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Research Paper

CLINICAL ASSESSMENT OF '*DUSPARSHADI YOG*' (HERBAL COMPOUND) IN TROPICAL PULMONARY EOSINOPHILIA

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Tropical eosinophilia, has been known to physicians even prior to 1930. Eosinophilia is said to be when there is increase in absolute eosinophil count by $>600/\text{cumm}$. It can occur due to various pathologic conditions. Tissue eosinophil infiltration is an important feature of tropical pulmonary eosinophilia. Herbal drugs explained in Ayurveda provide a wide range of formulations for the management of such diseases. Present study was conducted to assess the efficacy and safety of an Ayurvedic compound formulation '*Dusparshadi Yog*' in tropical pulmonary eosinophilia. This article accounts the data of 30 patients diagnosed for tropical eosinophilia that underwent a full clinical, radiological, and pathological study and treated with the drug. There was a significant result in eosinophil and neutrophil count along with other criteria resolute for the study including respiration rate, PEFr, etc. ($p < 0.001$).

Keywords: Tropical Eosinophilia, *Dusparshadi Yog*, Ayurveda, Medicinal Herbs

INTRODUCTION

The clinical conditions designated as tropical eosinophilia, eosinophilic lung, pulmonary eosinophilosis, and Weingarten's syndrome is familiar to chest physicians' since 1930 (Weingarten, 1943) However the condition was recognized as distinct identity of respiratory system in late 1940 (Frimodt-Moller and Barton, 1940; and <http://dev.chestpubs.org/>). Cough is attributed as the most common symptom of respiratory distress which is initiated by the

stimulation of sensory nerves in the mucosa of respiratory tract (Madison and Irwin, 2005). It is also observed after oesophageal reflux, post nasal drip, asthma, viral infections and in 10-15% of patient who are taking ACE inhibitors (Morice *et al.*, 2006)

Cough can be observed in its two definite phases with or without expectoration. When associated with expectoration it indicates definite changes either in lungs, bronchi or upper respiratory passages. Otherwise it indicates the

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early stage of certain pulmonary disorder, simple congestion of throat or larynx or presence of pleurisy or some of reflex irritation (Samuel *et al.*, 1958).

Eosinophils are terminally differentiated, non-dividing granulocytes, normally constitute a tiny proportion of the peripheral blood leukocyte (Asem A Abdeljalil, 2008). Eosinophilia is a condition indicating increase in absolute eosinophil count by >600/cumm (Shirish M Kawthalkar, 2006). There is variation in the count of eosinophils depending on the daytime. Lowest count is observed in morning where as the highest count may be seen in night (Dacie and Lewis, 2006). Tropical Pulmonary Eosinophilia, is a typical condition characterized by very high raised absolute eosinophilic count with severe spasmodic bronchitis and leucocytosis (Vijayan, 2008). Tropical Pulmonary Eosinophilia may also be associated with cough, nocturnal wheezing and dyspnoea, diffuse reticulo-nodular infiltrates in chest radiographs and marked peripheral blood eosinophilia (Vijayan, 2006); Udwadia, 1975; Ottesen and Nutman, 1992; Vijayan, 2007).

THE CAUSES OF EOSINOPHILIA

Etiology eosinophilia is based on two theories as follows (Sanjivi *et al.*, 1955).

1. An infection theory, possibly of virus origin – Parasitic infections due to nematodes, filariae, and helminths may cause pulmonary infiltrates and eosinophilia. Such infections include strongyloidiasis, ascariasis, paragonimiasis, schistosomiasis, dirofilariasis, ancylostomiasis, trichomoniasis, clonorchiasis, and visceral larva migrans (Gorgolas *et al.*, 2009)
2. Extrinsic causes favoring an allergic state closely allied to bronchial asthma –

Eosinophilic immune response can be initiated by inhaled or ingested substances like medications, drugs (e.g., cocaine), food (e.g., contaminated cooking oil), dietary supplements (e.g., L-tryptophan)(Kaliterna *et al.*, 2009).

