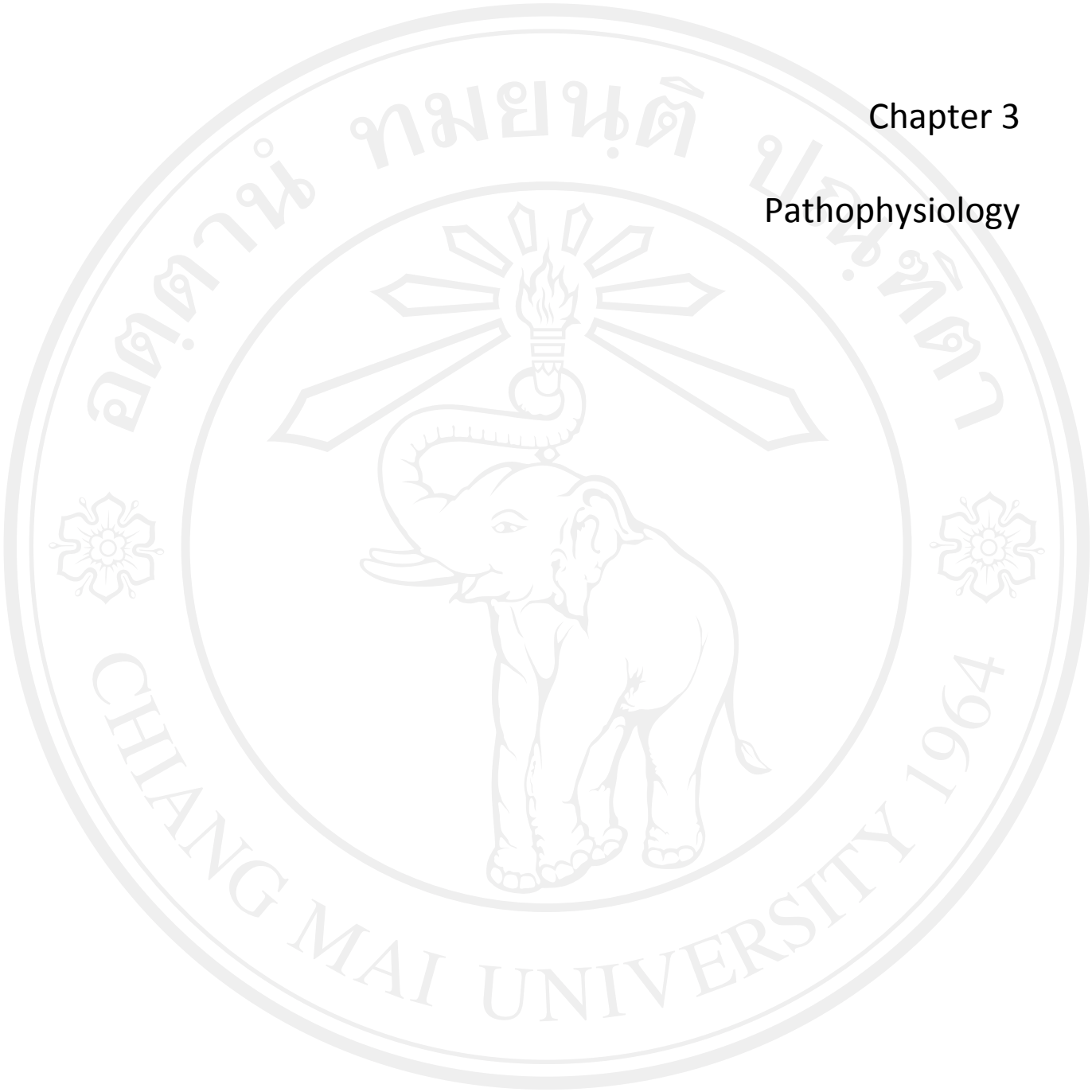
Chapter 3

Pathophysiology



Women with reproductive aging is associated for the most part, however not fully, with the decrease of a finite variety of biological germ cells among the women ovary.[1]This can be slightly decline, however generally the method seems to progress at bound periods during a daily life. To giving birth, there's an identified decrease of just about 50% the existing pool of follicle, after that the decreasing method; atresia, slows to some extent, till an early 40 year old once the full variety of remaining follicles seems to be within the thousands. At this time in life, abnormality appears to progress steady and apace once more and older women movement forwards through the menopausal transition to primarily zero oocytes by age at a median 52.4 years.[2]Menopausal problems are associated with a decrease of procreative hormones created by ovary. This chapter, therefore, presents the method of the menses cycle during a woman's procreative amount, hormonal changes (particularly steroid hormone deficiency), and their effects on women's lives, that are related to menopausal transition.

