ISSN 2706-0225 (Print)

SLJOM

The Sri Lanka Journal of Menopause

Volume 1, Issue 2

March 2020

Published by Menopause Society of Sri Lanka

SLJOM

The Sri Lanka Journal of Menopause

Volume 01, No 02, March 2020

Editorial Address
No.112, Model Farm Road,
Colombo 8.
Sri Lanka
Telephone/Fax+94112 699211
E mail: slanerolle@hotmail.com
Website: www.mensocsl.lk

This journal is published biannually.
ISSN 2706-0225 (Print)
ISSN 2714-1659 (Online)

SLJOM
The Sri Lanka Journal of Menopause

General Information

The Sri Lanka Journal of Menopause (SLJOM) is an editorially independent publication owned by Menopause Society of Sri Lanka. The journal publishes peer reviewed work in all areas of Menopause including urogynaecology, oncology and clinical practice.

Submission for Publication
Full instructions for submitting a manuscript can be found on the website at: http://www.menopause.lk. Please note that SLJOM does not accept paper submissions.

Editorial Note
Editors who submit manuscripts, either as corresponding author or contributing author, take no part in any stage of the editorial processing of their manuscript.

Other information about SLJOM can be found by visiting: http://www.menopause.lk. General inquiries may be directed to the Menopause Society of Sri Lanka, No. 112, Model farm Road, Colombo 08, Sri Lanka.
(Tel +940112699211 Fax +940112699211, Email: menosoc.srilanka@gmail.com)

Disclaimer
The publisher, Menopause Society of Sri Lanka cannot be held responsible for errors or any consequences arising from the use of information contained in this journal; the views and opinions expressed do not necessarily reflect those of the publisher, Menopause Society of Sri Lanka and editors, neither does the publication advertisements constitute any endorsement by the publisher,Menopause Society of Sri Lanka and the products advertised.

Advertisement
SLJOM accepts display and classified advertising. The advertising and product information in Journal does not constitute and endorsement or approval by the journal or the publisher of the quality or value of the said product or claims made for it by the manufacturer. It reserves the right to reject any advertisements considered unsuitable according to the set policies of the journal and guidelines related medical advertising laid down by the Government of Sri Lanka.

Subscription information
Copies of the journal are provided free of cost to life members of Menopause Society of Sri Lanka.

Published by:
Menopause Society of Sri Lanka
No.112, Model Farm Road,
Colombo 8, Sri Lanka
Telephone/Fax+94112 699211
E mail: menosoc.srilanka@gmail.com

Printed by:
Lakcom Print
No.88, Pepiliyana Rd,
Gangodawila, Nugegoda, Sri Lanka.
Telephone : 011 2825666 / 0715 555558
E mail: *pushpakumara@gmail.com*

SLJOM
The Sri Lanka Journal of Menopause

Contents

SLJOM
The Sri Lanka Journal of Menopause

Message from the Editor in Chief

Dear authors, reviewers and readers.

It gives me a great pleasure to release issue 2 of volume 1, Sri Lanka Journal of Menopause. At the outset let me thank assisting editors Dr. Sharadha Jayalath and Dr. Chanil Ekanayake for their hard work and their contribution to make this issue.

The global pandemic of novel coronavirus disease 2019 has transformed post reproductive health care around the world into a challenging situation. Medical management, notably women going through the perimenopause and menopause, has come to a new dimensions.

Menopause is a time of transition marked by fluctuating physiologic changes that impact the quality of life of many women with vasomotor symptoms, sleep problems, sexual problems and mood disturbances as well as long-term changes such as genitourinary symptoms, osteoporosis, increase risk of ischaemic heart disease, stroke and sarcopenia.

We must recognize that these difficult times are marred with many uncertainties in terms of social, health and financial security. Uncertainties lead to fear. Excessive fear leads to chaos and total disruption of post reproductive health care in Sri Lanka.

Amidst the pandemic waging through the country and the world, Menopause Society of Sri Lanka continues to serve the post reproductive women in Sri Lanka.

I extend my sincere gratitude to all the authors and contributors to this volume.

Thanking you,

Dr. Sanath Lanerolle
Editor in Chief,
Sri Lanka Journal of Menopause.

Leading Article

Menopause Transition – Physiology, Symptomatology and Management

Sathanadan M[1]

[1]*Consultant Gynaecologist, Reproductive Endocrinologist and Fertility Specialist*

***Corresponding Author** – Dr Sathanandan M (FRCS, FRCOG, FFFP, MPHIL, FSLCOG)*

Email - satha55@btconnect.com

Menopause marks the permanent cessation of menstruation (Final menstrual period = FMP) and can only be diagnosed clinically one year after FMP. Menopause heralds the transition in a woman's life from a reproductive state to a nonreproductive one. Across the world menopause occurs in early 50s, and is only truly affected by smoking and medical or surgical induction of the menopausal state. Clinical symptoms of menopause may precede FMP and the physiological changes of menopause transition may begin several years prior to the onset of any manifestation (usually around 45years and 5 to 6 years prior to FMP). It is the depletion of ovarian follicles to a critical level that heralds menopausal transition [1-3].

In order to understand the context in which the physiological changes of menopausal transition are happening, it is necessary to consider the definitions and stages associated with reproductive aging.

The premenopause is the phase of woman's life from the menarche (onset of menstruation) until the beginning of the perimenopausal stage.

The perimenopause comprises the time from a woman's mature reproductive state at the point when she begins to experience variability in the length of her cycle or a characteristic symptoms of the menopausal transition, to the year following her final menstrual period (FMP). It is only following this 12 month period of amenorrhoea that a diagnosis of menopause can be made. The term menopause and postmenopause are often used interchangeably to describe the phase of woman's life from this point[1,3].

Straw Classification

In 2001, the Stages of Reproductive Ageing Workshop (STRAW) met to propose criteria for defining the stages of reproductive life. The STRAW staging system provides healthcare providers and women with a guide in the assessment of fertility and contraceptive requirements. The latest staging is called STRAW+10.

STRAW+10 staging system is divided into 3 phases.

1) the reproductive phase
2) the menopause transition
3) the postmenopausal phase.

The reproductive stage is subdivided into three stages (-5 to -3). The early reproductive stage (-5) refers to the period immediately following menarche, before menstrual cycles become regular.

During peak reproductive stage (-4) menstrual cycles are regular.

The late reproductive stage (-3) marks the time when fertility begins to go into a decline. It is subdivided into 2 stages. During stage -3b, menstrual cycles are regular but Anti Mullerian Hormone (AMH) levels continue to fall (a process that starts from menarche) as a result of a gradual depletion of antral follicular count.

Stage -3a is characterised by subtle changes in menstrual cycle length and flow. FSH levels rise with increasing variability, whilst levels of antral follicle AMH and inhibin B are low[1].

STRAW -2 is the onset of early menopausal transition where cycle variability increases with a persistent difference of 7 days or more in the length of consecutive cycles. Anatomical and biochemical changes are similar to those of stage -3a, but with increasing variability of FSH levels.

The late menopausal transition (STRAW -1) is characterised by an interval of amenorrhoea lasting at least 60 days[1]. There is increased prevalence of anovulation and further variability in cycle length and hormonal levels. During this stage FSH levels are greater than 25 IU/L and are often associated with high Estragon (E2) levels. However E2 levels start to fall over the last 1-3 years. It is during this time that menopausal in particular vasomotor symptoms usually arise.

Late menopausal transition concludes with FMP (STAW 0). Postmenopausal phase starts from FMP (STRAW +1 to +2). STRAW +1 is defined as the early postmenopausal stage. It is subdivided into three stages. Stage +1a lasts 1 year from FMP and the end of this stage is defined as menopause and marks the end of perimenopause. During stages +1a and +1b (which also lasts one year) , FSH levels continue to rise, while E2 levels continue to fall[1-3]. Thereafter the levels of these hormones begin to stabilise. Vaso Motor Symptoms (VMS) are most likely to occur during this period.

Stage +1c marks a period of stabilization in levels of FSH and E2 which lasts between 3 to 6 years.

The late postmenopausal stage (+2) lasts for the remaining life span of a woman, during which FSH levels tend to fall gradually. Generalised somatic ageing processes rather than reproductive ageing characterise this period. However the prevalence of urogenital symptoms increase at this time[1].

Physiological Changes in the Menopausal Transition

During this period, there is a gradual reduction in the number and quality of ovarian follicles to the critical level[2]. Oocyte production stops at 20 weeks of gestational age when the level is 6 to 7 million follicles. Thereafter the level decreases through a combination of follicular atresia and oocyte release, until fewer than 100 follicles remain in each ovary at the onset of perimenopause (menopausal transition). In addition the oocyte and its surrounding layer of granulosa cells are thought to become increasingly incompetent with age[2].

With decline in antral follicle count in the late reproductive stage and early menopausal transition, there is a reduced amount of inhibin B production by the granulosa cells[2]. Inhibin B usually has a negative feedback mechanism in the pituitary to reduce rising levels of FSH.

