Menopause: Treatment options, dietary aspects and clinical implications

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Menopause refers to the cessation menstruation. It is a counterpart of menarche which marks the beginning of menstruation. The current understanding of the physiology of menopause is that there is a depletion of primary Oocytes in the ovary by atresia as an effect of aging coupled with decreased sensitivity of the remaining Oocyte to Gonadotropins. This is then reflected as a decrease in the levels of oestradiol and progesterone. Oestradiol is currently known to be central to the pathogenesis of most of the symptoms encountered during the climacteric period. Because the currently understood theory of the pathogenesis of the symptomatology is cessation of production of oestradiol by primary Oocytes, the management of these symptoms has been hormonal replacement therapy (HRT) though of recent, other options including diets and supplements have been found to have a potential to minimize or relieve symptoms. This article will review the physiology, symptomatology and treatment options of the climacteric symptoms.

Key words: Menopause, climacteric, premenopausal, post-menopause, hormone replacement therapy.

INTRODUCTION

Menopause refers to permanent cessation of menstruation resulting from the loss of ovarian follicle development. The diagnosis is typically made retrospectively after a woman misses her normal menses for at least 12 years (Sherwin, 2001; Spinelli, 2004) at around her menopausal age. This commonly happens at an average age of 47.5 (Baram, 1997) though there are variations due to race, ethnicity, geographical environment and other factors. Menopause is only one event surrounded by period prior to and after it. It is preceded by a fairly long period of symptoms called the perimenopausal period, commonly called menopausal transition period (MTP) (Butler and Santoro, 2011; Santoro and Randolph, 2011) and after menopause follows the post menopause period. It is during the perimenopausal or transition period when most severe disturbing symptoms happen and they may diminish in severity in the postmenopausal period. Studies have demonstrated that symptoms may begin up to 6 years before the final menstrual period and continue for a variable number of years after the final menstrual period (Butler and Santoro, 2011; Santoro and Randolph, 2011; McKinley et al., 1992) but as the post menopause years progress, with an accompanying loss of ovarian response to gonadotropins the associated affective symptoms of menopause tend to decline. The effects of cessation of oestradiol production are much more pronounced in tissues with oestrogen receptors such as bones, brain, blood vessels, central nervous system and the skin. The symptoms seen in women in this group are mostly noted in these organs. It should be noted at this point that menopause is just one the manifestations of the so called climacteric syndrome.

Frequently, the term "climacteric" has been widely used when discussing issues related to menopause (Butler et al., 2011). It is a period before and after menopause during which the symptoms associated with cessation of oestradiol production manifest. Usually it occurs over a period of one year prior to menopause, (though as pointed out earlier in this article, the time intervals vary from one to six years before menopause) and may extend beyond menopause for five to ten years. At the centre of the physiology of menopause is the depletion of primary oocytes in the ovary by atresia as an effect of
aging coupled with decreased sensitivity of the remaining oocyte to gonadotropins (PonJola et al., 2014). This is then reflected as a decrease in the levels of oestradiol and progesterone. Oestradiol is currently known to be central to the pathogenesis of most of the symptomatology of the climacteric syndrome (Perimenopausal, menopausal and post-menopausal symptoms). Climacteric is a period covering Perimenopause (transition towards menopause), menopause (a cessation of menses) and post-menopause (Santoro et al., 2011).

Age of on set

Mean age at menopause vary substantially between women across different countries or across different ethnic groups (Belitz, 1977; Gray and Doyle, 1983; Hunt and Newcomer, 1984; Danker, 1986; Ulijaszek et al., 1991; Flint, 1997; Morabia et al., 1998). Reasons behind this international variability remain poorly understood. The mean age in low income countries is estimated to range from 40 - 48 according to available studies done in India. (Singh and Ahuja, 1980; Sengupta and Gogo, 1993) while in developed countries it ranges between 48 - 52 years (Kim et al., 2003; Malacara et al., 2002). It has been long since when the debate on the factors affecting the age of onset of menopausa started, but it is now widely accepted that age of menarche, type of menstrual cycle, the number of pregnancies, marriage, contraceptive use, height, weight, social and economic status do not influence the age of onset of menopause but it appears that familial, racial, cigarette smoking are likely to affect the age of onset.

