



Stress and fertility-Past conviction, present cognizance and future orchestrations

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ABSTRACT

Different studies have been done to study the effect of stress on reproductive physiology and fertility. Pathogenesis of stress-induced infertility /decrease fecundity is explained by various neuro-hormonal axis and theory of oxidative stress, but proper management of stress and regulation of these neurohormonal axis along with oxidative stress is lacking in modern medical science. A better understanding of stress and its relation with body physiology, especially fertility, is attempted in light of *Ayurveda* to get knowledge about the etiopathogenesis of stress-induced infertility and its holistic management. In *Ayurveda* concept of stress is not only confined to psychological factors, but it is the state of disturb body homeostasis, i.e. the state where *doshas*, *dhatu*s, *malas* & *agni* are not in their proper functioning. Diet and lifestyle have their role in maintaining body homeostasis. Along with diet and lifestyle various drugs, therapeutic procedure (*panchakarma*) & non-materialistic treatment (*achar rasayan*-rules and beliefs to be followed in life) have been described in *Ayurveda* to manage disturbed body homeostasis, and thus it helps in the management of stress in a holistic way. Concept of stress management by *Ayurvedic* concepts like diet, lifestyle, *Agni*, body purification methods along with *rasayan* and *ojo-varadhak* objects (diet, lifestyle, and drugs) will open a vast area of research about the applicability of these concepts in stress management by the holistic way. It will help to serve society by providing not only cure of stress-related infertility but also give a healthy reproductive life.

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INTRODUCTION

In today's world where modernization is making each and every field of life easy and smooth inspite of these advancements incidence of stress is increasing day by day. Fast and disturbed life style, changing food habits, changing family and social structure along with increasing competition in the work field are the basic cause of stress. Chronic stress, whether it is physical or psychological alters body physiology. Various type of Neuro-hormonal secretion gets activated in the response of stress those have an inhibitory action on body physiology. Infertility or reduced fecundity is also one of the conse-

quences of disturbed body physiology in response to chronic stress (Buck *et al.*, 1997; Rosenfeld and Mitchell, 1979).

Various mechanisms have been proposed about the relation of stress and reproductive physiology, but concept about regulatory factors of stress and their implication in stress management needs more researches. In the present era where researches are focusing on a single molecule or gene model of disease pathogenesis and treatment but as stress has multi system effect on the human body in response to various type of stimuli, needs holistic approach towards understanding its pathogenesis and management.

As *Ayurveda* has a holistic approach towards life and disease management. Diet and life style have their impact on the functional unit of body (*vata*, *pitta*, *kapha*) (Shastri, 2005j). Fine tuning of these functional units are important for maintenance of health and any alteration in their equilibrium results in disease (Tripathi, 2011). Avoidance of these factors, diet and life style opposite to the qualities of these disturbed *doshas* along with specific drugs, treatment procedure and non materialistic objects are various treatment options for any disease in *Ayurveda* (Pandey and Chaturvedi, 2005n). Variety of these treatment options is beauty of *Ayurveda* because selection of these treatment options is also described on the basis of severity of *doshic* disturbance and state of disease (Pandey and Chaturvedi, 2005f). Individualistic approach of treatment is also a beauty of *Ayurveda* where treatment is planned according to particular person (Pandey and Chaturvedi, 2005a).

In present review different parallels were drawn from the concepts like *vata dusti* (vitiation of *vata dosha*) (Shastri, 2005i) *agni dusti* (improper digestion) (Pandey and Chaturvedi, 2005l), *stroto-dusti* (blockage in channels carrying nutrition for different tissue in body) (Pandey and Chaturvedi, 2005m) and *ojo-kshaya* (reduced immunity of body because of improper nutrition of body tissue) (Pandey and Chaturvedi, 2005e) to the pathogenesis of stress induced infertility. So that holistic management of the particular person can be planned.

