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Research Paper

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PATHOPHYSIOLOGY OF ASRIGDAR W.S.R. DISTURBED INFLAMMATORY RESPONSES OF ENDOMETRIUM

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Declaration

The Declaration of the author for publication of Research Paper in Asian Journal of Modern and Ayurvedic Medical Science (ISSN 2279-0772) Dr. Sarita Mishra the author of the research paper entitled PATHOPHYSIOLOGY OF ASRIGDAR W.S.R. DISTURBED INFLAMMATORY RESPONSES OF ENDOMETRIUM declare that , I take the responsibility of the content and material of my paper as I Myself have written it and also have read the manuscript of my paper carefully. Also, I hereby give my consent to publish my paper in ajmams , This research paper is my original work and no part of it or it's similar version is published or has been sent for publication anywhere else. I authorise the Editorial Board of the Journal to modify and edit the manuscript. I also give my consent to the publisher of ajmams to own the copyright of my research paper.

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Abstract

Asrigdara is a disease manifest as excessive bleeding per vagina during menstrual period. It is a debilitating disease in woman and disturbs their routing life.

To understand the pathophysiology (*samprapti*) of disease is very important . *Samprapti* is the process in which the *doshas* get vitiated and manifest as the disease. A better treatment can be given only after prevention of vitiation of *doshas* and pacification of vitiated *doshas* .

In this article pathophysiology of *Asrigdara* is discussed w.s.r. to dysfunctional uterine bleeding. Pathophysiology of *Asrigdara* is very similar to that of dysfunctional uterine bleeding which is very common now a day and treatment option is mainly hormonal treatment and finally hysterectomy.

According to modern science aetiology of DUB is unknown, disturbed inflammatory response and altered vascular endothelial growth factor in endometrium is thought to it's resion.

Inflammatory response is very much similar to altered functioning of *pitta* and *vata* and altered growth of vessel is similar to improper functioning of *vata*.

So for *samprapti vighatan* one should take care of vitiated *vata* and *pitta* which is expressed is term of disturbed inflammatory response and endothelial growth factor, by *chikitsa siddhanta* of *Asrigdara* we can provides better, safer treatment for

heavy bleeding during menses (*Asrigdara* w.s.r. to DUB) and a new area of research will open i.e. to assess drug described in *Asrigdara* and their action on inflammatory response and endothelial growth factor is endometrium.

Key word- *Samprapti, Asrigdara,* DUB, *Pitta, Vata,* Inflammatory response

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Introduction

To understand *samprapti* of *Asrigdara*, concept of *Artava*(i.e. synonymous with *Asrika*), *doshisk* predominance in different phase of menstrual cycle is necessory. Understanding of vitiation of *doshas* by *nidan* will help for better understanding of *samprapti* of *Asrigdara* w.s.r. to DUB and its pathology and then only we understand and realise the scientific vision of our *Acharyas* about the *samprapti* of disease,which is very true till today and proven by various researches by taking helps of modern tool technologies.

Concept of *Artava*

ऋतौभवम्इतिआर्तवम[1],

The word, *Ritu* –Particular or specific time, *Bhavam*- Occurrence.

Definition of *Artava*

In female, the periodical bloody discharges having blackish colour and specific odour through vagina by *vayu*, is known *Artava*.[2]

Status of *doshas* during menstrual cycle-

Raja srava kala(menstrual period) – it mainly influenced by *vata*. Excretion or movement of any substance from one place to another is the function of '*vata*' [3]. *Rajopravritti* is main function of *Apana vata* [4](type of *vata*). According to modern gynaecological aspect, regression of endometrium, increase vascular fragility, increase inflammatory reactions and mediators are seen in this phase. [5]

Ritukala (Period till ovulation)-

Ritukala starts with establishment of '*Navin raja*' [6]. The '*Navin raja*' may be considered with proliferation of endometrium followed by ovulation.

During proliferation phase reconstruction of endometrium starts and endometrium become spongy.

It is known that *prithvi* and *jala mahabhuta* are required for regeneration and *bhautik* components of *kapha* are *prithivi* and *jala*. So in proliferative phase, *kapha* dominance is proved.

Ritu vyatita kala (Period after ovulation till next mense get start) -

After *ritukala*, *Artava* becomes *agneya* and in this period '*purana raja*' is present in *Garbhashaya* [7].Secretory activity due to various enzymatic action increases during this period [8] .These enzymatic activities are very similar to function of *pitta*.

It can be said that the stage is govern by *pitta.*

Proper balance of all the three *doshas* during whole month is responsible for normal menstruation. Disturbance in their balance leads to *vayadhi*.

Asrigdara is one of the diseases which are caused by the *doshik* disturbance and manifest as excessive bleeding per vagina.

Pathophysiology of *Asrigdara*

Asrigdara is *rakta pradoshaj vayadhi* [9] and is due to *pittaavritta apana vayu* [10]/ *pitta samyukta apana vayu*. It is the condition in which

menstrual blood excretion (*dirana*) is in abundant quantity.

