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Ayurvedic Management of Thalassemia Major (*Beeja Dushtijanya Pandu*) As An Adjuvant Therapy - A Case Study

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ABSTRACT: -

Introduction: Thalassemia is a gathering of acquired issues of hemoglobin combination that outcomes from an adjustment in the pace of globin chain creation and unusual amalgamation of the globin chains of hemoglobin. In Ayurveda, infection like Thalassemia isn't portrayed, however in light of applied Children brought into the world with Thalassemia major typically creates serious weakness, insufficient erythropoiesis, jaundice and haemosiderosis which brings about greenish earthy colored appearance. The cutting edge clinical administration of Thalassemia is blood bonding (BT) treatment, the main treatment with haemosiderosis (iron over-burden) as an inconvenience. Iron chelators utilized in current medication are exorbitant and related with antagonistic medication responses. Understanding, it very well might be perceived as a *Beejadoshajanya*, *Adibala pravritta* and *Sahaja vyadhi* and classification instituted as *Beejadushtijanya Pandu*. It tends to be perceived that *Pitta Pradhana Tridosha* influences the elements of *Raktavaha srotasa* and eventually the course of arrangement of *Rakta Dhatu* is influenced and brings about *Raktavikriti*.

Materials and methods: A Case study on 11-year-old male child who have been diagnosed Thalassemia major. His complaint was severe anemia and he was on regular blood transfusion every 30 days, liver and spleen enlarged, and the serum iron and serum ferritin values were above normal limits according to investigation.

Observation and Result: At the end of three months of therapy, his blood report and the symptoms of the disease showed very promising results.

Conclusion: This case study revealed that *Gandhakadi Yoga* with *Pippali* is effective in *Beejadoshajanya Pandu* (Thalassemia major). Marked improvement was found in subjective and observed parameters.

Keywords: *Beejadushtijanya Pandu*, Thalassemia Major, *Gandhakadi Yoga* with *Pippali*



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INTRODUCTION

Thalassemia are a heterogeneous group of inherited disorders characterized by abnormal synthesis of hemoglobin that result from an alteration in the rate of globin chain production. A decrease in the rate of production of the globins [mainly alpha (α) and beta (β)] impedes hemoglobin synthesis leading to early excessive destruction of red blood cells. This causes hypochromic, microcytic anemia, one of the characteristic presenting symptoms of thalassemia. The thalassemia results from inherited defects in the synthesis of the globin chains of hemoglobin. Humans have different hemoglobin at various stages of development. Normal adults have a major hemoglobin (Hb) called HbA, comprising about 90% of the total, and a minor component, HbA₂, which accounts for 2–3%. The main hemoglobin in fetal life is HbF, traces of which are found in normal adults too. There are three embryonic hemoglobin and all of these different hemoglobin are tetramers of two pairs of unlike globin chains^[1].

Ayurveda texts do not describe any disease similar like to Thalassemia But when the pathophysiology and clinical features of the disease is examined under the lens of physiology and pathology concepts of Ayurveda, it may be understood as a *Beejadoshajanya*, *Adibala pravritta* and a *Sahaja vyadhi*, whose nomenclature may be coined as *Beejadushtijanya Pandu*. It is a *Pitta Pradhana Tridoshaja* disease,

where- in the process of formation of *Rakta Dhatu* is affected due to *Sahaja Karana*, affecting the functions of *Raktavaha Srotasa* and results in *Raktavikriti*. In *Rasashastra*, a subject deal with metals and mineral preparations in Ayurveda, the preparations of *Loha* (iron), the toxic effects of it when used in excess, i.e. in terms of dose and duration or in wrong way, are also mentioned. *Ayurveda Prakasha*^[2], a text authored by *Acharya Madhav*, special internal medications for toxic effects of iron are mentioned, one such medication suggested as *Loha Sevanajanya Vikara Prashamana* (i.e. clearing the toxic effects of iron, which may be equated to or appears similar to iron overloading) is modified in to *Gandhakadi Yoga* with *Pippali*, the adjuvant drug used in this case study.

The case study of an 8-year-old male child, suffering with Thalassemia major is presented here. He was on regular blood transfusion every 30 days and had severe anemia, liver and spleen enlarged with serum iron and serum ferritin values above normal limits. Other complaints were general weakness and loss of appetite. Both father and mother were carriers of Thalassemia, i.e., Thalassemia minors. The child was on regular blood transfusion with interval of 30 days along with modern medical management deferriximine (500mg). He was administered with *Gandhakadi Yoga* with *Pippali* Tablets, the Ayurveda management for three months as adjuvant therapy.