Need of this study

This study is about past conviction, present cognizance and future orchestrations of stress and fertility. Present insight about stress that is based on disturbance of neurohormonal axis is lacking its applied aspects in area of management of stress. Whereas *Ayurvedic* concept of *dosha-vaishamya*, *Agni dusti*, *stroto-avrodh* and *ojo-kshaya* are (having similar symptoms as that of stress induced neurohormonal signals) having more applied concepts be-

cause it has been mentioned in *Ayurvedic* texts in detail that what are the diet and life style changes one should follow to regulate these pathological factors. Regulation of diet and life style (*nidan parivarjan*) is stated as first and foremost principal of management of any disease (Shastri, 2005a) even when it is not in its expressed form (state of *sanchaya*, *prakop* and *prasara of dosha*) (Shastri, 2005l). Management principal of stress induced infertility i.e. diet and life style modification along with drug, therapeutic procedure and non materialistic object can give a holistic management of stress. These concepts of management will open a new area of research where clinical assessment along with neurohormonal effects of these factors can be studied for validation of these time proved *Ayurvedic* theories, and thus a holistic management protocol can be established to regulate reproductive physiology despite of tremendous medical advancement.

Stress and its impact on fertility

Stress affects the human body in the form of physical, social and psychological forms (Sharma *et al.*, 2013). Physiologically stress affects the body homeostasis (Tsigos and Chrousos, 2002). As this paper is the review article about stress and infertility studies performed between time period of 2005-2019 based on human studies were searched (Table 1) by the help of key words-life style, diet, stress, infertility, oxidative stress, fertility and female are showing that how changing life style, diet and stress affects reproductive physiology and fertility.

All these studies are concluding that diet (based on plant origin, rich in vitamin B, C and E with micronutrients like selenium, zinc, manganese along with full of antioxidant property) weight loss exercises, cessation of smoking and prevention of alcohol and caffeine consumption have their role in fertility outcome. Body responds to these stressors in the form of disturbed homeostasis of the endocrine, immune and nervous system (Coe and Laudenslager, 2007). To draw parallels from *Ayurvedic* concepts about the stress, it is important to explain the neurohormonal response of the body against stress. The nervous system gets activated first in response to any type of stress, whether it is physical or psychological. The autonomic nervous system, the hypothalamic-pituitary-adrenal axis (HPA axis) and adrenergic nervous system get stimulated as a stress response. HPA axis is controlled by corticotrophic-releasing hormones (CRH) and Anti-vasopressin hormone (AVP). Along with this, various peripheral mediators are also get activated like glucocorticoids (GCs), neurotrophins and catecholamines (Benschop *et al.*, 1996). Studies are showing that psychological

stress in work field (Walter *et al.*, 1999), malnutrition, heavy exercises for a long time (Rivest and Rivier, 1995) stimulates the HPA axis and inhibit hypothalamic-pituitary-ovarian axis (HPO axis) (Makino *et al.*, 2002). Various researches are showing relation between long term hyper activation of components of HPA axis (i.e. corticotropin-releasing hormones (Marti *et al.*, 1999), glucocorticoids (Rabin *et al.*, 1990), corticotrophins (Mann *et al.*, 1985) and beta endorphins (Chen *et al.*, 1992) results in impaired fertility in females. Along with these neurohormones various pro-inflammatory cytokines (Rivier and Rivest, 1991a) and deficiency of growth hormone – induced insulin like growth factors -1 (GH IGF-1) (Sahlin, 1995) have their role in regulation of reproductive physiology.

Effect of Stress on HPO axis via CRH, ACTH and Glucocorticoids

CRH neurons (present in the para ventricular nucleus of hypothalamus and in other brain areas like norepinephrine and central sympathetic system in the brain stem have regulatory role on HPA axis and peripheral sympathetic system (Chrousos, 1992). CRH secretions are regulated by mutual interaction among the various components of stress system. It activates HPA axis either by beta endorphins or catecholamines that results inhibition of reproductive axis at all levels (Mastorakos *et al.*, 2006). GnRH secretion, i.e. inhibited by CRH in response of chronic stress results in decreased pulsatile secretion of LH that disturbs the process of ovulation (Chatterjee *et al.*, 1994). CRH receptors are also found in female reproductive tissues i.e. ovaries, uterus and placental trophoblast (Chrousos, 1995). When exposed to psychological stress increased CRH (Bromberger *et al.*, 1997) reduces ovarian steroidogenesis (Ghizzoni *et al.*, 1997). At uterine level increased CRH disturbs the process of endometrial decidualization and implantation defect (Zoumakis *et al.*, 2001) results in infertility and pregnancy losses.

