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Impact of Nasya on the Hypothalamic-Pituitary-Ovarian Axis In Infertility (Anoulatory cycle) -A Review Article

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ABSTRACT: Nasya not only targets the local effects in the nasal cavity but also interacts directly with the hypothalamus and pituitary gland. The hypothalamic-pituitary-ovarian (HPO) axis is critical for normal ovulatory function, and disruptions in this axis can contribute to infertility. Anovulation or oligo-ovulation refers to disrupted ovarian activity, significantly impacting fertility. Ovulation is the release of ovum from a matured Graafian follicle. Menstruation is not related to ovulation. Though menstrual cycles are regular, they can be anovular. Anovulatory cycles are generally painless and with excessive bleeding. The diseases like polycystic ovarian syndrome or disease (PCOS) and Dysfunctional uterine bleeding (DUB) have anovulatory cycles. Anovulatory cycles are one of the common causes for infertility. Chronic anovulatory cycles may cause endometrial carcinoma due to unopposed estrogens, deficient progesterone and thus endometrial hyperplasia with excessive bleeding. Hence there is a great need for treating anovulatory cycles. There is also a disturbance of Hypothalamo-Pituitary-Ovarian axis. As nasya or nasal route of medicine may stimulate this axis, any vatahara taila may be used in anovulatory cycles, thus can simultaneously treat infertility that occurred due to anovulatory cycles. In the present article, Impact of Nasya on the Hypothalamic-Pituitary-Ovarian Axis in Infertility (anovulatory cycle) is discussed.

KEY WORDS: Nasya, H-P-O axis, PCOS, DUB, anovulatory cycle, infertility.

INTRODUCTION

Nasya not only targets the local effects in the nasal cavity but also interacts directly with the hypothalamus and pituitary gland. The hypothalamic-pituitary-ovarian (HPO) axis is critical for normal ovulatory function, and the delivery of the active compounds from Nasya can stimulate neurosecretory cells in the hypothalamus, promoting the release of GnRH. This cascade effectively enhances the secretion of FSH and LH from the anterior pituitary, thereby facilitating ovulation and improving overall fertility.

Anovulation or oligo-ovulation refers to disrupted ovarian activity, significantly Infertility is a condition in women's life which indi-cates inability to procreate. Infertility is generally de-fined as one year of unprotected intercourse without conception. Sub-infertility is described as Women or Couples who are not sterile, but exhibit decreased re-productive efficiency¹. The normal secretion of gonadotropins, regulated by the hypothalamus, is essential for ovulation. The process commences with the release of gonadotropin-releasing hormone (GnRH), which stimulates the anterior pituitary gland to produce follicle-stimulating hormone (FSH) and luteinizing hormone (LH). In cases of anovulation, the absence of ovulation leads to a lack of corpus luteum formation and insufficient progesterone, resulting in a non-receptive

endometrium for embryo implantation. Conditions such as luteal phase defects and luteinized unruptured follicle syndrome further complicate the ovulatory process, necessitating interventions that can restore hormonal balance.

Aim and Objective: To understand Impact of Nasya on the Hypothalamic-Pituitary-Ovarian Axis In Infertility (Anoulatory cycle).

Methodology: Reviewing the Anovulatory Female Infertility and Role of *Nasya* in it through *Ayurvedic* classics, commentaries also recently published books and Research journals and modern science literature, the collection done and attempt to get co-relation between *Ayurveda* and Modern literature.

AYURVEDA

According to Vachaspati the word Nasaya means being in the nose or the things beneficial to the nose. Acharya to Acharya Sushruta medicines or medicated oils ad-ministered through the nose is known as Nasya. Nasya is considered as the gateway of Sirah³. Shringataka marma formed by the union of Siras (Blood vessels) supplying to Ghrana (Nose), Jinhva (Tongue), Akshi (Eye) and injury to this marma is fatal. Indu has mentioned Shringataka as a 'Shirasu Antarmadhyam'. Acharya Sushruta states that excessive Sanga, **Udbhavasthana** –Pakvashaya, **Adhisthana** –Tryavartava Yoni, **Vyaktisthana** – Beejagranthi, **Marga** – Abhyantara.

Nasya is said to exert its beneficial effects through multiple pathways. The administration of medicated oils via the nasal route promotes absorption through the nasal mucosa, reaching the olfactory epithelium and ultimately influencing the central nervous system. The absorption mechanisms include passive diffusion, transcytosis, and vascular transport. The high vascularization of the nasal cavity ensures rapid uptake of the drug, bypassing first-pass metabolism in the liver. Furthermore, the combination of external treatments such as "Abhyang" and "Sweda" enhances drug absorption by increasing blood flow and vasodilation.

