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An Open Label Single Arm Clinical Study on the Combined Effectiveness of *Chitrakadi Vati* and *Avipathi Churnam* in the Management of Hypothyroidism

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ABSTRACT

Background: Hypothyroidism in Ayurveda can be understood as *kapha pradhana tridoshaja, agnimandya janya vyadhi* making the *dushti* of *dhatus* predominantly *rasa* and *medas*. *Chitrakadi vati* was selected as it contains *pancha lavana* and *kshara dvaya* which help in agni deepana and *ama pachana* at *koshta* and *dhatu level*.*Avipathi churnam* was selected for the purpose of *koshta shodhana* and it helps in *suka virechana* and *vata anulomana* due to the presence of *trivrut*

Aims and Objectives: To study the combined effectiveness of Chitrakadi vati and Avipathi churnam in the management of hypothyroidism.

Methodology: Among 23 registered patients, 20 of them completed the course of treatment. They were administered with *Chitrakadi vati* 1 tablet (250 mg) half an hour before food with warm water twice daily (morning and evening) for a period of 84 days and *Avipathi churnam* 12 gms in early morning empty stomach with honey once in a month for 3 consecutive months. Subjective parameters were assessed by Cochran's Q and Mc Nemar tests. Objective parameters were assessed by Repeated Measures Anova and Paired T Test.

Result: There was statistically significant improvement in the signs and symptoms of Hypothyroidism and thyroid profile. ($p<0.05$ was observed)

Conclusion: *Chitrakadi vati* and *Avipathi churnam* are effective in the management of hypothyroidism.

KEYWORDS

Agni mandyam, Avipathi churnam, Hypothyroidism, Chitrakadi vati

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INTRODUCTION

Hypothyroidism is a clinical condition resulting from reduced production of thyroid hormone. Hypothyroidism is most common with prevalence of 5.4%.Women are affected approximately six times more than men[1].

The signs and symptoms of hypothyroidism are found to be similar with specific conditions described in classical *ayurvedic* textbooks. *Acharya Charaka's* concept of *asta nindita purusha* includes many of the endocrinal presentations. Description of *galaganda* available in classics coincides with the goitric manifestation of Hypothyroidism. Symptoms seen in the hypothyroidism patients are found in the classical description of different conditions such as *amajeerna, kaphaja pandu, kaphaja shopha, avarana* and *bahudoshavastha*. *Acharya Charaka* emphasizes on the ability of the *vaidya* to comprehend the *dosha-dushya* of the *vyadhi* than mere naming of the *vyadhi*. The critical analysis of the pathogenesis and symptomatology of hypothyroidism reveals that it is basically caused due to the dysfunctioning of the agni. Hypofunctioning of *jatharagni*, which in turn, affects *dhatvagni*, eventually, brings out pathological sequence & ultimately, the diseased condition[2].

Chitrakadi vati is explained in the *grahani chikitsa* in charaka samhita. The main action of *Chitrakadi vati* is *ama pachanam* and *agni deepanam*. According to *acharya Sarangadhara*, *Chitraka* is mentioned as the ideal drug for *deepana* and *pachana*. The two *kshara dravyas* contribute for the *lekhana* and *ksharana swabhava* of the *oushdha*. The drug possess *sukshma*, *teekshna* and *vyavayi guna* due to the presence of *pancha lavanas* and *trikatu*. In general the drug is having action over the *samana vata*, *pachaka pitta* and *kledaka kapha*. The main site of action of the drug will be *annavaha srotas* that helps in correcting the *jaatharagni* and its component in the *dhatwagni*[3].

Avipathi churnam is explained in the *virechana kalpam adhyayam* of *ashtanga hrudayam*. The main ingredient of the yoga is *Trivrt*. It helps in the *suka virechanam* and thus bring *Vata anulomanam*. The other ingredients of the yoga like *Trikatu*, *Musta* and *Amalaki* is *kapha hara* and possess *deepana karma*. Due to the presence of *Trijataka*, the yoga is *pittahara* and *rakta prasadana* in nature. The indications of the drug are *mutra krchra, jwara, chardi, kasa, bhrama, shosha, pandu* and *alpa agni*. It is specifically indicated for *paitika vikaras*. The study was carried out to study the combined effectiveness of *Chitrakadi vati* and *Avipathi churnam*[4].

OBJECTIVES

- To study the combined effectiveness of *Chitrakadi vati* and *Avipathi churnam* in the management of hypothyroidism.
- To understand the pathophysiology of hypothyroidism with the principles of Ayurveda.

