Proper digestion as a regulator of female reproductive physiology-An Ayurvedic perspective

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ABSTRACT

Neuro-hormonal regulation of female reproductive system is a well-established theory till today which believes that Gonadotropin-Releasing Hormone (GnRH) is the primary signal that control the activity of Anterior Pituitary Gonadotrops which regulates secretion of Follicular Stimulating Hormone (FSH) and Luteinizing Hormone (LH). Further FSH and LH regulate growth of ovarian follicle and their proper balance results in ovulation. There is consensus among experts about hypothalamus that secret GnRH is the primary site that regulates female reproductive physiology. Now researchers are focused on the factors regulating HPO axis. Since last one decade role of GIT in regulation of HPO axis became the area of interest for researchers. Various studies have been done showing relationship between GIT and HPO axis. In Ayurvedic samhitas artava dhatu and artava-vaha strotasas are considered as the factors regulating reproductive physiology. In present study literature review of Charak Samhita, Sushruta Samhita and Ashtanga Hridaya was done to understand concept of artava dhatu and its regulatory factors. It was found that artava dhatu is formed only after proper digestion. Various factors e.g. type of diet, life style and Agni (status of digestive capacity) having their role on digestion that indirectly influencing artava and artava-vaha strotas. It can be concludes that Ayurvedic concept of ahar, agni and digestion have their regulatory role on female reproductive physiology by regulating formation of artava dhatu.

INTRODUCTION

Human body is made up of different systems which act in cumulative ways to perform body activity but in modern medical world, specialty and super specialty have segregated human body. For proper functioning of body fine-tuning between each system is necessary. Various external and internal factors are influencing body homeostasis. Ayurveda being the life science believes in promotion of health of healthy one and pacification of disease of ill person (Pandey and Chaturvedi, 2005b) It has holistic approach towards body and life. There is no system wise segregation of body. As per Ayurveda body is made up of 3 doshas (vata, pitta, kapha), 7 dhatus (rasa, rakta, mamsa, meda, asthi, majja,
shukra) & 3 malas (mutra, purish, sweda) (Shastri, 2005b) Doshas are functional unit and dhatu&mala are structural unit of body. Each dosha, dhatu&mala has their specific function (Shastri, 2005d). Homeostasis between them is required for proper functioning of body (Shastri, 2005c). Each dosha have certain qualities i.e. responsible for proper functioning of dosha (Pandey and Chaturvedi, 2005c). These qualities of doshas get disturb by various factors i.e. diet, life style & mental status of body. Concept of Agni and strotasas are also two important concepts for regulation of dosha, dhatu & mala in body. A thorough understanding of dosha, dhatu, mala, Agni & strotasas are important before understanding reproductive physiology.

Concept of doshas

Physiological unit of body is termed as tridosha in Ayurveda, when they get disturbed results in diseases (Tripathi, 2011a). Vata is responsible for all movement in body and as regulator of body physiology (Pandey and Chaturvedi, 2005i). Functions related to digestion and energy expenditure are regulated by pitta (Pandey and Chaturvedi, 2005k). All anabolic activities are under control of kapha (Pandey and Chaturvedi, 2005i).

Vitiating factor of doshas

It is beauty of Ayurveda where regulating factors of doshas (physiological unit of body) in terms of diet, life style & mental status have been described in very detail and during management of disease avoidance of these factors is considered as first line of management (Shastri, 2012). This concept of causative factors for disturbing body physiology is lacking in modern physiology. Researchers have been started in this area but are in very preliminary stage. Ayurvedic concept of nidan, disturbing body physiology and causing specific disease (Pandey and Chaturvedi, 2005f) can give a new area of research for understanding links between external factors and body physiology & along with this it can help in filling gap between interlinked physiologies of different body system and give a more holistic picture of body physiology.

Factors Vitiating Doshas in Body

As per Ayurveda certain diet and life style have their role in aggravation of particular dosha.

1. Vataj nidan: (Shastri, 2005i).

Vata vardash vihara nidan

Factors related to life style i.e. ati-maithuna (excessive coitus), ati yanavaroahana, Ati-margagamana (excess travelling), ati-bharavahana (carrying excess weight), apatarpana (Excess fastin), ratri jagarana (awakening in night) aggravates vata dosha in body.

Vata vardash manasik nidan:

Shastri (Shastri, 2005j).

Pitta vardash ahara nidan

Rasa –Excessive use of amla (sour), lavana (salty) and katu (pungent) rasa

Guna – ushna (hot), tikshna (spicy) etc. diet provokes pitta

Pitta vardash vihara nidan

Factors related to life style i.e. Viruddha bhojana (eating food item those are opposite in Nature), ati madya sevana (excess alcohol), aggravates pitta dosha in body.

