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Research Article

EFFECT OF *DHATRYADI GHRITHM* IN "DIMINISHING OVARIAN RESERVE"

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ABSTRACT

Background: Diminishing ovarian reserve (DOR) describes women of reproductive age with regular cycles, mostly ovulatory, whose response to ovarian stimulation is reduced compared to women of comparable age. The most appropriate correlation of DOR can be done with *Dhatukshaya Vandya. Dhatraydi Ghrithm* mentioned in *Sahasra Yogam* is said to have implicit effect in enhancing reproductive potential.

Objectives: To evaluate the effect of *Dhatryadi Ghrithm* in "Diminishing ovarian reserve".

Materials and methods: It was a pre and post interventional study done during the time period July 2017 to December 2018 with a sample size of 20. Females between the age group of 20-35 years, diagnosed with DOR attending Outpatient Department of Govt. Ayurveda College Hospital for Women and Children, Poojappura, Thiruvananathapuram were selected. Serum Anti Mullerian Hormone (AMH), Serum Estradiol, Antral Follicular Count (AFC) and LH/FSH ratio, Ovarian volume was assessed on the 2nd day of the cycle after completing 90 days of *Ghritha* administration. Paired t test was used to analysis the data statistically.

Results: 55 % of total study population were in the low fertility group and 45% confined to the very low fertility group.7 out of 20 patients obtained satisfactory level of fertility after 3 months of treatment. There was a considerable increase in mean value of AMH before and after treatment (2.62-→9.01), p-value 0.001. AFC was also significantly increased after three months of treatment, p-value <0.002. 3 patients were conceived during the study period.

Conclusion: Study concluded that the *Dhatryadi Ghrithm* was found to be effective in increasing AMH and AFC, but it did not have any effect on serum Estradiol, LH/FSH ratio and in Ovarian volume.

INTRODUCTION

Ovarian reserve refers to the reproductive potential left within a woman's two ovaries based on number and quality of eggs. Diminishing ovarian reserve (DOR) is the loss of normal reproductive potential in the ovaries due to a lower count or quality of the remaining eggs[1]. DOR can occur approximately 1% of women worldwide. But nowadays 10-30%of female infertility is due to DOR [2]. This has several major medical consequences including infertility, decreased bone mass with risk of fracture, abnormal uterine bleeding from lack of regular ovulation, and hot flashes. [3]

In *Ayurveda* there is no direct reference of DOR but condition can be most appropriately correlated with *Dhatukshaya Vandhya*, one among 6 types of *Vandhya* explained in *Haritha Samhita* [4]. It is due to depletion of *Dhatus* or due to inadequate formation of *Dhatus*, especially *Arthava* and *Sukradhatu* which in turn leads to reduction in fertility potential and ultimately *Anapathyatha.* In DOR, the physiological function of *Pitta* is impaired earlier and there is early domination of *Vata* which results the findings of *Dhatukshaya* like low AMH level, low AFC, short cycles, irregular cycles and ultimately leads to stoppage of periods. *Dhatryadi Ghrithm* mentioned in *Sahasra Yoga*[5] is said to have implicit effect in enhancing reproductive potential *(Vandhya Cha Peetwa Labathe Cha Garbham).*

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The objective of the study was to evaluate the effect of *Dhatryadi Ghrithm* in "Diminishing Ovarian Reserve'' in females of age group 20-35 yrs.

Ethics

The study was approved by Institute Ethics Committee (Ref. No. AVC IEC 273/2017) and informed written consent was obtained before enrolment.

MATERIALS AND METHODS

Single Group, Pre and post interventional study with sample size of 20 was conducted in the OPD of Government Ayurveda college Hospital for Women and Children, Poojappura,Thiruvananthapuram.

Inclusion Criteria

- Females in the age group of 20-35 years, diagnosed with "DOR" during the time period July 2017-December 2018 were included in the study.