Epidemiology

With improvement in life expectancy and increase in the number of senior citizens, it can be deduced that the population of women in their peri-menopause, menopause and postmenopausal ages will in no doubt increase. For example in the United States alone about 1.3 million women attain menopause each year (Soares, 2004). Similar increases in numbers of women in their menopause age are also expected in other high income countries. In medium and low income countries figures may be lower. This figure is however expected to increase as life expectancy improves. This means that there will come a point in time when much more women will require treatment for the menopausal symptoms. Some studies have even come to a conclusion that with this improvement of life expectancy, women spend almost a third of their life in menopause (Us Census Bureau, 1996) which means that a population of women in need of treatment of menopausal symptom is higher that years before.

Physiology

Menopause results from loss of ovarian sensitivity to gonadotropin stimulation, which happens in relation to depletion of ovarian follicles. The oocytes in the ovaries undergo atresia throughout a woman’s life cycle, resulting in a decline in both the quantity and the quality of follicles which translates into reduction of hormonal production (Oestrogen) that leads the manifestations in menopause. This is called physiological menopause. Artificial menopause is said to have happened when surgical removal of both ovaries for some medical indications or following treatment with chemo or radiotherapy. As pointed out earlier in this chapter, menopause has to happen at an age above 40, therefore if it happens earlier than that it is called premature menopause and it is advised that in this case, the diagnosis should not be concluded until other causes of amenorrhea have been excluded.

Although the major symptoms of menopause is cessation of menstrual flow, irregularities in hormonal serum levels during peri-menopausal period is thought to bring silent morphological and physiological changes in the body before the time of onset menopause. Systems that are commonly affected include the bones, blood vessels, heart, brain, urinary tract, gastrointestinal tract, skin and reproductive system (Nicks et al., 2010). The morphological changes that occur are commonly associated with complaints that in some cases need medical attention (Burger, 1999; Nicks et al., 2010).

CLINICAL MANIFESTATIONS AND DIAGNOSIS

During the perimenopause, menopause and postmenopausal periods, women experience a wide range of symptoms which may begin as far as six years prior to menopause and persists for sometimes thereafter. As the post-menopause years progress, with an accompanying loss of ovarian response to gonadotropins, symptoms of menopause may begin to decline (Butler and Santoro, 2011; Santoro and Randolph, 2011), however chronic pathologies like osteoporosis and cardiovascular diseases usually will persist and even worsen as time goes if no treatment is offered.

The range of symptoms experienced by menopausal women include: Hot flushes or flushes, insomnia, weight gain and bloating, mood changes, irregular menses, mastodynia, depression and headache. The severity of this set of symptoms and individual symptoms differs significantly among women and the severity is usually measured using the Kupperman index or the menopausal
rating scales (MRS) (Kupperman, 1953; Hauser, 1994; Potthoff, 2000).

Our current knowledge on the morphological and physiological changes seen throughout the perimenopause, menopause and postmenopausal periods has centered on the ovary and cessation of production of oestradiol by the ovarian follicles, but there is a mounting scientific evidence that there are other bio-active substances that may be responsible for the process and explain the changes and clinical presentation (Ipyana et al., 2013).

Changes in menstrual cycles

Menopause, by definition, is final menstrual period and should be regarded as just one of the manifestations of the climacteric period. It marks the irreversible termination of female reproductive capability that affects all aged women.

The physiological mechanism responsible for menopause is the continuous loss of ovarian follicles to that point at which menstrual cycles completely cease (O’Connor, 2001).

Most often cessation of menses is heralded by a gradual decrease in the amount and frequency of blood loss during several months or years. A shorter menstrual cycle (< 25 days) is the most common change in menstrual cyclicity that occurs during the perimenopausal or menopausal transition period in women who have no pelvic pathology and who continue to be ovulatory (Santoro et al., 1996). Excessive and prolonged bleeding may be a feature of normal perimenopausal or approaching menopause but menstrual function ceasing suddenly without warning is rare if all it can happen.

Hot flashes (Flushes)

It is generally acknowledged that hot flashes are the commonest symptoms experienced by women in their menopausal transition and even after the menopause. Studies have shown that that 50 - 70% of postmenopausal women experience hot flushes and night sweats of varying severity (Hunter, 1986; McKinlay, 1992), and that approximately 20% still have these climacteric complaints even 10 to 20 years after the menopause (Berg, 1986).

Hot flashes may be the cause of discomfort, sleep disturbances and emotional changes especially if they are severe or if they occur frequently or if no treatment is offered. A woman whose flashes are severe enough to cause major sleep disturbances may also complain of cognitive or affective disorders resulting from lack of sleep.