Gandhakadi Yoga with *Pippali* is a modified

form of the drug suggested for *Loha Sevanajanya Vikara Prashamana* (Iron overloading) in *Ayurveda Prakasha* [3], the

contents and brief details of manufacturing and posology are given below:

Table 1: Showing ingredients of Gandhakadi Yoga with Pippali:

Sr.No.	Drug Name	English / Latin	Part used	Quantity
1	<i>Shuddha Gandhaka</i>	<i>Sulphur (purified)</i>	As whole	1 part
2	<i>Vidanga</i>	<i>Embelia robusta</i> Taxonomist	Dry fruit powder	1 part
3	<i>Agastya</i>	<i>Sesbenia Grandiflora</i> Linn.	Green Leaves	Q.S. for <i>Bhavana</i>
4	<i>Pippali</i>	<i>Piper longum</i> Linn.	Dry fruit powder	1/20 parts
5	<i>Bhringaraja</i>	<i>Eclipta alba</i> (L.) Hassk. (syn. <i>Eclipta prostrate</i> L.)	Green Leaves	Q.S. for <i>Gandhaka</i> <i>Shodhana</i>

Q.S.= Quantity sufficient

MATERIALS AND METHOD

Preparation of Gandhakadi Yoga with Pippali tablets: The *Gandhaka* was purified through *Bhringaraja Swarasa* following the standard method [4], the purified *Gandhaka* and dry powder of *Vidanga* and *Pippali* fruits were triturated in the leaf juice of *Agastya*, and then converted into tablet form, each tablet weighing 250 mg.

Posology: The *Gandhakadi Yoga with Pippali Vati* was administered along with the modern medical management as an adjuvant drug, in the dose of 250mg per day (dose calculated following Young's Formula) [5] in divided doses for 12 weeks; *Ushnodaka* (warm water) was used as vehicle of administration.

OBSERVATIONS AND RESULTS

The child had been administered with *Gandhakadi yoga with Pippali* tablets along with modern medical management for three month duration. It was observed that the Blood transfusion interval was increased by 5-6 days during the treatment period.

In the table no.1 shows improvement in CBC parameter and table no.2 shows the changes in biochemical parameters before and after treatment in the patient. The results showed that decrease in serum ferritin, serum iron and increase TIBC level after the three months of treatment period. Figures 1 to 4 are showing the actual reports of the investigations.

Table 2: CBC investigation Table 2 Biochemistry investigation

Lab. Investigation	B.T	A.T.	
Hb%	5.3	7.9	(gm %)
Total RBC	1.99	3.04	(mil/cumm)
Total WBC	6100	3730	mil/cumm
PCV	15.9	22.7	%
MCV	77	74.7	-
MCH	26	26	-
MCHC	34	34.8	-
S. Tot. Protein	7.15	7.05	gm/dl
S. Albumin	4.13	4.29	gm/dl
S. Globulin	3.02	2.75	gm/dl
A/ G Ratio	1.37	1.56	
S. G. O. T.	87	46	iu/l
S. G. P. T.	147	44	iu/l
S. Alkaline Phosphatases	91	121	iu/l
S. Bilirubin T	1.66	1.8	mg/dl
S. Bilirubin D	0.46	0.44	mg/dl
S. Creatinine	0.57	0.45	mg/dl
S. Iron	234	156	µg/dl
S. TIBC	298	194	mcg/dl
S. Ferritin	2827	1382	ng/ml

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("NABH"-Accredited Hospital)

Opp. B-Division Police Station Gurudwara Road, Jamnagar-361008

Patient's Name: HARSHI BHOSHPAL
Physician: DR. KALPANA PATEL
Date Name/Ref No: KALPASHRITVA
Specimen Rec. Time: 01/02/2021 11:34
Biologist/Center: Dr. UGANTA MEENA

Age/Sex: 8 Years/Male
IP/OPD No: 4788
Date of Collection: 01/02/2021
Report Release Time: 02/02/2021 09:54
Reg. ID: P-2886-21