MATERIALS AND METHODS

Source of data: Patient were recruited from outpatient department of *Kayachikitsa,* Sri Dharmasthala Manjunatheswra college of Ayurveda and Hospital, Hassan.

Method of collection of data: 59 patients (Table 1) were screened and selected based on the screening form prepared. Data was collected using specially prepared case report form.

Table 1 Demographic details of 23 patients of Hypothyroidism

Geographic Observation	Predominance	No of Patients (%)
Age	18-30 years 31-40 years	11 (48%) 5 (22%)
Gender	Female	20 (87%)
Educational Status	Graduates	14 (61%)
Marital Status	Married	19 (82%)
Economic Status	Middle class	20 (87%)
Occupation	Home maker	11 (44%)

The demographic details of 23 enrolled patients of hypothyroidism such as age, gender, educational status etc are represented in table below (Table 1).

The observations related to the personal history and disease details of the 23 patients of hypothyroidism are represented in table below (Table 2).

Table 2 Observations related to personal history and disease

Family history	Absent	16 (70%)
Nature of diet	Mixed	19 (83%)
Dietary habit	*Vishamashana*	16 (70)
Nature of Agni	*Vishama* *Manda*	15 (65%) 7 (30%)
Hair loss	Present	18 (79%)
Weight gain	Present	12 (52%)
Muscle ache and stiffness	Present	16(70%)
Tiredness	Present	22 (96%)
Serum T_3	90-120 Nano gram / dl	6 (26%)
Serum T_4	6 - 9 micro gram/ dl	10 (44%)
Serum TSH	5-30 micro IU/ml	14 (70%)
BMI	18-24.9 Kg/m^2 25-29.9 Kg/m^2	11 (49%) 7 (30%)

Diagnostic Criteria:

TSH value**:** 5.5 – 150 micro IU/ml[5] (Hypothyroidism).

Both clinical and subclinical hypothyroidism

Symptoms[6]

Tiredness, weakness, dryness of skin, feeling cold, hair loss, constipation, weight gain with poor appetite, hoarseness of voice, muscle aches/stiffness ,menstrual disturbances

Signs

Bradycardia, periorbital puffiness

Inclusion Criteria

Between the age of 18-60 years, patients of either gender, patients already diagnosed as hypothyroidism with or without medication, patients with Primary hypothyroidism, patients with sub clinical hypothyroidism. (Elevated serum TSH level with normal serum T_4 level), patients who are ready to sign the informed consent form.

Exclusion Criteria

Patients suffering from systemic diseases like Ischemic Heart Disease, Diabetes mellitus, carcinomas etc., patients suffering from congenital hypothyroidism, pregnancy and lactation, patients with stress induced hypothyroidism, rapid progressive case of myxedema, hypothyroidism due to drug therapy (e.g. amiodarone, lithium, interferon), hypothyroidism due to infiltrative diseases like sarcoidosis, scleroderma, haemochromatosis. Patients who have under gone any type of thyroid surgery.

Ethics: Ethics clearance was obtained form Institutional Ethics Committee before initiation of the study, (IEC No: SDM/IEC/53/2015-2016). The trial was registered with Central Trial Registry of India (CTRI/2017/10/010066 dated 10.12.2017).

Study Design: The study was an open label single arm clinical study at OPD level with convenient sampling, pre and post-test design with sample size of 23 hypothyroidism patients.

Intervention: The trial drugs *Chitrakadi vati* and *Avipathi churnam* were collected from SDM pharmacy Uduppi, a GMP certified pharmacy.

Method of preparation:

Chitrakadi Vati

The fine powders of all the ingredients were prepared separately and mixed together thoroughly by triturating in *Khalva yantra*. Then they were triturated with *Matulunga Swarasa/Amla Dadima Swarasa*. Then pills of two *Ratti* (250 mg) by weight were prepared and then dried in shade. After drying these pills they were stored in air tight containers[7].

Avipathi Churnam

The fine powders of all the ingredients were prepared in the form of dry drugs separately, mixed together and filtered through cloth. After preparing the powder, it was stored in air tight containers[8].

Treatment plan:

Chitrakadi Vati was administered as 1 tablet (250 mg) twice daily half an hour before food with warm water for 84 days in combination with *Avipathi churnam* 12 gms early morning empty stomach with honey as *anupana* once in a month for 3 consecutive months.