Pitta vardash manasik nidan:

Kaptha (anger), Ersha (jealousy)

3. Kapha vardash ahara vihar: (Shastri, 2005k).

Kapha vardash ahara nidan

Rasa –Excessive use of madhura (sweet), amla (sour) and lavana (salty) rasa

Guna – Guru (heavy), snigdha (oily/fatty), abhishyandi (diet having ability to obstruct stotasa) etc. diet provokes kapha

Kapha vardash vihara nidan

Factors related to life style i.e. sedentary life style, adhyashana (eating before digestion of Previous food), ajeerana (indigestion), divaswapna (sleeping during day time) aggravates kapha dosha in body.

Kapha vardash manasik nidan:

Lobha (greed)

Concept of Agni and Dhatu:

Agni that is present in body, termed as kayagni is divided into three as (Pandey and Chaturvedi, 2005e).

Jatharagni: It looks after digestion and absorption of food.

Bhootagni: It converts all vijateeya panchabhaustic drayvas to sajateeya drayvas.

Dhatvagni: It is present in their respective dhatus and performs synthesis and breakdown of dhatus.
There are four functional state of _agni_ according to predominance of _dosha_ and _duskya_ (Pandey and Chaturvedi, 2005d) i.e.

**Samagni**: It is due to influence of normally equilibrated _dosha_. It ensures complete digestion of food ingested at proper time without any irregularity leads to proper functioning of _dhatus_.

**Visamagni**: It is due to influence of predominance of _vata dosha_. In this state function of _agni_ is irregular and fitful. It sometime helps the process of complete digestion and other time improper digestion. Thus leads to improper formation of _dhatus_.

**Tikshnagni**: It is due to influence of predominance of _pitta dosha_. In this condition _agni_ is excessively excited, it easily digests even a very heavy meal, in very short span of time and when it gets no food to digest it starts digesting _dhatus_ and thus cause _dhatus_ shosha.

**Mandagni**: It is due to influence of predominance of _kapha dosha_. In this state _agni_ in unable to digest even a small quantity or otherwise even easily digested food leads to _vidaha_.

Functions of _jatharagni_ includes

- Digestion of food
- Saarakitta vibhajana

After function of _jatharagni_ ahara rasa get form, and then _bhootagni_ and _dhavagni_ comes into play so _vijateeya ahara rasa_ get converted into _sajateeya_ to different _mahabhutas_ of body and after functioning of _dhatu paka_ gives nourishment to body tissue.

But when proper functioning of _agni_ gets disturbed, _ama_ gets formed at various levels in body that leads to different pathological conditions.

- Apakva ahara in amashaya
- Apakva ahara rasa in amashaya
- Ama at dhatu level

When food gets properly digested it forms _sara_ and _kitta bhaga_. _Sara bhaga_ get absorb and after digestion with _dhavagni_ forms _sthayi_ and _asthayi poshaka dhatu_. _Sthayi_ poshaka _dhatu_ gives nutrition to permanent _dhatu_ i.e. _sthayi_ rasa _dhatu_ gives nutrition to _rasya dhatu_ proper and _asthayi rasa dhatu_ after functioning of _raktagni_ forms _sthayi_ and _asthayi rakta dhatu_, in the same manner other _dhatu_ get form and get their nutrition from their previous _dhatus_. _Dhatus_ are structural unit of body and have their specific function. _Rasa_, _rakta_, _mamsa_, _meda_, _asthi_, _majja_ and _shukra_ are 7 _dhatus_ described in _Ayurveda_, each have their specific function (Shastri, 2005e).

Disturbance in function of _agni_ at any level i.e. _jatharagni, bhutagni_ and _dhavagni_ leads to formation of _ama_ that is causative factor of different pathological conditions. But gross digestion takes place in _amashaya_, that’s why _Acharya_ has described formation of _ama_, primarily in _amashaya_.

Due to improper functioning of _agni_, food remain undigested and form _ama_ which is foul in smell, very slimy and vitiates _doshas_ and _dhatus_ when get absorbed (Tripathi, 2011b).

**Symptoms of Ama**

- Srotarodha
- Weakness
- Heaviness
- Coated tongue
- Improper digestion

This _Ama_ is responsible for vitiation of all the _doshas_ and _dhatus_ (Tripathi, 2011c).

Concept of _agni_ is very different concept in comparison to of modern concept of digestion. In modern Gastroenterology digestion takes place in body by the help of various types of enzymes. There is no direct evidence about the longevity, health, cheerfulness, plumpness, luster vitality etc. having relation with proper digestion as _Ayurvedic_ concept about function of _agni_ is (Pandey and Chaturvedi, 2005a). But new researches has shown and giving glimpse that has been well elaborated in _samhitas_ in relation to concept of _agni_ and _ama_. Researchers has shown that apart from digestion digestive system has control on immunity, brain and hormonal secretion.

**Concept of Srotas**

It is very unique concept of _Ayurveda_. _Srotasas_ are the structures in human body through which _dhatu_ and _doshas_ moves. _Srotasas_ allows materials to pass through them very slowly. _Acharya Charak_ has described thirteen major _srotasas_ (Pandey and Chaturvedi, 2005m) along with it _Acharya Sushruta_ has described 2 extra pair of _srotasas_ in female i.e. _Artavavaha srotas_ and _Stanyavaha srotas_. _Artavavaha srotas_ are two in numbers and having their root in _garbhashaya_ and _artavavahi dhamanis_ (Shastri, 2005a).