Lower levels of inhibin B fail to keep this mechanism in check which leads to higher levels of FSH during the early follicular phase. This in turn leads to increased activity of a single dominant follicle or the recruitment of multiple dominant follicles, and thus higher levels of E2 production. As E2 levels rise to a critical level.

At an earlier stage, the LH surge occurs earlier and the follicular phase is shortened, which in turn reduces the overall cycle length[2]. The luteal phase does not change in duration until later in transition. This shortened menstrual cycle does not occur in all women entering perimenopause.

As women move onto late menopausal transition, menstrual cycle becomes progressively longer in duration. The proportion of cycles which are anovulatory also increases. This may be due to a variety of reasons.

1) A progressive deregulation of positive and negative feed back mechanisms in the hypothalamic pituitary ovarian axis. High levels of E2 which elicits an LH surge in the middle of the cycle has failed.

2) A fall in E2 in the luteal phase has also failed to lower the circulating levels of LH due to hypothalamic-pituitary insensitivity.

3) In the ovary, high levels of FSH may also prevent ovulation occurring inspite of LH surge.

Progesterone levels appear to fall steadily throughout menopausal transition. This may be due to reduced Progesterone production from corpus luteum as well as increase in the frequency of anovulatory cycles[2].

Levels of E2, only falls in the 2 years preceding FMP (this has been noted in the prolonged ovulatory cycles) whilst FSH levels continue to rise. Only 12 months following FMP, the E2 levels are persistently low. In the postmenopausal women, it is the estrone (E1) that predominates in the circulation. This is generated by conversion of Androgens (secreted by adrenal glands and postmenopausal ovaries) in the adipose tissue and liver.

FSH levels undergo slow decline in the late menopausal transition[2]. Whilst there is little change in the levels of testosterone across the transition, levels of SHBG (Sex Hormone Binding Globulin) falls leading to an increased proportion of free testosterone[3].

AMH produced by antral follicles is not directly involved in feedback mechanisms. AMH is high at menarche and then declines after 26 years. It is almost undetectable in the 5 years preceding menopause.

Symptoms of Menopausal Transition

Meopausal transition and postmenopausal period are characterised by broad range of physical and psychological symptoms which can be extremely debilitating.

A woman has about 400000 potential oocytes in her ovaries at menarche. She loses these at a rate of 1000 per month regardless of whether she takes oral contraceptive pills which inhibits ovulation but does not spare oocytes.

Symptoms of menopausal transition also called climacteric, are usually reported as a continuum and can be classified into several types:-

- VASOMOTOR SYMPTOMS:- include hot flushes, palpitations, night sweats, altered sleep pattern and fatigue.

- NEUROMUSCULAR :- these include headaches, joint and muscular pain. other degenerative changes may also occur such as hair and skin changes, which can include a crawling sensation (formication) and itchy skin.

- PSYCHOGENIC :- these include poor concentration, forgetfulness, depression, anxiety, claustrophobia, agoraphobia, irritability, difficulty in coping, tearfulness and lack of drive including sex drive.

- UROGENITAL :- symptoms of vaginal dryness, uterovaginal prolapse and urinary symptoms of urge incontinence / overactive bladder.

- INDIRECT SYMPTOMS :- of menopausal osteoporosis – repeated fractures.

There is a huge variation in the frequency and severity of menopausal symptoms between different women.

About 20% have no significant symptoms, 60% have mild to moderate symptoms and 20% have very severe symptoms.

Menopause induced by surgery or chemo/radiotherapy usually have more severe symptoms.

Vasomotor Symptoms

Hot flushes adversely affect many women in menopausal transition (MT). These symptoms persist for 5 years on average. It is thought that the alpha adrenergic system, specifically noradrenaline, is the chemical trigger triggered by decreasing Estrogen levels. Hot flushes can be aggravated by stress, anxiety, diet, lifestyle and other medications.

Although night sweats can keep women awake at night, insomnia associated with menopause is likely to be due to a separate mechanism (loss of neuronal modulation of energy metabolism), and one can occur without the other[4].

Neuromascular Symptoms

Joint pain is a common complaint in perimenopausal women. Estrogen is thought to attenuate inflammation and promote cartilage turnover[5].

Headaches and migraine are also common symptoms in the perimenopause. In migraine, continuous hormone replacement therapy should be considered, preferably using a non-oral route and lowest effective dose. Estrogen gives variable results for headaches.

If Estrogen is contraindicated, migraine can be treated with serotonin reuptake inhibitors such as venlafaxine, fluoxetine and paroxetine, which all have shown efficacy[6]. Lifestyle changes alone or in combination with isoflavones may be used for prevention of migraine in MT. Gabapentin also reduces frequency and severity of migraine.

Psychogenic Symptoms

During perimenopause, psychogenic symptoms such as fear of ageing (and wrinkles), changing body shapes, financial pressures, relationship issues, and changing roles with children becoming independent. Estrogen imbalance may aggravate any or all of these. Women who have a past history of depression, or have a history of premenstrual syndrome are more likely to experience psychogenic changes during the perimenopause providing HRT will alleviate Estrogen deficiency, but cannot compensate for many of the factors which may be responsible for low mood. However, certain types of depression which are due to Estrogen deficiency are best treated by HRT[7].

Urogenital Symptoms

Vaginal problems are common and under reported.

Vaginal dryness due to Estrogen deficiency, can cause sexual problems due to lack of lubrication and loss of tissue elasticity.

Loss of normal vaginal secretions can also be associated with an overgrowth of vaginal commensal organisms, resulting in vaginal discharge.

In addition to the vagina, urogenital tract is also affected by lack of Estrogen and this may present as urgency or urge incontinence.

Urogenital problems respond best to local Estrogen therapy. Which includes creams, tablets and vaginal rings. Only Vagifem 10 microgram inserted into the vagina twice a week, is licensed to be used without additional progesterone, lifelong in women with an intact uterus.

Osteoporosis

Women lose 1% of their bone mass each year after ovarian failure and Estrogen replacement can inhibit this.

Quantifying Symptoms

To document the severity of symptoms, a quantitative score sheet has been developed. This enables women to self-score their symptoms on a scale of 0 to 3 and for the total score to be calculated. Not only this allows the severity of symptoms to be accurately assessed, but it also allows follow up of any change / improvements as a result of any therapy.

Menopausal Symptomatology Score Sheet

Symptom	*Score (0 = nil, 1= mild, 2=moderate, 3=severe)*
VASOMOTOR SYMPTOMS	
Hot flushes	
Night sweats	
Crawling feeling under the skin	
Dry skin	
NEURO MUSCULAR SYMPTOMS	
Muscle pains	
Backache	
Headaches	
Joint pains	
PSYCHOLOGICAL SYMPTOMS	
Depression	
Irritability	
Mood swings	
Anxiety	
Inability to sleep	
Tiredness	
Loss of sex drive	
Unloved feelings	
Tearfulness	
UROGENITAL SYMPTOMS	
Dry vagina	
Painful sex	
Urinary frequency/urgency	
Total Score	

Differential Diagnosis

Before we describe a woman's symptoms as being due to climacteric (Menopausal Transition / Perimenopause) we need to be sure we are not missing a medical problem. The three commonest medical problems that can be confused with menopausal symptoms are hypothyroidism, anaemia and depression. Depression is particularly difficult as it is very common in women during perimenopause.

Conclusion

Take a good history about symptoms of menopause.

Using the score sheet is a valuable way of quantifying the symptoms. Take a detailed history with

respect to risk factors for breast cancers, thromboembolic disease and osteoporosis.

Ordering a series of expensive hormone tests in women undergoing physiological menopause is a waste of resources.

Firstly, FSH levels are variable and single raised level is not meaningful.

Secondly, Estrogen levels vary a lot from day to day and its blood level bear no relationship to the symptomatology.

Thirdly the results of hormone tests will not change the management of the patient. This should be determined by the women's symptoms.

The initial prescription of HRT is a therapeutic trial. Using the score sheet is a more objective way of evaluating any improvement in symptoms during treatment. Maximum possible score is 60.

If there is improvement, continue the prescribed treatment. If there is no improvement, a different preparation of HRT could be tried.