3.1 Pathophysiology of climacteric symptoms

The menstrual cycle

The cycle could be a continual cycle of physical changes that occur in reproductive-age females.[3]A woman's initial menses is termed menarche, and happens generally around age 12.[4]The cycle, necessary for reproduction, is controlled by the system. There are 3 distinct phases: (1) menses, (2) follicular phase, and (3) luteal phase.[4]These phases vary long between women, and therefore the cycles also vary in individual women. The typical cycle is 28 days.[4]Ovulation; biological process, delineates the transition from the follicular phase to the luteal phase. It aroused by step by step to increase a great amount of estrogen within the phase of follicular, discharge slowly and then stop, after that also the lining of the female internal reproductive organs thicken. Amounts of follicle within the ovary begin to develop underneath an influence of a complicate interaction of hormone, and when many day one or sometimes 2 to come change dominant (follicles by non-dominant become dying). When the LH (LH) surges, sometimes at mid-cycle, the dominant follicle releases an ovum regarding 24-36 hours later. This can be known as ovulation. While not fertilization, the egg is simply viable for a hold day or less. In the same place of the dominant follicle within ovaries to come to be a corpus luteum that produces massive amounts of progesterone. Progestin (progesterone) prepares the mucous membrane for potential implantation of associate embryo. If, when two weeks, there's no implantation, the corpus luteum can die, inflicting each progestin and steroid hormone levels to decrease speedily. Once this happens, menses happens because the lining of the female internal reproductive organ is shed. Menses ends at 45 or 50 for many women: then they enter climacteric.[4]

The restricted variety of follicles inside the ovary plays an expressing norm in terms of ovulation and dynamics of hormone. To reduce a pool of the follicle leads

to a total loss to produce inhibin B, that successively releases a pertaining to physiology 'restraint' on follicle stimulating hormone (FSH) releasing.[2]Increasing in gonadotrophin, characteristics in menopausal transition, may end up in an exceedingly the spectrum functions of the follicle. If the responsive follicles are show, it is attainable to own excessive to produce sex steroids or amounts of folliculogenesis. If also part responsive follicles are show, folliculogenesis might not happen to completion with no ovulation or corpus luteum. Lastly, if no responsive follicles are present, folliculogenesis does not occur and amenorrhoea results. It is necessary to know there are 2 types of follicles—those that are sensitive to and people that don't seem to be sensitive to gondatropin signals. This explains the variability in cycles throughout menopause: why a woman might not menstruate some months and so bleed unremarkably for many a lot of months.[5-11] In early menopausal transition, proof shows the CNS (central nervous system) does not respond unremarkably into sex hormone, failing to provide the mandatory pre-ovulatory LH (luteinizing hormone)surges.[6]Hormonal dynamics across the complete menstrual cycles in an exceedingly a cohort study in community in women with an early stages of the menopausal transitions were studied mistreatment daily urinary sampling with permission of the SWAN(Study of Women's Health Across the state). Cycles of luteal function was analyzed in these women. Subjects' age and body size were prognostic of endocrine cycles. Women of larger body size had usually lower hormone excretion. Hormonal dynamics across the complete menstrual cycles in an exceedingly community-based cohort of women within the early stages of the menopausal transition were studied mistreatment daily urinary sampling with permission of the Study of Women's Health Across the state (SWAN). Cycles of luteal functions were analyzed in these women. Subjects' age and body size were prognostic of endocrine cycles. Women of larger body size had usually lower hormone excretion.[12]SWAN and Melbourne Women's Health Project found terribly closely related to drops in oestradiol and rises in gonadotrophin within the late transition to postmenopause stage.[8, 13]

Clinically, there is necessary to recollect the completion of reproductive system, also not simply the amounts of ovary, is experience modification. Indeed, a number of the foremost common symptoms related to perimenopause are caused by reproductive hormonal fluctuations.