Hot flashes are characterized by the sudden onset of intense warmth that begins in the chest and may progress to the neck and face. They are often accompanied with anxiety, palpitations, profuse sweating, and red blotching of the skin. Hot flash symptoms can be severe enough to affect a woman’s ability to work, impair her social life, her sleep pattern, and her general perception of health (Stein et al., 2000) and therefore treatment is imperative in such situations.

The severity and disturbance the hot flashes cause have also been reported to be the most common reason for women to use Hormonal replacement Therapy (HRT) (Koster, 1990). It has been further reported that for women who are able and willing to use HRT, it will successfully relieve symptoms by about 80% to 90% (Tait et al., 2000).

Central nervous system symptoms in menopause

Memory function impairment and estrogen deficiency seen in menopausal women is still a gray area that calls for further research because it is well established that normal aging itself induces a decline in certain cognitive capabilities. However some studies have shown that postmenopausal women receiving HRT have shown better performance on memory testing than postmenopausal control subjects not receiving estrogen therapy (Sherwin, 1997). The probable effect of estrogen is to slow the decline of preserved memory function though the Women’s Health Initiative (WHI) data do not show improved cognitive function in women taking HRT (Rossouw, 2002).

During the menopausal transition women go through a period of depressive symptoms arising from effects of hormonal changes such as estrogen-related sleep disturbance and vasomotor symptoms. Regardless of whether the criteria for a definitive diagnosis of major depression are met, depressive symptoms should always be considered in the context of level of functioning; any functional impairment calls for consideration of intervention (PonJola et al., 2014).

In most instances, symptoms caused by menopause may not be easily distinguishable from symptoms caused by primary depression. It is scientifically established that treatment of depressive symptoms with estrogen in perimenopause, the postpartum period, and premenstrual syndrome is common (Gregoire, 1996), with observed resultant improvement in functioning and mood.(PonJola et al., 2014). It should be noted at this juncture that clinical depression requires treatment with antidepressants, with estrogen being used just as adjuvant therapy (Cohen, 2003). The effective use of estrogen in the treatment of these cases implies that estrogen deficiencies play a remarkable role in the causation of depressive illness in menopausal women.
Migrane headache in menopause

There is a mounting evidence that migraine headache is associated with hormonal changes observed during menses in menstruating women as well as women in their menopause because oestrogen level fall during these periods (Bernstein, 2010) but the confusion still remains as many menstruating and perimenopause women do not experience any headaches. Strong support of the theory of low oestrogen and migraine headache is supported by the fact that women with migraine come to relief when started on HRT (WHI, 2002).

Some studies have further found that fluctuating levels of hormones in perimenopausal period triggers headaches and make them more severe and frequent (Calhoun, 2004) while some Clinical observations found the fact that attacks of migraine in some women correlate with the menstrual cycle and improve when hormonal cycling ceases during pregnancy and may even disappear later on after menopause when hormone levels are relatively stable (Edelson, 1985). However it should not be ignored that those hormonal changes may not be the only triggering factor as many women do not experience it at any time during their reproductive ages and during and after menopause meaning that there could be other bioactive substances involved in the process making treatment of this condition particularly challenging.

Osteoporosis and osteopenia

Osteoporosis simply means thinning or decreased bone density. It is scientifically defined as a bone mineral density (BMD) equal to or greater than 2.5 standard deviations (SDs) below the peak bone mass, or T score while osteopenia is defined as a BMD that is 1.0-2.49 SDs below the T score (WHO, 1994). Osteopenia is therefore a condition where bone mineral density is lower than normal but not low enough to be classified as osteoporosis and is considered by to be a precursor to osteoporosis (WHO, 2000). However, it should be known that not every person diagnosed with osteopenia will develop osteoporosis.