References

1) Harlow SD, Gass M, Hall JE, et al. Executive summary of the stages in Reproductive Aging Workshop +10: addressing the unfinished agenda of staging in reproductive aging . The Journal of Clinical Endocrinology and Metabolism 2012; 97:1159-1168

2) Butler HG, Santoro N, The Reproductive Endocrinology of menopausal transition. Steroids 2011; 76:627-635

3) Burgher HG, Hale GE, Robertson DM, Dennerstein L. A review of hormonal changes during the menopausal transition: focus on findings from the Melbourne Women's Midlife Health Project. Human Reproductive Update 2007; 13:559-565

4) Bourney RE, Primary menopausal insomnia: definition, review and practical approach Endocrine Practise 2011; 17:122-131

5) Kaunitz AM, Should new onset arthralgia be considered a menopausal symptom? Menopause 2013; 20:591-593

6) MacGregor EA, Headache and hormone replacement therapy in the postmenopausal women. Current Treatment Options in Neurology 2009; 1;10-17

7) Stud J, Personal view: hormones and depression in women. Climacteric 2015; 18(1):3-5

Volume 1, Issue 2
March 2020

SLJOM The Sri Lanka Journal of Menopause

Review

Sexual Functions in Perimenopause

Randombage P[1], Jayawardane M[2]

[1]Senior Registrar in Obstetrics and Gynaecology, Colombo South Teaching Hospital, Kalubowila.

[2]Consultant Obstetrician and Gynaecologist and Senior Lecturer, Faculty of medical sciences, University of Sri Jayewardenepura

***Corresponding Author** - Dr. Prabath Randombage*

E mail - prabathrandombage@gmail.com

No conflicts of interest

Abstract

Sexual dysfunction is a rising problem especially in those who are at perimenopausal age. It goes hand in hand with aging, medical and surgical comorbidities, psychological factors as well as relationship factors. More and more women seek the opinion of doctors since it has disrupted their quality of life. The prevalence is hard to determine since women are reluctant to come up with the complaint of sexual dysfunction. Remedies have been coming up such as topical moisturizer applicants to newer hormone replacement therapies. Psychological phenomenon has been further explored since many women are suffering from depression and other infirmities of the mind. Even though studies have been done, the problem is far from resolved and further studies and newer methods should be produced to improve quality of life and provide a long lasting solution for sexual dysfunction.

Key words

Sexual functions, perimenopause

Introdution

Sexual functions of women's life have received increased attention from medical, pharmaceutical and public health fields during recent decade. It is regarded as an integral part of a woman's life and studies are being conducted to access the sexual functions and their quality of life. In the Study of Women's Health Across the Nations in America (SWAN) has revealed that more than 75% of women in their middle age think sex is either moderately or extremely important to their functioning of life[1].

Menopause is a physiological phenomenon of women. However beyond that it causes many biopsychological changes which results in reduction of quality of life. Sexual dissatisfaction leads among these changes[2,3].

Sexuality is an important aspect of life. It is affected by biological, physical, hormonal, emotional and social factors[4]. Moreover current relationship with the partner, male sexual dysfunctions and polypharmacy at this age also affect sexual behavior[5].

Sexual dysfunction increases with age due to reduction of Estrogen which is physiological during menopausal transition. Thus both aging and natural menopause have negative effect on aspects of sexuality like libido, arousal, desire, orgasm and sexual activity. If the physical activity of women remain high it will positively affect the sexual functions[6]. Estrogen is also important for awareness and receptivity of sexual functions. Further the depletion of Estrogen results in vaginal dryness and deep dyspareunia. Other than that urogynaecological issues like pelvic muscle weakness, prolapse and urinary incontinence have negative impact in sexuality and quality of life[7,8].

It has proven that use of HRT improves the sexual functions in many aspects like orgasm, lubrication and pain relief. It has also shown among the sexually active women the hormonal treatment may result in sexual dysfunction due to the decline in androgen levels. So the exact role is still unclear[9].

Relationship between sexual function and severity of menopausal symptoms can be assessed using the Female Sexual Function Index (FSFI) and the Menopause Rating Scale (MRS).

Prevalence

It is a difficult task to measure the exact prevalence of sexual dysfunction in community since many women are reluctant to disclose their personnel and private information. A study done recently showed 24 percent of Caucasian and African American women aged between 20 and 65 years reported distress associated with sexual relationship[13].

Sexual dysfunction and frequency of symptoms increase directly with age in both men and women whereas the personal distress about these symptoms diminishes as women age.

Most women had never spoken to a doctor about their sexual functions and Nusbaum and colleagues found that only 14% to 17% of women reported their sexual functions. The patient was nearly twice as likely as the physician to have initiated the discussion on their sexual functions if the topic has been raised[14].

Menopause vs. Perimenopause

Consecutive 12 months of amenorrhea in the absence of physiological causes like pregnancy and lactation, and in the absence of pathological causes like hysterectomy which results in termination of menstruation and declining of ovarian functions epidemiologically defines the menopause. Perimeopause however is not clearly defined in the literature. It is manifested with menstrual irregularities and occurrence of vasomotor symptoms during the transitional period to menopause. More recent research has distinguished between early and late perimenopause based on a more rigorous, consensus-based staging system (Stages of Reproductive Aging Workshop - STRAW) for reproductive aging in women[15].

Overview of Sexual Functions

Sexual performance according to the perspectives of Masters and Johnson, illustrates a linear model. It reflects male sexuality more accurately than female, where it is more qualitative. The linear model being a progression from desire to arousal and excitement leading to orgasm followed by a refractory period.

This complex subject is usually studied in aspects of desire with sexual thoughts and fantasies, arousal, frequency and sexual activity which includes intercourse, masturbation, orgasm and satisfaction. However there are wide variations among attitudes towards sexuality and pathologies like pain during intercourse and difficulty to reach the orgasm, which also affect negatively for the poor functioning[16].

Some studies have broadly divided this into two: libido and potency. Libido comprises sexual interest, desire, drive, motivation and pleasure and potency is the physiologically measurable events like arousal, activity, and overall sexual response. Also the other measures of potency like dyspareunia and vaginal dryness has clear relationships with the menopause[17].

An international consensus group has highlighted the importance of intimacy and sexual stimuli for innate female sexual drive, which is an expansion to the already developed models in the latter part of 20th century. In a woman's perspective, it is not necessary to have an innate sexual drive or libido for a healthy and satisfying sexual life. This grants the improved understanding of true female psychosexual disorders that represents the reality of woman's sexual lives. Sexual motivation of a relationship includes the desire to reinforce physical and emotional intimacy and sexual stimuli then can be processed in the mind, influenced by biological and psychological factors. As a result

arousal and desire occur, which could easily disrupted by physical and mental pain[18].

Factors Contributing to Sexual Dysfunction

There are several factors that contribute to sexual dysfunction among women. Hormonal effects have a major impact on sexual response as it alters the normal physiology of a woman and cause adverse effects.

Different non communicable diseases such as diabetes mellitus and communicable diseases also have an effect on sexual functions on both genders. Side effects of pharmaceuticals for the diseases might have an adverse effect on sexual functions and may cause a significant deterioration as the disease and the drugs having a synergistic effect.

Psychosocial and aging factors are often reported as more important determinants than ovarian function among mid-aged women. Aging is inevitable and with it the overall sexual function deteriorates significantly.

Factors such as availability of a partner, previous sexual behaviour and enjoyment, relationship quality, psychological function, general physical health and ethnicity also contribute to the sexual functioning of a woman[19].

Women tend to disregard the psychological factors as well as infirmities in the mind due to the stigma that is present in the community. Depression and other psychological symptoms cause less desire and lower frequency of sexual intercourse. Smoking is one of the important factor related to reduced desire and frequency of sexual intercourse due to the negative effects on sex steroids[20].

Sexual satisfaction promotes further sexual activity by breaking the cycle of negative feedback. Pressures from other influences, including the media, proposing alternative criteria for 'normal' sexual behavior can increase performance anxiety and dissatisfaction in women as well as in men.

Painful intercourse is a common complaint in particular among perimenopausal women. Study done on middle aged women found an inverse relationship between sexual desire and painful intercourse beginning in the late perimenopause, as well as an increase in masturbation during early perimenopause. Also vaginal dryness was highly associated with pain and lower sexual arousal and pleasure.

Wide understanding of these factors and how it affects normality of the sexual functions are paramount important in patient counselling and deciding future management options[21].

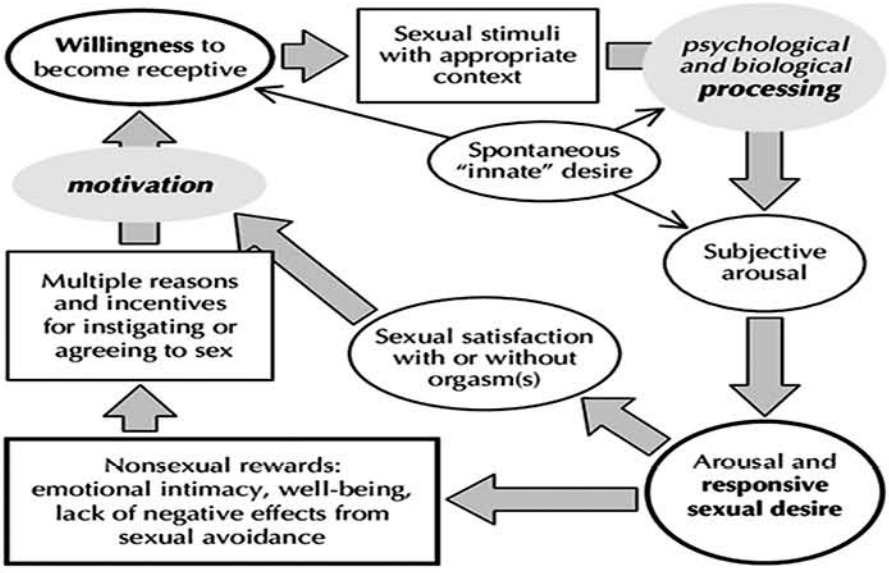

Figure 1: International consensus model of female sexuality[22].