Current concentration of FSH, LH, oestradol (E_2), progestin (P), and therefore the inhibins throughout the traditional menstrual cycle are delineating. The menstrual cycle is characterised by comparatively consisting and lower values for E_2 and INH-A throughout the primary 50% of the follicular phase, as a resultant increase to a mid-cycle peak all day before the mid ovulatory phase of LH surge. When a sudden falls, secondary peaks of E_2 and INH-A secretion are parallel throughout the luteal phase, with a resultant drop resulting in the beginning of menstruation. On the opposite hand, INH-B concentrations are nearly associated to increase and fall of FSH within an early follicular period. They peak at mid-cycle so decrease to the lowest levels

throughout the luteal period. The form of E_2 and INH-Aare maintained in women with regular cycles as they age. It absolutely was found in an exceedingly massive for the study; cross-sectional of frequently cycling amounts of woman aged 24 - 50 year old that the concentrations of E_2 within the early follicular phase were unchanged. The oldest subjects really had a better concentration of E_2 even supposing the circulating follicle-stimulating hormone was raising. In another study, that compared older and young women, showed a rise level of urine estrogens and a fall in urine chemical compound throughout the luteal period. One study has found that the decline in current INH concentration with age most moderately explains the consistent or perhaps higher E_2 concentration in spite of rising follicle-stimulating hormone. Follicular-phase LH concentrations rise solely within the oldest cluster of frequently cycling women. Mensuration of E_2 and INH in each venous blood vessels of frequently cycling women has shown that E_2 concentrations are considerably higher within the vein exhausting the ovaries to contain the most follicle as compared to the contralateral ovarian vein, whereas INH concentrations are equivalent in each ovarian veins despite the aspect as a dominant follicle. Though each E_2 and Inhibins are presented to produce an ovarian granulose cells, differential mechanism are seem as manipulate to secret the 2 Inhibins. According to INH-B seems to develop follicles, meanwhile an INH-A beside E2 comes notably from the dominant cyst. Its postulated to concentrate the current of INH-B that could mirror an amount of follicles to recruit from the primal pools, variety to decreases as age increase.[14]

Consequently, losing E_2 embrace an event of oestrogen deficiency symptoms and undesirable health outcomes, like loss of bone and raised susceptibleness to myocardial infarct and coronary artery disease. Weaken of INH-B production in older women as elevated FSH concentrations within the follicular period of the cycle are often postulated to extend secretion of FSH, that successively provides raised drive to keep up E_2 secretion because the overall ovarian follicle range decreases.[14]

Hormones dynamic

(1) Endocrine dynamics in the common reproductive cycle[15]

Understanding the common secretion dynamics of the hypothalamic-pituitary-ovarian axis is resultant observation throughout perimenopause period. Pituitary gland is regulated by the secretion pulsatile of GnRH (gonadotropin-releasing hormone) from hypothalamus. LH and FSH regulate female internal reproductive organ function. These gonadotropins are subjected to preponderantly negative feedback by sex steroids progestogen and oestrogen. FSH, as shown once isolated pituitary gonadotrophs, is maintained in long-run cell culture within the absence of GnRH. They still turn out important numerous of FSH; however the secretion of LH speedily drops to undetectable levels. LH is therefore entirely GnRH dependent. FSH is subject to feedback negative management that is mediated by Inhibins and sex steroid hormones. Female internal reproductive organ is mirrored by produce sex

steroids and peptide hormones (i.e., Inhibin and activin). Sex steroids embrace oestradiol made by the follicle, progestogen made by corpus luteum when the maturation of androgens, the dominant ovarian follicle, primarily testosterone, and androstenedione which secreted by the theca interna and therefore an ovarian stroma. Appreciation as crucial norm competes as female internal reproductive organ glycoproteins that Inhibin and activin may be comparatively early development. The function of Inhibins includes regulation of gonads, pituitary, and closely long loop for FSH with negative feedback of pituitary. The most important norm of Inhibin is the negative feedback regulation of pituitary FSH secretion. FSH is administrating to stimulate the production of Inhibin that is reciprocally related to FSH concentrations.