Other Major causes responsible for Eosinophilia are

- 1) Medications that have been implicated to trigger the condition are Antibiotics, NSAID, Antidepressants, Contraceptives, Antihypertensives, Leukotriene inhibitors and Anticonvulsants (Kaliterna *et al.*, 2009).
- 2) Skin diseases e.g., pemphigus *dermatitis*, *herpetiformis*, *erythema multiforme*.
- 3) Loeffler's syndrome.
- 4) Haematopoietic diseases e.g., *polycythemia vera*, *pernicious anaemia*, Hodgkin's disease following splenectomy.
- 5) Malignant disease with metastasis.
- 6) Irradiation.
- 7) Miscellaneous disorders e.g., *polyarteritis nodosa*, *rheumatoid arthritis*, *sarcoidosis*.
- 8) *Acute schistosomiasis*.
- 9) Onchocerciasis and Clonorchiasis.
- 10) Strongyloidiasis
- 11) Acute migratory phase of intestinal nematodes (e.g., *Ancylostoma duodenale*, *Necator americanus*, *Ascaris lumbricoides*) etc.

Etiopathogenesis

Eosinophilia is a condition arises when microfilariae are trapped in the pulmonary capillaries and destroyed by intense allergic

inflammation in the lung parenchyma. As TPE occurs only in those individuals who are highly sensitized to filarial antigens, it is proposed that this represents an immune-pathological response rather than as a result of direct damage by microfilariae. These microfilariae may sometimes be seen at lung biopsy (Webb *et al.*, 1960)

Broncho-alveolar lavage of affected individuals reveals that polyclonal IgE, and filarial specific IgM, IgG and IgE, accumulate in the lung at high levels, together with a striking eosinophilic alveolitis (Nutman *et al.*, 1989). The recent identification and characterization of a major IgE-inducing filarial antigen of *B. maluyi* which is prominently expressed in microfilariae and not in the adult worm (Lobos *et al.*, 1992).

Clinical Features

The symptoms present are paroxysmal cough, wheeze and fever. These symptoms mostly found in the night but occasionally also present in the day. The chest radiograph shows miliary changes or mottled opacities. Lung function tests show a restrictive picture. If in this condition patient is not treated, this progresses to debilitating chronic interstitial lung disease. In this condition there is not specific therapy but the lymphatic damage can be managed actively as outlined for filarial elephantiasis.

Non specific systemic features include fever, malaise, and weight loss. The absolute eosinophilic count in hyperacute cases can be as high as 50000/mm³. The non-pulmonary manifestations of Tropical Pulmonary Eosinophilia include hepatosplenomegaly, lymphadenopathy, muscle pains and muscle weakness and occasionally diarrhoea with weight loss. Tropical Pulmonary Eosinophilia involves many organ systems, e.g., Liver, spleen, lymph glands but mainly involves the lungs.

Ayurveda classifies respiratory diseases under various heads. Among them, it elaborates *Kasa* as one of the ailment affecting respiratory system. Ayurveda also prescribes various medicaments for the alleviation of the symptoms arising as a result of involvement of respiratory system. The present research was aimed to evaluate the effect of *Dusparshadi yoga* (Chakrasamhita) indicated especially for Vataja Kasa on Tropical Pulmonary Eosinophilia. The herbal compound prescribed by *Charaka Samhita* (*Chikitsa Sthana*, 18/51) contains *Dusparsha* (*Solanum xanthocarpum*), *Pippali* (*Piper longum*) *Musta* (*Cyperus rotundus*), *Bharangi* (*Clerodendron serratum*), *Karkatshringi* (*Pistacia integerrima*) and *Shati* (*Hedychium spicatum*).

MATERIALS AND METHODS

Patients of Tropical Pulmonary Eosinophilia, attending Out Patient Department (OPD) and In Patient Department (IPD) of Government Ayurved Hospital, Raje Raghuj Nagar, Nagpur were selected randomly, irrespective of caste, sex, educational and socio-economical status. Clinical research proforma for recording the detail history of patients was prepared and diagnosis of the patients was confirmed with the help of modern techniques.

Criteria of Diagnosis

The diagnosis detailed history of the patients was taken. Laboratory investigations such as total leucocyte count, differential leucocyte count, erythrocyte sedimentation rate, haemoglobin percentage, urine and stool examinations were carried out to rule out other pathology. As well as X-ray of chest was done. All the investigations were done before and after the treatment.