Exclusion Criteria

- Peri menopausal women
- Fragile X syndrome
- Patients with systemic illness like diabetic mellitus, thyroid disorders
- DOR due to administration of chemotherapy, radiation therapy
- Patients who had massive ovarian interventions
- Auto immune disease, malignancy

Procedure

Females in the age group of 20-35 yrs having complaints of primary infertility, secondary infertility, short cycles were selected from Outpatient Department of Govt. Ayurveda College Hospital for Women and Children, Poojappura, Thiruvananthapuram. Detailed clinical examination was done on the day of first visit. Lab investigations and USG were taken on the second day of menstruation. Patients diagnosed with DOR after getting informed written consent were selected for the study. The patients were asked to report on the first day of next menstrual cycle. The enrolled patients were given *Deepana* and *Pachana* drugs (*Ashtachoornm*)[6] 5g twice daily for duration of 2-5 days followed by *Dhatryadi Ghrithm* 15 gram twice daily for a period of 3 months. All of them were followed up after completing 90 days of drug administration.

Assessment

AMH, Serum estradiol, AFC and LH/FSH ratio, and Ovarian volume were assessed on the 2nd day of the cycle when the patient gets menstruation after completing 90 days of drug administration.

Primary Outcome

- Changes in Basal serum AMH level and Basal AFC after administration of *Dhatryadi Ghritha*

Secondary Outcomes

- Changes in Basal LH/FSH ratio.
- Changes in Basal Serum Estradiol
- Changes in Basal Ovarian Volume

Statistical Analysis

Data was analysed statistically using Paired t test.

Drug Review

Table 1: *Dhatraydi Ghrithm*

No	Drug	*Rasa*	*Guna*	*Veerya*	*Vipaka*	*karma*
1	*Dhatri*	*Pancha Rasa* except *Lavana, Amla* mainly	*Ruksha*	*Sita*	*Madhura*	*Tridoshahara*
2	*Vidari*	*Madhura*	*Guru Snigdha*	*Sita*	*Madhura*	*Vatapittahara*
3	*Ikshu*	*Madhura*	*Guru Snigdha*	*Sita*	*Madhura*	*Pittahara*
4	*Satavari*	*Madhura Tiktha*	*Guru Snigdha*	*Sita*	*Madhura*	*Vatapittahara*
5	*Kushmandam*	*Madhura*	*Laghu Snigdha*	*Sita*	*Madhura*	*Vatapittahara*
6	*Mridwika*	*Madhura*	*Guru Snigdha*	*Sita*	*Madhura*	*Vatapittahara*
7	*Yastimadhu*	*Madhura*	*Guru Snigdha*	*Sita*	*Madhura*	*Vatapittahara*
8	*Chandana*	*Madhura Tikta*	*Laghu Ruksha*	*Sita*	*Kadu*	*Kaphapittahara*

RESULTS

The most common age group enrolled was in between 31-35 years which constituted around 55% of the study population (Table 2). Majority of them were following sedentary life style habits. 60% of the patients were of *Madhyama Satwa* & 40% of them possessed *Avara Satwa* status. 75% of patients were having poor appetite and only 25% were having normal appetite. Most of the patients (80%) were *Vata-Paithika Prakruthi*, 20% had *Kapha-Vata Prakruthi*. Psychological statuses of patients were also assessed.60% were anxious, 25% were stressed and 15%were depressed. 60 % were preferring *Katu Rasa* and 25% *Amla Rasa*. Most of the patients had disturbed/ reduced sleep. Majority had *Krura Koshta* (80%). 80 % of patients had primary infertility.

Table 2: Baseline characteristics of the study

Age (Yrs)	**Frequency**	**Percentage**
20 - 25	2	10%
26 - 30	7	35
31 - 35	11	55
Nature of work		
sedentary	11	55
Moderate	6	30
Hard work	3	15
Prakruthi		
KV	4	20
VP	16	80
PK	0	0
Type of Infertility		
Primary	16	80
Secondary	4	20

Table 3: Percentage Distribution regarding menstrual pattern

Presenting complaints		**Frequency**	**Percentage**
Menstrual interval (in days)	19 - 22	1	5
	22 - 25	9	45
	26-29	7	35
	30-33	1	5
	More than 33 days	2	10
Cyclic pattern	Regular	18	90
	Irregular	2	10
Menstrual duration(in days)	1 – 3 days	13	65
	4 – 6 days	6	30
	6-9 days	1	5
Amount of bleeding	Spotting	1	5
	Scanty	12	60
	Moderate	5	25
	Mild	1	5
	Excessive	1	5
Dysmenorrhoea	Present	7	35
	Absent	13	65

