Original Article

Evaluation of *Gandhakadi Yoga* as an adjuvant therapy in the management of *Beejadushtijanya Pandu* (thalassemia major)

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Abstract

Introduction: Thalassemia major is a malignant type of genetic disorder and iron overload is the main complication of the disease which results due to frequent blood transfusions. *Gandhakadi Yoga* has been proved effective against iron overload in experimental studies and pilot voluntary study, hence, taken for clinical evaluation in the present study. **Aim:** The aim of this study is to evaluate the efficacy of *Gandhakadi Yoga* as an adjuvant therapy in the management of thalassemia major. **Materials and Methods:** A total of 46 patients of age group 2–12 years were registered and randomly divided into two groups. Group A (trial group-*Gandhakadi Yoga* with blood transfision (BT)) and Group B (control Group-with BT and iron chelation therapy). The assessment was done based on the subjective and objective parameters after12 weeks of treatment, with a follow-up of 12 weeks. The data obtained in clinical study was analyzed using Student's "*t*" test. **Results:** Trial drug provided highly significant result ($P < 0.001$) in most of the subjective parameters and BT interval was prolonged. In Group A, the maximum improvement was found in three patients (13.04%); moderate improvement in 15 patients (65.22%) and mild improvement in five patients (21.74%). No adverse drug reaction was reported during the clinical study. **Conclusion:** *Gandhakadi Yoga* provided better results than control in subjective and objective parameters, BT interval and general health status, hence, has an effective role as an adjuvant in the management of thalassemia major.

Keywords: *Beejadushtijanya Pandu, Gandhakadi Yoga*, thalassemia major

Introduction

Thalassemia is one of the most challenging hematological disorders which do not have a definite cure in the contemporary medical science. The scientific community is looking at traditional holistic system of medicines for a satisfactory approach. Till date, totally five research works have been carried out on thalassemia major. In these previous studies, a trial was made to develop a systematic approach for the proper understanding of the pathology from the Ayurvedic point of view and to find out better regimen for the disease. The present study is one more approach in this direction.

A disease having signs and symptoms similar to Thalassemia is not described as such in Ayurveda. Following the methodology described by *Acharya* Charaka in *Vimanasthana*, thalassemia may be correlated to *Tridoshajanya Panduroga*.[1]

The pre-clinical studies of *Gandhakadi Yoga* have already been carried out and also this formulation has been evaluated for iron sorbitol induced iron overload in albino rats with promising results[2] and hence, it has been taken for clinical trial on patients of thalassemia major in the present study.

The aim and objective of the study is to evaluate the efficacy of *Gandhakadi Yoga* as an adjuvant therapy in the management of thalassemia major.

Materials and Methods

Selection of the patients

Pre-diagnosed patients of thalassemia major attending the outpatient department of Kaumarbhritya and patients registered in the Thalassemia ward, fulfilling the criteria of selection, were registered in the study irrespective of sex, caste etc.

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Ethical clearance

The present study has been started after getting clearance from the Institutional Ethics Committee (IEC No. PGT/7-A/Ethics/2013-14/1767, dated 10/09/2013) and was also registered in Clinical Trial Registry of India (CTRI/2014/02/004383, dated 06/02/2014). Written informed consent of the parents of each patient was taken before starting the treatment. Basic information of the disease and treatment was provided to the patients before the trial.

Criteria for selection of patients

1. Diagnosed cases of thalassemia major
2. Age group: 2-12 years of either sex.

Criteria for exclusion of patients

1. Children below 2 years and above 12 years of age
2. Cases having HIV, Hepatitis B infection, hepatic failure, diabetes mellitus, tuberculosis etc.
3. Patients having blood transfusion interval for ≤12 days
4. Patients undergone for splenectomy.

Grouping and posology

The selected patients were randomly divided into two groups using coin toss method, namely treated and control group and examined clinically along with laboratory investigations.

1. Trial group (Group A): In this group, along with blood transfusion (BT), *Gandhakadi Yoga* tablets were orally administered with lukewarm water as *Anupana* for 12 weeks. Adult dose of *Gandhakadi Yoga* was taken 1 g/day and child dose was calculated according to young's formula[3] for different age group [Table 1]
2. Control group (Group B): In control group, regular BT along with contemporary iron chelators were continued as per standard protocol.

Duration of treatment in both the groups was 12 weeks with a follow-up period of 12 weeks.