It can be concluded that stress induces CRH that have its effect on fertility by inhibition of LH surge, ovarian steroidogenesis, endometrial decidualization and implantation. Beta endorphins which are activated by CRH also inhibit GnRH secretion and finally restrain LH surge (Petraglia *et al.*, 1986). ACTH is also induced by chronic stress that also restrains LH surge by inhibiting responsiveness of pituitary gonadotropes to GnRH (Mann *et al.*, 1985).

Increase level of glucocorticoids in serum also restrains HPO axis (Dubey and Plant, 1985). Glucocorticoids receptors are present over different levels of HPO axis i.e. hypothalamic GnRH neurons (Chandran *et al.*, 1994), pituitary gonadotropes (Breen

et al., 2004), ovaries (Schreiber *et al.*, 1982) and ovarian granulosa cell cytosol that results in decreased responsiveness of gonadotropes to GnRH (Breen *et al.*, 2007) and thus impairs LH surge (Melis and Paoletti, 1987). Direct effect of increased level of glucocorticoids over ovaries results atresia of follicles (Meurer *et al.*, 1991). Increased level of Glucocorticoids also have role in expression of estrogen receptors (Zamorano *et al.*, 1992), tissue uptake of estrogen and estrogen stimulated DNA synthesis in uterus (Biggsby, 1993). Levels of synthesis of estrogen get reduced by the inhibitory effect of glucocorticoids over granulosa cell aromatase activity (Hsueh and Erickson, 1978). This glucocorticoids mediated estrogen deficiency not only disturbs luteal steroidogenesis but also affects expression of estrogen and progesterone receptors in uterus (Bergman *et al.*, 1992) those are important for blastocyst implantation, endometrial preparation for maintenance of pregnancy and parturition (Chatterjee *et al.*, 1993).

Effect of stress on GH-IGF-1 axis

Insulin like growth factor-1 (IGF-1) is mainly synthesized by liver, and its synthesis is stimulated by GH. IGF-1 receptors are present in hypothalamus, pituitary, ovaries and reproductive tract (Codner and Cassorla, 2002) & it has role in release of GnRH, gonadotrophins secretions, follicular growth, steroidogenesis and ovulation. In chronic stress, increased level of glucocorticoids suppresses GH secretion and thus IGF-1 synthesis get also reduced (Laron, 2002) that results in disturbed HPO axis.

Effect of stress on interleukins

During stress, HPA axis is regulated by pro-inflammatory cytokines IL-18. Under stressful conditions secretion and surge of LH is get suppressed by hypothalamic IL expression, elevated pituitary IL-18 synthesis and TNF synthesis. Chronic stress induced cytokines directly activates corticotrophin and glucocorticoids secretion (Tsigos and Chrousos, 1994). Thus, cytokines have inhibitory role on female reproduction system at all levels, i.e. increased secretion of CRH from hypothalamus, ACTH & β endorphin secretion from pituitary, peripheral secretion of glucocorticoids and inhibition of ovarian steroidogenesis (Rivier and Rivest, 1991b).

Effect of stress on nervous supply of the reproductive organ

Sympathetic and parasympathetic innervations of pelvic viscera is modulated by stress and thus have control on reproductive physiology. In ovaries

perivascular interstitial areas and follicular surrounding have rich supply of autonomic terminals. Hence, ovarian blood supply; ovarian contractility, follicular size and ovulation are controlled by autonomic innervations. β Adrenergic receptors are present in all secretory compartments of ovaries, and thus, their activation influences follicular development and hormone secretion (Coleman *et al.*, 1979). Stress-induced epinephrine and corticosteroids have down regulatory role on this receptor (Burden, 1985). Autonomic nerve terminal are found abundantly over ampuloisthmic junction, uterotubal junction and over uterus, which have their role in transport of ova through the oviduct and process of implantation.