Diagnosis

The doctor should be mindful enough to ask the sexual problems as the patients may be reluctant to discuss them. Developing trust between patient and healthcare professional allows greater exploration of fears, fantasies and difficulties that often do not need referral. Taking a good sexual history is the corner stone and another way is by using questionnaires.

Female Sexual Function Index (FSFI) and the Menopause Rating Scale (MRS) can be used to assess the problems of these aspects[10]. The MRS has been standardized and translated into many languages and widely used in many researches. It has Subjective complaints of which 11 items are classified into 3 domains[10]:

- Psychological (4 symptoms: depressed, irri table, anxious, exhausted)
- Somatic (4 symptoms: sweating or hot flushes, cardiac complaints, sleeping disorders, joint and muscle complaints)
- Urogenital symptoms (3 symptoms: sexual problems, urinary problems, and vaginal dryness).

Female Sexual Function Index (FSFI-19) is used to assess sexual functions among women aged 18 to 70 years. FSFI consists of 19 questions evaluating 6 domains of female sexual function: sexual desire, arousal, lubrication, orgasm, satisfaction and pain in the previous 4 weeks[11,12].

Management Options

Increasing number of women seeks medical advice for sexual dysfunction. There are several treatment modalities available. However there is a paucity of research on the treatment of sexual dysfunction, specifically in the perimenopause.

Estrogen therapy in all forms (i.e. oral, transdermal and vaginal) is effective in treating vaginal pain and dryness. However it is less effective in other aspects of sexual function[23,24].

Even a good doctor patient relationship can allow resolution of the symptoms of a woman. Concomitantly, hormonal and pelvic interventions can act synergistically to improve the sexual dysfunction of the woman.

For urogenital symptoms, treating vaginal atrophy and urinary tract infections is the mainstay. As last resort, surgery can be considered.

Psychological Treatment

Psychological treatment itself can improve the well being of a woman. As the first step, education of anatomy, physiology, and expectations can be addressed. Next, disparities in sexual desire between partners can be addressed in couple's therapy. For women whom never had or rarely experienced orgasm, a technique which is known as directed masturbation can be used either alone or with the partner and has shown a success rate of 65%[25].

Other women who are able to have an orgasm while masturbating, but find the pressure of a sexual encounter with their partner too anxiety provoking, Masters and Johnson's sensate focus (SF) method can be a useful tool. It consists of progressive levels of touching, starting with nonsexual touching, progressing to more sexual touching, and eventual intercourse or other direct genital stimulation.

For women experiencing pervasive anxiety, or other mood symptoms, cognitive behavioral therapy (CBT) can be used[26].

Non Hormonal Pharmacotherapy

In a study done on premenopausal women who is with SSRI induced arousal or orgasmic problems, Sildenafil has been found to have a superior effect than placebo on arousal and orgasmic dysfunction. Despite more than 80% of the women complaining of decreased desire at study baseline, low desire was unaffected by sildenafil treatment[27].

Hormonal treatments

Menopausal replacement therapy (MRT) is the current treatment of choice. There is an increased risk of having a serious side effect of hormone replacement therapy such as cardiovascular disease, cerebrovascular disease, deep vein thrombosis and breast and ovarian cancers. Risks versus benefits should be compared if the patient has severe postmenopausal symptoms, as the risk of the adverse effects occurs in a very small percentage. This issue was addressed by the Women's Health Initiative. Due to the benefits of MRT, clinicians and patients warrant the use of exogenous hormones as a treatment, at least through the perimenopause[28]. Several trials have reported that MRT leads to increased desire for sex in postmenopausal women[29].

For women experiencing vaginal atrophy and who do not wish to take systemic Estrogen, topical Estrogen creams has remarkable effects improving symptoms. Low-dose local vaginal Estrogen delivery as treatment for vaginal atrophy is effective and well tolerated[30].

However, clinicians should be more aware of the risk of breast cancer, even can be attribute by vaginal Estrogen according to the recent meta-analysis of epidemiological studies[31].

A recent study has shown an increase in sexual desire and frequency of satisfying sexual encounters by using a testosterone patch in surgically menopausal women. Though androgenic adverse events (e.g. acne, hirsutism) was higher in the testosterone group, most were mild. Although it improved sexual functions, the testosterone patch failed to gain FDA approval in 2004 due to concerns over long-term safety[32].

Tibolone is a synthetic steroid sex hormone with Estrogenic, Androgenic, and Progestogenic effects. Studies have shown Tibolone to be superior to HRT in improving of sexual performance, including general sexual satisfaction, sexual interest, sexual fantasies, sexual arousal and orgasm, with decreased frequency of vaginal dryness and dyspareunia[33].

Upcoming Methods

Vaginal lubricants and moisturisers have a place in reducing vaginal dryness and pain during intercourse in women with mild to moderate valvo-vaginal atrophy. Lubricants and moisturisers work in different ways and are particularly helpful for women who are not medically suitable to take Estrogen. Although lubricants do not have long-lasting effects; it mainly provides short-term relief during intercourse.

Vaginal erbium and CO2 lasers have been used to treat valvo-vaginal atrophy and studies suggest a significant improvement in symptoms, including vaginal dryness and dyspareunia. However larger studies and strong evidence are lacking how these treatment options improve the sexual functions among perimenopause[34].

Selective Estrogen receptor modulators (SERMs) act as Estrogen agonists / antagonists. Raloxifene and Tamoxifen are well known SERMs, but are not effective in the treatment of valvo-vaginal atrophy. Recent studies have shown reduced dyspareunia in postmenopausal women treated with Lasofoxifene. The Selective Estrogen Menopause and Response to Therapy 1 (SMART-1) study have shown that Tissue-selective estrogen complexes improved vaginal atrophy with reduced incidence of dyspareunia at 2 years compared with placebo[35].

Conclusion

Sexual dysfunction among women is a rising problem especially those who are at perimenopausal age. The dysfunction can be related to the anatomy, physiology or the psychological factors of the woman. Many studies have been done to seek the root cause of the pathologies as well as to seek management modalities. Newer methods have risen as management options, but the problem seems far from being solved. Studies should be done addressing different aspects of a woman's life to conjure an effective treatment, to improve their quality of life significantly.

References

1. Cain VS, Johannes CB, Avis NE, Mohr B, Schocken M, Skurnick J, et al. Sexual functioning and practices in a multi-ethnic study of midlife women: Baseline results from swan. Journal of Sex Research 2003; 40(3):266–276. Available from: https://doi.org/10.1080/00224490309552191

2. Dąbrowska-Galas M, Dąbrowska J, Michalski B. Sexual Dysfunction in Menopausal Women. Sexual Medicine 2019; 7(4):472–479.

3. Dennerstein L, Dudley E, Burger H. Are changes in sexual functioning during midlife due to aging or menopause? Fertil Steril 2001; 76(3):456–460. Available from: http://www.sciencedirect.com/science/article/pii/S0015028201019781

4. Yánez D, Castelo-Branco C, Hidalgo LA, Chedraui PA. Sexual dysfunction and related risk factors in a cohort of middle-aged Ecuadorian women. Journal of Obstetrics and Gynaecology 2006; 26(7):682–686. Available from: https://doi.org/10.1080/01443610600914021

5. Thornton K, Chervenak J, Neal-Perry G. Menopause and Sexuality. Endocrinology and Metabolism Clinics of North America 2015; 44(3):649–661. Available from: https://doi.org/10.1016/j.ecl.2015.05.009

6. Jamali S, Rahmanian A, Javadpour S. Examining the sexual function and related attitudes among aged women: A cross- sectional study. International Journal Reproductive Biomedicine 2016; 14(1):29–38.

7. Wróbel B. Assessment of painful sexual intercourse occurrence among women in gynaecological practice Ginekologia Polska 2008; 79(11):762-767. Available from: https://journals.viamedica.pl/ginekologia_polska/article/view/46674

8. Aukee P, Penttinen J, Airaksinen O. The effect of aging on the electromyographic activity of pelvic floor muscles: A comparative study among stress incontinent patients and asymptomatic women. Maturitas 2003; 44(4):253–257. Available from: http://www.sciencedirect.com/science/article/pii/S0378512203000446

9. Schwenkhagen A. Hormonal Changes in Menopause and Implications on Sexual Health. Journal of Sexual Medicine 2007; 4(s3):220–226. Available from: https://doi.org/10.1111/j.1743-6109.2007.00448.