Preparation of *Gandhakadi Yoga* tablets

Gandhakadi Yoga is a combination of *Shudha Gandhaka* (Purified Sulfur), *Vidanga* (*Embelia robusta* Burm. f.), and *Agastya* (*Sesbenia grandiflora* Linn.). Originally *Agastyapatra Swarasa Bhavita Vidanga Churna* is suggested in the text Ayurveda Prakasha[4] for *Apakva Loha Sevanajanya Vikara Prashamana* (symptoms produced after intake of improperly prepared *Loha Bhasma* as well as improper digestion of *Loha Bhasma* or Iron overload). However, in the present study, *Shudha Gandhaka* was incorporated in the original formulation.

All the drugs were authenticated for quality and purity by Pharmacognosy laboratory, IPGT and RA, GAU, Jamnagar by employing Ayurvedic Pharmacopoeia of India standards.[5,6]

First of all known quantity (1.5 kg) of raw *Gandhaka* was melted by adding a specified quantity of *Goghrita* (cow-ghee-1/4th of *Gandhaka*). After complete melting, liquefied *Gandhaka* in *Goghrita* was poured in to *Bhringaraja* (Eclipta alba (L.) Hassk) *Swarasa* through a clean cotton cloth**.** *Gandhaka* settled at the bottom of the vessel was collected and the process was repeated for six times as per the textual reference.[7] *Gandhaka* obtained at the base of the vessel after 7th repetition was collected, washed with hot water and dried properly.

Then, the powder of *Shudha Gandhaka* and *Vidanga* were taken in equal quantity and triturated with juice of *Agastya* leaves. *Bhavana* (trituration) process was repeated for two times. Granules were prepared by sieve (No. 20) and then, tablets were prepared by following standard operating procedure and physico-chemical analysis of the finished product was carried out in the pharmaceutical laboratory [Table 2].

Assessment criteria

A special proforma was prepared to study the etiopathogenesis and to assess the response of given treatment and any complications. The effect of therapy was assessed by adopting standard scoring pattern for subjective parameters.[8]

Subjective parameters

The subjective parameters include *Panduta* (pallor), *Hriddravatva* (palpitation), *Daurbalya* (weakness), *Balakshaya* (loss of strength), *Akshikutashotha* (puffiness around the orbit), *Jwara* (fever), *Aruchi* (anorexia), *Udarashula* (abdominal pain), *Pleehavridhi* (splenomegaly), *Yakritvridhi* (hepatomegaly), *Atisara* (loose motion), *Pindikodweshtana* (leg cramps) *Sandhishula* (arthralgia) and *Vivarnata* (discoloration of skin).

Objective parameters

Following investigations were performed before and after the treatment.

Table 1: Doses of *Gandhakadi Yoga* tablets according to different age group

Age group (years)	Dose	*Aushadha Kala*
2-4	200 mg in 2 divided doses	*Bhojana Purva* (Before meal)
4-6	300 mg in 2 divided doses	
6-8	375 mg in 2 divided doses	
8-10	425 mg in 2 divided doses	
10-12	500 mg in 2 divided doses	

Table 2: The physico chemical analysis of *Gandhakadi Yoga* tablets

Parameters	*Gandhakadi Yoga*
pH	4.00
Loss on drying (at 110°C)	5.25%w/w
Ash value	7.96%w/w
Acid-insoluble ash	1.49%w/w
Water-soluble extractive	15.27%w/w
Methanol- soluble extractive	10.95%w/w
Solubility in carbon disulfide	11.24%w/w
HPTLC	At 254 nm: 5 spots At 366 nm: 6 spots

HPTLC: High performance thin layer chromatography

1. Routine hematological investigations
2. Biochemical investigations which includes.

Liver function test (LFT): to assess the hepatic toxicity of the drug, renal function test (RFT): to assess the renal toxicity of the drug, serum iron, serum total iron binding capacity and serum ferritin: to assess iron overload in the body.

Dietary advice

Patients were advised to take low iron diet and to avoid the possible aggravating factors of thalassemia.

Assessment of total effect of therapy

The assessment was done after completion of course of treatment, i.e. after 12 weeks. An assessment scale was made to assess the rate of improvement in clinical signs and symptoms. At the end of treatment, the result in view of the percentage of relief in clinical signs and symptoms was classified [Table 3].

Statistical analysis

Paired *'t'* test was used for the assessment of results in individual groups and unpaired *'t'* test was used for comparative effect of therapy of both groups were applied.

