

**ROLE OF AN INDIGENOUS GRANULE FORMULATION ON RAJONIVRITTI-JANYA
LAKSHANAS (HYPOESTROGENISM)**

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Article Received on 21/05/2019

Article Revised on 11/06/2019

Article Accepted on 01/07/2019

ABSTRACT

Menopause is the permanent cessation of menses due to physiological changes of ageing due to depletion of oocytes. *Rajonivritti* is the term mentioned in *Ayurved* which denotes *Swabhavika raja kshaya*. It is estimated that as many as 85% of postmenopausal women have experienced a menopause related symptom in their lifetime. Conservative therapies include Hormonal replacement therapy and self-management techniques. Prevalence of HRT use among menopausal women is 45 years and above. As HRT has got its own limitations, so effort is been done to replenish the oestrogen through Phytoestrogen to post-menopausal women. To enhance palatability and ease the mode of administration the drugs were modified as *khanda kalpana* i.e. granules. Literary review of menopausal changes and phytoestrogenic activity of indigenous granule formulation. To formulate simple, economical, palatable health drink for postmenopausal women and to evaluate its efficacy in improving the QoL. A single blind clinical study on 40 menopausal women with pre-test and post-test design with an indigenous granule formulation administered 10gms twice daily with milk for the period of 3 months. This *khanda kalpana* showed marked improvement in 82.5% of women, with improvement in both subjective and objective parameters. This study shows that the drug is effective in post-menopausal women, the statistical data was significant with $P < 0.0001$. No adverse effect of the drug was observed during the study. Thus the health drink formulated with the indigenous drugs was beneficial in improving menopausal symptoms along with increasing the serum oestradiol and calcium levels.

KEYWORDS: Hormone replacement therapy, *Khanda kalpana*, Phytoestrogens, *Rajonivritti*, *Raja kshaya*.

INTRODUCTION

Menopause has achieved a greater significance in today's prospective. Life expectancy has gone up to 80 years of age and women are living around 30 to 40 years or more in post menopause, estrogen depleted state and with it comes all the problems of menopause.^[1] *Rajonivritti* explained by *Acharya Sushruta* and in his commentary is that the age mentioned is 50 years which should be considered as a probable age and not a fixed one. There may be some variations in this regard. Considering the variations and factors influencing it, can be logically quoted as either environmental (*kaal*) or the individuality of a woman (*swabhava*). The menstrual flow gradually declines with irregular or scanty flow of menses. More importance has been given to *Ahara* and *Vihara* in the maintenance of health, these factors too, should be

considered for this fluctuation.^[2] As we know the management for Menopausal symptoms is Hormone Replacement Therapy (HRT) which can be given only for a shorter period as it has adverse effects on prolonged use.^[3]

Importance: *Jaravastha* is the period dominated by *Vata dosha*. And the selected drugs like *Shatavari*, *Yashtimadhu*, Soyabeans, finger millet, *Atasi*, *Brahmi* and *Kukkutanda twak bhasma* are *vayasthpaka*, *vajeekara* and by their properties help to alleviate *Vata dosha* and remove the obstructions in the *srotas* by the virtue of their *veerya* thus aiding for the free flow of *vata*. According to the contemporary medical science the above drugs are said to be rich in Phytoestrogens. Phytoestrogens are estrogens of plant origin and have

weak estrogenic properties which can be utilized to our advantage in the management of Menopausal Problems. They are classified into three main groups: Isoflavones, Lignans and Coumestans.^[3] With the rising walk-ins of the women facing menopausal symptoms in to the gynecology clinics, there arises a need to develop a health supplement which has therapeutic effects in improving the symptoms of menopause by replenishing the estrogen in a safe manner, supplementing the calcium, iron and also having some effects on the equilibrium of the mental condition. With this intention the present study has been undertaken.

AIMS AND OBJECTIVES

- The aim of the present study was to evaluate the therapeutic efficiency of health drink formulated with the above Indigenous drugs in Menopausal Women and formulate Simple, Economical, Palatable and Best Possible Health drink for Menopausal age group women.
- An objective was to evaluate phytoestrogenic activity of selected drugs *Shatavari*, *Yastimadhu*, Soyabeans, Finger Millet, *Atasi*, *Brahmi*, *Kukkut anda twak bhasma*, *Guda* on Menopausal women.