Effect of Oxidative Stress on Female Reproductive System

As per modern physiology, any form of stress whether it is mental or physical get expressed in the form of oxidative stress. Oxidative stress has its role in reproductive physiological disturbances. In a healthy body, there is balance of reactive oxygen species (ROS) and antioxidants.

Oxidative stress is the condition where generation of reactive oxygen species and other free radical species exceeds the scavenging capacity of antioxidants in the organism. This balance gets disturbed due to excessive production of ROS and / or inadequate intake or increased utilization of antioxidants. Most of the ROS are produced in electron transport chains in the mitochondria, endoplasmic reticulum, plasma and nuclear membranes (Lushchak, 2011). Physiology of female reproductive system is controlled by balance between cellular reactive oxygen species and their antioxidant, this balance plays an important regulatory role through various signaling and transduction pathway in folliculogenesis, oocyte maturation, corpus luteum, uterine function, embryogenesis, embryonic implantation and fetoplacental Development. Imbalance between ROS production and antioxidant are considered as the cause of pathological processes affecting female reproductive physiology (Sugino *et al.*, 2004).

Oxidative stress and ovarian function

ROS and antioxidants have regulatory role in oocyte maturation, folliculogenesis, ovarian steroid genesis and luteolysis because in aerobic metabolism utilization of oxygen is necessary for development of gametes. Various antioxidant enzymes such as copper zinc superoxide dismutase (Cu, Zn - SOD), manganese superoxide dismutase (Mn-SOD) and glutathione peroxidase have their role in oocyte maturation. These enzymes neutralizes reactive oxygen species (Riley and Behrman, 1991). In

a study (Agarwal and Allamaneni, 2004) hydrogen peroxide was added to culture of hCG stimulates luteal cells it was observed that production of progesterone and estradiol hormones get reduced. Level of oxidative stress biomarkers, i.e. conjugated dyes, lipid hydro peroxide and Thiobarbituric acid is lower in follicular fluid as compared to their level in serum. Antioxidant defence is more in pre-ovulatory follicle (Jozwik, 1999).

Oxidative stress and endometrium

Expressions of antioxidant get changes in response to cyclical changes in the endometrium. Thioredoxin enzyme has higher expression in early secretory phase. In late secretory phase activity of superoxide dismutase get decreased thus ROS level increases that triggers the release of prostaglandin F2 (Sugino *et al.*, 1996). Decidualisation and preparation of endometrium for implantation by regulation of endometrial, myometrial and microvascular function is controlled by nitrogen monoxide (Tseng *et al.*, 1996).

Fallopian tube function and oxidative stress

Various studies have shown the presence of cytokines, prostaglandin and metabolite of lipid peroxidation and ROS in fluid samples of fallopian tube (Tamate *et al.*, 1995). For fertilization and transport of pre-embryo, equilibrium of these components is required. For proper functioning of fallopian tubes, an endogenous nitrogen monoxide system exist in fallopian tube, deficiency of NO may cause tubal motility dysfunction, resulting in retention of the ovum, delayed sperm transport and infertility (Rosselli *et al.*, 1995).

Modern studies have also started accepting that nutrition and metabolism have regulatory role on reproductive physiology. Studies related to role of ahar, proper functioning of *agni, vata* and *stroto-shodhan* should be done to evaluate their role in regulation of reproductive physiology. These studies can give a better and holistic management of female reproductive disorders.

Above reference related to effect of stress on reproductive physiology of female are concluding that any type of physical or psychological stress disturbs various neuro hormonal axis and activates reactive oxygen species resulting oxidative stress in body. Pathophysiology of these stress responses of the body is explained in very detail, but regulatory factors of this external stress and its management needs more exploration.