Bone loss normally accelerates in the late menopausal transition and continues for the first few years after menopause (Finkelstein, 2008). It is one of the most common and disabling conditions leading to falls and fractures in older women but unfortunately it is commonly ignored. With proper intervention, osteopenia as a precursor of osteoporosis, is a largely preventable sequela of menopause. Commonly used drugs are Bisphosphonates including Alendronate, Risedronate and Ibandronate; selective estrogen receptor modulators (SERMs) such as raloxifene, estrogen, calcitonin, and teriparadine (Rosen, 2005). Calcium, vitamin D, calcitonin, monoclonal antibodies have also been used (Andersen, 1999). Prior to treatment risk assessments from the World Health Organization (WHO) Fracture Risk Assessment Tool (FRAX) is done (FRAX-WHO, 2010). According to these recommendations, consideration of therapy should be made for postmenopausal women, and men older than 50 years of age, if any one of the following is present (National osteoporosis foundation, 2010).

i.) Prior hip or vertebral fracture
ii.) T-score of 2.5 at the femoral neck or spine, excluding secondary causes
iii.) T-score between 1.0 and 2.5 at the femoral neck or spine

Clinicians' judgments in combination with patient preferences indicate treatment for people with 10-year fracture probabilities above or below these levels.

The onset of menopause leads to rapid loss of BMD because bone resorption is accelerated while formation remains at premenopausal rate. Trabecular bone is affected more than cortical bone; thus, bone loss is more commonly observed at vertebral, coaxial, and radial sites (PonJola et al., 2014).

The overall effect of menopausal bone loss is reduction of bone strength, leading to an increased risk of fracture particularly that of the vertebra and the neck of femur. Osteoclasts have been shown to have estrogen receptors, and these are hypothesized to be the mechanism by which estrogen replacement protects against osteoporosis. One meta-analysis study found a 27% reduction in risk of non-vertebral fractures in older women who received hormone therapy for hip and wrist fractures, the risk reduction was 40% (Grady, 2001).

The severity of osteoporosis is also related to race, being worse in whites than in Asians and least severe in women with dark complexions. Other risk factors are smoking and slender build. Similarly, the lower the woman’s bone mass is when a woman enters menopause, the more severe the osteoporosis will be. (PonJola et al., 2014).

Other features of menopause

The vaginal epithelium changes to become pale because of a reduced number of capillaries. Rugation also diminish, and therefore the vaginal wall becomes smooth.

- Vaginal changes often result in insertional dyspareunia.
- The menopausal ovary diminishes in size and is no longer palpable during gynecologic examination.
- Atrophic cystitis, when present, can mimic a urinary tract
infection
- In older women, a general loss of pelvic muscle tone occurs, sometimes manifested as prolapse of reproductive or urinary tract organs
- The uterus becomes smaller.
- A decrease in urine pH leading to a change in bacterial flora may result in pruritus and a malodorous discharge.
- Weight gain due to age-related decline in Basal Metabolic Rate (BMR).
- Body fat redistribution into the abdomen which by itself increases the risk for diabetes type 2, Heart diseases, and cancer (Mahan and Escott-Stump, 2008).
- Sarcopenia: Age-related loss of lean body mass. Inadequate protein intake and sedentary lifestyle augment sarcopenia in menopause women.
- Mood changes or swings are also observed in menopausal women.

Diagnosis of menopause

The diagnosis is typically made retrospectively after the woman has missed menses for 12 consecutive months (Butler and Santoro, 2011). This is usually coupled with other symptoms like Hot flashes or flushes, Insomnia, Weight gain and bloating, Mood changes, Irregular menses, Mastodynia, Depression as well as other minor features (PonJola et al., 2014).

The laboratory indication that menopause has occurred is a rise in the measured FSH level. The FSH level rises more than the LH level because of the reduced renal clearance of FSH in comparison with LH. Both hormones rise to even higher values than those seen in the surge during the menstrual cycle. Repeated measurement of FSH and LH levels at 2 to 3 months intervals is helpful for establishing whether the woman is progressing through menopause. The FSH rise precedes the LH rise. FSH is the diagnostic marker for ovarian failure. LH is not necessary to make the diagnosis (Butler and Santoro, 2011).

The levels of circulating estradiol have very different ranges before and after menopause, and these levels are obviously much lower in menopause. The levels of inhibition are also observed to be low. (Santoro and Randolph, 2011)

Other markers of ovarian aging include anti-Müllerian hormone (AMH) and Müllerian-inhibiting substance (MIS), which are produced by granulosa cells of all follicles. Assessment of these markers may be the earliest and most effective way of measuring progress toward menopause. At present, however, these testing are not sufficiently developed to be considered a standard of diagnosis and care. (PonJola et al., 2014).