**Functions of Srotas**
Srotasas have important role in formation, maintenance and nutrition of dhatu. Acharya Charaka defines Srotas as transporting channels of dhatus (tissue elements) undergoing transformation (Pandey and Chaturvedi, 2005h). This transformation of element occurs with the aid of specific Agni (digestive power specific to each element) located at the base or root of each Srotas. They are variously called as Poshaka dhatus (providing nutrition), Asthaya dhatus (circulating metabolites) and Margag dhatus (moving through channels). Growth and development, depletion of body tissues take place only through Srotasas (Pandey and Chaturvedi, 2005j). Thus, proper functioning of srotasas is necessary to maintain the health.

Faulty diet, life style and psychology vitiates srotasas and certain gunas of specific doshas and when that specific dosha reaches at particular vitiated site of srotas causes srotodushti (Pandey and Chaturvedi, 2005f). The main signs of the vitiation of the srotas are (Pandey and Chaturvedi, 2005g) 1. Atipravrutti–increased flow of contents of the srotas. Sanga–Obstruction in the flow of contents in the srotasas 3. Sira granthi–Appearance of nodular growth in the srotasas 4. Vimarga gamana – Diversion in the flow of contents of srotas.

Ayurveda opines that vitiation of doshas are prime for generation of disease. Concept of Anshamsa dusti of Doshas (Tripathi, 2011d) and Kha-Vaigunya and srotodushti is also a very important concept for a disease process. Every Dosha has its specific gunas and in a disease, specific guna get vitiated by particular nidan sevana (Pandey and Chaturvedi, 2005f) Abnormalities at particular site of body (very similar to concept of Kha-Vaigunya of Srotasas) are also starts with nidanesevana. Such treatment that gives consideration to whole disease process (i.e. Samprapti Vighatana) is beauty of Ayurveda whereas in Modern Medicine after effect of causative agent on body is treated, they have no concept about management of body homeostasis which gets disturbed in the state of Disease.

**Formation of artava**

Proper functioning of reproductive physiology can be assessed by proper functioning of artava dhatu and artava-vahā srotasas. Artava is final outcome of reproductive physiology either in form of regular menstruation or proper conception, because in samhitas conception is considered as function of aartava (Shastri, 2005f).

Factors which regulate formation of artava also regulate whole reproductive physiology. To understand these regulatory factors process of artava formation should be understood in detail. It is clearly explained in Ayurveda that after proper digestion of rasadi dhatu, raja / artava forms in female every month (Shastri, 2005h). Here monthly formation of artava indicates ovulatory cycle because after ovulation if conception has not taken place menstrual bleeding takes place every month.

Dhatus moves in body through their respective channels. It is clearly described in samhitas that raja is formed from rasa dhatu in body during digestive process that accumulates in garbhashay throughout the month by fine vessels present in uterus and get excreted every month for three days through yoni.

**Role of diet in controlling reproductive physiology in light of role of leptin and its relation with HPA axis**

Ayurveda opines that generalized health, nutrition and proper digestion have relation with artava formation (Satyapal, 2008a). In girl, before onset of puberty, as yoni (reproductive organ) is underdeveloped artava is not expressed, it is present in whole body. Due to effect of diet and generalized body health this artava comes in yoni at the age of twelve year and get excreted through vagina (yoni mukha) every month (Satyapal, 2008b).

Artava get form from rasa dhatu after proper functioning of Agni. This artava reaches every month to uterus by aartava–vahi dhamanis where fine blood vessels provide nutrition to uterus, artava get accumulate throughout the month to provide nourishment to the fetus if conception taken place and if it not happens this accumulated artava get excreted through yoni mukha every month (Shastri, 2005g).

Proper functioning of agni is responsible for proper artava formation. Modern physiology also started accepting that nutrition affects HPO axis and thus have effect on formation of sex hormones. Liver that is important organ related with metabolism and detoxification plays important role in regulation of reproductive physiology.

Estrogen and progesterone are two basic hormones which are important for various reproductive functions i.e. development of reproductive organ, proper menstrual flow, oocyte development for fertilization, capacitation, fertilization, embryo implantation and development.

It is proven now that reproductive physiology depends on the energy reserves stored as fat in adipose tissue. In 1994, leptin was discovered that was the first adipokine which linked missing link between body nutrition and reproduction. Leptin is a 16kDa peptide hormone secreted mainly from adipose tissue plays important part in regulation of body weight and energy expenditure (Friedman and...
Halaas, 1998). Plasma level of leptin is regulated by feeding and fasting. Leptin not only regulates body weight homeostasis, but also thermo genesis, angiogenesis, hemopoiesis, osteogenesis, chondrogenesis, neuroendocrine and immune function (Bouhoumé et al., 1998; Fantuzzi and Faggioni, 2000; Sagawa et al., 2002; Khan et al., 2012). Leptin have regulatory role in ovarian function, occytes maturation, embryo development as well as implantation and placentation (Cervero et al., 2005). Researchers have demonstrated that leptin plays an integral role in the normal physiology of the reproductive system with complex interaction at all levels of hypothalamic pituitary gonadal axis (HPG), stimulatory effects at the hypothalamus and pituitary and inhibitory action at the gonads. Thus leptin explains relation between metabolic status with the reproductive axis that is very similar to the concept of aartava dhatu formation which is under control of ahar, status of agni and ahar rasa formed after proper digestion.