Criteria for Selection of Patients

The signs and symptoms of raised eosinophilic count were considered for selection of patients.

Criteria for Rejection of Patients

Those patients who were in status asthmaticus were excluded from the study. The patients having less haemoglobin percentage, raised blood sugar level were also rejected.

Groups of Management

After obtaining informed consent, the patients of study were divided randomly into two groups.

Table 1: Drugs Used

S. No.	Sanskrit Name	Latin Name	Proportion
1	Dusparsha	<i>Solanum xanthocarpum</i>	1
2	Pippali	<i>Piper longum</i>	1
3	Musta	<i>Cyperus rotundus</i>	1
4	Bharangi	<i>Clerodendron serratum</i>	1
5	Karkatshringi	<i>Pistacia integerrima</i>	1
6	Shati	<i>Hedychium spicatum</i>	1

Figure 1: *Solanum xanthocarpum*



Figure 2: *Piper longum*



Figure 3: *Cyperus rotundus*



Figure 4: *Clerodendron serratum*



Figure 5: *Pistacia integerrima***Figure 6: *Hedychium spicatum***

Present paper highlights the effect obtained in a group treated with medicine- *Dusparshadi yoga*. Thirty patients satisfying the criteria for Tropical Pulmonary Eosinophilia were treated under this group.

DRUG PROFILE

Following table shows the drugs prescribed to the patients -

Matra (Dose)

Three grams of compound *Churna* (powder) of

Dusparsha (*Solanum xanthocarpum*), *Pippali* (*Piper longum*) *Musta* (*Cyperus rotundus*), *Bharangi* (*Clerodendron serratum*), *Karkatshringi* (*Pistacia integerrima*) and *Shati* (*Hedychium spicatum*) was given daily three times a day.

Bheshaj Sevan Kala (Time of Drug Administration)

The *Churna* (powder) was given at morning 8 am, at afternoon 2 pm and at night 10 pm. with lukewarm water.

Duration of Treatment

The compound *Churna* (powder) of *Shati* (*Hedychium spicatum*), *Shunthi* (*Zingiber officinale*) and *Sugandhavala* (*Pavonia odorata*) was administered for total 21 days.

Criteria of Assessment

The assessment of the patients was done two day prior starting the treatment. Patients were examined at length and symptoms were noted. All clinical and laboratory investigations were carried out within these two days. After completion of the duration of the treatment all these investigations were repeated.

OBSERVATIONS AND RESULTS

All the patients were examined as per proforma prepared for clinical study. Following results were observed.

Effect on Respiration Rate

22.6 + 1.919 respiration per minute was noted before treatment in control group which after treatment was reduced to 17.533 + 1.634 respiration rate per minute. Difference of mean was 5.0667. This difference was tested statistically by paired 't' test, 't' was 27.346 (P<0.001).

Table 2: Effect of Therapy on Various Parameters by Paired 't' Test

S. No.	Parameter	Mean \pm SD		Diff. of Mean (BT-AT)	SE	Paired 't'	'P' Value
		BT	AT				
1	Respiration Rate	22.6 \pm 1.919	17.533 \pm 1.634	5.0667	0.1852	27.3461	< 0.001
2	Sustained Maximal Inspiration	660 \pm 306.93	773.33 \pm 276.59	-113.33	22.860	4.951	< 0.001
3	Peak Expiratory Flow Rate	118.33 \pm 35.912	308.33 \pm 63.086	-190	12.9986	14.6168	< 0.001
4	Inspiration Time	3.7 \pm 0.9153	4.633 \pm 0.6149	-0.933	0.1585	5.8871	< 0.001
5	Expiration Time	2.2667 \pm 0.884	3.633 \pm 0.6149	-0.9667	0.1552	6.2269	< 0.001
6	Expansion of Chest	80.233 \pm 3.910	85.3667 \pm 3.6717	-5.133	4.0338	1.2725	> 0.10
7	Breath Holding Time	10.333 \pm 1.825	40.5 \pm 14.8178	-30.1667	3.09422	9.7525	< 0.001
8	Total Leucocyte Count	9753.33 \pm 614.05	8496.66 \pm 577.4398	1256.67	87.3206	14.3915	< 0.001
9	Neutrophil Count	57.733 \pm 4.777	59.1667 \pm 4.1112	-1.433	0.9716	1.4751	> 0.10
10	Lymphocyte Count	25.8 \pm 4.7	31.6 \pm 3.970	-5.8	1.2057	4.8104	< 0.001
11	Monocyte Count	0.3 \pm 0.6512	0.4 \pm 0.7239	-0.1	0.12998	0.7693	> 0.10
12	Eosinophil Count	16.8333 \pm 2.2141	9.1667 \pm 2.5472	7.667	0.4077	18.8047	< 0.001
13	Haemoglobin gm %	11.033 \pm 0.626	11.3667 \pm 0.7203	-0.346	0.03022	11.476	< 0.001
14	Absolute Eosinophilic Count	1547.87 \pm 358.99	838 \pm 347.556	703.867	54.1832	12.9904	< 0.001