Hormonal replacement therapy (HRT)

For a long time there has been a hot and confusing debate regarding the use of Menopausal Hormone Therapy (MHT) or Hormone Replacement Therapy (HRT). This has been so because the use of HRT is associated with a number of risks such as Deep venous thrombosis (DVT), Pulmonary embolism (PE), stroke, breast cancer, endometrial cancer, ovarian cancer depending on the type of hormone used, thus evaluation on patients on cardiovascular diseases, smoking habit, potential benefits and anticipated complications are critically important prior to initiation of therapy (Barclay, 2013). On the other hand Potential benefits of HRT include reduction of incidences or risks for hot flashes, urogenital symptoms, sleep problems, reduce cholesterol, relieve vaginal dryness, osteoporotic fracture and generally improve the quality of life.

These Hormones can be administered either several routes. Common ones are systemically, the oral, transdermal, topically via the vaginal route in a cream, ring, and implants forms. Patches and tablet are also available. Topical preparations are used solely to treat vaginal symptoms.

Trying to solve the mystery surrounding HRTs, The Global Consensus Statement on Menopausal Hormone Therapy had issued a document that may be used to guide the use of HRT. (T. J. de Villiers, 2013). The document serves to emphasize international consensus regarding HRT or MHT and is aimed at empowering women and healthcare practitioners in the appropriate use of MHT. The document emphasizes that:

i.) MHT is the most effective treatment for vasomotor symptoms associated with menopause at any age, but benefits are more likely to outweigh risks for symptomatic women before the age of 60 years or within 10 years after menopause.

ii.) MHT is effective and appropriate for the prevention of osteoporosis-related fractures in at-risk women before age 60 years or within 10 years after menopause.

iii.) Randomized clinical trials and observational data as well as meta-analyses provide evidence that standard-dose estrogen-alone MHT may decrease coronary heart disease and all-cause mortality in women younger than 60 years of age and within 10 years of menopause. Data on estrogen plus progestogen MHT in this population show a similar trend for mortality but in most randomized clinical trials no significant increase or decrease in coronary heart disease has been found.

iv.) Local low-dose estrogen therapy is preferred for women whose symptoms are limited to vaginal dryness or associated discomfort with intercourse.

v.) Estrogen as a single systemic agent is appropriate in women after hysterectomy but additional progestogen is required in the presence of a uterus.
vi.) The option of MHT is an individual decision in terms of quality of life and health priorities as well as personal risk factors such as age, time since menopause and the risk of venous thromboembolism, stroke, ischemic heart disease and breast cancer.

vii.) The risk of venous thromboembolism and ischemic stroke increases with oral MHT but the absolute risk is rare below age 60 years. Observational studies point to a lower risk with transdermal therapy.

viii.) The risk of breast cancer in women over 50 years associated with MHT is a complex issue. The increased risk of breast cancer is primarily associated with the addition of a progestogen to estrogen therapy and related to the duration of use. The risk of breast cancer attributable to MHT is small and the risk decreases after treatment is stopped.

ix.) The dose and duration of MHT should be consistent with treatment goals and safety issues and should be individualized

x.) In women with premature ovarian insufficiency, systemic MHT is recommended at least until the average age of the natural menopause.

xi.) The use of custom-compounded bioidentical hormone therapy is not recommended.

xii.) Current safety data do not support the use of MHT in breast cancer survivors.

Diet: Osteoporosis

Osteoporosis cannot be treated but rather prevented if the intervention is started early. As pointed out earlier in this chapter, during menopause there is accelerated bone loss while the rate of bone formation remains fairly that of young adults. Calcium helps the body to mineralize the new cells. Calcium may be obtained in supplements, but dietary sources are also available. Daily calcium requirement for menopausal women is about 1200mg.

Dietary sources of calcium include: Milk, low fat cheese, yogurt, Oysters, salmon, lobster, Brazil nuts, spinach and other green leafy vegetables.

Though exercise may help prevent rate of osteoporosis, other measures include; reducing red meat, eating more cereals, grains, pasta, vegetable, avoiding concentrated sugar, ,stop smoking, limit coffee, tea and alcohol.

Diet: Sensory changes

Loss of taste and loss of smell can occur as part of menopause though menopause is not the only known cause of this condition (Mahan and Escott-Stump, 2008). A change in sensory function can affect a woman’s dietary choices in many different ways. Sensory changes can decrease appetite, leading to loss of lean body mass, or they can increase consumption if satiety is reduced, leading to increased body weight. Women can work to overcome loss of test and smell with increased use of ingredients such as herbs, spices, vinegars, and/or hot sauce that do not negatively impact health.