(2) Endocrine Dynamics within the menopause[15]

Though important movement forward has created in recent years, hormone options in menopause are still processed. In current understanding encircle, the gametocyte are decline in numbers of climacteric approaches, as described as unsteady female internal reproductive organ hormone production. These are altered to feedback a regulation of pituitary as a result of approaching female internal failure reproductive organ. Roles to decline an inhibin levels are critical, as it reduced negative feedback on pituitary leading to a raised FSH production.

Traditional ideas regarding the endocrine changes characterizing perimenopause enclosed step by step declining oestrogen level and gonadotropins rise. Moreover, to increase the proof that oestrogen and the rise of FSH levels throughout peri-menopause. A number of the longitudinal information is primarily based totally on urinary steroid profiles. Many researchers have elevated oestrogen to produce within the multiple follicles developing in peri-menopausal women. In recent observations, profiles of urinary LH, gonadotrophin, oestrogen and pregnanediol glucuronide in traditional participants in varied steps of menopausal period. Particularly the cycle day of an important follicular period as a rise of oestrogen excretion, therefore the secretion of oestradiol into the circulation is related to reciprocally with FSH. Higher levels of FSH are also related to a long period to rise in oestrogen secreation.

An unsteady endocrine profiles will justify varies symptoms, as well as all those in keeping for transient oestrogen excessing and therefore a huge incidence of female internal reproductive organ hemorrhage. Rises within the frequent of folliculo-development by elevated sex hormone and FSH levels have additionally been found in adolescents. Preservation of E_2 secretion would be fascinating for as long as attainable in females. Consequently, losing E_2 embrace to develop oestrogen sufficient symptoms, and unlikely quality of life outcomes like loss of bone and raised susceptibleness to coronary artery disease and myocardial infarct. Given the confirmation that Inhibin B production by the ovary declines considerably any functions of accelerating women age in frequently cycling, whereas E_2 production is

preserved, it are often postulated that to decline Inhibin-B levels resulted to rise in follicle stimulating hormone when its raised the FSH drive that enables E2 secretion to be maintained as female internal reproductive organ follicle numbers fall. supported the preceding proof, it was hypothesized to fall the levels of Inhibin (propably primarily Inhibin-B) happens by reproductive aging women owing to decline amounts of follicle, permitting an increase in FSH, that results in accelerated follicle development and raised oestrogen excretion in peri-menopausal women. Progestin levels fall as a lot of cycles to be change to anovulatory, and androgens show inconsistent modification.

Traditionally, natural climacteric has been outlined as 12 consecutive months of amenorrhoea. A range of terms and definitions are utilized in medical literature to outline the period before climacteric once a woman's hormonal level is related to irregular expelling cycles and raised episodes of amenorrhoea.[16] In conclusion, the Stages of reproductive Aging Workshop + 10 suggested that in an updates of the 2001 Stages of procreative Aging Workshop (STRAW) criteria by simplified the criteria of hemorrhage in early and late menopausal period. These criteria divided the Stage –3 as late reproductive stage and therefore the Stage+1 as early postmenopause stage, to provide data for the length of Stage–1 and Stage +1 as early postmenopause and suggested the applications are not standing with women's age, ethnicity, body size, or life-style characteristics.[17]

The subsequent given the definition to the staging of criteria:[17]

Stage –3 (Late reproductive stage): late stage of reproduction marks the period once fertility begins to decrease and through that there is also changes in an exceedingly woman's menstrual cycles.

Stage–2 (Early menopausal transition): described by a persistent distinction of a hole week or a lot of within the length of consecutive cycles.

Stage –1 (Late menopausal transition): this stage is indicated by the prevalence of amenorrhoea of more than 60 days. FSH levels are unsteady. It typically elevated into the menopausal vary and nonetheless typically resembling earlier years of reproduction, especially once seeing a rise of oestradiol level. It is throughout this stage that vasomotor symptoms most typically occur. On average, this stage lasts 1 to 3 years.

Stage +1a, +1b, +1c (Early postmenopause): In early postmenopause, continues to decrease FSH and oestradiol till roughly a pair of years when the FMP, when that the amount of those hormones stabilize. Stage +1a begin after amenorrhoea12-monthsbut this period needed to define that the FMP has happened. It corresponds to stop as the "perimenopause", it is still used months when FMP occurred. The Stage +1b include the amount of speedy to make the form in average levels of FSH and oestradiol. Supported researches in changing of hormone, Stages +1a and +1b along are calculable to last, on average, 2 years. Stage +1c that last from 3-6 years sometimes represent stabilization duration of a high level of FSH and low values of oestradiol. In all, early climacteric sometimes lasts between 5-8 years.