10. Heinemann LAJ, Potthoff P, Schneider HPG. International versions of the Menopause Rating Scale (MRS). Health and Quality of Life Outcomes 2003; 1:1–4.

11. Wiegel M, Meston C, Rosen R. The Female Sexual Function Index (FSFI): Cross-Validation and Development of Clinical Cutoff Scores. Journal of Sex and Marital Therapy 2005; 31(1):1–20. Available from: https://doi.org/10.1080/00926230590475206

12. Rosen R, Brown C, Heiman J, Leiblum S, Meston C, Shabsigh R, Ferguson D, D'Agostino R. The Female Sexual Function Index (FSFI): A Multidimensional Self-Report Instrument for the Assessment of Female Sexual Function. Journal of Sex and Marital Therapy 2000; 26(2):191–208. Available from: https://doi.org/10.1080/009262300278597

13. Bancroft J, Loftus J, Long JS. Distress about Sex: A National Survey of Women in Heterosexual Relationships. Archives of Sexual Behaviour 2003; 32(3):193–208.

14. Albertsen PC. The Changing Nature of Women's Sexual Health Concerns Through the Midlife Years. Journal of Urology 2005; 174(5):1969.

15. Soules MR, Sherman S, Parrott E, Rebar R, Santoro N, Utian W, et al. Executive summa-

ry: Stages of Reproductive Aging Workshop (STRAW). Climacteric 2001; 4(4):267–272. Available from: https://doi.org/10.1080/cmt.4.4.267.272

16. Davidson JM. Sexual behavior and its relationship to ovarian hormones in the menopause. Maturitas 1985; 7(3):193–201. Available from: https://doi.org/10.1016/0378-5122(85)90040-4

17. Masters WH, Johnson VE. Human sexual response, Boston (Little, Brown and Company) 1966. Available from: https://opus4.kobv.de/opus4-Fromm/frontdoor/index/index/docId/15944

18. Domoney C. Psychosexual disorders. Obstetrics, Gynaecology and Reprodive Medicine 2018; 28(1):22–27. Available from: https://doi.org/10.1016/j.ogrm.2017.10.004

19. Dennerstein L, Dudley E, Burger H. Are changes in sexual functioning during midlife due to aging or menopause? Fertil Steril 2001 [cited 2020]; 76(3):456–460. Available from: https://www.sciencedirect.com/science/article/pii/S0015028201019781

20. Johnston JR CC, Hui Siul, Witt RM, Appledorn R, Baker RS, Longcope C. Early Menopausal Changes in Bone Mass and Sex Steroids*. Journal of Clinical Endocrinology and Metabolism 1985; 61(5):905–911. Available from: https://doi.org/10.1210/jcem-61-5-905

21. Avis NE, Green R. The Perimenopause and Sexual Functioning. Obstetrics and Gynecology Clinics North America 2011; 38(3):587–594. Available from: http://dx.doi.org/10.1016/j.ogc.2011.05.009

22. Damjanović A, Duišin D, Barišić J. The evolution of the female sexual response concept: Treatment implications. Srp Arh Celok Lek 2013; 141(3–4):268–274.

23. Huang A, Yaffe K, Vittinghoff E, Kuppermann M, Addis I, Hanes V, et al. The effect of ultra low-dose transdermal estradiol on sexual function in postmenopausal women. American Journal of Obstetrics and Gynecology 2008; 198(3):265-265. Available from: http://www.sciencedirect.com/science/article/pii/S0002937807011830

24. Gast MJ, Freedman MA, Vieweg AJ, De Melo NR, Girão MJBC, Zinaman MJ, et al. A randomized study of low-dose conjugated Estrogen on sexual function and quality of life in postmenopausal women. Menopause 2009; 16(2). Available from: https://journals.lww.com/menopausejournal/Fulltext/2009/16020/A_randomized_study_of_low_dose_conjugated.7.aspx

25. McMullen S, Rosen RC. Self-administered masturbation training in the treatment of primary orgasmic dysfunction. Journal of Consulting and Clinical Psychology 1979; 47:912–918.

26. McCabe MP. Evaluation of a Cognitive Behavior Therapy Program for People with Sexual Dysfunction. Journal of Sex Marital Therapy 2001; 27(3):259–271. Available from: https://doi.org/10.1080/009262301750257119

27. Nurnberg HG, Hensley PL, Heiman JR, Croft HA, Debattista C, Paine S. Sildenafil Treatment of Women With Antidepressant-Associated Sexual Dysfunction: A Randomized Controlled Trial. JAMA 2008; 300(4):395–404. Available from: https://doi.org/10.1001/jama.300.4.395

28. Wassertheil-Smoller S, Hendrix S, Limacher M, Heiss G, Kooperberg C, Baird A, et al. Effect of Estrogen Plus Progestin on Stroke in Postmenopausal WomenThe Women's Health Initiative: A Randomized Trial. JAMA 2003; 289(20):2673–84. Available from: https://doi.org/10.1001/jama.289.20.2673

29. Modelska K, Cummings S. Female sexual dysfunction in postmenopausal women: Systematic review of placebo-controlled trials. American Journal of Obstetrics Gynecology 2003; 188(1):286–93. Available from: http://www.sciencedirect.com/science/article/pii/S0002937802714476

30. The Board of Trustees of The North American Menopause Society (NAMS). The role of local vaginal estrogen for treatment of vaginal atrophy in postmenopausal women. Menopause 2007; 14(3):357–369. Available from: http://content.wkhealth.com/linkback/openurl?sid=WKPTLP:landingpage&an=00042192-200714030-00008

31. Type and timing of menopausal hormone therapy and breast cancer risk: individual participant meta-analysis of the worldwide epidemiological evidence. Lancet 2019; 394(10204):1159–1168. Available from:http://www.sciencedirect.com/science/article/pii/S014067361931709X

32. Braunstein GD, Sundwall DA, Katz M, Shifren JL, Buster JE, Simon JA, et al. Safety and Efficacy of a Testosterone Patch for the Treatment of Hypoactive Sexual Desire Disorder in Surgically Menopausal Women: A Randomized, Placebo-Controlled Trial. JAMA Internal Medicine 2005; 165(14):1582–1589. Available from: https://doi.org/10.1001/archinte.165.14.1582

33. Nijland EA, Weijmar Schultz WCM, Nathorst-Boös J, Helmond FA, Van Lunsen RHW, Palacios S, et al. Tibolone and transdermal E2/NETA for the treatment of female sexual dysfunction in naturally menopausal women: results of a randomized active-controlled trial. Journal of Sexual Medicine 2008; 5(3):646—656. Available from: https://doi.org/10.1111/j.1743-6109.2007.00726.x

34. Khanjani S, Panay N. Vaginal estrogen deficiency. The Obstetrician and Gynaecologist 2019; 21(1):37–42.

35. Mirkin S, Komm BS. Tissue-selective estrogen complexes for postmenopausal women. Maturitas 2013; 76(3):213–220. Available from: http://www.sciencedirect.com/science/article/pii/S0378512213001874

Review

How Accurately Can You Suspect Endometrial Carcinoma in PMB?

Ilukpitiya IGDC[1]

[1]*Post graduate trainee, Registrar in Gynaecology and Obstetrics, Professorial Unit, University of Sri Jayawardenepura, Colombo South Teaching Hospital, Kalubowila.*

***Corresponding Author** - Dr Ilukpitiya IGDC*

E mail – ilukpitiyad@yahoo.com

Abstract

Endometrial carcinoma is the second commonest gynaecological carcinoma worldwide, which is more frequently present as postmenopausal bleeding in early stages. Evaluation of endometrial thickness by 2D and 3D transvaginal ultrasonography, saline infusion sonography, MRI, blind and hysteroscopic guided endometrial biopsy are the investigations available to evaluate postmenopausal bleeding. Many studies has been conducted to assess and compare the accuracy of each investigation and found to have differences in sensitivity, specificity and predictive values on diagnosing endometrial malignancies. Therefore, systematic analysis of symptoms, risk factors and supportive investigations will give a better prediction of endometrial carcinoma in women presenting with postmenopausal bleeding.

Key words

postmenopausal bleeding, endometrial carcinoma, sensitivity, specificity, predictive value

Introduction

Endometrial carcinoma is the second most common female genital tract malignancy worldwide, but it is the commonest gynaecological malignancy in western countries as they are having well establish cervical screening programmes for cervical carcinoma, which is the number one gynaecological cancer among other countries[(1)]. In Sri Lanka, endometrial Carcinoma is the eighth commonest carcinoma among females, where cervical and ovarian carcinoma are the leading genital tract malignancies[(2,3)]. Most of the endometrial cancers are diagnosed in early stages, as most of them are presented as post-menopausal bleeding (90%), even though only 10% -15% of post-menopausal bleeding is associated with endometrial carcinoma [(4,5,6,7)]. According to the data from year 2018, deaths due to endometrial carcinoma is 1% of all deaths due to malignancies in Sri Lanka[(3)].