MATERIAL AND METHODS

The study was single blind clinical study with pre-test and post-test design to evaluate the therapeutic effect of indigenous granule formulation for post-menopausal women. The study was approved by the Institutional Ethics Committee for Human research (PU/PIA/IECHR/2017/24 on 10th April 2014), in Parul Institute of *Ayurveda*, Parul University, Vadodara. It was carried out with WHO-good clinical practice guidelines. The clinical trials has also been registered in Clinical Trail Registry of India. (CTRI/2018/04/013049 on 04/04/18).

Source of data

- The total 40 patients were selected from the O.P.D. of the department of the *Prasuti Tantra Evum Stri Roga* of Parul *Ayurved* Hospital, Limda-Waghodia

POSOLOGY & DURATION OF THERAPY

Table No. 01: Granule Administration.

FORMULATION	ROUTE	DOSE	MEDIUM	TIME	DURATION
Indigenous granules	Orally	10gm	<i>Godugdha</i> /Milk	Twice a day	3 months

- *Aushadh Sevan Kaal* – 8am and 8pm; before food, after the previously eaten food of previous *Annakala* is digested.
- The patients were assessed by Subjective and Objective Parameters before treatment, during follow ups and after the treatment.
- Investigations were carried out before treatment and after treatment.

Follow up

The patients were observed for a month after completion of treatment.

fulfilling the diagnostic criteria of *Rajonivritti-janya lakshanas*.

- All the ingredients of the trail drug were collected from market sample of Vadodara and processed and later prepared in the GMP certified Pharmacy of Parul Institute of *Ayurved*, Waghodia.

Preparation of drug-

- *Kukkutanda twak bhasma* was prepared after *shodhan* for 5 days in saline water followed by *marana* i.e. *Bhavana* with *Ghrutakumari swarasa* till formation of *Chakrika* which was subjected to *maha puta* for 5 times with intermediate *bhavana*.
- Soyabean, *Shatavari*, *Ragi* were taken in 3 parts; *Atasi* in 2 parts; *Yashtimadhu and brahmi* 1.5 parts and *Bhasma* of *kukkutanda twak* 0.5 parts with quantity sufficient *guda* was formulated in granule form in Pharmacy of Parul Institute of *Ayurveda*.

CRITERIA FOR SELECTION OF PATIENTS

The patients who fulfilled diagnostic criteria of symptoms from inclusion in a woman with Amenorrhea of one year.

INCLUSION CRITERIA

Post-menopausal women between 40-60 years having 3 or more symptoms from the below list:

Physical: Vaginal dryness, Hot flushes, Muscle pain, Joint pain/back ache, Decreased Libido, Dyspareunia
Psychological: Insomnia/ Sleep disturbances, Irritability, Depression, Anxiety, Cancer Phobia

EXCLUSION CRITERIA

Women with Type II Diabetes Mellitus, Artificial Menopause, Malignancy and other Systemic disease.

INVESTIGATIONS

1. Haemoglobin
2. Serum Oestradiol
3. Serum Calcium
4. Vaginal Smear

ASSESSMENT CRITERIA

Subjective Parameters: MENOPAUSAL RATING SCALE.^[4]

Objective Parameters

- a) Body weight
- b) Blood Pressure
- c) Pulse rate
- d) Haemoglobin level
- e) Serum Oestradiol
- f) Serum Calcium
- g) Vaginal smear

OVERALL EFFECT OF THERAPY

The overall effect of therapy was grouped into 5 types.

1. No change or Less than 25% changes in the signs and symptoms.
2. Mild improvement: 26-50% relief in the signs and symptoms.
3. Moderate improvement: 51-75% relief in the signs and symptoms.
4. Marked improvement: 76-99% relief in the signs and symptoms.
5. Complete remission: 100% relief in the signs and symptoms.

STATISTICAL ANALYSIS

The information collected on the basis of observation, were subjected to statistical analysis in terms of percentage of relief, Mean, Standard Deviation (SD) and standard Error (SE) and by the use of student paired 't' test, to evaluate the significances at different levels. The obtained results were interpreted as insignificant result - $P > 0.05$, significant result - $P < 0.05$. Analysis was carried out using statistical package for social sciences (SPSS) 20.0 version.