Sensory changes can also affect gastrointestinal function. When the capacity to taste or smell is reduced, salivary, stomach, and pancreatic secretions are also reduced and could lead to impaired digestion and absorption of food.
Diet: Gastrointestinal changes

More than 30% of men and women over 50 years of age suffer from achlorhydria (Mahan and Escott-Stump, 2008). Achlorhydria means inadequate production of gastric acid. Inadequate gastric acid increases the risk of incomplete digestion of food and impair vitamin B12 absorption and subsequently leading to vitamin B12 deficiencies.

Diverticulosis, out pouches in the intestinal tract caused by straining associated with constipation, is even more common than achlorhydria, with more than 60% of adults over 60 years of age suffering from the condition. Diverticulosis is more common in women than men at same age (Mahan and Escott-Stump, 2008).

Constipation is a common complaint of menopausal women. Constipation is defined as painful bowel movements, straining at elimination, decreased frequency of bowel movements, hard stool, and incomplete emptying. Constipation is generally a symptom of other underlying issues. Treatment of constipation with fiber pills or laxatives does not help identify the underlying problem. Recent studies have found that high fiber and fluid intake can improve the condition (Hana, 2014).

Vitamin B12

Vitamin B12 requires intrinsic factor and hydrochloric acid to be absorbed and used. Intrinsic factor and gastric acid production may be blunted as women age (Mahan and Escott-Stump, 2008), thus compromising the absorption of vitamin B12 taken through food and supplements.

RDA of vitamin B12 is about 2.4 mcg. Nutritional sources of vitamin B12 include: Beef, Crab, Oysters.

Folic acid

Folic acid is another vitamin that may be lacking in women of old age. Adequate folic acid, vitamin B12 and vitamin B6 are required to metabolize homocysteine appropriately. Deficiencies in any of these B series vitamins lead to increased homocysteine, which is associated with increased risk for cardiovascular disease and Alzheimer's disease (Mahan and Escott-Stump, 2008).

RDA of folic acid is about 400mcg. Nutritional sources are white beans, spinach.

Vitamin D

Vitamin D deficiency has been estimated to affect 60 - 70% of women over the age of 40 (Martins et al., 2007). The deficiency is related to increased risk for osteoporosis, type 2 diabetes, and cancer, in addition to autoimmune conditions, depression, and impaired mobility. Of specific concern for women with osteoporosis is an increased risk for bone loss, bone fractures, falls, and reduced muscle strength and coordination. When serum vitamin D levels are maintained well above the standard cut-off for deficiency, there is the potential to reduce disease risk, improve mood, reduce sarcopenia, and decrease the rate of falls associated with aging (Dawson-Hughes, 2008).

RDA for vitamin D is about 400IU. Sources include sunshine, salmon and catfish

Calcium

Calcium is crucial for preventing or treating osteoporosis and may reduce hypertension. Only 4% of women meet the RDA for calcium (Mahan and Escott-Stump, 2008). Even though supplements of calcium are often necessary to meet the RDA, dietary sources of calcium provide many essential nutrients, unlike supplements, which provide calcium alone or in combination with only a few other nutrients. For example, dark, leafy greens provide fiber, potassium, and folic acid in addition to calcium. RDA for calcium is about 1200mg. Sources includes Yogurt, Sardines, white beans, low fat cheese, and spinach.

Magnesium and Zinc

Magnesium and zinc are two critical minerals that may be low in diets. Magnesium is involved in bone development and preventing osteoporosis, as well as regulating mood and muscle relaxation. Zinc is important for strengthening the immune system, building strong bones, and healing wounds. Deficiencies in zinc lead to reduced appetite and decreased sense of smell. Multivitamin and mineral formulas may not have adequate magnesium and zinc to enhance bone health, mood, and the immune system. Dietary Sources include: Brown rice, spinach, cooked oat bran, groundbeef, oysters, Turkey, pork.

Conclusion

As aging population increase due to improvement in life expectancy with a resultant increase in the number of women in their menopause age, there is a need to expand our knowledge on the physiology, pathophysiology, clinical features and possible available treatment options to care for the increasing population of women in the extreme age group.
There is emerging scientific evidence that treatment beyond pharmacological agents can be used to treat or manage menopausal related symptom and therefore our knowledge expansion will provide a wide room for selection of management options for specific patients with specific set of menopausal symptoms.

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