Observations

In the present study, total 46 patients were registered, 25 in Group A, and 21 in Group B. Out of these, 44 completed the course of treatment (23 in Group A and 21 in Group B). Two patients discontinued the course of treatment in Group A due to irregularity in the subsequent visits as having difficulty to reach the hospital. Maximum, 45 (45.65%) patients were from the age group of 5-10 years, 24 (52.17%) were males and 22 (47.83%) were from the lower socioeconomic background. Majority of the patients, i.e. 31 (67.39%) were diagnosed of thalassemia before the age of 1 year. Most of the patients, i.e. 21 (45.65%) had received BT up to 50 times. Thirty-four (73.91%) had febrile reactions to BT. Among the 46 patients, 21 (45.65%) were taking iron chelator, i.e. deferasirox. History of consanguineous marriage was found in 12 (26.09%) patients. The parents of all the patients (100%) had done naked eye single tube red cell osmotic fragility test and among them, (86.96%) of the patients had identified father and mother carriers of thalassemia. *Vishamashana* was found in 36 (78.26%) patients, and *Amla Rasa* predominant diet was observed in 31 (67.39%) patients, while *Ruksha Guna* in 35 (76.09%) patients. Anger was found in 26 (56.52%) patients. *Vata Pitta Prakriti* was found in 27 (58.70%) patients, *Avara Abhyavaharana Shakti* was observed in 25 (54.35%) patients, *Vata Pitta Dosha* predominance was observed in 27 (58.70%) patients. Majority of the patients, 29 (63.04%) had *Mandaagni*. *Rasavaha* and *Raktavaha Srotodushti* was found in all the (100%) patients while *Medavaha* and *Asthivaha Srotodushti* was observed in 24 (52.17%) and 9 (19.57%) patients, respectively.

Panduta, *Yakritvriddhi* and *Vivarnata* was found in all the 46 (100%) patients. *Pleehavriddhi* was found in 45 (97.83%) patients, *Daurbalya* in 44 (95.65%) patients, *Hriddravatva* in 41 (89.13%) patients, *Aruchi* in 39 (84.78%) patients, *Pindikodweshtana* in 31 (67.39%) patients, *Sandhishoola* in 21 (45.65%) patients, *Balakshaya* in 29 (63.04%) patients, *Akshikootashotha* in 19 (41.30%) patients, *Udarashoola* in 13 (28.26%) patients, *Atisara* in 13 (28.26%) patients) and *Jwara* in 11 (23.91%) patients.

Table 3: Overall assessment criteria

Overall assessment	Score
Maximum improvement	>75% improvement
Moderate improvement	51%-75% improvement
Mild improvement	26%-50% improvement
No improvement	0%-25% improvement

Results

Effect of therapy on subjective parameters

Trial drug provided relief in all the subjective parameters while in control group *Udarashula*, *Atisara*, *Jwara* and *Aruchi* was found to be relieved and rest of the parameters were aggravated [Tables 4-6].

Effect of therapy on body mass index

Body mass index was highly significantly ($P < 0.001$) increased in trial group while decreased ($P > 0.05$) in control group [Table 7].

Effect of therapy on objective parameters

a. Hematological parameters: Hb., total red blood cell (TRBC) and packed cell volume (PCV) were increased significantly ($P < 0.05$) while ereythrocyte sedimentation rate (ESR) was decreased in trial group. Control drug provided an insignificant increase ($P > 0.05$) in Hb, TRBC, PCV, platelet count, and ESR
b. Biochemical parameters: In trial group, serum bilirubin, SGOT and serum albumin were decreased while SGPT, serum alkaline phosphatase, serum total proteins, and serum globulin were increased. However the result was insignificant ($P > 0.05$). In control group, SGPT, serum alkaline phosphatase and serum globulin were decreased while serum bilirubin, serum total proteins, and serum albumin were increased. Moreovere, the result was also insignificant ($P > 0.05$). SGOT was decreased significantly ($P < 0.05$). Insignificant decrease ($P > 0.05$) found in serum creatinine and blood urea in trial group, while insignificant increase in control group. In trial group, serum iron was decreased while serum Total iron binding capaicty (TIBC) and serum ferritin were increased, but the result is insignificant ($P > 0.05$) in all of three parameters. In control group, highly significant increase ($P < 0.001$) was found in serum TIBC, significant decrease ($P < 0.05$) in serum iron and insignificant increase ($P > 0.05$) was found in serum Ferritin. Both groups provided decrease in serum Iron and increase in serum TIBC, but better improvment was found in control group. Serum ferritin was increased in both groups, but the rate of elevation was