OBSERVATIONS AND RESULTS

The observation made on 40 patients having *Rajonivrittijanya lakshana's* showed the maximum

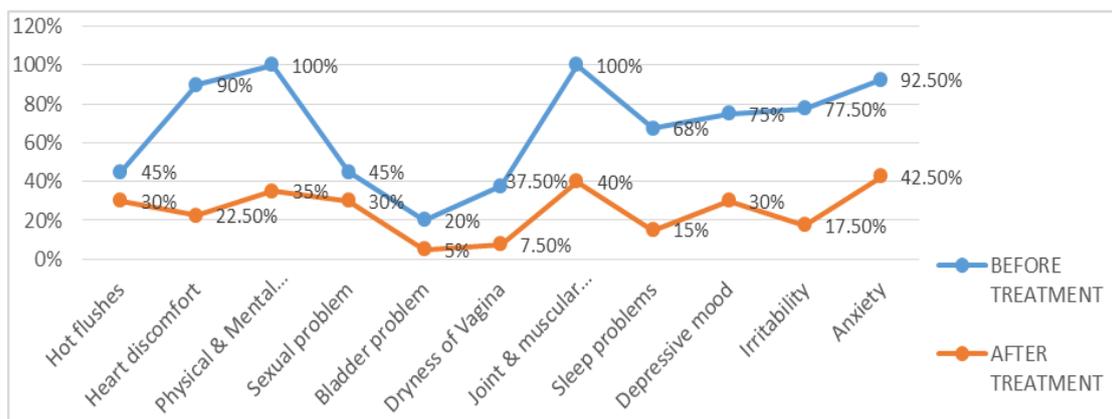
number of patients i.e. 30% belonged to age group of 55-60 years, from *Jangala desha* i.e. 60%; religion belonging to Hindu i.e. 90%; Married women (97.5%), 92.5% women were literate. The maximum socioeconomic status of the patients were rich and middle class patients were 32.5%. The menopausal duration of 1-4 years were maximum i.e. 60%, with menopausal age from 40-45 years and 45-50 years were majority i.e. 40% each. Many patients i.e. 87.5% had their Menarche at the age of 11-13 years. Among 40 patients, 57.5% patients had irregular peri-menopausal history.

EFFECT OF THERAPY

The productive result of Indigenous health drink was observed in all the features of menopause syndrome in menopausal rating scale.

On Subjective parameters

Before treatment to after treatment: The result was observed statistically significant ($P < 0.001$) by paired 't' test. (Table no. 02).



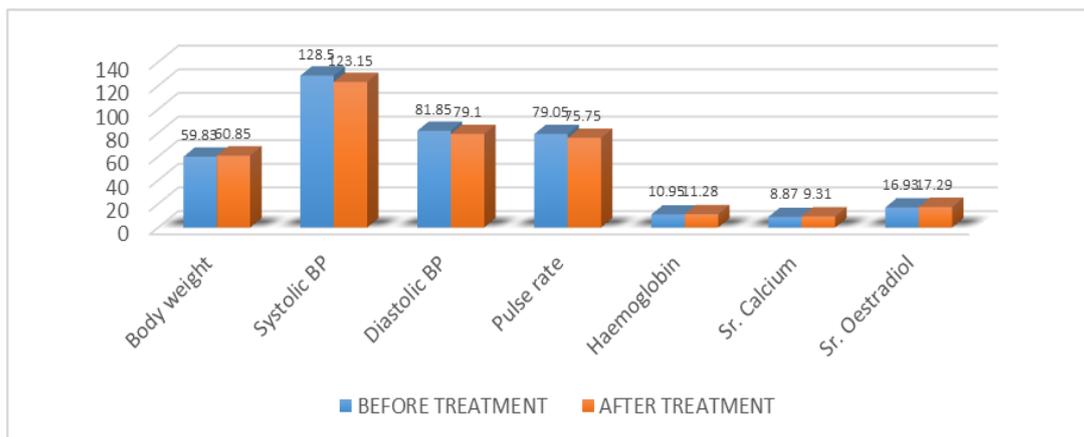
Graph No. 01: Result on Subjective Parameter's (Mrs) of 40 *Rajonivritti* Patients.