Role of Leptin in the Regulation of HPG Axis

Gonadotropin Releasing Hormone (GnRH) cells of the hypothalamus are the primary regulators of reproductive axis, these cells reside in the brain in the preoptic area of the hypothalamus. GnRH is secreted into the hypophyseal portal blood vessels and controls secretion of the Pituitary Gonadotropines Luteinizjing Hormone (LH) and follicle stimulating hormone (FSH) (Chehab et al., 1996). Studies are showing that in human, patients lacking leptin protein (Strobel et al., 1998) or functional leptin receptor (LEPRs) (Clément et al., 1998) do not attain pubertal maturity and have low serum level of FSH & LH. A threshold leptin concentration is important for initiation of the menstrual cycle and the function of reproductive system. Leptin receptor (LEPR) is expressed abundantly with in arcuate and ventromedial hypothalamic nuclie which controls both sexual behaviour and food intake (Mercer et al., 1996). This evidence explains and gives experimental evidence about the Ayurvedic concept which states that ar tava formation (which is responsible for reproductive function and menstruation) is regulated by ahar and proper functioning of Agni, vata and strotasas.

Leptin has direct effect on the anterior pituitary (Jin et al., 1999). Pituitary tissue culture studies showed that leptin induces a dose-related increase in LH, FSH and prolactin release via nitric oxide synthase activity in the gonadotropes (Yu et al., 1997). Several studies showed that restricted feeding inhibits LH secretion but leptin treatment in these subject results in LH surge (Amstalden et al., 2002). In leptin deficient (ob/ob) mice leptin administration accelerates sexual maturation and puberty in normal female mice (Ahima et al., 1997). Rodents with LEPR deficiency have hypothalamic hypogonadism, resulting in delayed pubertal development and infertility too. It has been found that there is synchronicity of LH, estradiol and leptin rhythmicity during mid-to-late follicular phase of the menstrual cycle in healthy woman (Licinio et al., 1998). These studies are showing that regulation of LH secretion (important for ovulation) is regulated by leptin and thus establishes the link between nutrition and generalized health of body on regulation of reproductive physiology.

Role of leptin in ovarian function

Leptin receptors (LEPRs) have been identified in granulosa, theca and interstitial cells of the human ovary (Sir-Petermann et al., 1999) and leptin protein has been found in follicular fluid, with concentrations same as present in serum (Cioffi, 1997). Leptin plays role in follicular development as well as in luteal function because leptin transcription has been detected at early follicular states whereas leptin protein appears only in mature follicle. (Archenco et al., 2003) various in vitro studies have shown that treatment with medium-high physiologic doses (starting from 10ng/ml) of leptin inhibited steriodogenesis in human granulosa and theca cells (Agarwal, 1999) and results in marked decline in the number of ovulated oocytes (Duggal et al., 2000). These studies show that ovarian estradiol production get suppressed by high leptin concentration, this reduced estradiol production interfere with the development of dominant follicles and oocyte maturation and finally results an anovulation.

Therefore, the condition where excess energy stores or metabolic disturbances are there like obesity and PCOS, leptin have an inhibitory effect on ovaries and in suboptimal nutritional status like anorexia nervosa, exercise induced amenorrhoea and functional hypothalamic amenorrhoea, leptin deficiency results in HPG dysfunction (Farooqi et al., 1999).

So, it can be concluded that the relation between leptin and nutritional status of body along with proper metabolism, and role of leptin in regulation of HPG axis (which controls reproductive physiology) are probably experimental evidence about Ayurvedic concept that states how optimal nutrition with proper functional of agni and vata are responsible for suddha aartava dhatu in body and it reaches to garbhashaya through avra-vaha strotas where it performs its action that in fetus formation after conception or get excreted as menstrual blood.

Role of agni w.s.r. liver in regulation reproductive physiology

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No proper consideration has been given to proper metabolism in management of disorder related with reproductive physiology. As it has been explained in this article that leptin is a missing link between metabolic regulations of reproductive physiology. Estrogen and progesterone are the two basic hormones involved in reproductive physiology. Metabolism of estrogen is also very important because disturbed metabolism of it is also associated with disturbed folliculogenesis, impaired oviduct function, impairment of growth of embryo and placenta, abortion, endometriosis, PCOS etc (Rosselli and Dubey, 2006). Liver in involved in metabolism and detoxication of estrogen, any disturbances in this process disturbs reproductive physiology. In modern physiology liver is considered as regulator of all metabolic process likewise in Ayurveda all the functions related to metabolism are conducted by Agni present in body at different level. So disturbed liver functions and their impact on reproductive physiology should be investigated under umbrella of Ayurveda that will give possible explanation about how disturbed Agni and vata in body alters reproductive physiology. Proper production of estrogen, metabolism and excretion are important for normal reproductive function.