A single stressor activates various pathways in body. Management of stress needs regulation of entire pathways. Therapy based on single molecule, hor-

Table 1: Review articles about stress and infertility studies performed between time periods of 2005-2019 based on human studies

Study	Reference
The impact of lifestyle factors on reproductive performance in the general population and those undergoing infertility treatment: a review.	(Homan <i>et al.</i> , 2007)
Stressful life events are associated with a poor in-vitro fertilization (IVF) outcome: a prospective study.	(Ebbesen <i>et al.</i> , 2009)
Oxidative stress as a life-history constraint: the role of reactive oxygen species in shaping phenotypes from conception to death.	(Metcalf and Alonso-Alvarez, 2010)
Lifestyle factors in people seeking infertility treatment—a review.	(Anderson <i>et al.</i> , 2010)
Epigenetics and lifestyle	(Alegría-Torres <i>et al.</i> , 2011)
Efficacy of a short-term yoga-based lifestyle intervention in reducing stress and inflammation: preliminary results.	(Yadav <i>et al.</i> , 2012)
The effects of oxidative stress on female reproduction: a review.	(Agarwal <i>et al.</i> , 2012)
Lifestyle factors and reproductive health: taking control of your fertility.	(Sharma <i>et al.</i> , 2013)
Association of western diet & lifestyle with decreased fertility.	(Nazni, 2014)
Impact of stress on oocyte quality and reproductive outcome.	(Prasad <i>et al.</i> , 2016)

none or drug is not sufficient because management of entire axis require a vast approach that not only suppresses these activated pathways but also helps to maintain body homeostasis.

Concept of stress in Ayurveda

Ayurveda believes that body is consists of *doshas* (*vata*, *pitta*, *kapha*), *dhatu* (*rasa*, *rakta*, *mamsa*, *meda*, *asthi*, *majja*, *suka*) and *malas* (*sweda*, *pureesh*, *mutra*) (Shastri, 2005f). Proper homeostasis of these *doshas*, *dhatu* and *malas* are required for health and any disturbance in their equilibrium results in disease. Diet and life style have their impact on status of *dosha*, *dhatu* and *srotas* (Pandey and Chaturvedi, 2005g). Diet and life style which are having qualities similar to particular *dosha* (Shastri, 2005b) aggravates that *dosha* when consumed in exclusive way and result in disturbed body homeostasis.

Doshas get influenced by diet and life style further vitiates *agni*, *dhatu* and *srotas* of body those are further responsible for disturbed body homeostasis. As stress is expressed in the form of disturbed body homeostasis, in Ayurveda disturbed body homeostasis get expressed in form of *dosha vaishamy*, *agni dusti* Pandey and Chaturvedi (2005b), *sroto-dusti* and *dhatu dusti* (Pandey and Chaturvedi, 2005g).

Ojo-kshaya (Shastri, 2005e) is the concept of most severe form of disturbance in body homeostasis. Initially any type of *nidan* disturbs *dosha*, *agni*, *srotas* and *dhatu* (Pandey and Chaturvedi, 2005h). To understand basic pathology of stress on female reproductive physiology role of *dosha*, *agni*, *srotas*, *dhatu* and *ojasa* should be explained.

Reproductive physiology of female is under control of *vata dosha* (Pandey and Chaturvedi, 2005s) because *aartava dhatu* that is responsible for all reproductive function i.e. menstruation or conception is under regulatory control of *vata dosha* (Pandey and Chaturvedi, 2005p). Best factor for conception is *Saumansya* (*gladness*) and *daurmanasya* (depressive state of mind) is stated as causative factor of infertility (Pandey and Chaturvedi, 2005r). Both of these mental qualities are under control of *vata*. In *samhitas* it is clearly explained that *vata* in regulatory factor of *manas* (Pandey and Chaturvedi, 2005p). So any type of vitiating in *vata* influences *manas* and have effect on reproductive physiology (Pandey and Chaturvedi, 2005p).