To understand pathophysiology of *Asrigdara* w.s.r. to DUB (altered response of inflammatory mediator and endothelial growth factor) we have to understand

- Pathophysiology of both separately then only we can understand importance of principle of treatment of *pitta* and *vata* in *Asrigdara*.
- Use of drug those are explained by our *Acharyas* for *Asrigdara* instead of modern drug those have various side effect.
- We can prove effect of our drug on parameter like inflammatory mediator, vascular fragility, vascular endothelial growth factor etc. by various biochemical as immunohistochemical method.

Pathophysioloy of *Asrigdara* [11]

The woman who consumes excessive salty, sour, hot, *vidahi* (producing burning sensation) and unctuous substance, meat of domestic, aquatic and fatty animals, *Krishara* (made up with rice and pulses) *payasa* (rice cooked with milk and sweetened) curd, *shukta* (vinegar), *mastu* (curd water) and vine, her aggravated *vayu*, with holding *rakta* (blood) which get vitiated due to above cause, increases its amount and then reaching *raja* carrying vessels (branches of ovarian and uterine arteries) of the uterus, increases immediately the amount of *raja* (*artava* or menstrual blood) in other words the increase in amount of *raja* is due to its mixture with increase blood. This increase in menstrual blood is due to relative more increase of *rasa*, in this condition, excessive blood is discharged hence it is known as *pradara*.

Doshik disturbance by *Nidan*

Increase in *dravata* of *Rakta*

Rakta pramana utkramana

Increase amount of *raja* in *garbhashya*

From the these pathology it can inferenced that *chala* [12]*guna* of *vayu* along with *sara* [13]and *drava* [14] *guna* of *pitta* plays an important role in forming the basic *samprapti* of *Asrigdara chala guna* is for increase movement and *shara guna* disturbes stability and causes depletion of *dhatus* (tissue) [15]

Drava guna – It increases the liquid part of *dhatu* [16].

Entire process of the development of the disease can be summaries in the following ways –

Because of various causative factors *tridoshas* get vitiated and leads to *Agni mandya* which leads to *rasagani vaishamya* and this again leads *vikrita rasa dhatu* formation.Hence, the *artava* i.e. *upadhatu* of *rasa* also get vitiated and *rakta*, due to its *rasabhavata* gets vitiated and increase in amount by the *pitta prakopaka nidan sevan*, the *rasa* and *drava guna* of *pitta* get vitiated. These factors affects the uterine vascular apparatus leading to uterine congestion and increasing uterine circulation along with this *pittavrita apana vayu* and its *chala guna* leads to excessive and irregular bleeding which is termed as *'Asrigdara'*

Mechanism of normal menstruation w.s.r. to inflammatory response and endothelial growth factors of endometrium-

Menstruation is endometrial response following the withdrawal of oestrogen and progesterone subsequent to normal ovulatory cycle. These hormone act predominantly through receptors those are expressed at cellular and vascular level of

endometrium, any disturbance at these level disturbes normal menstrual process.

- Progesterone withdrawal causes shrinkage of tissue and spiral arteriol vasoconstriction under the influence of PGF2x and endothelin leading to reduce blood flow.[17]
- Specific vasoconstriction and relaxation of arteriols takes place leading to ischemia and reperfusion damage causes release of cytokines various metaloproteinases (MMP) are upregulated by falling progesterone level, casusing degradation of extracellular matrix (tissue break down) [18]
- Endometrial lysasomes get raised due to falling progesterone level, releases hydrolytic enzyme.
- Endometrial macrophages, polymorphs and granulated lymphocytes get increase greatly around the time of menstruation and influences vascular permeability and tissue breakdown. [19]
- Mast of cell commonly degranulate around the onset of mensturation, releasing tryptase, chymase and several other molecules which influences endothelial and tissue integrity. [20]
- Cytokines (IL-8) released adjacent to blood vessels in the endometrium are chemotactic for leukocytes and influential to leukocyte migration to facilitate tissue breakdown, remodelling and repair.
- Fibrin – platelet plugs appears within the superficial vessel. The balance between generation of coagulation factor and fibrinolysis, get shift towards fibrinolysis during menstruation. [21]
- Prolonged vasoconstriction, release of local growth factors and n effect of increasing oestradiol terminates the blood loss and tissue repair.
- Angiogenic growth factor, such as vascular endothelial growth factors involves in repair process by the stimulation cause by hypoxia, these are produced by migratory leukocytes in endometrium. [22]

In these inflammatory responses; division, cell interaction, constriction and dilation are function related to *vata* and enzymatic activity and inflammatory response is related to normal functioning of *pitta*, if this balance get disturbed it causes disturbance in normal menstrual bleeding pattern. According to *Ayurveda* vitiated *pitta* and *vata* in uterus causes disease known as *Asrigdara* it's sign and symptoms are very similar to Dysfunctional Uterine Bleeding (DUB). The pathology of DUB that is established by various modern tool and technique is very much similar to that of *samprapti* of *Asrigdara* that was explained approx 2000 year ago.