Table 4: Effect of therapy on subjective parameters in Group A

Cardinal feature	*n*	Mean score±SEM			Percentage change	*t*	*P*
		BT	AT	Actual change			
Panduta (pallor)	23	2.304±0.132	1.478±0.165	0.826±0.102	35.85↓	8.068	<0.001**
Hriddravatva (palpitation)	20	1.250±0.123	0.350±0.109	0.900±0.100	72↓	9.00	<0.001**
Daurbalya (weakness)	22	1.136±0.074	0.0455±0.045	1.091±0.0627	96↓	17.390	<0.001**
Balakshaya (loss of strength)	14	1.286±0.125	0.143±0.0971	1.143±0.143	88.89↓	8.00	<0.001**
Akshikootashotha (puffiness around the orbit)	10	1.300±0.153	0.800±0.200	0.500±0.167	38.46↓	3.00	<0.05*
Jwara (fever)	6	1.000±0.000	0.000±0.000	1.000±0.000	100↓	Inf.	<0.001**
Aruchi (anorexia)	22	1.909±0.112	0.000±0.000	1.909±0.112	100↓	17.01	<0.001**
Udarashoola (abdominal pain)	5	1.200±0.200	0.000±0.000	1.200±0.200	100↓	6.00	<0.01*
Pleehavriddhi (splenomegaly)	23	1.957±0.183	1.348±0.173	0.609±0.104	31.11↓	5.850	<0.001**
Yakritvriddhi (hepatomegaly)	23	1.696±0.193	1.087±0.153	0.609±0.122	35.90↓	5.007	<0.001**
Atisara (diarrhaea)	6	1.333±0.333	0.000±0.000	1.333±0.333	100↓	4.00	<0.01*
Pindiko dweshtana (leg cramps)	14	1.571±0.202	0.143±0.143	1.429±0.173	90.91↓	8.272	<0.001**
Sandhishoola (arthralgia)	11	1.364±0.244	0.273±0.195	1.091±0.211	80.00↓	5.164	<0.001**
Vivarnata (discoloration of skin)	22	1.773±0.197	1.455±0.205	0.318±0.102	17.95↓	3.130	<0.01*

**Highly significant (<0.001), *Significant (*P*<0.01, *P*<0.05). BT: Before treatment, AT: After treatment, ↑: Increase, ↓: Decrease, SEM: Standard error of mean

Table 5: Effect of therapy on subjective parameters in Group B

Cardinal feature	*n*	Mean score±SEM			Percentage change	*t*	*P*
		BT	AT	Actual change			
Panduta	21	1.952±0.161	2.000±0.154	0.047±0.047	2.43↑	−1.00	<0.05*
Hriddravatva	19	1.316±0.134	1.421±0.139	0.105±0.072	8.00↑	−1.455	>0.05
Daurbalya	19	1.15±0.115	1.368±0.137	0.211±0.096	18.18↑	−2.191	<0.05*
Balakshaya	14	1.286±0.221	1.429±0.173	0.143±0.097	11.11↑	−1.472	>0.05
Akshikootashotha	9	0.778±0.147	1.111±0.111	0.333±0.167	42.85↑	−2.00	>0.05
Jwara	4	1.000±0.000	0.250±0.250	0.750±0.250	50.00↓	3.00	>0.05
Aruchi	16	1.625±0.125	1.500±0.158	0.125±0.155	7.69↓	0.808	>0.05
Udarashoola	7	1.143±0.143	0.429±0.297	0.714±0.184	50.00↓	3.873	<0.01*
Pleehavriddhi	20	1.900±0.143	1.900±0.143	0.000±0.000	0.00	0.00	>0.05
Yakritvriddhi	21	1.619±0.161	1.619±0.161	0.000±0.000	0.00	0.00	>0.05
Atisara	5	1.200±0.200	0.000±0.000	1.200±0.200	100↓	6.00	<0.01*
Pindikodweshtana	14	1.714±0.194	1.786±0.187	0.071±0.071	8.00↑	1.00	>0.05
Sandhishoola	11	1.455±0.207	1.455±0.207	0.000±0.000	0.00	0.00	>0.05
Vivarnata	21	1.905±0.181	1.952±0.176	−0.047±0.047	2.5↑	1.00	>0.05

**Highly significant (<0.001), *Significant (*P*<0.01, *P*<0.05). BT: Before treatment, AT: After treatment, ↑: Increase, ↓: Decrease, SEM: Standard error of mean

less in trial group compared to control group. Although, the difference is statistically insignificant in all of three parameters [Tables 8-10].

Effect of therapy on blood transfusion interval

BT Interval was increased by a mean of 5.65 days in trial group which is statistically highly significant ($P < 0.001$) while it was significantly decreased ($P < 0.01$) by a mean of 3.33 days in control group [Table 7].

Follow-up details

Follow-up was done after 12 weeks after active treatment. No further increase in the severity of signs and symptoms was observed in the trial group. No adverse effects were reported by any of the patients in trial group.

Overall effect of therapy

In trial group, 3 (13.04%) patients had maximum improvement, 15 (65.22%) patients showed moderate improvement, 5 (21.74%) patients had mild improvement and no patient remained unchanged while in control group. Changes were found in subjective and objective parameters as described previously but when considering overall effect of therapy, no improvement was found in any of the patient. Thus, all the 21 (100%) patients remained unchanged [Table 11].