Pathology

The most common (80%) histological type of endometrial carcinoma is endometrioid adenocarcinoma (type 1), and they are associated with nulliparity, obesity, insulin resistance, and hyper estrogenic environment. They are graded from 1-3 according to the degree of differentiation and nuclear features. Type 2 tumours include serous, squamous, undifferentiated carcinomas, carcinosarcomas and endometrial stromal sarcomas. They are less common, more aggressive and have a poor prognosis. They are associated with old age and not associated with the risk factors for type 1 cancers. Type 1 tumours usually have a background of endometrial hyperplasia and found to have about 50% of severe atypical endometrial hyperplasia. Endometrial carcinomas are usually primary and very rarely can be secondaries from breast, ovary, lung, gastric, colorectal carcinomas and melanomas.

Endometrial carcinoma spreads locally into the myometrium, to the cervix and vagina (haematogenous spread as well can be seen in the vagina as drop lesions). Deeper myometrial invasion can penetrate the serosa and involves the parametrial tissues. Endometrial carcinoma spread through the lymphatics to the external iliac, internal iliac, obturator and para-aortic lymph nodes and this spread is directly proportional to the degree of myometrial involvement. Trans-tubal spread is also possible to the peritoneum and to the ovaries. Lungs are the commonest site of haematogenous metastasis and, type 2 endometrial carcinomas have the highest tendency to spread even with a minimum myometrial invasion.

Screening and Diagnosis

Routine mass screening of the population is not practical due to very low prevalence of endometrial carcinoma and its precursor lesions (complex hyperplasia of the endometrium). Therefore, proper assessment of symptomatic females, specially associated with risk factors, is the mainstay of the diagnosis.

The commonest cause for postmenopausal bleeding is atrophic endometritis or vaginitis, accounting for 60-80% of all cases[30]. Exogenous Estrogen contribute in 15-25%, endometrial hyperplasia in 5-10% and cervical or endometrial polyps in 2-12% for postmenopausal bleeding. Bleeding may arise from extra genital arears such as urethra, bladder and rectum. The possibility of cervical carcinoma is always should be kept in mind on investigating for postmenopausal bleeding, especially in Sri Lanka, as a third world country. Even the risk is 10-15%, 75% of endometrial carcinomas occur in postmenopausal period and 90% of them present as postmenopausal bleeding, making them to seek medical advice in early stage of the disease.

Obtaining a comprehensive history including risk factors with proper clinical examination of the lower genital tract, including assessment of the cervix, vagina and perineum in combination with the investigations, will provide a good predictive value than the predictive values of individual component[28,29]. The pre-test probability of endometrial carcinoma is reduced from 10-15 % up to 1% post-test with negative results. But it varies with the coexisting risk factors and advancing age, where there is 1% risk if the age is <50 years and 25% if the age is > 80years. The risk is 18% in obese, 21% in diabetic and 29% in obese & diabetic in combination[6].

Surgery is the mainstay of management of endometrial carcinoma including, obtaining peritoneal washing for cytology, extra fascial total hysterectomy, bilateral salphingo-oophorectomy, with or without pelvic and para-aortic lymph node dissection which will provide surgico-pathological staging of the disease. Post-operative adjuvant radiotherapy (external beam or brachy-therapy) would be decided depending on the grade, type and the degree of myometrial invasion of the tumour. Still there are some controversies of the management of endometrial carcinoma, where many studies been focused currently on adjuvant chemotherapy, chemoradiation when compared to radiotherapy alone.

The overall 5 year survival of all stages of the endometrial carcinoma is 80% and it varies with the grade and myometrial invasion. Survival in stage I disease is approximately 85-90%, and it reduces up to 70-75% in stage II, 45% in stage III and <30% in stage IV, which reflect the importance of early detection of the disease.

Trans Vaginal Sonography (TVS)

Multiple logistic regression analysis showed that time since menopause and endometrial thickness were statistically significant predictors of endometrial carcinoma[8].

Transvaginal ultrasonography is a known less invasive investigation which is freely available and

has a very good patient acceptancy. Usually it is sufficient for an initial evaluation of postmenopausal bleeding if the ultrasound images reveal a thin endometrial echo (less than or equal to 4 mm). The patient can be reassured, given that an endometrial thickness of 4 mm or less has a greater than 99% negative predictive value for endometrial cancer[9]. Some studies show 100% sensitivity when using 4mm thickness of the endometrium as the cutoff value, therefore none of the patients found to have endometrial cancer after the ultrasonography became negative[10].

According to systematic analysis done by Gupta JK et al. only 4 studies from 21, which used 5mm as the cutoff endometrial thickness, had high quality criteria. Using the pooled estimates only from these four studies, a positive test result raised the probability of carcinoma from 14% to 31.3%, while a negative test reduced it to 2.5%[11]. This shows when the thickness of both endometrial layers at < or = to 5 mm, the negative result will rule out endometrial pathology very well, but it should be always corelated with the associated risk factors and recurrence of postmenopausal bleeding. But positive results will not always give an accurate diagnosis of endometrial carcinoma.

The most cited meta-analysis by Smith-Bindman et al. included 5892 women from 35 prospective studies that compared endometrial thickness measured by TVS to presence or absence of endometrial carcinoma on histology[12]. At 5 mm cut-off, the overall summary mean weighted estimates of the sensitivity for detecting endometrial cancer was 96% for a 39% false-positive rate. This would reduce a pre-test probability of 10% for endometrial cancer to a post-test probability of 1%. Therefore, expectant management (without the need for tissue sampling) is recommended for these women.

There is only one study that looked at follow-up of women with PMB and an endometrial thickness of < or = 4 mm[13]. It showed that none of the women with the expectant management developed cancer over 1 year of follow-up. But endometrial malignancy was missed by TVS in 1 patient among 163 patient (0.6%) who was diagnosed by cervical cytological examination. If the endometrial thickness is > 4mm, the presence of fluid in endometrial cavity is a good marker in diagnosing pathological changes in the endometrium. Curcic´ et al. concluded that, if the endometrial thickness is < 4mm no further evaluation is indicated if the clinical picture supports[24].

Sonographic examination of endometrium is not always accurate as there can be inter and intra examiner variation. Level of experience, skill of the examiner and some patient factors are unfavorable for the procedure. Transvaginal ultrasonography is also not always reproducible. Therefore, in all the cases where ultrasonography is not possible, considering the risk factors and continuation of per vaginal bleeding, an alternative method should be advised.

Saline Infusion Sonogram (SIS)

Saline infusion sonogram is done by infusing saline into the uterine cavity using a catheter through the cervix before performing trans vaginal ultrasonogram. This will separate two endometrial lining and allows to measure endometrial thickness more accurately and visualize intracavitary lesions such as polyps and fibroids.

The meta-analysis done by de Kroon et al. on the accuracy of SIS on analyzing the endometrium in patients with abnormal uterine bleeding, concluded that its ability in evaluating uterine cavity in pre and postmenopausal women[17]. But it was more feasible on premenopausal women than post menopausal women (success rate 95% and 86% respectively). The pooled sensitivity and pooled specificity of SIS in uterine cavity evaluation were 95% and 88% respectively, the likelihood ratios were 8.23 and 0.06 respectively and the post-test probabilities were 0.91 and 0.07 respec-

tively. But this method can be little discomforting among postmenopausal women than conventional TVS reducing patient's acceptance and technical failure can also be encountered.

Gel instillation sonography is a feasible, accurate alternative for SIS in the evaluation of women with abnormal bleeding, and has fewer technical failures[18].

Endometrial Sampling

Dilatation and curettage was used in the past to obtain endometrial sampling as a blind procedure. But this method is now outdated, as it is considered as a minor surgical procedure which required the patient to get admitted and to undergo general or regional anaesthesia, while there are novel methods that has been developed for endometrial sampling as outpatient procedure. Complications due to anaesthesia, uterine perforation and bleeding are the main possible complication of dilatation and curettage. A Clinical trial conducted by Sanam et al. revealed that dilatation and curettage has 100% sensitivity, specificity, positive and negative predictive values and accuracy, where the values with Pipelles sampling was comparable with the results which is a very cheap, easy and reliable method with high patient acceptancy[25].

The Pipelles device consists of a disposable plastic outer tube measuring 3mm in diameter, within it, is a closely fitting rod. When the rod is withdrawn, it creates a vacuum that sucks in a section of endometrium, sufficient to give a histological report. Because of its smaller diameter it is very easier to insert through the cervix without needing any anaesthesia and cervical grasping. A meta-analysis done by Dijkhuizen et al. shows Pipelle device and the Vabra device (an endometrial aspiration device) has shown a very good detection rates on diagnosing endometrial carcinoma 99.6% and 97.1% respectively[19]. Pipelle was the most sensitive device with the sensitivity of 81% and the specificity of both methods was >98%. But insertion of the device may be difficult in postmenopausal women as the cervix gets narrowed and it is not an infrequent thing that the histology report mentions as insufficient sampling.