Table 4: Percentage Distribution Regarding Gynaecological Complaints

Complaints		**Frequency**	**Percentage**
Abnormal vaginal discharge	Present	9	45
	Absent	11	55
Dyspareunia	Present	6	30
	Absent	14	70

Primary outcome measured was the changes in Basal serum AMH level and Basal AFC after administration of *Ghritha*. Among the 20 patients before treatment nobody was in the class of 15.7-28.6 (satisfactory fertility), but after treatment 7 patients obtained satisfactory level of fertility. After three months of treatment considerable increase in value AMH was found. Mean value of AMH was 2.62 before treatment. It was increased to 9.01 after the treatment period of three months. As the paired t test showed a p-value 0.001, statistically significant.

Before treatment none of the subjects had normal antral follicle count. Majority was having mean AFC level 3-4 & 5-6. After treatment 7 patients belongs to mean AFC level of 5-6. 3 patients had AFC level 7-8. 0ne patient had AFC level of 9-10. After three months of treatment considerable increase in the number of antral follicles were found. Before treatment the mean value of AFC was 3.41. It was increased to 5.29 after the treatment period of three months. As the paired t test showed a p-value <0.002, statistically significant.

Table 5: AMH and AFC values before and after treatment

S.No	AMH value before treatment (pmol/L)	AMH value after treatment (pmol/L)	AFC before treatment	AFC after treatment
1.	1.6628	1.9324	5	8
2.	5.1681	16.99	4	5
3.	1.1235	1.9706	4	4
4.	1.1235	16.54	1	2
5.	5.4602	15.88	5	8
6.	3.9997	conceived	0	conceived
7.	7.86	11.76	5	6
8.	.4494	.2247	1	2
9.	4.5389	conceived	0	conceived
10.	4.5165	8.8307	5	6
11.	2.294	16.6	4	6
12.	3.6626	11.5	2	3
13.	1.1235	1.01	3	2
14.	2.1346	2.471	2	4
15.	2.3818	16.08	3	7
16.	.2247	1.327	2	6
17.	2.6964	13.53	4	5
18.	2.247	17.4	2	10
19.	.2921	2.247	6	6
20.	2.1122	conceived	5	conceived

Table 6: Statistical data of AMH

	N	AMH		Paired difference		Paired t test	
		Mean	sd	Mean	sd	T	p
BT	17	2.62	2.10	6.395	6.196	4.256	0.001
AT	17	9.01	6.98				

Table 7: Statistical data of AFC

	N	AFC		Paired difference		Paired t test	
		Mean	sd	Mean	Sd	t	p
BT	17	3.41	1.54	1.882	2.088	3.717	0.002
AT	17	5.29	2.29				

Secondary outcomes measured were

- **FSH/LH Ratio**- Out of 20 patients nobody had a normal LH/FSH ratio of 1:1. 3 patients had ratio of 1:1 after treatment. But there was no considerable change in FSH/ LH ratio. (p value:0.637)
- **S. Estradiol**- No considerable increase in value of serum estradiol was found after three months of treatment. Mean value of serum estradiol before treatment was 47.83 and was increased to 52.84 after treatment. As the paired t test showed a p-value 0.298 (i.e., p >0.05), it can be concluded that it was statistically insignificant.
- **Ovarian volume**- All patients had normal level of ovarian volume (<15 cc) before treatment. Majority were under the group 3-6 cc and after treatment was no significant increase was observed.

Other Relevant Findings:

- 3 patients were conceived
- 7 patients with dysmenorrhea had complete cure after treatment

DISCUSSION

Ovarian reserve is an indirect measure of future fertility and predictor of onset of menopause. It describes the functional potential of the ovary and is a complex clinical phenomenon influenced by age, genetics, and environmental variables[7]. Ovarian reserve screening is generally done on day 2,3,4 of the menstrual cycle[8]. DOR also known as poor ovarian reserve, is a condition of low fertility characterized by decreased quality and quantity of oocytes in the ovaries. DOR has been recently defined by ESHRE, the Bologna's criteria, according to which at least two of the following three features should be present (1) Age > 40 years (2) abnormal ovarian function test i.e., AFC, AMH (3) poor ovarian response in a previous stimulated cycle[9], i.e., less than 3 follicles after standard gonadotropin stimulation.DOR presents no symptoms in most women. However, patients with this condition might experience any of the following symptoms:

- Difficulty getting pregnant
- Late or absent menstrual periods
- Shorter menstrual cycles such as from 28 days to 25 days
- Heavy Menstrual Flow
- Miscarriage

Reports suggest that patients with a diminished ovarian reserve have the only option of IVF with a donor egg [10]. Regarding the *Dosa* concept in reproduction, it is well understood that *Vata* has a prime role in reproduction as *Apana* does the function of *Arthava* and *Garbanishkramana* [11], *Sukrartava Ambuvaha Srotovichari* by *Samana* [12] and *Vyana Vayu* influences various movement including *Beejagathi* and *Poshana*[13]*.* The *Agneya* character of *Arthava* and preconceptional preparation using *Pittala* stuff shows the inevitable role of *Pitta* in conception. All the endocrine activities including maturation of graffian follicles, ovulation, formation of corpus luteum and associated changes in the uterus, menstruation, influence on estrogen, progesterone at different phases can be attributed to normal functions of *Pitta*.

The normal state of *Doshas* is disturbed due to improper *Maidhuna*, suppression of natural urges, abnormalities in diet such as excessive, inadequate, unwholesome, incompatible, etc, excessive intake of rough, bitter, astringent, salty, sour, hot foods, and psychological abnormalities like fear, anxiety, anger, etc leading to the vitiation of *Vata* and qualitative decrease of *Pitta* which ultimately causes *Vandhyatwa*. Analyzing *Vandhyatva* in *Ayurveda* is not limited to the non-achievement of pregnancy but also includes failure of a successful continuation of pregnancy. The treatment principle adopted should normalize the vitiated *Vata* and *Pitta*.

The most appropriate correlation of DOR can be done with *Dhatukshaya Vandhya*. Condition like *Rasa Dhatu Rupa Arthava Kshaya* can be considered as a reduction in reproductive potential manifested due to oxidative stress and infections etc. which are seen in occult primary ovarian reserve condition and diminished ovarian reserve condition. *Sarvadhatu Pariksheena* can be seen in patients who have undergone chemotherapy etc. where DOR main reason for infertility. Later stages of *Balakshaya Vandhya* can be correlated with premature ovarian failure where *Sarva Dhatu Pariksheena Avastha* can be seen. *Vandhyatwa* due to *Beeja Dushti* as seen in *Shanda, Vartha*, etc can be correlated with POF seen in X – linked chromosomal abnormalities. *Garbhakosha Bhanga* and *Vandhyathwa* due to *Arthavavaha Srothovedha* can be correlated with DOR manifested due to depletion of primordial follicles after massive ovarian surgery. Symptoms like *Daaha, Santhaapa* (hot flushes) *Rajo Athipravruthi* (shortening of menstrual cycle) are seen in early stages of DOR [14]. In the early stages *Dhatukshaya Vandhya* is manifested as *Rasakshaya, Arthavakshaya* and in *Vyadhyavastha, Rasadhi Saptha Dhatu Pariksheena* occurs. Finally, it leads to *Bala kshaya*. When untreated and *Apathya Sevana* (unwholesome habits) leads to reduction in fertility potential and ultimately *Anapathyatha*.

Markers of ovarian reserve are considered as the most important parameter for assessing the effect of treatment in "DOR". Out of twenty patients 3 patients were conceived during the study period. It was the best result of the study, because there were no other interventions, only *Dhatryadi Ghritha* was given for a period of 3 months. There were significant changes observed in the values of AMH and AFC after treatment i.e., P value was significant.

Dhatryadi Ghritha contains *Amalaki, Vidari, Ikshu, Satavari, Kushmandakam, Mridwika, Yashtimadhu*, *Chandana, Sitha Ksheeram* and. *Ghrithm* Contents of the *Dhatryadi Ghrita* are mainly *Madhura Rasa, Guru Snigdha Guna, Sita Virya, Madhura Vipaka,* and *Vata Pitta Hara. Amalaki, Vidari, Satavari* have *Rasayana* property and all the drugs are *Vrishya.* All the ingredients of *Dhatryadi Ghrita* maximally have action on central nervous system as anti-psychotic, anti-alcoholic and as an antioxidant. Most drugs in this formulation are found to have rich array of anti-oxidants, which slows down aging process, promote good general health and longevity. *Ghritha* enhances reproductive potential and its ingredients are proved to possess antipsychotic property.