DUB, According to europian society of human reproduction and embryology is 'excessive bleeding (excessively, heavy, prolonged or frequent) of uterine origin which is not due to demonstrable pelvic disease, complication of pregnancy or systemic disease. It is of two types-

1- Anovulatory DUB - disturbed HPO axis and unopposed

oestrogen are found in this condition. Unopposed oestrogen has direct effect on the uterine blood supply by reducing vascular tone [24]and possibly an indirect effect through inhibiting, inhibitory vasopressin [25]release leading to vasodilation and increase blood flow. Excessive endometrial proliferation and hyperplasia with increased and dilated draining veins and suppression of spiral arterioles with increased fragility. Unopposed oestrogen increases expression of Vascular Endothelial Growth Factors which may contribute to disturbed angiogenesis.

Endometrium exposed to prolonged unopposed oestrogen, synthesize less Prostaglandins and high proportion of PGE than PGF ,increase synthesis of Nitric oxide (endothelium derived relaxing factor)

2-Ovulatory DUB – No disturbance of HPO axis and no hormonal imbalance is there.

Main defect appears to be in the control of process regulating the volume of blood lost during menstrual breakdown of endometrium, primarily the process of vasoconstriction and haemostasis.

Reduced level of endothelin causes increase in blood volume. Endometrial PG release is greatly influenced by circulating steroid level, increase in PG release and disproportionate rise of PG E2 causes vasodilatation and PG I 2 causes reduce platelet aggregation and increase fibrinolytic activities. Mast cell degranulate at menstruation, there is increase number of substances including heparin, which reduces fibrin formation and histamine which causes endothelial cell contraction, resulting in increase gap between the vascular endothelial cells and both transudation and blood cell loss.

DISCUSSION

According to modern studies disturbed HPO axis, altered hormonal balance altered haemostatic process, altered vascular fragility, disturbed expression of vascular endothelial growth factor and various altered inflammatory mediator are cause of DUB.

Ayurveda opines that all *yoni rogas* and *rajo doshas* are due to *vata prakopa*.

- In *Ayurveda*, causes related to diet, physiology and psychology are given i.e. *katu* (pungent) *rukchha*(dry), *amla* (sour) *tikchhna,* (spicy), *snigdha* (oily) meat and dairy product, excessive sexual intercourse , depression, excessive sleeps in day time, Improper eating habits disturbing *doshas* in body.

Modern science also accepts that stress disturbs HPO axis of body and causes menstrual abnormalities.

Stress and nutritional deficiency causes depletion of adrenal gland (source of body progesterone) and depletion of body progesterone.

Fast food, food that is heavy to digest and acidifying food, increases body estrogens by decreasing its excretion from body.

- About pathophysiology of *Asrigdara, Ayurveda* opines that vitiated *rakta* get increase in its amount and goes in uterus and *rajovaha shiras*.

Modern science also says that unopposed oestrogen has direct effect on the uterine blood supply and increases blood flow.

- About the treatment *Ayurveda* says that in all

yoni vyapad and *rajo doshas, vata* should be treated first.

Modern science also except that regularization of HPO axis is very important in female disorder that influences hormonal level of body and function of HPO axis are very similar to that of vata.

In treatment of *asrigdara pitta vatashamak* treatment has advice.

Apart from hormonal treatment the drug which reduces the degradation of fibrin / platelet clots to fibrin degradation product, reduces menstrual blood loss. Lysis and disturbed fragility is govern by *pitta* and *vata* in body so *vata pitta shamak* drugs describe in *Asrigdara* will be helpful, this may be new area of research in this field.

Conclusion.

In spite of vast researches in field of DUB not any safe treatment is present for it. Though modern scientists have identified altered inflammatory responses and altered vascular growth as a pathological causes but they have no treatment for it, but from above discussion it can be said that these pathological factors are very similar to function of altered *pitta* and *vata* and *Ayurveda* have treatment to pacify this *pitta* and *vata* and can give safe and better treatment in case of heavy menstrual bleeding.

It can be concluded that changes at endometrial level are very similar in menorrhagia (due to DUB) to that of disturbed function of *vata* and *pitta* in case of *Asrigdara*. Increase fragility of vessel, decrease vasoconstriction and disturbed angiogenesis (vascular endothelial growth factors) are very similar to disturbed *chala guna* of *vata* and defective haemostatic process, increase inflammatory response and increase volume of blood, unstable endometrium is similar to disturbed *drava* and *sara guna* of *pitta.* So if we treat the candition by considering *Ayurvedic* concept of *yoni roga* chikitsa i.e. *vatashamak* and *chikitsa* of *asrigdara* i.e. *vata pitta shamak* we can treat the disease better way without any side effect of hormonal treatment.

By giving consideration to these pathological event that is inflammatory response, vascular fragility and vascular endothelial growth factor we can assess action of drug described for treatment of *Asrigdara* at various biochemical and immuno histological level and can provide a better and safer treatment.

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