Table 3: Total Effect of Therapy

S. No.	Effect of Therapy	No. of Patients	Percentage
1	Cured	00	00.00
2	Markedly Improved	00	00.00
3	Improved	22	73.33
4	Unchanged	08	26.67
5	LAMA	00	00.00

Effect on Sustained Maximal Inspiration

660 + 306.93 was the reading of sustained maximal inspiration before treatment, which after treatment increased to 773.33 + 276.59. Difference of mean was 113.33. This difference was tested statistically by paired 't' test and was found to be highly significant 't' was 4.951 (P<0.001).

Effect on Peak Expiratory Flow Rate

Present study highlighted that increase in the peak expiratory flow rate by 190 after treatment was also highly significant ('t' = 14.6168, P<0.001).

Effect on Inspiration Time

Inspiration time rose from 3.7 + 0.9153 to 4.633 + 0.6149 after administration of *Dusparshadi Yoga* for 21 days as described earlier. Increase

in the inspiration time in control group was also highly significant ('t' = 5.8871, P<0.001).

Effect on Expiration Time

The group also highlighted highly significant increase in the expiration time ('t' = 6.2269, P<0.001).

Effect on Expansion Of Chest

This expansion of chest in the group was also increased by 5.133 cm which was insignificant as 't' = 1.2725, P>0.10.

Effect on Breath Holding Time

The group also highlighted highly significant ('t' = 9.7525, P<0.001) increase in the breath holding time by 30.1667 s from 10.333 + 1.8257 to 40.5 + 14.8178 s.

Effect on Total Leucocyte Count

The group showed reduction in TLC by 1256.67 / mm³ which was also highly significant as 't' was 14.3915, P<0.001

Effect on Neutrophil Count

The patients of this group exhibited marginal increase in neutrophil counts by 1.433%. This marginal increase was insignificant. (P>0.10)

Effect on Lymphocyte Count

In this group lymphocyte count raised by 5.8% from 25.8 + 4.7 to 31.6 + 3.970, 't' = 4.8104, P<0.001 suggested highly significant increase.

Effect on Monocyte Count

In this group the results were insignificant 't'=0.7693, (P>0.10).

Effect on Eosinophilic Count

Eosinophilic count was 16.833 + 2.2141 before starting the treatment. After completion of duration of treatment of *Dusparshadi Yoga*, it reduced to

9.1667 + 2.5472 't' was 18.8047, (P<0.001). This reduction was highly significant.

Effect on Haemoglobin Gram Percentage

Group also highlighted highly significant ('t'=11.476, P<0.001) increase in the haemoglobin g% from 11.033 + 0.6260 to 11.366 +0.7203 g%.

Effect on Absolute Eosinophilic Count

Study also exhibited reduction of 703.867 in absolute eosinophilic count which was highly significant ('t' = 12.9904, P< 0.001).

TOTAL EFFECT OF THERAPY

In this study the patients from the group of *Dusparshadi Yoga* 73.33% patients were improved and 26.67% patients were unchanged. It is obvious from the Table 3 that no patient was observed in cured, markedly improved category, in control group.