**Role of Liver in Metabolism of Estrogen**

Under normal condition, 2-methoxyestradiol which is metabolite of estrogen is very low at local level but under influence of certain exogenous factors, enzyme CYP (that is responsible for conversion of estrogen to 2-methoxyestradiol) get activated and level of 2-methoxyestradiol rises at local level. Some of its Adverse effect on reproductive physiology are as follows Improper nutrition of developing follicle

Proper angiogenesis in ovaries is under control of estrogen that is important for nutrition of developing follicle. 2-methoxyestradiol metabolite of estrogen derived from liver impairs this angiogenic process and leads to condition like PCOS and failed ovulation resulting in infertility (Dubey and Jackson, 2001).

**Effect on oviduct**

Proper cell growth of oviduct is important because it is the site where fertilization takes place. Catatol metabolite of estradiol impairs the cell growth in oviduct that impairs its ciliary and contractile function which is important for movement of ovum and sperm. 2-methoxyestradiol hampers the function related to oviduct in process of fertilization i.e. rhythmic contraction and ciliary movement within the lumen of oviduct, capacitation process, early embryo development, gene expression, implantation and placental development (Zhu and Conney, 1998; Dubey and Jackson, 2001).

**Estrogen in blood**

Estrogen in blood exists mainly in the bound form with carrier proteins but only unbound form of estrogen is physiologically active and it can only enter in cell. Sex hormone binding globulins (SHBG’s) are one of such protein which regulates the unbound form of estrogen in blood. These SHBG’s are synthesized in liver and has half-life of seven days. SHBG in affected by circulating androgen concentration. Several physiological and pathological conditions causes shift in the circulating level of this high affinity binding protein and cause several androgen abnormality (Maruyama et al., 1987). SHBG gets suppressed by elevated testosterone level while stimulated by high estrogen level. SHBG has high affinity for testosterone as compared to estrogen level because of this in case of PCOS where testosterone level is high, SHBG level get decrease and because of that blood concentration of free estrogen that is biologically active get increases.

SHBG level get suppressed in conditions like obesity, PCOS, hypothyroidism, hirsutism, acne vulgaris, acromegaly and androgen secreting ovarian tumours. Levels of SHBG in blood get elevated in conditions like anorexia nervosa, hyperthyroidism, androgen insensitivity / deficiency and primary biliary cirrhosis (Cumming and Wali, 1985).

Liver also takes part in detoxification of estrogen that is very important for normal reproductive physiology. Liver metabolizes the estrogen in phase-I (hydroxylation) and phase-II (methylation, glucuronidation and sulphation) pathway and finally it get excreted through urine and stool (Wood, 1996). Alteration in these detoxification process disturbs estrogen metabolism and disorder related to increased estrogen level that get manifested as menstrual irregularity, endometrial hyperplasia, endometriosis, PCOS, fibroid uterus, fibrocystic breast disease, abortion and problem related to infertility.

**Future perspective of research in field of leptin and estrogen metabolism in light of Ayurveda**

For proper functioning of reproductive physiology proper functioning of HPA axis is important. Any disturbance in it results in reproductive disorder like menstrual irregularities, hormonal imbalance, PCOS, fibroid uterus, endometriosis, infertility etc. Established principle of management of diseases in modern medical science is not sufficient because there is no permanent cure of these diseases and incidence of these problems are increasing day by day. It is need of the day that factors regulating HPA
axis should be identified so that management can be done at root cause of pathogenesis. Ayurveda being a life science and having holistic approach towards body explains effect of external and internal factors (diet, life style, psychology) on body physiology. Avoidance of causative factor is first line of management of any disease as per Ayurveda. This step is very important to break pathogenesis of disease and to establish body homeostasis because Ayurveda believes that disease is nothing but the state of altered body homeostasis. Proper digestion is the first requirement for maintenance of body homeostasis because diet and life style influences physiological units of body i.e. tridoshas. Tridoshas has influence on agni (digestive process), dhatu and strotas. Importance of diet, life style, agni and strotas are explained in chapters of Ayurvedic samhitas such as Dincharya Adhyaya, Ritucharya adhyaya, Matrashteyee adhyaya, Navegannadharaaneyee adhayaya, Doshadhaturmala kshaya vridhhi vigyanee adhyaya, Strотовиман adhyaya. Concepts explained in these chapters helps in maintaining proper homeostasis of body. New researches related to role of leptin and liver in regulation of reproductive physiology are attempt to search a new line of management of reproductive disorders. Researchers are showing that level of leptin in body is regulated by feeding and nutrition. Ayurveda can help in the area about regulation of leptin level and its relation with different type of ahar vitiating a particular dosha i.e. what is the difference in leptin level in particular person after eating vata/pitta/kapha vardhaka ahar or what is the difference in leptin level in particular person after doing activities that vitiates particular dosha / what is change in leptin level when a particular food item is given to persons having different type of agni like samagni, vishamagni, teekhanagni and mandagni. These researches help to control leptin level by selection of food according to predominance of dosha in body and status of Agni in particular person. Disturbed estrogen metabolism is cause of various reproductive disorders as described earlier and liver has regulating role in its transport, metabolism and excretion. But no proper management principle is present in modern medical science to regulate these functions of liver like SHBGs synthesis, estrogen metabolism and excretion. Ayurvedic concept of agni and shodhan (body purification) can help in these area because functions related to metabolism can be correlated to functions of agni and pitta and body purification processes like virechana (medicated purgation) can help to remove excess estrogen from body because it is proven now that estrogen is excreted through body via stool. So researches should be done to study role of status of Agni in estrogen metabolism, detoxification and SHBGs synthesis. Role of virechana should be investigated in case of disorders having estrogen excess in body.