Assessment Criteria:

Subjective Parameters:

Assessment of subjective parameters were done on 1st day, 10th day, 41st day, 71st day and 90th day with the help of a suitable clinical scoring of hypothyroidism – 'BILLEWICZ SCORE'[9]. The parameters in BILLEWICZ SCORE are the following signs and symptoms:

Symptoms:

Diminished sweating, dry skin, cold intolerance, weight increase, constipation, hoarseness, deafness

Signs:

Slow movements, coarse skin, cold skin, periorbital puffiness, pulse rate, ankle jerk

Objective parameters

Assessment of objective parameter will be done on the 1st and 90th day based on the changes in the laboratory parameters like thyroid profile and body weight with respect to BMI.

OBSERVATIONS AND RESULTS

In the present study, among the 59 patients screened, 23 patients were registered. Of them 20 have completed their course of treatment.

The effect of the therapy in 20 patients of Hypothyroidism are shown in the table below:

Cochran's Q test was applied to note the significant changes in the signs and symptoms during treatment (1st day, 10th day, 41st day, 71st day and 90th day) and post hoc analysis was done with Mc Nemar test with significant level at $P < 0.05$ (Table 3)

Table 3 Effect of therapy on signs and symptoms

Parameter	N	Cochran's Q Value	P Value	Remarks
Dryness of skin (1st day – 90th day)	17	49.106	.000	S
Diminished sweating (1st day- 90th day)	8	21.400	.008	S
Cold Intolerance (1st day-90th day)	11	28.462	.004	S
Weight gain (1st day-90th day)	11	35.733	.002	S
Constipation (1st day -90th day)	10	28.923	.002	S
Slowness of movement (1st day- 90th day)	3	4.000	.406	NS
Coarseness of Skin (1st day – 90th day)	8	26.000	.008	S
Cold Skin (1st day -90th day)	5	14.462	.006	S

Periorbital Puffiness (1st day- 90th day)	12	34.909	.000	S

The effect of therapy on Gross Billewicz score of 20 patients of hypothyroidism is presented in the table below (Table 4). Repeated measure anova with a Green House Geisser correction was applied to determine the effect of therapy on Gross Billewicz Score and also helped to determine the interval where maximum benefit was obtained with the same.

Table 4 Effect of therapy on Gross Billewicz score

Parameter	F value	P value	Mean difference					Remarks
			1st day- 10th day	10th day- 41st day	41st day- 71st day	71st day- 90th day	1st day- 90th day	
Gross Billewicz Score	40.052	0.0	4.850	13.55	8.30	3.50	30.20	S

S = Significant

The effect of therapy on Thyroid profile and BMI before and after treatment is presented in the table 5. Paired T test was applied to determine the effect of therapy on Thyroid profile and BMI.

Table 5 Effect of therapy on thyroid profile and BMI

Parameter	Mean		Mean Diff	SD (±)	SE (±)	t	p	Remark
	BT	AT						
Serum T_3	87.53	102.65	15.11	36.76	8.21	1.83	>0.05	NS
Serum T_4	5.15	8.24	3.09	3.65	.81	3.78	<0.05	S
Serum TSH	45.91	11.98	- 33.93	45.38	10.14	-3.34	<0.05	S
Serum TSH without thyronorm intake (9 patients)	35.41	10.11	24.40	2.34	.524	1.87	>0.05	NS
Serum TSH with thyronorm intake (9 patients)	64.69	14.58	50.11	52.39	17.46	2.86	<0.05	S
BMI	24.6	24.2	0.4	2.34	.524	.655	>0.05	NS

S = Significant, NS= Not Significant, SD= standard deviation, SE= standard error

DISCUSSION

Statistically significant improvements were observed on majority of the subjective and objective parameters with administration of *Chitrakadi Vati* and *Avipathi Churnam.* All signs and symptoms were assessed at 5 intervals i.e baseline, 10th day, 41st day, 71st day and 90th day.

Chitrakadi vati and *Avipathi churnam* helped in pacifying dryness of skin in 17 patients. Both *Chitrakadi vati* and *Avipathi*

churnam due to their ama pachana and sroto shodhana swabhava helped in removing Kapha avarana in *rasa* and *rakta vaha srotas*. Thereby helped in relieving the symptom.

Chitrakadi vati and *Avipathi churnam* pacified diminished sweating in 8 patients. *Chitrakadi vati* contains *pancha lavanas* and *dviksaharas which does kapha medo harana and agni vardhana.* Moreover, the *Vyavayi* action of the *pancha lavanas* will help in the *sweda pravartti*. *Avipathi churnam* also helps in correcting the *agni mandyam* at koshta and dhatu level thereby brings the *samana vata* to the *prakruta avastha*. The *prakruta samana vata* helps in the *samyak sweda pravrutti*.