Discussion

Hemoglobinopathies constitute to be a major public health problem internationally and particularly in the developing world. Thalassemia is such a disease and if corrective steps are not taken,

Table 6: Comparative efficacy on subjective parameters of Group A with Group B

Symptoms	*n*	Mean score±SEM		Mean difference	Percentage change	*t*	*P*
		Group A	Group B				
Panduta	44	0.826±0.102	0.047±0.047	0.874	106.78↓	7.500	<0.001**
Hriddravatva	39	0.900±0.100	0.105±0.072	1.005	111.11↓	8.073	<0.001**
Daurbalya	41	1.091±0.0627	0.211±0.096	1.301	118.94↓	11.633	<0.001**
Balakshaya	28	1.143±0.143	0.143±0.097	1.286	112.50↓	7.445	<0.001**
Akshikootashotha	19	0.500±0.167	0.333±0.167	0.833	211.41↓	3.525	<0. 01*
Jwara	11	1.000±0.000	0.750±0.250	0.600	50.00↓	1.662	>0.05
Aruchi	38	1.909±0.112	0.125±0.155	1.784	92.31↓	9.579	<0.001**
Udarashoola	13	1.200±0.200	0.714±0.184	0.700	50.00↓	1.859	>0.05
Pleehavriddhi	44	0.609±0.104	0.000±0.000	0.656	108.45↓	5.557	<0.001**
Yakritavriddhi	44	0.609±0.122	0.000±0.000	0.609	100.00↓	4.779	<0.001**
Atisara	11	1.333±0.333	1.200±0.200	0.133	0.00↓	0.325	>0.05
Pindikodweshtana	29	1.429±0.173	0.071±0.071	1.663	108.80↓	10.372	<0.001**
Sandhishoola	24	1.091±0.211	0.000±0.000	1.414	123.44↓	6.564	<0.001**
Vivarnata	43	0.318±0.102	0.047±0.047	0.366	113.93↓	3.209	<0.001**

**Highly significant (<0.001), *Significant ($P < 0.01$, $P < 0.05$). BT: Before treatment, AT: After treatment, ↑: Increase, ↓: Decrease, SEM: Standard error of mean

Table 7: Effect of therapy on other parameters in Group A and Group B

Parameter	*n*	Mean score±SEM			Percentage change	*t*	*P*
		BT	AT	Actual change			
BT interval (days)							
Group A	23	23.739±1.834	29.391±1.968	5.652±0.852	23.81↑	−6.635	<0.001**
Group B	21	26.810±1.575	23.476±1.243	3.333±1.074	12.43↓	3.103	<0.01*
BMI (kg/m^2)							
Group A	23	14.651±0.320	15.342±0.333	0.691±0.121	4.72↑	−5.722	<0.001**
Group B	21	13.904±0.263	13.753±0.290	0.151±0.158	1.08↓	0.955	>0.05

**Highly significant (<0.001), *Significant (P<0.01, P<0.05). BT: Before treatment, AT: After treatment, ↑: Increase, ↓: Decrease, SEM: Standard error of mean, BMI: Body mass index

Table 8: Effect of therapy on objective parameters in Group A

Parameters	*n*	Mean score±SEM			Percentage change	*t*	*P*
		BT	AT	Actual change			
Hb (g%)	23	7.983±0.410	8.891±0.297	0.909±0.409	11.38↑	−2.219	<0.05*
TRBC (10^6/cumm)	23	3.096±0.142	3.424±0.130	0.329±0.150	10.62↑	−2.194	<0.05*
PCV (%)	23	23.326±1.209	25.952±0.862	2.626±1.169	11.26↑	−2.246	<0.05*
Platelets (10^3/cumm)	23	291.957±29.041	323.00±27.024	31.043±27.979	10.63↑	−1.110	>0.05
ESR (mm/h)	23	25.625±3.072	19.565±3.329	6.000±2.505	23.47↓	2.395	<0.05*
Serum bilirubin (mg/dl)	23	1.883±0.255	1.730±0.137	0.152±0.216	8.08↓	0.705	>0.05
SGOT (IU/L)	23	76.609±8.038	71.304±10.596	5.304±10.365	6.92↓	0.512	>0.05
SGPT (IU/L)	23	55.739±8.721	76.043±20.140	20.304±14.471	36.43↑	−1.403	>0.05
Serum alkaline phosphatase (IU/L)	23	143.391±14.301	153.435±11.768	10.043±14.011	7.00↑	−0.717	>0.05
Total proteins (g/dl)	23	6.743±0.100	6.765±0.087	0.021±0.083	0.32↑	−0.260	>0.05
Albumin (g/dl)	23	3.796±0.052	3.752±0.061	0.043±0.061	1.15↓	0.703	>0.05
Globulin (g/dl)	23	2.965±0.0983	3.013±0.0729	0.047±0.064	1.61↑	−0.743	>0.05
Serum creatinine (mg/dl)	23	0.409±0.020	0.383±0.018	0.026±0.018	6.38↓	1.447	>0.05
Blood urea (mg/dl)	23	27.261±1.882	25.478±1.270	1.783±1.555	6.54↓	1.146	>0.05
Serum iron (µg/dl)	23	127.857±8.382	116.748±7.134	11.109±5.978	8.69↓	1.858	>0.05
Serum TIBC (µg/dl)	23	285.000±8.000	297.043±7.684	12.043±6.050	4.23↑	−1.991	>0.05
Serum ferritin (µg/ml)	23	2867.304±349.606	2872.696±331.703	5.391±85.940	0.19↑	−0.062	>0.05