Stage +2 (Late postmenopause: shows the duration of restricted changes in reproductive endocrine perform and therefore the processes of physical aging dominate.

(3) Changes in hormone during reproductive aging[18]

Change in FSH: Increasing FSH happens step by step across the middle reproductive years, changing into pronounced in women more than 40s. This etiology is often currently usually approved as GnRH (gonadotropin-releasing hormone) is played a role to stimulate two factors of LH and FSH. Any divergence in their secretion can be described by

- LH and FSH sensitivities; to validate by dose or amounts of pulsatile GnRH excretion,
- Gonadal hormone surroundings, as well as steroid and no steroidal factors, and/or
- Affordable within the tone of pituitary activin and/or follistatin.

To keep as these conclusions, the monotropicis increase in FSH that results from a larger sensitivity to decrease female internal reproductive organ feedback onto hypothalamic-pituitary ovarian axis compared with LH. As a result of the rise in FSH it happens with traditional conjunction and/or perhaps induces levels of oestradiol. Probably that is diminishing to input factors of non steroidal, notably to decrease Inhibin pool of follicles, are accountable for the dampened restrictive character of female internal reproductive organ feedback.

Changes in LH: increasing regular cycle of LH excretion in women were a lot of equivocal than for FSH. Within an exceedingly research of 94 participants' ages 24 s-50s, there was a major rise in average FSH excretion that detected by age 35s, as no aging affects ascertained in LH excretion till age 45s. Another research of 500 frequently cycling unproductive women by identical authors, the rise of FSH levels was ascertained to start in early age at 28s. Additionally, a statistically important rise in average of LH level throughout the follicular period can detect by age 35s, and additional rise in women older than 40s. Not like previous examines, the researchers terminated a rise of FSH and LH concentrations that happened in women with normal ovulatory cycles. It quite early in reproductive lives and will use to be the earliest endocrine markers for aging reproduction.

In present report showed that to regulate LH excretion is comparatively proof against to appear decrease of female internal reproductive organ reserve, with maybe solely a refined rise in concentrations till simply before climacteric. When the ovarian pool is decrease steeply in oestradiol and endocrine Inhibin, an actual fact described for oophorectomy in pre-menopausal women are related to increase (four-to six fold) in the levels of LH. Inside the surgery between 1-4 weeks, any research has proof that female internal reproductive organ inhibin is by far the most input to the GnRH-mediated regulation of LH excretion. It ought to be expected that within the loss of negative feedback signals (oestradiol and Inhibin).When

ovariectomy, the pulse generator of endogenous GnRH could influenced favor FSH excretion.

Changes in ovaries, hypothalamic-pituitary, and cerebral function[19]**:** Once the brain is amongst particular tissues target with sex hormones. Oestrogen, progestin, and androgen also ready inducing many affects in the brain areas (CNS: central nervous system), through to bind for specific receptor. Sex hormones are notaction strictly to regulate the functions of endocrine and sexual activity behavior. To identify oestrogen, progestogen, and androgenic hormone receptor outside the CNS areas, like hypothalamus and pituitary, might justify function roles for totally control in the different of brain functions. Especially specific receptors for gonadal steroids are localized within the amygdaloid nucleus, cortex basal forebrain hippocampus, midbrain rafe nuclei, cerebellum locus coeruleus, glial cells, and central gray matter; by confirm to involve sex hormones. Theses mechanisms are for the controlling quality of life, psychological mechanism and processes of memory in physiological-pathological situations.

The functions of those sex steroids within central nervous system are comparable within peripheral targets organ, manufacturing of non genomic and genomic affects. Within genomic function, steroids also induce comparatively a long mechanism on neurons by activating particular intracellular sex hormone receptors(ER$\alpha$and ERβ).These mechanisms are modulating genome transcription and synthesized protein. Therefore, sex steroids synthesize, reduce and metabolize most of neuroactive transmitters and neuropeptides. According to express the mechanism of receptors. Moreover, sex steroids exert seriously affects in brain that cloud not be attributed to gene functions. Effects of genome steroids are modulate colligation functioning, electrical excitability, and morphological options. In recently, the particularmolecular and cellular functions are underlying the non-genomic mechanisms. Oestrogen has begun to elucidate and can utilize membrane mechanisms directly, like to activate with G-protein-coupled second messenger systems and ligand-gated particle channels, included to regulate neuron-chemical transporters.