CONCLUSION

Identification and timely intervention of DOR is crucial as, such women have a lower pregnancy rate and higher pregnancy loss compared to age matched controls with normal ovarian reserve. Majority of

women have to undergo procedures like In Vitro Fertilisation (IVF) which may require repeatedly trials, adversely affect women health, highly expensive and even with low success rates. The potential implication of our Ayurveda treatment for human reproduction could be significant not only for the preservation of fertility status but also for the prevention of diverse spectrum of health problems that emerge in women after depletion of ovarian reserve. *Samana Chikitsa* which normalises *Vata* and *Pitta*, promotes *Rasa Dhatu, Arthava Upadhatu, Sukla Dhatu* is highly beneficial in the treatment of DOR. Drugs which has *Vrishya Guna, Rasayana* property will increases the reproductive potential. Management of DOR by adopting the treatment concepts of *Dhatukshaya Vandhya* was effective in increasing AMH level, AFC count while it was not effective in increasing S.Estradiol, and regularising FSH/LH ratio and in changes of ovarian volume. The successful conception rate of the study was 15% only. No treatments can slow ovarian aging and truly prevent diminished ovarian reserve. However treatments opted for regularising the markers of ovarian reserve can improve the quality of ovum which may enhance the success rate of conception and in preventing associated health issues.

REFERENCES

1. Diminished Ovarian Reserve | Women & Infants' Fertility [Internet]. Women & Infants' Fertility Center. Available from: https://fertility.womenandinfants.org/services/women/diminished-ovarian-reserve
2. Diminished Ovarian Reserve-Department of Obstetrics and Gynecology_Available from www.columbiaobgyn.org/condition_treatments/diminished-ovarian-reserve
3. What is Diminishing Ovarian Reserve (DOR)? [Internet]. ARC Fertility. 2015 Available from: https://www.arcfertility.com/diminishing-ovarian-reserve
4. Prof (Dr) Gyanendra Pandey. Acharya Harita Samhita. First edition 2014. Vol. II. Varanasi: Chaukhamba sanskrit series office; chapter 48/1-3 page no 1312
5. Dr Nishteswar K, Dr Vidyanath R Sahasrayogam text with English translation; 4th ed. Year 2014; Varanasi, chaukhamba Sanskrit series office; page no 64
6. Aravattzhikathu K V Krishnanvaidyan, Aanekaleelil S Gopalapilla. Sahasra Yogam Sujanapriya Commentary. 27th ed. Aalapuzha: Vidhyarambham publishers; 2007, Page no 81
7. Tal R, Seifer D. Ovarian reserve testing: A user's guide. American Journal of Obstetrics and Gynecology. 2016 Oct 14. Available from https://doi.org/10.1016/j.ajog.2017.02.027
8. Testing and interpreting measures of ovarian reserve: Fertil Steril 2015; 103: e9-e17 Available from http://www.asrm.org/globalassets/asrm/asrm-content/news-and-publications/practiceguidelines/fornnonmembers/testing_ and_interpreting_measures_of_ovarian_reserve_a_committee_opinion-noprint.pdf
9. Rasool S, Shah D. Fertility with early reduction of ovarian reserve: the last straw that breaks the Camel's back. Fertility Research and Practice. 2017; 3:15 doi:10.1186/s40738-017-00411
10. Broekmans FJ. Testing for ovarian reserve in assisted reproduction programs: The current point of view. Facts Views Vis Obgyn. 2009;1: 79–87
11. Prof.Srikanthamurthy K.R Astanga hrdayam of Vagbada Sutra Sthana. Chaukhamba Krishnadas Academy; chapter 12/9 Page no 167
12. Prof.Srikanthamurthy K.R Astanga Samgraha of Vagbada sutra sthana. Vol. I. chaukhamba Orientalia; chapter 20/2 Page no 368
13. Prof.Srikanthamurthy K.R Astanga Samgraha of Vagbada sarira sthana. Vol. II. Chaukhamba Orientalia; chapter 2/2 Page no 17
14. Divya U et. al., Effect of Ayurvedic Treatment Protocol on Diminishing Ovarian Reserve. International Journal of Ayurvedic Medicine, 11(2), 228–234.

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