**Highly significant (<0.001), *Significant (P<0.01, P<0.05). BT: Before treatment, AT: After treatment, ↑: Increase, ↓: Decrease, Hb: Hemoglobin, TRBC: Total red blood corpuscles, PCV: Packed cell volume, ESR: Erythrocyte sedimentation rate, SGOT: Serum glutamate oxaloacetate transaminase, SGPT: Serum glutamate pyruvate transaminase, TIBC: Total iron binding capacity, SEM: Standard error of mean

Table 9: Effect of therapy on objective parameters in Group B

Parameters	*n*	Mean score±SEM			Percentage change	*t*	*P*
		BT	AT	Actual change			
Hb (g%)	21	8.500±0.431	8.757±0.269	0.257±0.380	3.02↑	−0.676	>0.05
TRBC (10^6/cumm)	21	3.215±0.164	3.304±0.116	0.089±0.128	2.76↑	−0.696	>0.05
PCV (%)	21	24.843±1.248	25.681±0.776	0.838±1.045	3.37↑	−0.802	>0.05
Platelets (10^3/cumm)	21	253.095±26.108	280.952±20.210	27.857±30.018	11.00↑	−0.928	>0.05
ESR (mm/h)	21	19.524±3.095	20.381±3.063	0.857±0.788	4.39↑	−1.088	>0.05
Serum bilirubin (mg/dl)	21	1.405±0.098	1.476±0.126	−0.071±0.113	5.08↑	−0.630	>0.05
SGOT (IU/L)	21	105.714±18.315	67.619±5.789	38.095±17.874	36.03↓	2.131	<0.05*
SGPT (IU/L)	21	72.667±11.121	69.238±7.692	3.429±11.606	4.71↓	0.295	>0.05
Serum alkaline phosphatase (IU/L)	21	149.286±8.116	140.429±11.952	8.857±8.908	5.93↓	0.994	>0.05
Total proteins (g/dl)	21	6.752±0.105	6.833±0.072	−0.081±0.089	1.19↑	−0.903	>0.05
Albumin (g/dl)	21	3.795±0.049	3.881±0.048	−0.085±0.045	2.25↑	−1.867	>0.05
Globulin (g/dl)	21	2.957±0.095	2.952±0.067	0.004±0.079	0.16↓	0.059	>0.05
Serum creatinine (mg/dl)	21	0.433±0.023	0.457±0.027	0.023±0.030	5.49↑	−0.794	>0.05
Blood urea (mg/dl)	21	23.810±1.824	27.143±2.161	3.333±1.603	14.00↑	−2.080	>0.05
Serum iron (µg/dl)	21	141.662±10.840	122.529±9.427	19.133±6.060	13.50↓	3.157	<0.01*
Serum TIBC (µg/dl)	21	292.581±7.643	313.952±6.593	−21.371±5.453	7.30↑	−3.919	<0.001**
Serum ferritin (µg/ml)	21	2831.629±293.709	2841.933±344.69	−10.305±283.818	0.36↑	−0.036	>0.05

Hb: Hemoglobin, TRBC: Total red blood corpuscles, PCV: Packed cell volume, ESR: Erythrocyte sedimentation rate, SGOT: Serum glutamate oxaloacetate transaminase, SGPT: Serum glutamate pyruvate transaminase, TIBC: Total iron binding capacity, SEM: Standard error of mean, BT: Before treatment, AT: After treatment, ↑: Increase, ↓: Decrease