Chitrakadi vati and *Avipathi churnam* helped in relieving weight gain in 10 patients. Chitrakadi vati and *Avipathi churnam* contains drugs with *ushna veerya katu vipaka* and does the rasa dhatwagni deepana. The *pancha lavanas* and *dvi kshara* present in *chitrakadi vati* helps in the *karshana* of *medo dhatu* thereby helping in relieved the symptoms.

Chitrakadi vati and *Avipathi churnam* pacified constipation in 10 patients. *Chitrakadi vati* contains *ushna teekshna guna yukta dravyas* which help in *Ama paachana* and *Agni deepana*. *Avipathi churnam* contain *Trivrut* as the major ingredient, which will help in *vata anulomana* thereby relieved the symptom.

Chitrakadi vati and *Avipathi churnam* helped in relieving periorbital puffiness in 12 patients. periorbital puffiness in hypothyroidism is due to the mucinous deposits. It can be understood as a rasa *vruddhi lakshana* due to *Rasa dhatwagnimandyam*. *Chitrakadi vati* and *Avipathi churnam* contains drugs like *Trikatu, Trijataka* and *Pancha lavana* which does the *kleda shoshana* and thereby relieved the symptoms.

Chitrakadi vati and *Avipathi churnam* relieved cold intolerance in 11 patients. Cold intolerance can be understood as "*sheeta dvesha* or *shaitya*" in ayurveda. It is caused due to the *vruddhi* of *kapha dosha* and *rasa dhatu*. *Pitta kshaya* also contributes to the manifestation of cold intolerance. *Chitrakadi vati* contains drugs like *trikatu, dvikshara* and *pancha lavanas* which are basically *kapha hara* in nature.It also help in correcting the *rasa dhatwagnimandyam*. *Avipathi churnam* contain drugs with properties like *ushna veerya, katu vipaka*. Hence both the drugs help in relieving the symptom.

Chitrakadi vati and *Avipathi churnam* were found to reduce the serum TSH level from a mean value of 45.91 micro IU/ml before treatment to 11.98 micro IU/ ml after treatment. The overall reduction in serum

TSH between 1st day and 90th day was 33.93 microIU/ml which was statistically significant. In 9 patients of hypothyroidism who were not under thyronorm, Serum TSH was 34.51 micro IU/ml before treatment and it decreased to 10.11 micro IU/ml after 90 days of treatment with decrease of 24.40 micro IU/ml. The decrease in the value was not statistically significant. (P>0.05). In 9 patients of hypothyroidism who were under thyronorm, Serum TSH was 64.69 micro IU/ml before treatment and it decreased to 14.58 micro IU/ml after 90 days of treatment with decrease of 50.11 micro IU/ml. The decrease in the value was statistically significant. (P<0.05).Both the drugs also increased the serum T_3 and T_4 levels after treatment. The overall increase in the level of serum T_3 was 15.11 ng/dl but it was not statistically significant. The overall increase in the level of serum T_4 was 3.09 micro gram/dl which was statistically significant.

Chitrakadi vati and *Avipathi churnam* were found to reduce the BMI from a mean value of 24.6 kg/m^2 to 24.2 kg/m^2 after treatment. The overall reduction in BMI was 0.4 kg/m^2 which was not statistically significant (p >0.05).

Administration of *Chitrakadi vati* in combination with *Avipathi churnam* was found to reduce the Gross Billewicz Score, where the maximum result was obtained between 10th day and 41st day. Repeated measures Anova with a Green House - Geisser correction determined that Gross Billewicz score differed statistically at time point F= 40.052, P = 0.000.Between 10th day and 41st day the overall reduction in Gross Billewicz Score was 13.55 which was statistically significant.

CONCLUSION

- Administration of *Chitrakadi vati* for 3 consecutive months relieved the signs and symptoms of Hypothyroidism namely – dryness of skin, diminished sweating, cold intolerance, weight gain, constipation, coarseness of skin, cold skin and periorbital puffiness.
- There was no statistical difference in signs and symptoms namely -bradycardia, slowness of movement, hoarseness of voice , deafness and sluggishness of ankle jerk
- Both the drugs reduced the TSH level and increased the level of serum T_4 after 90 days of treatment.
- But both the drugs didn't show any statistical difference in serum T_3 levels and BMI after 90 days of treatment.
- Hypothyroidism can be understood as a state of *mandagni* at the level of *koshta* and *dhatu.*
- Hence administration of *Chitrakadi vati* 1 tablet (250 mg) twice daily (morning and

evening) before food with warm water and *Avipathi churnam* 12 gm with honey in early morning empty stomach once in a month for 3 consecutive months is effective in the management of hypothyroidism.

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