CONCLUSIONS

It can be concluded that feeding and fasting by means of leptin regulates reproductive physiology by regulating HPA axis as well having direct role in regulation of ovarian function, oocyte maturation, embryo development, implantation and placentaion. Along with this liver is playing important role in synthesis of SHBGs, metabolism, detoxification and excretion of estrogen because alteration in these step results in menstrual irregularity, endometrial hyperplasia, endometriosis, PCOS, fibroid uterus, fibrocytic breast disease, abortion and problem related to infertility. But researches in field of regulation of reproductive physiology by leptin (indirectly nutrition) and liver are in very primary phase. Ayurveda can help in this area because artava and artava-vaha strotas are responsible for reproductive functions and there is very elaborate description about role of proper digestion and metabolism in formation of artava dhatu and function of artava-vaha strotas. Role of diet and life style on status of Agni and doshas are explained in very detail. Vitiation of doshas and Agni by these etiological factors i.e. diet, life style and psychological status have their role in formation of artava and function of artava-vaha strotas. Ayurveda believes in avoidance of etiological factors as first line of management. This concept of management is lacking in modern medical science. So role of diet, life style and status of Agni and their relation with regulation of leptin and liver function can give a new area of research and management principle of reproductive disorders.

REFERENCES

Agarwal, S. K. 1999. Leptin Antagonizes the Insulin-Like Growth Factor-I Augmentation of Steroidogenesis in Granulosa and Theca Cells of the Human Ovary. Journal of Clinical Endocrinology & Metabolism, 84(3):1072–1076.

Ahima, R. S., Dushay, J., Flier, S. N., Prabakaran, D., Flier, J. S., et al. 1997. Leptin Accelerates the Onset of Puberty in Normal Female Mice Rapid Publication Leptin Accelerates the Onset of Puberty in Normal Female Mice. J. Clin. Invest, 99:391–396.

Amstalden, M., Garcia, M. R., Stanko, R. L., Nizielski, S. E., Morrison, C. D., Keisler, D. H., Williams, G. L., et al. 2002. Central Infusion of Recombinant Ovine
Leptin Normalizes Plasma Insulin and Stimulates a Novel Hypersecretion of Luteinizing Hormone after Short-Term Fasting in Mature Beef Cows. Biology of Reproduction, 66(5):1555–1561.

Archanco, M., Muruzábal, H. C. A., Lafontan, M., Busse, R. 1998. Leptin, the Product of Ob Gene, Promotes Angiogenesis. Circulation Research, 83(10):1059–1066.

Cervero, A., Horcajadas, J., Domínguez, F., Pellicer, A., Simón, C. 2005. Leptin system in embryo development and implantation: a protein in search of a function. Reproductive BioMedicine Online, 10(2):60943–60944.

Friedman, J. M., Halaas, J. L. 1998. Leptin and the regulation of body weight in mammals. Nature, 395(6704):763–770.

Jin, L., et al. 1999. Leptin and Leptin Receptor Expression in Normal and Neoplastic Human Pituitary: Evidence of a Regulatory Role for Leptin on Pituitary Cell Proliferation. Journal of Clinical Endocrinology & Metabolism, 84(8):2903–2911.

Khan, S. M., Hamnvik, O.-P. R., Brinkoetter, M., Mantzoros, C. S. 2012. Leptin as a Modulator of Neuroendocrine Function in Humans. Yonsei Medical Journal, 53(4).

Licinio, J., Negrao, A. B., Mantzoros, C., Kaklamani, V., Wong, M. L., Bongiorno, P. B., Gold, P. W., et al. 1998. Synchronicity of frequently sampled, 24-h concentrations of circulating leptin, luteinizing hormone, and estradiol in healthy women. Proceedings of the National Academy of Sciences, 95(5):2541–2546.

Maruyama, Y., Aoki, N., Suzuki, Y., Ohno, Y., Imamura, M., Saika, T., Yamamoto, T. 1987. Sex-steroid-binding plasma protein (SBP), testosterone, oestradiol and dehydroepiandrosterone (DHEA) in prepuberty and puberty. Acta Endocrinologica, 114(1):60–67.