As Per Modern concept

Ovarian cycle 1

The development and maturation of a follicle, ovulation and formation of corpus luteum and its degeneration constitute an ovarian cycle. For the ovulation to occur, there are series of changes that occur before release of the ovum - like recruitment of groups of follicles, selection of dominant follicle, its maturation and then ovulation.

Role of hormones in ovulation⁴

LH Surge: Sustained peak level of oestrogens for 24-48 hours in the late follicular phase results in LH surge from the anterior pituitary.

FH rise: Pre - ovulatory rise of $17 - \alpha$ - hydroxy progesterone facilitates the positive feedback action of oestrogen to induce FSH surge increase in plasminogen activator plasminogen plasmin helps in lysis of the wall of the follicle.

Thus the combined LH/FSH midcycle surge is responsible for the final stage of maturation, rupture of the follicle and expulsion of the oocyte (ovulation).

Anovular menstruation⁵

In an anovulatory cycle, the follicles grow without any selection of dominant follicle. The oestrogen is secreted in increased amount. There may be imbalance between oestrogen and FSH or because of temporary unresponsiveness of the hypothalamus to the rising oestrogen, Gonadotrophin releasing hormone (GNRH) is suppressed and thereby no ovulation. The possible causes of anovulation are – PCOD, elderly women, women with premature ovarian failure, corpus luteum insufficiency, resistant ovarian syndrome (follicles are present but FSH receptor is either absent or resistant).

Hypothalamo – Pituitary – Ovarian axis (H-P-O axis) ⁶:

The hypothalamus is connected with the anterior lobe of the pituitary through a special hypothalamo pituitary portal system of vessels.

It is directly connected with the posterior lobe of the pituitary by the supra-optic and para ventricular nuclei. The hormones liberated from the hypothalamus, pituitary and ovary are dependant to one another. A well co-ordinated axis is formed called H-P-O axis. The secretion of hormones from these glands is modified through feedback mechanism operating through this axis. This axis may also be modified by hormones liberated from the thyroid or adrenal glands.

Induction of ovulation⁷ - measures are:

☐ General – psychotherapy to increase the emotional causes, if any

☐ Drugs – Clomiphene citrate (CC), hMG, FSH, GnRH analogues
□ Surgery – Laparoscopic ovarian drilling (LOD), or laser vaporization, wedge resection, surgical removal of ovarian or
adrenal tumor, uterovaginal surgery, bariatric surgery.

Pathway⁸

Drug Through nasal route (gateway of Head) Reaches the *Shringataka marm (Siro Antarmadhyam)* Spread thought the *siras* of nose, ear, eyes and tongue. Reaches in *Shira* (Head)

Rutukala⁹ – Rutustu dwadasha raatram bhavathi drushtartavaha

Adrushtartavaapyasteetyeke bhashanthe - Su.sa.3/6

- ➤ *Ritukala* is 12 days when artava is visible.
- > Ritukala can occur without menstruation also.
- According to some it is 16 days and entire month also.
- > Ritukala denotes proliferative phase including ovulation.

Nasya and its importance¹⁰

Urdhwa jatru vikareshu viseshaannasyamishyante

Naasaahi siraso dwaram thena tadvyaapya hanthi tha<mark>an – As.Hr.20/1</mark>

- Nasya is specially mentioned for urdhwa jatru gata vikaras.
- Nose is like a door to *siras i.e.* head.
- Nasya dravya enters through the nose and cures these rogas.

Marsha sneha and its parimana¹¹:

- ➤ Utkrushta matra 10 bindu
- ➤ Madhyama matra 8 bindu
- ➤ Hrasva matra 6 bindu

Ayogya for nasya 12:

- After intake of water, madya or garavisha, After meals,
- After head bath or about to take headbath, After procedure (raktamokshana)
- Peenasa rogi with recent history, During the vega of mala, mutra etc.
- > Sutika,Kasa, swasha peeditha rogi ,After vamana, virechana ,After vasti
- On cloudy days, nasya should not be done in the above said conditions.

Nasya yogya kala and dosha¹³

- Early morning in kapha dosha
- > Afternoon in pitta dosha & sheeta kaala
- ➤ Evening and night in *vata dosha*
- Morning in swastha avastha, sarat and vasant ritu
- Evening in greeshma kaala
- ➤ Whenever sun is seen in *varsha kaala*
- ➤ Morning and evening in vatajanya siro roga, hikka, apatanaka, manyastambha, swara bhramsha
- ➤ Alternate days in others.

Pratimarsha nasya¹⁴

Those who are suffering from *urakshata*, *nirbala*, *balaka* and those who lead comfortable life, anytime and even during rain *pratimarsha nasya* can be done.