6% out of 66 patients with insufficient sampling were diagnosed to have endometrial carcinoma or atypical hyperplasia subsequently by a prospective study performed by Van Doorn et al[20]. This finding implies that women with an insufficient sample and an endometrial thickness of 5mm should not be reassured. The patient can be reassured with inadequate sample if the hysteroscopic and sonographic findings are also reassuring only, according to the controlled regression analysis by Bakour et al[21].

Hysteroscopy

Hysteroscopy provides a direct visualization of the endometrial cavity compared to traditional blind procedures. It allows to take selective endometrial sampling only from the suspicious lesions, and therefore having a very low likelihood ratio of endometrial carcinoma when there is a negative hysteroscopy[22]. Study conducted by Epstein E et al. on the accuracy of TVS, SIS and Hysteroscopy on diagnosing endometrial pathology revealed that hysteroscopy is always superior to other two methods with regard to differentiating between malignant and benign lesions (sensitivity 84%, 44%, and 60%; false-positive rate 15%, 6% and 10%, respectively)[16]. Therefore, outpatient hysteroscopy and biopsy are still the methods of choice[17].

There are rigid and flexible hysteroscopes that can be used in outpatient procedures. Although flexible hysteroscopy is comparatively less painful, rigid hysteroscopy provides superior optical qualities and higher success rates. A liquid with low viscosity (normal saline) or gas (CO_2) can be used as expansion medium and continuous flow of fluid will distend the vagina and the cervical canal and allows the easy entry into the endometrial

cavity. Introduction of very small diameter hysteroscopes (3mm), and vaginoscopic non-touch method has reduced insertion of speculum and cervical grasp by tenaculum and has increased patient acceptancy and minimized the requirement of anaesthesia, making the office hysteroscopy as a currently popular method. In some instances, patient can develop pain due to cervical and uterine distension, therefore, a low threshold should be kept for local anaesthesia. Sometimes vision may be poor due to bleeding and fluid collection. In-patient hysteroscopy may be required if the outpatient hysteroscopy is inadequate or difficult. The sensitivity, specificity, accuracy and positive and negative predictive values of hysteroscopy are 94.4%, 97.0%, 96.8%, 68% and 99.6%, respectively, on diagnosing endometrial carcinoma or hyperplasia according to a systematic quantitative review conducted by Clark et al[22].

Three-dimensional Ultrasonography

Three-dimensional ultrasonography will provide a 3D view of the endometrium and the uterus, needs good technical skills than conventional 2D ultrasonography and availability is also limited. Studies show that the diagnostic performance of 3D ultrasonography is not superior to 2D ultrasonogram on differentiating benign and malignant endometrial lesions in women present with postmenopausal bleeding.

MRI (Magnetic Resonance Imaging)

MRI images help in differentiating endometrial polyps from endometrial malignancies by morphology and accurate detection of myometrial and cervical invasion. It has a mean sensitivity of 79%, specificity of 89%, accuracy of 86%, positive predictive value of 82%, and negative predictive value of 88% for diagnosis of carcinoma[33]. But MRI is not frequently used as a routine investigation in postmenopausal bleeding, as its limited availability and less cost effectiveness compared to other methods.

Table 1. Sensitivity, specificity, positive and negative predictive values of investigations, frequently used for the evaluation of postmenopausal bleeding in diagnosis of endometrial carcinoma.

Diagnostic test	Sensitivity	Specificity	positive predictive value	Negative predictive value
TVS (ET-4mm as cut off)	100%	61%	39%	100%
TVS (ET-5mm as cut off)[19,32]	88-95%	45-96%	31%	97.5%
SIS	95%	88%	16%	97%
Pipelle biopsy[31]	84-99.6%	98-99%	94%	94%
Novac Curratage	90-100%	100%	100%	98-100%
Hysteroscopic guided biopsy	94%	97%	68%	99.6%
MRI	79%	89%	82%	88%

(TVS - Trans Vaginal Sonogram, ET - Endometrial Thickness, SIS - Saline Infusion Sonography, MRI - Magnetic Resonance Imaging)

Summary and Conclusion

As a summary, when a postmenopausal woman comes with bleeding and having negative cervical smear, normal cervix and vagina on speculum examination, Trans-vaginal ultrasonography and endometrial thickness assessment can be offered as first line investigation. Even if the endometrial thickness is less than 4mm endometrial sampling can be considered if there are associated risk factors, such as, recurrence of bleeding, fluid in the cavity, irregular endometrium and other risk factors for endometrial carcinoma (lack of evidence yet). If the endometrial thickness is >4 mm, blind or hysteroscopic guided endometrial sampling, is recommended depending on the availability of the resources and to be managed according to the pathology. If the histopathology sample comes as insufficient, patient can be reassured provided there are hysteroscopic evidence of endometrial atrophy. If there is no evidence of atrophy or recurrence bleeding even with atrophy, inward hysteroscopy and biopsy is recommended for further evaluation[26]. The sensitivity, specificity, positive and negative predictive values of each investigation is summarized in Table 1.

References

1. James M, Mohamed K. Endometrial Cancer. Obstetrics, Gynaecology & Reproductive Medicine 2013; 23:263-269.

2. Samarakoon NK, Siriwikum LBDJ, Liyanage SK, Mahendra BAGG, Rathnayake RMUS, Hewavisenthi SJDeS. The pathological profile of endometrial carcinoma in a cohort of Sri Lankan patients. Journal of Diagnostic Pathology 2016; 11(2)50

3. The global cancer observatory, Sri Lankan data, May 2019, world health organization. Available from: https://gco.iarc.fr/today/data/factsheets/populations/144-sri-lanka-fact-sheets.pdf

4. Astrup K, Olivarius NDF. Frequency of spontaneously occurring postmenopausal bleeding in the general population. Acta Obstetricia et Gynaecologica Scandinavica 2004; 83:203–207.

5. Timmermans A, Gerritse MB, Opmeer BC, Jansen FW, Mol BW, Veersema S. Diagnostic accuracy of endometrial thickness to exclude polyps in women with postmenopausal bleeding. Journal of Clinical Ultrasound 2008; 36:286–290.

6. Smith-Bindman R, Kerlikowske K, Feldstein VA, Subak L, Scheidler J, Segal M, et al. Endovaginal ultrasound to exclude endometrial cancer and other endometrial abnormalities. JAMA 1998; 280:1510–1517.

7. Parkin DM, Bray F, Ferlay J, Pisani P. Estimating the world cancer burden: Globocan 2000. International Journal of Cancer 2001; 94:153–156.

8. Van Doorn LC, Dijkhuizen FP, Kruitwagen RF, Heintz AP, Kooi GS, Mol BW. Accuracy of transvaginal ultrasonography in diabetic or obese women with postmenopausal bleeding. Obstetrics and Gynecology 2004; 104:571–578.

9. Scottish Intercollegiate Guidelines Network. Investigation of Post- Menopausal Bleeding Section 5: Interpretation of Transvaginal Ultrasound (TVUS). Available from: https://pdfs.semanticscholar.org/702a/1d879bd13662aba45ddf7bab97d505a4fb16.pdf?_ga=2.218453210.2112398615.1597802323-1337495100.1597802323

10. Ilan Bruchim MD, Tal Biron-Shental MD, Marco M. Altaras MD, Ami Fishman MD. Combination of endometrial thickness and time since menopause in predicting endometrial cancer in women with postmenopausal bleeding. Journal of Clinical Ultrasound 2004; 32(5)219-224

11. The Role of Transvaginal Ultrasonography in Evaluating the Endometrium of Women

With Postmenopausal Bleeding – ACOG committee opinion no 734. Available from: https://pubmed.ncbi.nlm.nih.gov/29683909/

12. Peter SMD, Oddvar B, Gun H, Ulf U. Transvaginal Ultrasound for Identifying Endometrial Abnormality. Acta Obstetricia et Gynaecologica Scandinavica 1991; 70(7-8):591-594. Available from https://doi.org/10.3109/00016349109007922

13. Gupta JK, Chien PF, Voit D, Clark TJ, Khan KS. Ultrasonographic endometrial thickness for diagnosing endometrial pathology in women with postmenopausal bleeding: a meta-analysis Acta Obstetricia et Gynaecologica Scandinavica 2002; 81(9)799-816. Available from https://doi.org/10.1034/j.1600-0412.2001.810902.x

14. Smith-Bindman R, Kerlikowske K, Feldstein VA, Subak L, Scheidler J, Segal M, et al. Endovaginal ultrasound to exclude endometrial cancer and other endometrial abnormalities. JAMA 1998; 280:1510–1517.

15. Gull B, Carlsson S, Karlsson B, Ylöstalo P, Milsom I, Granberg S. Transvaginal ultrasonography of the endometrium in women with postmenopausal bleeding: is it always necessary to perform an endometrial biopsy? American Journal of Obstetrics and Gynaecology 2000; 182:509–515.