Roles for endogenous estrogens within the pathological process of high blood pressure are complicated. Indeed, the consequences of hormonal changes when climacteric are usually disguised as present as the different of cardiovascular risk factors, e.g., vascular in elderly, blood vessel stiffness, overweight, insulin sensitivity by age risk, and dyslipidemia.[20, 21]The results of endogenous oestrogen are mediate via oestrogen receptors (ERs), that embrace the “classic” receptors as ERα and ERβ.[22] ERα and ERβ are settled within the act in nucleus as transcription factors and plasma membrane that are mediate a speedy activation of intracellular signal cascade.[22]There unknown is presently perhaps what extent ERs-dependent or ERs-independent affects, e.g., antioxidant functions of oestrogens or inhibitory effects on SNS; sympathetic nervous system are concerned. The way of oestrogen

dependent signal pathways are controlling BP; blood pressure that altered throughout the different stages totally for human-life.

In postmenopause, neurotransmitters, peptides and steroids endure vital change by of the failure of gonadal hormone production consequently, conveyance of a specific symptoms as results of central nervous system derangement. Hot flushes, sweating, fatness and cardiovascular disease are change of the neuroendocrine within the hypothalamus consequence. Changing in mood, anxiety, mood depression, insomnia, headaches or/and migraine, alterations of psychological feature perform are all associated with postmenopause alterations of the limbic brain.

Change in gonadal hormones and neurosteriods[23]**:** neurosteroids are apply to sex steroids by shape and accumulate within the system of nervous from cholesterol precursors, and a minimum of partly, do thus independently excretion of peripheral steroidogenic gland. Many researchers have shown any psychological mechanisms and any symptom like mood depress, anxious and feeling discomfort will associate with neurosteroids, particularly DHEA and allopregnanolone. Thus, changing in mood, night sweats, anxious, feel depress, sleep disorder and association with psychological feature mechanisms are some potential reduce of regulative effects consequently; exert by gonado-or/and adrenal hormones in postmenopausal women.

Women within the perimenopausal years are a lot of seemingly to hunt medical consultation more than their pre-l or post-menopausal status. Hot flushes, night sweating, problems in sexual desire and psychological symptoms are raised within peri-menopause. These symptoms are demonstrating any by far the most instability, in all probability reflective unsteady hormone profiles. In peri-menopause, the frequent symptom is migraine which additionally unsteady attributed to hormonal profiles.[15]

Changing in the risk factors of cardiovascular disease seem firstly to be associated with women-age and BMI; body mass index, instead of related to the change of hormones over the transition period in menopause. The sole metabolic parameter associated with climacteric as such was the HDL level. All alternative of lipid profiles, BP, and Body-Mass-Index were associated with age, and FMP; final menstrual period.[15]

Metabolic change[16]: Most of women, the evidence of metabolic syndromes happens coincident by the sufficient of oestrogen. Health problems in associated with insulin, central fattiness, dyslipidemias, high blood pressure, and hypercoagulability. There is not thought of some illness being whether a constellation of connected risks factors as along as increasing some chance for disorders. Women in postmenopause have 1 hour raised a risk for metabolic problems, and close to 50%to develop CV; cardiovascular events. This etiology is still unknown, but several accept that underlying pathophysiologies are expounded to increase a visceral fatness and resistance of insulin.

Change in psychological aspects[24]: Oestrogen has directly and inductive effects with neurons. The direct effects of oestrogen on brain occur speedily. As sample, oestrogens altered electric activities with hypothalamus. In the other hand, to induce the oestrogen effects are both delayed to begin and take a long period. Modes of action are assumed to happen by its induce RNA; ribonucleic acid and synthesis protein. This means that the mechanisms of genome cause changes in the levels of particularly gene productionas neurochemical synthesizing enzymes. The study in rats showed that oestrogenmagnifies adrenergic functionswhich has additionally joined to psychological feature talents. Some mechanisms from sex hormone are action on chemistry in brain that offers potential explanations of this hormone on mood and memory.