Agni Vaishamy and Dhatu Poshan

All the vitiating factors of *vata* disturb proper functioning of *agni* in body because proper ignition of *agni* is controlled by *vata* (Pandey and Chaturvedi,

2005q). For proper formation of *artava dhatu* proper functioning of *agni* is required when this process get disturbed it hampers *artava dhatu nirman*.

Stroto-dusti

After proper digestion of *ahar rasa*, *artava dhatu* get formed and it gets accumulated in uterus throughout the month via *aartava-vahi dhamani* (Shastri, 2005h). No any specific description is available in *samhitas* about causative factors of *aartava-vaha stroto-dusti* but in references of *aartava-vaha stroto-viddha lakshan* (Shastri, 2005b), it is explained that infertility results when this *strotas* gets *viddha* thus factors causing infertility (improper diet, life style, *dushta artava*, *beeja dosha* and *daiva*) have their influence on *artava-vaha strotas*.

Oja-kshaya

Oja is considered as essence of all the *dhatu*s and it is responsible for natural strength of body and immunity (Pandey and Chaturvedi, 2005c). Qualities of *oja* are described in *Ayurveda* those have similar to quality of *Kapha* (Shastri, 2005c). Physical trauma, under nutrition, fear, sorrow, unnecessary thinking, excessive exercises are responsible for *ojo-kshaya* in body (Shastri, 2005d). Fears, depression, emaciation of body and disturbed thoughts are symptoms of *ojo-kshaya* (Pandey and Chaturvedi, 2005d).

It can be concluded that *dosha vaishamy*, *agni dusti*, *dhatu dusti*, *stroto-dusti* and *ojo-dusti* are response of body against the stress.

Pathogenesis of stress-An Ayurvedic understanding

As explained earlier in this article that as per modern physiology stress activates various neuro-hormonal axis and activates reactive oxygen species. Those have their effect on HPO axis and disturb LH surge, follicular maturation, ovulation and conception and finally results infertility or reduced fecundity. In *Ayurveda*, conception (*garbha nirman*) has been explained as function of *artava* (Shastri, 2005g). Factors regulating *artava dhatu* formation i.e. *ahar*, *agni*, proper functioning of *artava-vaha strotas* and *vata* along with mental calmness, are key regulatory factors of female reproductive physiology.

Physical and mental factor affecting artava dhatu nirmana

Formation of fetus is considered as main function of *aartava*. Factors which affect process of *garbha dharan* also have effect on *artava*. Mental disturbance has been considered as the main factors which disturbs potency of body and mental piece is explained

as best factor for conception.

Vata is considered as regulatory factor of *manas* and thus regulates *jeal* and *joy*; it also stimulates proper functioning of *agni*. Thus *vata* and *agni* have important role in reproductive physiology. When *vata* get disturb, it disturbs mental calmness, causes intrauterine death, fetal anomaly as fetal retention for long period (non initiation of labor). Vitiating *vata* is also responsible for fear, sadness etc. In all these references psychological factors have been given importance to control reproductive physiology. *Vata* has been considered as regulator of *manas* and when it gets vitiating it disturbs mental calmness (Pandey and Chaturvedi, 2005p). So *vata* has control on the body as well as on *manas* of a person and by disturbing psyche of a person or body function related to *vata*, *vata* disturbs reproductive physiology. It is proven now that stress in any form whether it is physical or mental it affects reproductive physiology.

It is clearly explained in *samhitas* that vitiating *vata* itself is responsible for psychological disturbance (Pandey and Chaturvedi, 2005p) and psychological factors (*bhaya*, *shoka*, *moha*) when present as an external stimulus (*nidan*) vitiates *vata dosha* (Shastri, 2005k). So, relation of *vata* with these psychological factors (*bhaya*, *shoka*, *chinta*, *moha*) is vice versa. It can be concluded that vitiating *vata* in body is root cause of stress (disturbed body homeostasis). All neuro-hormonal imbalances those are activated by stress resulting suppression of reproductive physiology can be correlated with disturbed functioning of *vata*. As functions of nervous system are similar to functions govern by function of *vata*, (Sumantran and Nair, 2019). So in case of vitiating of *vata*, reproductive physiology get disturbed that get expressed in form of improper *artava dhatu nirmana* and its disturbed function (improper menstruation or conception). Prime consideration of *vata dosha* during treatment of any gynecological disorder is also proving that reproductive physiology is under control of *vata*. *Nidan* of *ojo-kshaya* are very similar to *nidan* of *vata dusti* and have role in regulation of fertility. As described earlier that *dosha vaishamy*, *agni dusti*, *dhatu dusti* are stressors (disturbing body homeostasis of body) for body and are responsible for disease.