COMPLETE BLOOD COUNT

Test Name	Result	Units	Biological Reference Interval
Blood Counts			
Hemoglobin:	5.3	gm/dL	11.5 - 14.5
Total R.R.C.:	3.98	ml/cmm	4.0 - 5.5
Total W.B.C.:	6100	/cu mm	4000 - 12000
Platelet Count:	270000	/cu mm	1,50,000 - 3,50,000
Differential Count			
Neutrophils:	40	%	40 - 70
Lymphocytes:	54	%	20 - 40
Eosinophils:	03	%	1 - 4
Monocytes:	03	%	2 - 6
Basophils:	00	%	0 - 01
Absolute Eosinophil Count:	183	/cu mm	65-450
Blood Indices			
P.C.V.:	15.3	%	33 - 43
M.C.V.:	77.0	fL	76 - 90
M.C.H.:	26.2	pg	32 - 36
M.C.H.C.:	34.0	%	11.5 - 15.0
R.D.W.:	18.3	%	11.5 - 15.0
E.S.R. (Westergren Method)		mm	1 - 7
After one hour:			

Pathologist
Date of Reporting: 02/02/2021

figure no.1 (before treatment)

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Opp. B-Division Police Station Gurudwara Road, Jamnagar - 361008

Patient's Name: HARSHI BHOSHPAL
Physician: DR. KALPANA PATEL
Date Name/Ref No: KALPASHRITVA
Specimen Rec. Time: 20/02/21 11:38
Biologist/Center: Dr. UGANTA MEENA

Age/Sex: 8 Years/Male
IP/OPD No: 4788
Date of Collection: 20/02/2021
Report Release Time: 20/02/2021 11:59
Reg. ID: P-2886-21

COMPLETE BLOOD COUNT

Test Name	Result	Units	Biological Reference Interval
Blood Counts			
Hemoglobin:	7.3	gm/dL	11.5 - 14.5
Total R.R.C.:	3.85	ml/cmm	4.0 - 5.5
Total W.B.C.:	17200	/cu mm	4000 - 12000
Platelet Count:	330000	/cu mm	1,50,000 - 3,50,000
Differential Count			
Neutrophils:	40.0	%	40 - 70
Lymphocytes:	42.4	%	20 - 40
Eosinophils:	1.3	%	1 - 4
Monocytes:	2.1	%	2 - 6
Basophils:	1.8	%	0 - 01
Absolute Eosinophil Count:	18.09	/cu mm	65-450
Blood Indices			
P.C.V.:	22.7	%	33 - 43
M.C.V.:	82.4	fL	76 - 90
M.C.H.:	30.0	pg	25 - 31
M.C.H.C.:	36.4	%	32 - 36
R.D.W.:	20.4	%	11.5 - 15.0
E.S.R. (Westergren Method)		mm	1 - 7
After one hour:			

Pathologist
Date of Reporting: 20/02/2021

figure no.2 (after treatment)

INSTITUTE FOR POST GRADUATE TEACHING & RESEARCH IN AYURVEDA
("NABH"-Accredited Hospital)

Opp. B Division Police Station, Gurudwara Road, Jamnagar-361 008.

Patient's Name: HARSHI BHOSHPAL
Physician: DR. KALPANA PATEL
Date Name/Ref No: KALPASHRITVA
Specimen Rec. Time: 01/02/2021 11:59
Biologist/Center: Dr. UGANTA MEENA

Age/Sex: 8 Years/Male
IP/OPD No: 4786
Date of Collection: 01/02/2021
Report Release Time: 02/02/2021 13:44
Reg. ID: BIO-2803-21

BIO-CHEMISTRY

Test Name	Result	Units	Reference Range	Method
Renal Profile				
Urea	24	mg/dL	17 - 43	Urease
Uric acid	4.12	mg/dL	3.5 - 7.2	Urease
Creatinine	0.87	mg/dL	0.70 - 1.40	Jaffe
Hepatic profile				
Total Bilirubin	1.88	mg/dL	0.2 - 1.0	DCA
Direct Bilirubin	0.46	mg/dL	0 - 0.6	DCA
Indirect Bilirubin	1.42	mg/dL	0 - 0.5	Calculated
SGPT (ALT)	5.2	mg/dL	0 - 40	IJCC
SGOT (AST)	14.1	U/L	0 - 37	IJCC
ALP (ALP)	87	U/L	0 - 300	PAP
Alk. Phosphatase	91	U/L	0 - 300	IJCC
Total Protein	7.15	gms/dL	6.4 - 8.3	BCG
Albumin	4.13	gms/dL	3.4 - 4.4	BCG
Globulin	3.02	gms/dL	2.9 - 3.5	Calculated
A/G Ratio	1.37		0.9 - 2.3	Calculated