Time and dose of pratimarsha nasya14

Night or day ,After food ,After vamana ,After day sleep , After travel ,After tiredness, After coitus ,After *siroabhyanga* ,After *gandusha* ,After *mutratyaga* ,After *anjana* ,After *malatyaga*

Dose: 2 drops in each nostril

Result of pratimarsha nasya¹⁴

First 5 kaalas (upto diwaswapna) causes sroto sodhana

Next 3 kaalas (adhwa, srama and stree sanga) give relief from tiredness

Next 5 kaalas (siroabhyanga to mala tyaga) cause brightness in the eyes, keep the teeth strong and also causes samana of vata.

Marsha nasya should not be given below 7 years and more than 80 years of age 14

Pratimarsha nasya can be given to anyone starting from birth to death. If it is given daily, it works like marsha nasya.

- For a healthy individual, *nasya* with *taila* is best for daily purpose.
- The only difference of marsha nasya and pratimarsha nasya is seeghrakaaritwa and chirakaaritwa simultaneously i.e., marsha nasya works faster with better results compared to pratimarsha nasya which is slower in action.

Nasya guna – qualities (benefits) of nasya

Nasya increases thickness of skin and pleasantness of skin, strength to skandha, greeva, mukha, varsha and indriyas and hair remains black.

How to give *nasya* in anovulatory cycles

- ➤ 2 drops in each nostril from the day after complete stoppage of menstrual bleeding till day 10 of regular 28 day cycle.
- ➤ From day 10 to day 16 (or till ovulation) gradual increase of dose from 3 to 6 or 8 drops (D10 3 drops; D11-4 drops etc).
- ➤ If ovulation occurs before D13 or 14, *nasya* dose need not be increased, instead gradual decrease in dose like 7, 6, 5, 4, 3, and 2 should be given and 2 drops should be continued till next periods.
- While *nasya dravya* is given follicular study is done simultaneously from day 10 till ovulation.

Mode of action of nasya karma:

In nasya karma, the drug action may be understood that it reaches the sringaataka marma and from there spreads into various srotases. Vriddha Vagbhata is the first person who narrated the mode of action of nasya dravya.

- 1] By entering the general blood circulation after absorption.
- 2] Direct pooling into venous sinuses of the brain via inferior ophthalmic vein.
- 3] Absorption directly into the Cerebrospinal fluid.

It is known that the peripheral olfactory nerves are connected with limbic system of the brain including hypothalamus. This limbic system is concerned with multifunctional capabilities including behavioural aspects of human being and control over endocrine secretions. The experimental stimulation of olfactory nerves caused stimulation in certain cells of hypothalamus and amygdoloid complex. Keeping the head in lowered position and retention of medicine in naso-pharynx help in providing

sufficient time for local drug absorption. Any liquid soluble substance has greater chance for passive absorption through the cells of lining membrane. On the other hand, massage and local fomentation also enhance the drug absorption. The above said mechanism may help in stimulating H-P-O axis. To find the exact mechanism of *nasya* karma, pharmacokinetic studies are further required

DISCUSSION

Marsha nasya (10 *pravara* - 8 *madhyama* – 6 *avara*) is *sheeghra kari* in its function.

Hence ovulation may get stimulated with gradual increase in number of drops from 2 to 6 toor 10 depending on the tolerance of the patient to *nasya dravya*. *Nasya dravya* is given through nose and it may easily stimulate H-P-O axis working on ovaries, thus stimulating the growth of follicles and their rupture also. *Nasya* is started with small quantity and gradually increased so that it will not adversely affect and is tolerable by patient. In a patient with 28 day menstrual

cycle probable time of ovulation is around 14th day of cycle. Hence *nasya dravya* is given from day 10 to day 16 in gradual increasing dose so that follicle size also increases simultaneously. Ovaries are located in *apana vata sthana*. Drugs stimulating ovulation may have effect locally. *Nasya dravya* used through nasal route works directly on brain and can easily stimulate the H-P-O axis which plays main role in menatruation as well as ovulation.

SUMMARY AND CONCLUSION

It is understood that use of *pratimarsha nasya* after complete cessation of menstrual bleeding till day 10 of 28 day cycle and gradual increase in the number of drops till the time of ovulation and again gradual decrease to *pratimarsha nasya* dose may be effectively done in cases of anovulatory cycles. For the confirmation of ovulation, simultaneous follicular study also can be done. As the incidence of anovulatory cycles are increasing day-by-day leading to infertility in future like cases of PCOS etc., there is a great need of medicines that work faster without side effects. Though internal medicines work on ovaries locally stimulating ovulation, nasya dravya will work directly on H-P-O axis thus correcting anovular cycles and causing and ovulation.

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