After treatment to follow up: The statistical data was non significance in all parameters except in joint & muscular discomfort with 84% of relief and bladder problem showing 100% relief. Whereas in other menopausal symptoms, the relief found was below 70% after stoppage of trial medicine with reduction in severity of symptoms. (Table no. 02).

On Objective parameters: (Table no. 03)

The objective parameters were measured before and after treatment i.e. at the gap of 3 months. The statistical data of all parameters were significant and had improvement. The mean percentage of the change was increased of Body weight by 1.70Kg; Haemoglobin by 3.01gm%; Serum Calcium by 4.94mg/dl and Serum Oestradiol by 2.12pg/ml. Following were decreased mean percentage

in systolic blood pressure by 4.16 mm of Hg and diastolic blood pressure by 3.35 mm of Hg along with pulse rate by 4.17/min.



Graph No. 02: Result on Objective Parameter's of 40 Rajonivritti Patients.

Overall effect of therapy

The maximum patients i.e. 82.5% reported with markedly improvement of the post-menopausal

symptoms by Menopausal rating scale, 12.5% reported moderate improvement and 5% patients reported fully cured i.e. 100% relief.

Table No. 02: Paired 't' Test For The Subjective Parameter's.

SUBJECTIVE PARAMETER'S		MEAN RANK		Difference	% OF RELIEF	SD	SE	't' value	'P' value	Remark
1] Hot Flashes	BT-AT	1.53	0.35	1.18	77.12	1.375	0.217	5.403	0.000	S
	AT-FU	0.35	0.40	0.05	14.28	0.316	0.050	1.000	0.323	NS
2] Heart Discomfort	BT-AT	1.68	0.25	1.43	85.12	0.931	0.147	9.685	0.000	S
	AT-FU	0.25	0.35	0.1	40	0.304	0.048	2.082	0.044	NS
3] Sleep Problem	BT-AT	1.55	0.20	1.35	87.1	1.210	0.191	7.056	0.000	S
	AT-FU	0.20	0.28	0.08	40	0.267	0.042	1.778	0.083	NS
4] Depressive Mood	BT-AT	1.70	0.40	1.30	76.47	1.043	0.165	7.885	0.000	S
	AT-FU	0.40	0.45	0.05	12.5	0.221	0.035	1.433	0.160	NS
5] Irritability	BT-AT	1.55	0.20	1.35	87.09	1.122	0.177	7.609	0.000	S
	AT-FU	0.20	0.28	0.08	40	0.267	0.042	1.778	0.083	NS
6] Anxiety	BT-AT	2.65	0.53	2.12	80.00	0.966	0.153	13.916	0.000	S
	AT-FU	0.53	0.58	0.05	9.43	0.389	0.061	0.813	0.421	NS
7] Physical & Mental Exhaustion	BT-AT	2.28	0.35	1.93	84.65	0.656	0.104	18.564	0.000	S
	AT-FU	0.35	0.58	0.23	65.71	0.530	0.084	2.683	0.011	NS
8] Sexual Problem	BT-AT	0.80	0.33	0.47	58.75	0.716	0.113	4.198	0.000	S
	AT-FU	0.33	0.35	0.02	6.06	0.158	0.025	1.000	0.323	NS
9] Bladder Problem	BT-AT	0.55	0.05	0.5	90.90	1.062	0.168	2.977	0.005	S
	AT-FU	0.05	0.10	0.05	100	0.221	0.035	1.433	0.160	NS
10] Dryness of Vagina	BT-AT	0.55	0.08	0.47	85.45	0.679	0.107	4.425	0.000	S
	AT-FU	0.08	0.10	0.02	25	0.158	0.025	1.000	0.323	NS
11] Joint & Muscular Discomfort	BT-AT	3.10	0.45	2.65	85.48	0.662	0.105	25.311	0.000	S
	AT-FU	0.45	0.83	0.38	84	0.490	0.078	4.837	0.000	NS

Table No. 03: Paired 'T' Test for Objective Parameter's.