DISCUSSION

In present study 17 male and 13 female patients were included with 96.67% being from 21-50 years age group. Precise pathogenesis of tropical pulmonary eosinophilia is unknown in most of the cases of TPE. Patients with early disease show obstructive ventilatory deficiency while those with chronic disease may have a restrictive defect. Plausible effects obtained by the drugs can be attributed to the chemical constituents and Pharmacodynamic properties of individual herbs included in *Dusparshadi Yoga* based on the Ayurvedic principles.

PROBABLE EFFECT OF THE DRUGS

Solanum xanthocarpum contains a gluco-alkoloid C₄₄H₇₈O₁₉H termed as Solanarpine (Gupta and

Dutt, 1938) and Solamargine (Siddiqui *et al.*, 1983) is found in the fruits. On hydrolysis it gives crystalline compound and a sugar. The alkaloid is termed as Solacarpidin given an insoluble hydrochloride. A sterol $C_{30}H_{34}O_4$ which is also found is termed as "Carpesterol". The drug has proved the significant use in treatment of asthma (Mohan *et al.*, 2007). It also exhibits antihistaminic, anti-allergic property (Vadnere *et al.*, 2008). The drug is widely used by practitioners of the Siddha system of medicine in southern India to treat respiratory diseases (Nadkarni, 1954). The drug is also effective larvicide in the management of mosquito populations resulting in limiting the outbreak of various vector borne epidemics showing its antifilarial effect (Mohan *et al.*, 2006; Mohan *et al.*, 2005; Singh and Bansal, 2003; Rajkumar and Jebanesan, 2005).

Piper longum contains piperine 0.15 to 0.18%, Piplartine 0.13 to 0.20% and traces of a yellow crystalline pungent alkaloid. Other constituents found in the drug include triacontane, dihydrostigmasterol, an unidentified steroid reducing sugars and glycosides (Neelam and Krishnaswamy Kamala, 2001). It antagonized respiratory depression (Singh *et al.*, 1973; Dhanukar *et al.*, 1981; Dhanukar *et al.*, 1984) showing presence of some medullary stimulant factors in the extract (Kulshresta *et al.*, 1969 and 1971) *P. longum* showed an immune-regulatory potential with dose dependent decrease of lymphocytes (Devan *et al.*, 2007) and phagocytic activity (Agarwal *et al.*, 1994).

Cyperus rotundus contains fat, sugar, gum, carbohydrate, essential oil, albuminous matter, starch, fibre and ash. There are traces of an alkaloid. Proteins 5.21%, starch 22.62%, and carbohydrates 24.79% (Akperbekova, 1967). The

drug is found to be active against *Plasodium falciparum* (Weenen *et al.*, 1990).

It is also found to protect against broncho spasm induced by histamine aerosol (Singh N *et al.*, 1970).

Clerodendrum serratum contains the component of fatty acid are Myristic – 0.1, Palmitic – 12.9, Steraric – 4.2, Oleic – 58.5, Linoleic – 24.2 (Sharma *et al.*, 2002; The Ayurvedic pharmacopoeia of India, 1999; Rastogi and Mehrotra, 1999; Narayana, 2003; Gupta *et al.*, 2005) The drug is found to be useful with its anti-allergic and anti-inflammatory activity in diseases like asthma (Bhangare *et al.*, 2012). It also revealed significant inhibitory activity on histamine (Nal Bhujbal *et al.*, 2010).

Pistacia integerrima Essential oil 1.21%, crystalline hydrocarbon 3-4%, tannin substance 60% and gum mastic 5% (Anuradha *et al.*, 2010). The essential oil of a palegreenish yellow color with turpentine like odor and taste. The specific gravity of the oil is 0.8885 at 15°C. It contains α -terpinolene, Limonene, α -thujene (Abdur Rauf *et al.*, 2013). The crystalline principle obtained is insoluble in water in nearly all the organic solvents, is tasteless and has a sharp melting point 146°C. The tannins are of a yellowish crystalline appearance. The ethanolic extracts of the drug is found to inhibit the Gram positive bacteria better than the Gram negative bacteria. *B. cereus* was found to be more susceptible (Ramachandra *et al.*, 2010).