16. American College of Obstetricians and Gynecologists. ACOG Committee Opinion No. 426: The role of transvaginal ultrasonography in the evaluation of postmenopausal bleeding. Obstetrics and Gynaecology 2009; 113(2 Pt 1):462–464.

17. Epstein E, Valentin L. Gray-scale ultrasound morphology in the presence or absence of intrauterine fluid and vascularity as assessed by color Doppler for discrimination between benign and malignant endometrium in women with postmenopausal bleeding. Obstetrics and Gynaecology 2006; 28(1)89-95

18. Epstein E, Ramirez A, Skoog L, Valentin L. Transvaginal sonography, saline contrast sonohysterography and hysteroscopy for the investigation of women with postmenopausal bleeding and endometrium > 5 mm. Ultrasound in Obestetrics and Gynaecology 2001; 18(2):157-162.

19. De Kroon CD, De Bock GH, Dieben SW, Jansen FW. Saline contrast hysterosonography in abnormal uterine bleeding: a systematic review and meta-analysis. BJOG 2003; 110:938–947.

20. Werbrouck E, Veldman J, Luts J, Van HS, Van SD, Timmerman D, Van den Bosch T. Detection of endometrial pathology using saline infusion sonography versus gel instillation sonography: a prospective cohort study. Fertil Steril 2011; 95(1):285-288.

21. Dijkhuizen FP, Mol BWJ, Brölmann HAM, Heintz AP. The accuracy of endometrial sampling in the diagnosis of patients with endometrial carcinoma and hyperplasia: a meta-analysis. Cancer 2000; 89:1765–1772.

22. Van DHC, Opmeer BC, Burger CW, Duk MJ, Kooi GS, Mol BW. Inadequate office endometrial sample requires further evaluation in women with postmenopausal bleeding and abnormal ultrasound results. International Journal of Gynecology and Obstetrics 2007; 99:100–4.

23. Bakour SH, Khan KS, Gupta JK. Controlled analysis of factors associated with insufficient sample on outpatient endometrial biopsy. BJOG 2000; 10:1312–1314.

24. Clark TJ, Voit D, Gupta JK, Hyde C, Song F, Khan KS. Accuracy of hysteroscopy in the diagnosis of endometrial cancer and hyperplasia: a systematic quantitative review. JAMA 2002; 288:1610–1621

25. Camila TR, Júlio CR, Marcos FS, Ana CJ, Omero BP, Francisco JC, Antonio AN. Hys-

teroscopy as a standard procedure for assessing endometrial lesions among postmenopausal women. Sao Paulo Medical Journal 2007; 125:6. Available from https://doi.org/10.1590/S1516-31802007000600007

26. Curcić A, Durdević S, Mihaldzić-Tubić S, Mladenović-Segedi L, Maksimović M. Ultrasound detection of endometrial fluid in postmenopausal women. Medicinski Pregled 2009; 62:337–341.

27. Sanam M, Majid MMK, Comparison the Diagnostic Value of Dilatation and Curettage Versus Endometrial Biopsy by Pipelle - a Clinical Trial, Asian PacificJournal of Cancer Prevention 2015; 16(12)4971-4975. Available from DOI:10.7314/apjcp.2015.16.12.4971

28. Shagaf HB, Anne T, Ben WM, Khalid SK. Management of women with postmenopausal bleeding: evidence-based review. The Obstetrician and Gynaecologist 2012; 14(4)243-249. Available from DOI: 10.1111/j.1744-4667.2012.00129.x 2012;14:243–249

29. Ziegler D. Contrast ultrasound: a simple-to-use phase-shifting medium offers saline infusion sonography-like images. Fertil Steril. 2009; 92(1):369-373. Available from doi: 10.1016/j.fertnstert.2008.04.032.

30. Khan KS, Dinnes J, Kleijnen J. Systematic reviews to evaluate diagnostic tests. European Journal of Obstetrics and Gynecology and Reproductive Biology 2001; 95:6–11.

31. Khan KS, Chien PFW, Dwarakanath LS. Logistic regression models in obstetrics and gynaecology literature. Obstetrics and Gynecology 1999; 93:1014–1020.

32. Mohamed O, Joanna F, Jackie R, Hizbullah S, Jemma J. Endometrial pathology in the postmenopausal woman – an evidence based approach to management. The Obstetrician & Gynaecologist 2015; 17:29–38

33. Machado F, Moreno J, Carazo M, León J, Fiol G, Serna R, Accuracy of endometrial biopsy with the Cornier pipelle for diagnosis of endometrial cancer and atypical hyperplasia. European Journal of Gynaecological Oncology 2003; 24(3-4):279-281

34. Bruno C, Tiina R, Pentti L , Pekka Y. Transvaginal sonography and hysteroscopy in postmenopausal bleeding. Acta Obstetricia et Gynaecologica Scandinavica 1994; 73(5) 413-416. Available from https://doi.org/10.3109/00016349409006254

35. Ralf PG, Eric KO, Evan SS, David C, Laurence P, Shahid MH. Endometrial Polyps: MR Imaging Features and Distinction from Endometrial Carcinoma. Radiology 2000; 214(1): Available from https://doi.org/10.1148/radiology.214.1.r00ja3647

CME Questions

Menopause

Ekanayake C[1]

[1.]Consultant Obstetrician and Gynaecologist and Senior Lecturer, Department of Clinical Sciences, Faculty of Medicine, General Sir John Kotelawala Defense University.

E mail - cdekanayake2000@yahoo.com

1. Regarding menopause

   a. Vasomotor symptoms are present in 75% of women going through menopause.

   b. Estrogen alone preparations have a beneficial effect on high-density lipoproteins (HDL) and low-density lipoprotein (LDL).

   c. A significant amount of women with fracture neck of femur die within the first year.

   d. If the duration of treatment of Estrogen exceeds 1 year, it has to be under specific individualized indications with intense follow-up and monitoring.

   e. All women should have screening for BRCA gene mutation even if there is a negative history for breast and ovarian cancer.

2. The following are contraindications for hormone replacement treatment (HRT)

   a. Diabetes mellitus
   b. Past history of breast cancer
   c. Migraine
   d. Past history of deep vein thrombosis
   e. Essential hypertension

3. A 55-year old woman with hot flushes and night sweats presents to the gynaecology clinic. She underwent a mastectomy and radiotherapy for breast cancer 3-years back. She has a strong family history of osteoporosis. What is the best option to manage her symptoms?

   a. Hormone replacement treatment (HRT)
   b. Raloxifene
   c. Tamoxifen
   d. Norethisterone
   e. Transdermal HRT

4. A 60-year old woman with a documented history of Transient Ishaemic Attacks (TIA) complaints of vasomotor symptoms. What is the best treatment option,

   a. Hormone replacement treatment (HRT)
   b. Transdermal HRT
   c. Vaginal Estrogen
   d. Tamoxifen
   e. Phyto-Estrogen

5. A 45-year old woman with two children complains of headache, sweating and hot flushes. She had a hysterectomy five years back for menorrhagia. The general and gynaecological examination findings were normal. What is the most appropriate treatment regimen?

   a. Vitamin E
   b. Norethisterone
   c. Estrogen and progestogen HRT
   d. Combined oral contraceptive pill
   e. Estrogen only HRT

References

1. Patterson M. Menopause and hormone replacement therapy. In: Luesley DM, Baker PN, editors. Obstetrics and Gynaecology: An evidence-based text for MRCOG. 2nd ed. London: Hodder Arnold; 2010.

2. Luesley DM, Baker PN, editors. MCQs and Short Answer Questions for MRCOG. An aid to revision and self-assessment. 1st ed. London: Hodder Arnold; 2004.

3. Perera H. Ekanayake C. Menopausal hormone therapy with Estrogen and progestogen. Sri Lanka Journal of Menopause. 2019; 1 (1):5-12.

Answers

1. All true
2. FTFTT
3. D
4. B
5. E

* Table 01 shows a summary of menopausal treatment options

Table 01 : Menopause Treatment options

	HRT	Transdermal HRT	Vaginal oestrogens	Norethisterone	Tamoxifen	SERM	Tibolone	Clonidine	SSRI	Bisphosphonates	Plant oestrogens
Vasomotor symptoms	↓	↓		↓	↑	↑	↓	Slight ↓	↓		↓evidence?
Breast	↑	↑	-	↑	↓	↓					↑
Osteoporosis	↓	-	-	-	↓	↓				↓	↓
Cardiac risk	<60 - protective >60 – Risk ↑	= HRT		-							
Endometrial effects	O - ↑, O+ P -			↓	↑						
VTE	↑	-			↑						

SLJOM
The Sri Lanka Journal of Menopause

No. 112, Model Farm Road, Colombo 8, Sri Lanka.

9 772706 022006

Printed By