Mercer, J. G., Hoggard, N., Williams, L. M., Lawrence, C. B., Hannah, L. T., Trayhurn, P. 1996. Localization of leptin receptor mRNA and the long form splice variant (Ob-Rb) in mouse hypothalamus and adjacent brain regions by in situ hybridization. FEBS Letters, 387(2-3):473–478.

Pandey, K., Chaturvedi, G. 2005a. Grahani Chikitsa Adhayay 3rd,4th shloka . In Charak Samhita Vidyotini Hindi Vyakhya Chikitsa Sthana, page 452, Varanasi. Chaukhambha Bharti Academy.

Pandey, P. K., Chaturvedi, G. 2005b. Arthedashmamooliya Adhayay 26th shloka. In Charak Samhita Vidyotini Hindi Vyakhya Sutra Sthana, page 587, Varanasi. Chaukhambha Bharti Academy.

Pandey, P. K., Chaturvedi, G. 2005c. Deerghanjeviteeya Adhayay 59th -62th shloka . In Charak Samhita Vidyotini Hindi Vyakhya Sutra Sthana, pages 35–37, Varanasi. Chaukhambha Bharti Academy.

Pandey, P. K., Chaturvedi, G. 2005d. Grahani Chikitsa Adhayay 50th ,51st shloka. In Charak Samhita Vidyotini Hindi Vyakhya Chikitsa Sthana, page 461, Varanasi. Chaukhambha Bharti Academy.

Pandey, P. K., Chaturvedi, G. 2005e. Grahani Chikitsa Adhayay 8th ,13th , 16th shloka. In Charak Samhita Vidyotini Hindi Vyakhya Sutra Sthana, pages 453–456, Varanasi. Chaukhambha Bharti Academy.
Mishra, Sarita and Parameswarappa S. Byadgi. Int. J. Res. Pharm. Sci., 10(3), 2199-2208

Academy.

Pandey, P. K., Chaturvedi, G. 2005f. Strotoviman Adhayay 23rd shloka. In Charak Samhita Vidyotini Hindi Vyakhyा Viman Sthana, page 714, Varanasi. Chaukhabha Bharti Academy.

Pandey, P. K., Chaturvedi, G. 2005g. Strotoviman Adhayay 24th shloka. In Charak Samhita Vidyotini Hindi Vyakhyा Viman Sthana, page 714, Varanasi. Chaukhabha Bharti Academy.

Pandey, P. K., Chaturvedi, G. 2005h. Strotoviman Adhayay 3rd shloka. In Charak Samhita Vidyotini Hindi Vyakhyा Viman Sthana, page 709, Varanasi. Chaukhabha Bharti Academy.

Pandey, P. K., Chaturvedi, G. 2005i. Strotoviman Adhayay 6th shloka. In Charak Samhita Vidyotini Hindi Vyakhyा Viman Sthana, page 710, Varanasi. Chaukhabha Bharti Academy.

Pandey, P. K., Chaturvedi, G. 2005j. Strotoviman Adhayay 9th shloka. In Charak Samhita Vidyotini Hindi Vyakhyा Viman Sthana, page 712, Varanasi. Chaukhabha Bharti Academy.

Pandey, P. K., Chaturvedi, G. 2005k. Vatkalakaleeya Adhayay 11th shloka. In Charak Samhita Vidyotini Hindi Vyakhyा Sutra Sthana, page 251, Varanasi. Chaukhabha Bharti Academy.

Pandey, P. K., Chaturvedi, G. 2005l. Vatkalakaleeya Adhayay 12th shloka. In Charak Samhita Vidyotini Hindi Vyakhyा Sutra Sthana, page 252, Varanasi. Chaukhabha Bharti Academy.

Pandey, P. K., Chaturvedi, G. 2005m. Vatkalakaleeya Adhayay 6th shloka. In Charak Samhita Vidyotini Hindi Vyakhyा Sutra Sthana, pages 245–246, Varanasi. Chaukhabha Bharti Academy.

Rosselli, M., Dubey, R. K. 2006. Estrogen Metabolism and Reproduction—is there a Realationship? Journal für Fertilität und Reproduktion, 16(4):19–23.

Sagawa, N., Yura, S., Itoh, H., Mise, H., Kakui, K., Kori, D., Fujii, S. 2002. Role of Leptin in Pregnancy-A Review. Placenta, 23:80–86.

Shastri, A. 2005a. Jaatisutriya Adhayay 4rd shloka. In Kashyap Samhita Vidyatini Hindi Vyakhyा Sharir Sthana, page 79, Varanasi. Chaukhabha Sanskrita Sansthan.

Shastri, A. 2005b. Doshadhatumalkshavardhivigyaneeeya Adhayay 3rd shloka. In Sushrut Samhita Ayurvedatvavasandeepeika Hindi Vyakhyा Poorvardha Sutra Sthana, page 56, Varanasi. Chaukhabha Sanskrita Sansthan.

Shastri, A. 2005c. Doshadhatumalkshavardhivigyaneeeya Adhayay 48th shloka. In Sushrut Samhita Ayurvedatvavasandeepeika Hindi Vyakhyा Poorvardha Sutra Sthana, page 64, Varanasi. Chaukhabha Sanskrita Sansthan.