PARA-METER'S	MEAN RANK		DIFFERENCE	% OF CHANGE	SD	SE	't' value	'P' value	REMARK
	BT	AT							
Body Weight	59.83	60.85	1.02	1.70↑	1.050	0.166	6.176	0.000	Significant
Systolic BP	128.50	123.15	5.35	4.16↓	4.693	0.742	7.209	0.000	Significant
Diastolic BP	81.85	79.10	2.75	3.35↓	6.558	1.037	2.652	0.012	Significant
Pulse Rate	79.05	75.75	3.3	4.17↓	5.967	0.943	3.498	0.001	Significant
Haemoglobin	10.95	11.28	0.33	3.01↑	0.466	0.073	4.408	0.000	Significant
Serum Calcium	8.875	9.314	0.439	4.94↑	0.323	0.051	8.593	0.000	Significant
Serum Oestradiol	16.93	17.29	0.36	2.12↑	0.368	0.058	6.179	0.000	Significant

DISCUSSION

In *Ayurveda*, *Rajonivritti* is considered as *Swabhavika vyadhi* as its one of the physiological state of woman's life. The logic behind the age of *Rajodarshana* (Menarche) & *Rajonivritti* (Menopause) is that the *Raja* is a *upadhatu* of *rasa dhatu*, which functions better in *Tarunavastha* than the *Praudhavastha*, due change in *doshik* dominancy. There are other factors too specifically *kaal*, *swabhaav* and *vaya*. Therefore in a *Swabhavik Kshaya Avastha* and symptoms associated with this condition are a reflection of disturbed *Pitta* and *Kapha* by dominating *Vata*. *Rajonivrittijanya lakshana's* are the symptoms developed after *Artava kshaya* in *Vrudhawastha* due to *prakopit Vayu*. *Sharirik* as well as *Manasik lakshanas* are seen. In present era as females are leading altered life style i.e. excessive physical and psychological stress leads to early menopausal symptoms.

The formulation contains total 8 *aushadhi dravyas* among them 4 having Isoflavones i.e. *Rajashimbi*, *Shatavari*, *Yashtimadhu* and *Atasi*. They also acts as *balya* and *rasayan*. *Madhulika* as a base containing protein in large amount with dietary fibres in it with increase in *deepti* of *agni*. *Brahmi* acts as *medhya*, *smrutiprad* and *rasayan* helping in *manas lakshanas* of *rajonivritti* like anxiety, depression, irritability, insomnia etc. *Kukkutanda twak bhasma* having Calcium compound which helps in increasing the same in the body which is seen depleted in Menopausal period. *Guda* as sweetening agent and helps in enhancing digestion as well as increasing mild Haemoglobin. The *anupan* advised for this granule formulation was *Godugdha* as it helps in *dhatu vardhana karya*, and it is *balya*, *rasayan*, *ayukar*.

The symptomatic relief in this study was very good, many patients were satisfied with the therapy. The maximum relief was found in psychological symptoms with joint & muscular discomfort. Due to alleviation of the psychological symptoms even the heart discomfort; palpitation was relieved. The main action of oestrogen at the tissue level is a reduction of the rate of bone turnover by limiting osteoclasts to create new pits.^[5] Therefore the granules containing oestrogens of plant origin have helped in slight increasing the Serum Oestradiol level, which enhances the menopausal women health by decreasing Menopausal symptoms. The *Bruhan dravyas* also helps in further development of *dhatu* which in turn act as *rasayan* on body. Therefore there is decrease in all 11 menopausal symptoms was observed.

In Objective parameters, the Blood pressure and pulse rate was decreased or normalised. This may be due to the phytoestrogenic action of the formulation which helped in decreasing atherosclerosis. There was slight increase in body weight as the *dravya* in the granules included were having *bruhan karma*. The mild increase in Serum Oestradiol level was observed due to mild effect of phytoestrogens on the body as the study was for very

short period of time. There was good difference in improvement of the Serum calcium was observed as *Kukkutanda twak bhasma* which was direct supplement to Calcium, and along with that decrease in action of osteoclastic activity with the help of phytoestrogenic drug helps in decrease the rate of bone loss. Hence it may also result in slow & gradual formation of bones due to Calcium intake. Vaginal smear was done to detect any cervical pathology present before treatment to exclude the case in the study, and after treatment it was performed to see effect of phytoestrogen on cervix leading to any abnormal cervical pathology due to overdose of oestrogen which is seen as adverse effect of HRT. In this study, after treatment also there was no any change in report, suggesting that there is no adverse/abnormal effect on the cervix.

CONCLUSION

Health drink formulated with the indigenous drugs is beneficial in improving menopausal symptoms along with increasing the Serum Oestrogen and Calcium levels.

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