Note - Assays performed on "BX-3010" Fully Auto Chemistry Analyzer, SYSMEX, Japan

ANEMIA PROFILE

Test Name	Result	Units	Reference Range	Method
Iron	234	µg/dL	59 - 148	Ferene
TIBC	654	µg/dL	120 - 470	Ferene
U-Ferritin	298	µg/dL	250 - 450	Calculated

Note - Assays performed on "BX-3010" Fully Auto Chemistry Analyzer, SYSMEX, Japan

Note - Assays performed on "ALA-300" Fully Auto Fluorescent Immuno Assay Analyzer, TOSOH, Japan

Pathologist
Date of Reporting: 02/02/2021

figure no.3 (before treatment)

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Ministry of AYUSH, Govt. of India
("NABH"-Accredited Hospital)

Opp. B-Division Police Station Gurudwara Road, Jamnagar - 361008

Patient's Name: HARSHI BHOSHPAL
Physician: DR. KALPANA PATEL
Date Name/Ref No: KALPASHRITVA
Specimen Rec. Time: 20/02/21 11:58
Biologist/Center: Dr. UGANTA MEENA

Age/Sex: 8 Years/Male
IP/OPD No: 4788
Date of Collection: 20/02/2021
Report Release Time: 21/02/2021 14:21
Reg. ID: P-2886-21

BIO-CHEMISTRY

Test Name	Result	Units	Reference Range	Method
Renal Profile				
Urea	21	mg/dL	17 - 43	Urease
Uric acid	2.71	mg/dL	3.5 - 7.2	Urease
Creatinine	0.48	mg/dL	0.70 - 1.40	Jaffe
Hepatic profile				
Total Bilirubin	1.80	mg/dL	0.2 - 1.0	DCA
Direct Bilirubin	0.14	mg/dL	0 - 0.6	DCA
Indirect Bilirubin	1.66	mg/dL	0 - 0.5	Calculated
SGPT (ALT)	1.28	mg/dL	0 - 40	IJCC
SGOT (AST)	4.1	U/L	0 - 37	IJCC
ALP (ALP)	12	U/L	0 - 300	PAP
Alk. Phosphatase	12	U/L	0 - 300	IJCC
Total Protein	7.04	gms/dL	6.4 - 8.3	BCG
Albumin	4.08	gms/dL	3.4 - 4.4	BCG
Globulin	2.95	gms/dL	2.9 - 3.5	Calculated
A/G Ratio	1.36		0.9 - 2.3	Calculated

Note - Assays performed on "BX-3010" Fully Auto Chemistry Analyzer, SYSMEX, Japan

Pathologist
Date of Reporting: 20/02/2021

figure no. 4 (after treatment)

DISCUSSION

Blood Transfusion (BT), the only available management in conventional medicine, the interval of which was increased during the treatment period than earlier. This indicates the

reduced pace of destruction of RBC's and break down of hemoglobin which leads to repeated BT, and that patient got more benefit by administering Ayurvedic medicine as an adjuvant or supportive therapy with the existing management. *Rakta shodhana*, *Rakta prasadana*,

Shonita sthaapana, *Varnya* and *Pandughna* properties of the drug may be responsible for the increase in the BT interval. *Gandhakadi Yoga* with *Pippali* tablets showed improvement in almost all the cardinal features as well as in the laboratory parameters. *Agasyapatra Swarasa Bhaavita Vidangachurna* has been mentioned in *Ayurveda Praksha* in context to *Apakva Loha Sevanajanya Vikara Prashamana* (symptoms produced after intake of improperly prepared *Loha Bhasma* as well as improper digestion of *Loha Bhasma* (Iron overload)).^[6] These particular drugs may have chelating effect on iron; thereby their consumption helps to regulate the metabolism of iron and avoid its excess accumulation, thus reducing the chances of possible ADR's if any, thus showing a decrease in S. Iron, S. Ferritin level and S. TIBC.