Shastri, A. 2005d. Doshadhatumalkshavardhivigyaneeeya Adhayay 4th-8th shloka. In Sushrut Samhita Ayurvedatvavasandeepeika Hindi Vyakhyा Poorvardha Sutra Sthana, pages 56–57, Varanasi. Chaukhabha Sanskrita Sansthan.

Shastri, A. 2005e. Doshadhatumalkshavardhivigyaneeeya Adhayay 7th shloka. In Sushrut Samhita Ayurvedatvavasandeepeika Hindi Vyakhyा Poorvardha Sutra Sthana, page 57, Varanasi. Chaukhabha Sanskrita Sansthan.

Shastri, A. 2005f. Doshadhatumalkshavardhivigyaneeeya Adhayay 9th shloka. In Sushrut Samhita Ayurvedatvavasandeepeika Hindi Vyakhyा Poorvardha Sutra Sthana, page 58, Varanasi. Chaukhabha Sanskrita Sansthan.

Shastri, A. 2005g. Garbhavakranti Adhayay 8th shloka. In Sushrut Samhita Ayurvedatvavasandeepeika Hindi Vyakhyा Poorvardha Sutra Sthana, page 21, Varanasi. Chaukhabha Sanskrita Sansthan.

Shastri, A. 2005h. Shonitavarnaneeya Adhayay 6th shloka. In Sushrut Samhita Ayurvedatvavasandeepeika Hindi Vyakhyा Poorvardha Sutra Sthana, page 48, Varanasi. Chaukhabha Sanskrita Sansthan.

Shastri, A. 2005i. Vranaprashna Adhayay 19th shloka. In Sushrut Samhita Ayurvedatvavasandeepeika Hindi Vyakhyा Poorvardha Sutra Sthana, page 91, Varanasi. Chaukhabha Sanskrita Sansthan.

Shastri, A. 2005j. Vranaprashna Adhayay 21st shloka. In Sushrut Samhita Ayurvedatvavasandeepeika Hindi Vyakhyा Poorvardha Sutra Sthana, page 91, Varanasi. Chaukhabha Sanskrita Sansthan.

Shastri, A. 2005k. Vranaprashna Adhayay 23rd shloka. In Sushrut Samhita Ayurvedatvavasandeepeika Hindi Vyakhyा Poorvardha Sutra Sthana, page 91, Varanasi. Chaukhabha Sanskrita Sansthan.

Shastri, A. 2012. Aupadravikam Adhayay 25th shloka. In Sushrut Samhita Ayurvedatvavasandeepeika Hindi Vyakhyा Uttarardha Sutra
Page 1

**Uttara Tantra**, page 14, Varanasi. Chaukhamba Sanskrit Sansthan.

Sir-Petermann, T., Maliqueo, M., Palomino, A., Vantman, D., Recabarren, S. E., Wildt, L. 1999. Episodic leptin release is independent of luteinizing hormone secretion. *Human Reproduction, 14*(11):2695–2699.

Strobel, A., Issad, T., Camoin, L., Ozata, M., Strosberg, A. D. 1998. A leptin missense mutation associated with hypogonadism and morbid obesity. *Nature Genetics, 18*(3):213–215.

Tripathi, B. 2011a. Ayushkameeya Adhyaya 20th shloka. In *Ashtangahridayam Nirmala Hindi Vyakhya Sutra Sthana*, page 16, Jawahar Nagar Delhi. Chaukhambha Sanskrit Pratishthan.

Tripathi, B. 2011b. Doshopkramaneeya Adhyaya 25th shloka. In *Ashtangahridayam Nirmala Hindi Vyakhya Sutra Sthana*, page 188, Jawahar Nagar Delhi. Chaukhambha Sanskrit Pratishthan.

Tripathi, B. 2011c. Doshopkramaneeya Adhyaya 23rd-24th shloka. In *Ashtangahridayam Nirmala Hindi Vyakhya Sutra Sthana*, page 188, Jawahar Nagar Delhi. Chaukhambha Sanskrit Pratishthan.

Tripathi, B. 2011d. Sarvarognidan Adhyaya 10th shloka. In *Ashtangahridayam Nirmala Hindi Vyakhya Nidan Sthana*, page 431, Jawahar Nagar Delhi. Chaukhambha Sanskrit Pratishthan.

Wood, E. J. 1996. Harper’s biochemistry 24th edition. *Biochemical Education, 24*(4):80776–80781.

Yu, W. H., Walczewska, A., Karanth, S., McCann, S. M., et al. 1997. Nitric Oxide Mediates Leptin-Induced Luteinizing Hormone-Releasing Hormone (LHRH) and LHRH and Leptin-Induced LH Release from the Pituitary Gland. *Endocrinology, 138*(11):5055–5058.

Zhu, B. T., Conney, A. H. 1998. Is 2-methoxyestradiol an endogenous estrogen metabolite that inhibits mammary carcinogenesis. *Cancer Research, 58*:2269–77.