3.2 Pathophysiology of high blood pressure in menopause

Hypertension (HT) is usually unknown or unsuccessful to treat in women, particularly when climacteric once CV risks raises. For women with pre-menopausal status, an endogenous oestrogen also maintains vasodilation and therefore contributes to BP management. Elderly or/and therefore losing an endogenous oestrogen production, when climacteric, is amid to increase BP, causative by a high prevalence of high blood pressure in aging women. Throughout the menstruation cycles, BP level is reciprocally associated with oestrogen concentrations and lower if 17β-estradiol level get a peak,[25] its reflect the vasodilator mechanism of endogenous 17β-estradiol (E_2).[26] As same as to increase a production of endogenous oestrogen throughout gestation that contributed to maintain normal BP despite of increasing cardiac outputs and plasma volumes.[25, 27]

In primary decade, climacteric is rise in the course of BP.[28]Within the 7th decade, high blood pressure prevalence among women is also more than in men, notwithstanding ethnical backgrounds.[28]Particularly, they are pronounced that BP will increase SBP; systolic blood pressure and pulse pressure in women in post-menopause, meanwhile DBP; diastolic blood pressure remains the same level when compared with men (age-matched).[28]

Key risks of hypertension for climacteric period

Losing ovarian sex hormones during climacteric have several AEs; adverse effect on cardiovascular diseases (CHDs) risks factors. In clinical manifestations of CHDs happen around 10 years later in women when compared with men, therefore to increase the risks speedily at age of 63s.[29] High blood pressure is far and away the foremost vital risks factors that affected women in early post-menopausal year. Regarding 30-500women are developed high blood pressure (BP>140/90 mmHg) before age 60s.According to the onset of high blood pressure will caused a range of health problems which are usually associated to climacteric.[30] Delicate to moderate high blood pressure could cause complaints, like non specific chest pain, sleep

sdisturbance, headaches, palpitations, hot flashes, anxious, mood depress, and tiredness, etc.[31, 32]

Within the study of Women's Health, it was absolutely shown in nearly 40,000good health women (≥45s) who were elevated BP which seems to increases cardiovascular (CV) risks. Because high blood pressure may be predict robustly for the development of DM type-2.[33]Even though in women with pre-menopause, high blood pressure illness has shown to be a potential risk factors for arterial blood vessel disease.[34] Increasing SBP in ageing is principally cause to rise vascular stiffness arteries, including change in atherosclerotic within the vessel wall. SBP rises a lot of steeply in older women compared with the same in men, and it could be associated with the changing of hormone as such throughout climacteric.[35]Many another risk factors that related hormone have a result on the rise of BP throughout climacteric period.[21, 36] The decline within the oestrogen/androgens ratio are dilute with the effects of vasorelaxant of oestrogens on the vessels wall and to promote an assembly of vasoconstrictor factor like endothelia.[37]Male and female sex steroid hormones have a control effect of RAS; renin-angiotensin system. It has an effect on the production of angiotensin and Sodium metabolism. Declining oestrogen level around climacteric caused up regulation of RAS with a rise of plasmarenin activities.[38]It is important to represented that to elevate SBP is taken into account of sensitive predictor in future CV events than DBP.[39]Roles of oestrogens within pathological process for cardiovascular disease are complicated. Actually, consequences for changing hormone when climacteric is usually covert with the show of other CV risks factors, e.g., vascular in ole age, blood vessel stiffness, overweight, insulin sensitivity changes by age, and dyslipidemias.[20] In cross-sectional research indicated that climacteric will increase a chance for CVD by 2-folds, even when adjusted factors like age and BMI.[40]Early onset of climacteric and an extended post-menopausal time are related to higher BP level.[41]

In summary, the proximate years of climacteric are in the course of to increase BP and therefore the prevalence of CVD. These will cause patients who are usually associated with climacteric. To examine the CV risk for an individual woman ought to be a primary step to consider how to treat for peri-menopausal problems particularly treating by lifestyle modification. For women who complaint with severe menopausal problems and low risk of CHD, using HT; hormone therapy within the proximal years during climacteric period is also terribly useful.

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