Table 10: Comparative efficacy on objective parameters of Group A with Group B

Parameters	*n*	Mean score±SEM		Mean difference	Percentage change	*t*	*P*
		Group A	Group B				
Hb (g%)	44	0.909±0.409	0.257±0.380	0.652	73.46↑	1.160	>0.05
TRBC (10^6/cumm)	44	0.329±0.150	0.089±0.128	0.240	74.01↑	1.205	>0.05
PCV (%)	44	2.626±1.169	0.838±1.045	1.788	70.07↑	1.132	>0.05
Platelets (10^3/cumm)	44	31.043±27.979	27.857±30.018	3.186	3.48↓	0.077	>0.05
ESR (mm/h)	44	6.000±2.505	0.857±0.788	6.857	118.70↓	2.512	<0.05*
Serum bilirubin (mg/dl)	44	0.152±0.216	0.071±0.113	0.224	162.87↓	0.892	>0.05
SGOT (IU/L)	44	5.304±10.365	38.095±17.874	−32.791	420.66↑	−1.622	>0.05
SGPT (IU/L)	44	20.304±14.471	3.429±11.606	−23.733	112.93↓	−1.264	>0.05
Serum alkaline phosphatase (IU/L)	44	10.043±14.011	8.857±8.908	−18.901	184.71↓	−1.114	>0.05
Total proteins (g/dl)	44	0.021±0.083	0.081±0.089	0.0592	271.88↑	0.484	>0.05
Albumin (g/dl)	44	0.043±0.061	0.085±0.045	0.129	295.65↓	1.651	>0.05
Globulin (g/dl)	44	0.047±0.064	0.004±0.079	−0.052	109.94↓	−0.517	>0.05
Serum creatinine (mg/dl)	44	0.026±0.018	0.023±0.030	0.049	186.05↓	1.455	>0.05
Blood urea (mg/dl)	44	1.783±1.555	3.333±1.603	5.116	314.07↓	2.289	<0.05*
Serum iron (µg/dl)	44	11.109±5.978	19.133±6.060	−8.025	55.35↑	−0.941	>0.05
Serum TIBC (µg/dl)	44	12.043±6.050	21.371±5.453	−9.328	72.58↑	−1.137	>0.05
Serum ferritin (µg/ml)	44	5.391±85.940	10.305±283.818	4.913	89.47↑	0.017	>0.05

Hb: Hemoglobin, TRBC: Total red blood corpuscles, PCV: Packed cell volume, ESR: Erythrocyte sedimentation rate, SGOT: Serum glutamate oxaloacetate transaminase, SGPT: Serum glutamate pyruvate transaminase, TIBC: Total iron binding capacity, SEM: Standard error of mean, ↑: Increase, ↓: Decrease

it will burden the world's blood bank supplies and the health system in general. As iron overload is the main complication of thalassemia major, excess iron should be removed from the body. *Agasyapatra Swarasa Bhaavita Vidanga Churna* has been mentioned in Ayurveda Prakasha in the context of *Apakva Loha Sevanajanya Vikara Prashamana*.[4] These particular drugs may have chelating effect on Iron overload; thereby their consumption might help to regulate the metabolism of iron and avoid its excess accumulation, thus reducing the chances of possible adverse drug reactions if any. *Gandhakadi Yoga* has been evaluated for iron overload in experimental study with promising results.[2] Thus, it helps to decrease serum Iron, serum ferritin level and increases serum TIBC. *Gandhaka* has been used as *Lohamarana dravya* and is included in *Lohamaranagana*.[9] *Marana* is a process by which *Dhatus* are transformed into absorbable, adaptable and assimilable form.[10] Thus, *Gandhaka* interacts with metals at considerable temperature and brings about biotransformation of metals. Similarly, in human body, it may combine with free

Table 11: The overall effect of therapy in 44 patients

Assessment of result	Group A, number of patients (%)	Group B, number of patients (%)
Maximum improvement (>75%)	3 (13.04)	0
Moderate improvement (51%-75%)	15 (65.22)	0
Mild improvement (26%-50%)	5 (21.74)	0
No improvement (0%-25%)	0	21 (100)
Total	23 (100)	21 (100)

metals and convert them into soluble complexes, which may be easily excreted through urine or other modes of excretion. *Bhringaraja swarasa* was used for *Gandhaka Shodhana* before its inclusion in to *Gandhakadi Yoga*. *Bhringaraja* have hepatoprotective[11] and anti-inflammatory[12] activities and also it stabilizes human red blood cells (RBC) membrane.[13] Thus, it may help in reducing the hepatic damage encountered in thalassemic patients with tremendous iron overload. Fragile RBC's can also be taken care of to a certain extent by the virtue of its property of stabilizing human RBC membrane. Moreover, *Bhringaraja* has *Rasayana* property.[14] Recent concept of *Rasayana* equates it with immunomodulation and free radical scavenging activities. In thalassemic patients, 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. *Vidanga* contains embelin which is found to form complexes with nearly all metals under suitable pH giving rise to chelate structures. Embelin also showed iron chelating activity in some of the *Loha* preparations such as *Vidangadi Loha*, *Saptamrita Loha*.[15] Protective effect of *Agastya* against erythromycin estolate-induced hepatotoxicity has been reported.[16] Anxiolytic and anticonvulsive activity of *Agastya* leaves in experimental animals has also been proved.[17] Evaluation of *Agastya* for antiurolithiatic and antioxidant properties showed enthusiastic results.[18] *Agastya* leaf is reported to contain Ca (517 mg Ca in 100 g leaf protein concentrate-LPC).[19] Calcium antagonizes iron and is proven for its chelation.