H. spicatum, commonly known as Kapoor Kachri, contains α - pinene, β - pinene, limonene, 1, 8 - cineole, 2 - alkanones, linalool, camphor, linalyl acetate, β - terpineol, borneol, β - caryophyllene, γ - cadinene, humulene,

Table 4: Pharmacodynamic Properties of Drugs

S. No.	Name	Latin Name	Rasa	Vipaka	Vriya	Guna	Doshaghata
1	Dusparsha	<i>Solanum Xanthocarpum</i>	Tikta, Katu	Katu	Ushna	Laghu, Ruksha	Kaphaghna, Vataghna
2	Pippali	<i>Piper longum</i>	Katu	Katu	Anushna	Laghu, Snigdha, Tikshna	Kaphaghna, Pittakar, Vatahamaka
3	Musta	<i>Cyperus rotundus</i>	Tikta, Katu, Kashaya	Katu	Shita	Laghu, Ruksha	Pittaghna, Kaphaghna, Vatakar
4	Bharangi	<i>Clerodendron serratum</i>	Tikta, Katu, Kashaya	Katu	Ushna	Laghu, Ruksha	Kaphaghna, Vataghna
5	Karkatshringi	<i>Pistacia integerrima</i>	Kashaya, Tikta	Katu	Ushna	Laghu, Ruksha	Vataghna, Kaphaghna
6	Shati	<i>Hedychium spicatum</i>	Katu, Tikta, Kashaya	Katu	Ushna	Laghu, Tikshna	Kapha Vata Shamaka

Table 5: Properties of Drugs Used in Experimental Group

S. No.	Properties		Number	Percentage %
1	Rasa	Kashaya	5	83.33
		Tikta	5	83.33
		Katu	4	66.67
2	Guna	Laghu	6	100.00
		Ruksha	4	66.67
		Snigdha	1	16.66
		Tikshna	2	33.32
3	Virya	Shita	1	16.66
		Ushna	4	66.67
		Anushna	1	16.66
4	Vipaka	Madhura	0	00.00
		Katu	6	100.00
5	Doshaghata	Vataghna	3	49.99
		Pittaghna	1	16.66
		Kaphaghna	5	83.33
		Pittakar	1	16.66
		Vatakar	1	16.66
		Kapha Vatahamaka	2	33.32

terpinolene, p - cymene, benzyl cinnamate, benzyl acetate, linalyl acetate, γ - terpinene, β - phellandrene, methyl paracumarin acetate, cinnamic ethyl acetate, ethyl - p- methoxy cinnamate, ethyl cinnamate, d - sabinene, sesquiterpene - cadinene, sesquiterpene alcohols, sesquiterpene hydrocarbons, drimane and labdane derivatives (Balas, 1967; Dixit *et al.*, 1977; Garg *et al.*, 1977; Nigam *et al.*, 1979). Studies shows that most of the symptoms of pulmonary eosinophilia were relieved within one to three weeks, radiological findings and lymphadenopathy were also normalized (Shaw, 1980). Methanol extract of *H. spicatum* produced dose dependent anthelmintic activity (Sravani and Padmaa, 2011).

Dusparshadi Yog possesses Laghu, Ruksha and Tikshna guna with Katu Tikta rasa, Katu vipak and Ushna veerya. These properties act as Kaphavataghna. In this condition Dushti of Prana can be rectified by decreased formation of dushta Kapha and Vatanulomana. Pippali acts as Rasayana to Pranvaha srotasa. Considering the phytochemical and pharmacodynamic properties of the compound preparation prescribed in this research, the probable action can be attributed as antihistaminic and anti-inflammatory. Further studies are required for the precise claims.

CONCLUSION

The beneficial results exhibited by compound *Churna* of *Dusparshadi Yog* will be helpful to treat the patients of Tropical Pulmonary Eosinophilia. The present study showed herbs definitely produce positive results in tropical eosinophilia. No patients under this therapy showed any untoward effects of the drug. Comprehended etiology of eosinophilia for further management

of patient is decisive. Detailed history, thorough clinical examination along with blood and serological tests helps to rule out diverse aetiologies of eosinophilia.

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