and bleeding. For responders relapse is another issue. In the present study patient were under therapy for 18 months and followed up for 1 year without medicine, but only few of the patients reported sometimes loose motion, nausea, vomiting, mild cough, cold or fever and controlled easily from Ayurvedic therapy.

**Table I: Pretreatment characteristics of the study population (N = 11)**

Variable	Treatment Range
Age (yr)	11 - 58 years
M/F	7 / 4
Duration of symptoms (in months)	3 – 36
Fever*	5/ 11 (102 <sup>0</sup> F -105 <sup>0</sup> F)
Bleeding diathesis*	7 / 11
Pallor*	11 / 11
Hemoglobin (g/L)	17g/L – 72 g/L
Absolute Reticulocyte Count (X 10 <sup>9</sup> /L)	20 – 60 X 10 <sup>9</sup> /L
WBC Count (X 10 <sup>9</sup> /L)	1.4 – 2.5 X 10 <sup>9</sup> /L
ANC Count (X 10 <sup>9</sup> /L)	0.27 – 1.21 X 10 <sup>9</sup> /L
Platelets (X 10 <sup>9</sup> /L)	5 - 18 X 10 <sup>9</sup> /L

\*Before initiation of therapy; Values in numbers

**Table II: Outcome of patient treated with ayurvedic therapy (N=11)**

Evaluation	Response Type			Status		Remarks
	Complete Recovery	Partial Recovery	No Effect	Alive	Cumul. Mortality	
6 Months	1	9	0	10	1*	1 Developed Lymphoblastic Leukemia at 6 <sup>th</sup> Month
12 Months	3	6	0	9	1**	
18 Months	7	0	0	7	1***	
Last Follow up	7	0	0	7	0	

\*One patient died in the 5<sup>th</sup> month due to receiving infection repeatedly. \*\*One non responder to IST developed Plasmodium vivax infection and died in the 7<sup>th</sup> month. \*\*\*One patient with partial response relapsed and died at 13<sup>th</sup> month of therapy

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### Conclusion

The results of the treatment indicate that juice of *Tinospora cordifolia* + *Azadirachta indica* leaves, juice of *Emblica officinalis* fruits and *Terminalia chebula* powder with cow's urine are very much useful in management of AA. Though treatment has been given to a very small number of cases but recovery of patients who respond to therapy is excellent. This combination therapy has better effect than HSCT or IST. It is noninvasive, non hazardous, completely safe and eradicates the disease. Drugs are available in natural form everywhere in the world free or on a very nominal cost. The therapy has given the option for first and foremost choice of treatment to the patient suffering from AA in all age group. This study confirms our earlier claim for the management of AA. It is very safe economic and has the potential to cure the disease.



Figure 2: Photographs of the Patients

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**Table III: Aplastic Anaemia Patient's Investigation Report**

S. No	Su. No	Age	Sex	Com. Date	Hb g.%		TLC/cu mm		N %		L%		E%		M %		B %		PT /Cumm		Absolute reticulocyte count %		Wt in kg		Bone marrow biopsy	LF T	RF T	Widal Test		
					BT	AT	BT	AT	BT	AT	BT	AT	BT	AT	BT	AT	BT	AT	BT	AT	BT	AT	BT	AT				BT	AT	
1.	01	12	M	5-11-10	3.0	13.5	19.00	72.00	24	58	75	39	00	02	00	01	00	00	00	8x10 <sup>3</sup>	3.27 lac	0.08	1.5	28	42	Hypocellular	NA D	NA D	+	-
2.	02	14	F	3-11-12	3.9	12.1	25.00	65.00	28	60	68	30	02	09	02	01	00	00	18x10 <sup>3</sup>	2.82 lac	0.02	1.1	31	40	Hypocellular	NA D	NA D	+	-	
3.	03	58	M	28-01-13	7.2	8.4	27.20	29.00	36	48	54	45	33	53	63	02	04	00	15x10 <sup>3</sup>	0.50 lac	0.6	1.1	49	51	Hypocellular	NA D	NA D	--	--	
4.	04	15	F	4-02-13	2.0	8.6	26.00	52.00	59	60	36	37	02	02	03	01	00	00	35 x10 <sup>3</sup>	1.83 lac	0.06	1.2	30	36	Hypocellular	NA D	NA D	--	--	
5.	05	18	M	22-02-13	1.7	2.6	20.80	19.00	19	12	78	86	03	01	00	01	00	00	5 x10 <sup>3</sup>	0.03 lac	0.02	0.8	42	42	Hypocellular	NA D	NA D	--	--	
6.	06	24	F	2-03-13	4.4	3.9	14.00	19.30	49	40	45	55	02	02	04	03	00	00	9x10 <sup>3</sup>	0.05 lac	0.2	0.8	45	43	Hypocellular	NA D	NA D	+	-	
7.	07	11	M	26-04-13	3.8	7.5	30.40	46.00	22.4	57	73	38	02	03	46	02	00	00	7x10 <sup>3</sup>	2.46 lac	0.4	1.4	29	32	Hypocellular	NA D	NA D	--	--	
8.	08	15	M	22.10.13	4.3	13.8	17.00	46.00	16	33	80	54	02	00	02	03	00	00	50x10 <sup>3</sup>	1.04 lac	0.6	1.1	41	43	Hypocellular	NA D	NA D	+	--	
9.	09	11	M	02-04-14	4.8	9.8	26.00	46.00	74	62	21	32	05	03	00	03	00	00	10x10 <sup>3</sup>	1.52 lac	0.4	1.3	26	28.2	Hypocellular	NA D	NA D	+	-	
10.	10	40	F	28-07-14	2.9	10.5	24.90	47.00	59.9	56	33.7	39	04	02	60	03	00	00	206x10 <sup>3</sup>	2.86 lac	0.3	-	58	62	50% Cellularity	NA D	NA D	-	-	
11.	11	22	M	10-10-14	7.5	10.4	24.00	44.00	36	58	59	34	02	04	03	04	00	00	39x10 <sup>3</sup>	.87 lac	0.6	1.1	58.8	62	Hypocellular	NA D	NA D	-	-	

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### Informed Written Consent

We, the authors hereby declare that written informed consent has been obtained from the patient's parents for publication of this case report and accompanying images. A copy of written consent is available for review by the Editor-in-Chief of this journal.

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