Gandhaka is used as *Lohamaarana dravya* and included in *Lohamaarana gana*^[7]. *Maarana* is process by which *Dhatu*(metal) are transformed into absorbable, adaptable and assumable form^[8]. *Bhringaraja swarasa* was used for *Gandhaka shodhana*. *Bhringaraja* is proven for its hepatoprotective^[9] and anti-inflammatory^[10] activities and also it stabilizes human RBC membrane^[11]. Thus, it helps to reduce the hepatic damage encountered in Thalassemic patients with iron overload. Fragile RBC's are also taken care to a certain extent by the virtue of its property of stabilizing human RBC membrane. Moreover, *Bhringaraja* has *Rasayana* property^[12]. Recent concept of *Rasayana* equates it with immune modulation and free radical scavenging activities. In a Thalassemic patient excess free iron is unbound to ferritin, a specific protein enzyme and thus acts as free radical. This ionized iron causes tissue damage. Thus, *Rasayana* property of *Bhringaraja* can sustain the free radical damage

to a certain extent.

Other ingredients of *Gandhakadi Yoga* include *Vidanga*, *Pippali*, *Agastyapatra swarasa* and *Vidanga* which contains embelin. Free radical scavenging reactions and antioxidant activity of embelin has been reported. Embelin is found to form complexes with nearly all metals under suitable pH giving rise to chelated structures. Embelin also showed iron chelating activity in some of the *Loha* preparations like *Vidangadi lauha*, *Saptamrita lauha*^[13] etc.

Agastya was used as *Bhavana dravya*. Protective effect against erythromycin induced hepatotoxicity has been reported^[14]. Hence, this case study was planned to compare the efficacy of the *Gandhakadi Yoga* with *Pippali* and without *Pippali* and for clinical evaluation on patients of Thalassemia Major, against the standard conventional approach (i.e. Blood Transfusion & Iron chelation therapy), in order to find out the cost-effective supportive management through Ayurveda with no complication.

Hepatoprotective activity: The fruit extract improved the regeneration process by restricting fibrosis, but offered no protection against acute damage or against cirrhotic changes in rodents treatment with the ethanol extract of *P. longum* inhibits liver fibrosis induced by carbon tetrachloride (CCl_4).^[15] Piperine exerted a significant protection against tert-butyl hydroperoxide and carbon tetrachloride hepatotoxicity by reducing both in vitro and in vivo lipid peroxidation, enzymatic leakage of GPT and AP, and by preventing the depletion of GSH and total thiols in the intoxicated mice. Piperine also has shown lower hepatoprotective action.^[16] *Pippali* plays a major role in the *Raktvardhana* and *Raktshodhana* of the blood

due to its *Katu Rasa* and *Madhura Vipaka* and work in the splenomegaly due to its *Tikshana Guna* [17]. Calcium antagonizes iron and is proven for its chelation. In short, *Aamapaachana*, *Deepana*, *Pandughna*, *Jwaraghna*, *Vishagna*, and *Rasayana* properties relieve the signs and symptoms of Thalassemia Major. Iron chelation done through *Lohamaarana*, *Lohasevanajanya* *Vikara Prashamana* properties of the drug. *Raktashodhana*, *Krimighna*, and *Raktaprasaadana* properties decrease the rapid destruction of RBCs and thus prolonging the Life span of RBCs which increases the BT interval [18].

Thus, *Gandhakadi Yoga* with *Pippali* helps to decrease iron overload from body, normalize iron metabolism, prolong RBCs lifespan, relieve signs and symptoms of the disease, increase BT interval. All these factors increase the expectancy of good life as well as improve quality of life of Thalassemic patients.

In spite of *Ushna Veerya* drugs as major ingredients of *Gandhakadi Yoga* and long duration (12 weeks) of treatment, there was no any adverse effect was reported by any of the patients during the course of study. The toxicological study conducted has shown the safety aspect of the drug. This drug *Gandhakadi Yoga* with *Pippali* tablet has been evaluated for IronSorbitol induced iron overload in albino rats by Pramod Yadav et al [19].

CONCLUSION

This treatment protocol has been found effective in a single case of thalassemia major child along with the modern medical management. The medicine used for the management was found effective to increase the blood transfusion interval and to enhance the quality of life and life span of the child. The effect of the treatment protocol should be

evaluated on larger scale of the thalassemia patients.

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