In short, *Amapachana*, *Deepana*, *Pandughna, Jwaraghna, Vishagna,* and *Rasayana* properties relieve the signs and symptoms of thalassemia major. Iron chelation was done through *Lohamarana* and *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.

Although control drug found better in decreasing serum iron and increasing serum TIBC, the rate of elevation in serum ferritin is less in trial group as compared to control group. On the other hand, trial drug was found to be better in increasing BT interval and the improvement shown in the subjective parameters could be taken as signs of improvement in the quality of life of the patients.

Conclusion

Gandhakadi Yoga helps to decrease iron overload from the body, normalize iron metabolism, prolong RBCs lifespan, relieve signs and symptoms of the disease, increase BT interval. Hence, it is effective as an adjuvant therapy in the management of thalassemia major.

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Conflicts of interest

There are no conflicts of interest.

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हिंदी सारांश

बीजदुष्टिजन्य पांडु (थेलेसीमिया मेजर) के प्रबंधन में एक सहायक चिकित्सा के रूप में गंधकादि योग का मूल्यांकन

अंजना गोस्वामी, राजगोपाल एस., कल्पना एस. पटेल, वीरेन्द्र कुमार कोरी, प्रदीप कुमार प्रजापति

थेलेसीमिया मेजर एक घातक प्रकार का आनुवंशिक विकार है, जिसमें लौहतत्व अधिभार वृद्धि रोग का मुख्य उपद्रव है जो लगातार रक्त आधान के कारण होता है। प्रयोगिक अध्ययनों और प्राथमिक स्वैच्छिक अध्ययन में लौहतत्व अधिभार के विरुद्ध गंधकादि योग प्रभावी साबित हुआ है, इसलिए वर्तमान अध्ययन में चिकित्सकीय मूल्यांकन हेतु इसे लिया गया है। प्रस्तुत शोध कार्य थेलेसीमिया मेजर के प्रबंधन में एक सहायक चिकित्सक के रूप में गंधकादि योग की प्रभावकारिता का मूल्यांकन करने हेतु किया गया। अध्ययन के लिए कुल ४६ मरीजों को २-१२ वर्ष आयु वर्ग में पंजीकृत किया गया और उनको बिना पूर्वनिश्चित यादृच्छिक पद्धति से दो समूहों में विभाजित किया गया, 'समूह ए' (परीक्षण समूह-रक्त आधान के साथ गंधकादि योग) और 'समूह बी' (नियंत्रण समूह - रक्त आधान के साथ लोह चिलेशन थेरेपी)। बारह सप्ताह के उपचार के बाद व्यक्तिपरक और उद्देश्य मानदंडों के आधार पर विश्लेषण किया गया था साथ ही बारह सप्ताह के बाद अनुवर्ती कार्यवाही (फॉलो अप) की गयी। चिकित्सकीय अध्ययन में प्राप्त आंकड़ों का विश्लेषण "टी" परीक्षण द्वारा किया गया। परिणाम स्वरूप अधिकांश व्यक्तिपरक मापदंडों में परीक्षण दवा ने अत्यधिक महत्वपूर्ण परिणाम प्रदान किए और रक्त आधान अंतराल बढा हुआ मिला। 'समूह ए' में, तीन रोगियों में अधिकतम सुधार (१३.०४ %); पंद्रह रोगियों में मध्यम सुधार (६५.२२ %) और पांच रोगियों में अल्प सुधार (२१.७४ %) मिला। चिकित्सकीय अध्ययन के दौरान दवा की कोई प्रतिकूल प्रतिक्रिया नहीं मिली। इस प्रकार यह निष्कर्ष निकाला गया कि गंधकादि योग ने व्यक्तिपरक और उद्देश्य मानदंड, रक्त आधान अंतराल और सामान्य स्वास्थ्य स्थिति में नियंत्रण दवा से बेहतर परिणाम प्रदान किया, इसलिए थेलेसीमिया मेजर के प्रबंधन में सहायक के रूप में प्रभावी भूमिका निभाई।