Management principle

As any type of movement and its control along with psychological responses are under control of proper functioning of *vata*. This concept of vitiating of *vata* and its role in disturbing body homeostasis is primary cause of stress in body that results in reduced fertility. A holistic approach is required that can tar-

get all levels of disturbed physiology.

Principle of management should be –

1. Avoidance of caustive factors (Shastri, 2005a) Diet and life style factors should to be identified and be avoided which are responsible for vitiation of doshas especially vata.
2. Daivavyapashraya and satvavajaya chikitsa (Pandey and Chaturvedi, 2005n) Various types of rituals along with life style modification described under the heading of Achar rasayan (Pandey and Chaturvedi, 2005k) have been described to regulate *manas*.
3. Body Purification (Pandey and Chaturvedi, 2005o) To remove vitiated dosha body purification measures are described before the use of proper drug. These procedures clear strotas and remove vitiated doshas and help in generation of suddha dhatu and thus helps to maintain body homeostasis.
4. Rasayana (Pandey and Chaturvedi, 2005i) and ojo-*vardhak* drugs (Pandey and Chaturvedi, 2005j) To improve fertility and countervail effect of stress on body certain drugs which have their effect on *manas* (such as *medhya* drug) and *oja* have been described.

CONCLUSIONS

In conclusion, it can be said that choices about management of stress induced fertility are very limited in modern medical science, management portion in only limited to nutritional diet, weight control, proper exercise, use of vitamins like B, C & E along with micronutrients (such as Se, Zn, Mn) and antioxidants. Modern researches are still in research of fertile diet & life style. But as stress has its holistic effect on body physiology. It needs also a holistic approach for a particular person. *Nidan* factors which are responsible for disturbance of body homeostasis should be identified and their effect on *dosha*, *dhatu*, *agni* and *strotas* should be studied according to their symptoms of vitiation then only plan of management can be made according to the severity of *doshic* disturbances.

Present management (nutritional diet, exercise, weight management, avoidance of cigarette, alcohol, caffeine along with psychological counseling) of stress induced infertility needs more focus on its applied aspect. Because stress is individualistic response of particular person against environmental factors so it also needs individualistic approach of management. Individual based management is a

specialty of *Ayurveda* but validation of these concepts is need of the day to understand their effect on changing scenario.

Researchers in field of stress management and its effect on fertility based on *Ayurvedic* concept should be done that can open a new field of research and management protocol for management of stress induced infertility.

Incidence of causative factors related to Ayurvedic concept of doshik vitiation of *ahar* and *vihar* should be studied and identified in patients suffering from stress induced infertility. Incidence of symptoms of doshik imbalance, *agni dusti*, *strotodusti*, *artava dhatu dusti* and *oja-kshaya* should be identified in population suffering from stress along with fertility based issue.

Effect of management protocol as described in *Ayurveda* like *nidan parivarjan*, *achar rasayan*, *body purification*, *rasayana* and *oja-wardhak* drug should be studied individually and in group to understand their synergistic effect. Along with their effect on clinical parameter of stress, studies should be done about their effect on various neuro-harmonal axis like secretion of CRH, ACTH, Beta endorphins, IGF-1, and anti-oxidant level and on reproductive functions like LH surge, process of ovulation, folliculogenesis, tubal motility and implantation.

This study will help to understand relation between environmental factors and their effect on body which are involved in disturbance of reproductive physiology and provide a new area of research for better management of infertility.

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