ROLE OF PHYTOESTROGENS TO MITIGATE POSTMENOPAUSAL PROBLEMS: A REVIEW

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Abstract

To review the evidence that are available for the mitigation of postmenopausal problems with the phytoestrogens. PubMed, Medline, google scholar and Cochrane electronic database were searched related to role of phytoestrogens in combating the postmenopausal problems in women. Various researches were included related to the postmenopausal symptoms and risk factors like osteoporosis, osteopenia, cardiovascular diseases and cancer. Phytoestrogens act as prudent dietary alternative to Hormone Replacement Therapy (HRT). Soy isoflavones play an important role in the treatment of postmenopausal symptoms as well as in reducing plasma cholesterol levels and cancer prevention particularly breast cancer. Ipriflavone, a synthetic isoflavone responsible to increase in Bone mineral density. Diet rich in phytoestrogens play a beneficial role to mitigate the postmenopausal symptoms and its risk factors.

Keywords: Phytoestrogens, Postmenopausal, Mitigation and Isoflavones.

Introduction

Menopause is noteworthy events in woman's life which brings various physiological and psychological changes that affect the quality of her life (Punia, 2017). Menopause is the time when menstrual periods stop permanently causing cessation of pregnancy. In menopause, levels of estrogen and progesterone hormones decrease. Very low estrogen levels after menopause can affect women’s health and cause various symptoms including hot flushes in the chest and face, vaginal dryness, night sweats, headache, anxiety, depression, sleep disturbances and other symptoms which may lead to osteoporosis, hypertension, obesity, cardiovascular disease and cancer (Singh, 2014).

According to WHO, “post-menopausal women are those who have stopped menstrual bleeding one year ago or stopped having periods as a result of medical or surgical intervention (Hysterectomy/Oophorectomy) or both” (WHO, 1990). With the increased life expectancy, there is need for considerable improvement in attention to the menopausal health problems in growing population of post-reproductive women (Dalal, 2015). In 2026, projected figures have estimated menopausal population as 103 million among 1.4 billion population (Unni, 2008).

Hormone replacement therapy (HRT) is also suggested to avert post reproductive symptoms (Bairy, 2009). Now-a-days HRT is becoming more challenging because it has side effects as well. Through the diet rich in phytoestrogens, plant-based compound consisting isoflavones, coumestans and lignans plays a protective role to decrease the postmenopausal symptoms. Though various studies have been conducted to assess the post-menopausal symptoms, however literature is limited on the phytoestrogen rich diet to mitigate the post-menopausal problems.

Material and Methods

The PubMed, Medline, Cochrane and google scholar databases were searched for articles using the terms phytoestrogens, postmenopausal symptoms, osteoporosis in postmenopausal women, CVD and Cancer in Postmenopausal women and benefits of phytoestrogens. Published articles included for this review were based on the relevance of research on role of phytoestrogen to mitigate the postmenopausal problems.

Results and Discussion

Phytoestrogens

Phytoestrogens are estrogenic compounds found in plant and encompasses isoflavones, lignans and coumestans. Phytoestrogens are currently the most popular alternative to HRT. Researches have shown that isoflavones have a protective role as compared to lignans and coumestans against the development of various chronic diseases like osteoporosis, cardiovascular disease, and cancers (Duncan, 2003). There are two types of isoflavones i.e., daidzein and genistein. They are found in soy, clover, lentils, beans and chickpeas. A number of studies showed that plant-based diet rich in phytoestrogens is a contributing factor for the decreasing menopausal symptoms, cancer, osteoporosis and heart disease among Asian women.

Postmenopausal Symptoms

During post-menopausal stage, many symptoms occur like hot flushes, night sweats, irritability, sleep disturbance, muscle and joint pain, dry vagina, difficulty in concentrating, depression, mental confusion and headache (Dalal, 2015). A study by Syamala, 2007, observed that the mean age of menopause was 46.24 years. The most common menopausal problems were sleep disturbance i.e., 62.7%, 59.1% muscle

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and joint pain, then 46.4% and 45.6% hot flushes and night sweats respectively. Further, 32.1% postmenopausal women suffered from depression and 21% from anxiety. Another research conducted in Jamnagar district of Gujarat aimed at understanding various post-menopausal symptoms among women aged between 40 and 65 years. The symptoms were higher in urban areas followed by urban slums and rural areas. The common symptoms found were joint pain (64%), backache (58%), irritability (56.66%), forgetfulness and sadness (48%) and vasomotor symptoms like hot flushes and night sweats (47.33%) (Sarkar, 2014).

Phytoestrogen supplements are used as alternative to Hormonal Replacement Therapy (HRT) for the management of postmenopausal symptoms. Vasomotor symptoms like hot flushes, sleep disturbance and night sweats, these are consequences of estrogen deficiency may less observed in Asian women as compared to European or American women because they consuming phytoestrogen rich diet (Freeman et al., 2007; Messina et al., 2006). A study (Aso, 2012) was done on Japanese women, found that 10mg of equal supplement showed beneficial role on menopausal symptoms majorly hot flushes and shoulder or neck stiffness. Another study was done by the randomized double-blind controlled method in which 100mg of soy isoflavones extract was given and it showed significant reduction in hot flushes. So, it can be considered as safe and effective therapy for postmenopausal women (Nahas, 2007). Combination of isoflavones, cumicifuga racemose and lignans also showed an acute positive effect on reduction of postmenopausal symptoms (Sammaritino, 2006). Isoflavones from red clover (promensil) also responsible for the reduction in hot flushes of postmenopausal women (Van de weijer, 2002). Therefore, combination of phytoestrogens supplements with the exercise found as better strategy for reduction of postmenopausal symptoms and improving the postmenopausal quality of life (Riesco, 2011).

**Risk factors and complications in post-menopausal women**

The Study conducted by Bangalore’s institute for social and economic change found there was higher risk of being affected by obesity, osteoporosis, diabetes mellitus, hypertension, dyslipidaemia, cardiovascular disease, and various cancers at the age between 45 to 50 years (Syamala, 2007).

**Osteopenia and osteoporosis:** In Indian women, osteopenia and osteoporosis are prominent in post-menopausal period. With 35-40% of post-menopausal women to be diagnosed with osteopenia while 8-30% suffer from osteoporosis between 40 and 65 years of age due to diet deficiency (Unni, 2010). This can be reduced by supplementation and dietary changes mainly for calcium (1000-1500 mg daily) and Vitamin D (400-800 IU daily) (Dalal, 2015). As per Cauley (2001), found that Hormone replacement therapy (HRT) is effective in preventing and reducing osteoporosis related fractures by approximately 50% in postmenopausal women.

The reduction in bone mineral density can be prevented through the intake of natural plant-based compound i.e., phytoestrogens or estrogen like compounds in plants. Osteopenia may lead to another severe condition, osteoporosis that can be characterized by the low bone density and it cause due to deficiency of ovarian hormones (Al-Anazi, 2011). In post-menopausal women, soy isoflavones which having similar structure and functions as 17 Beta-estradiol, an alternative of hormone replacement therapy. These act on the osteoclast and osteoblast both through the genomic and non-genomic pathways and performing many beneficial effects in the reduction of bone density, turnover markers and mechanical strength of bones (Atmaca A, 2008).

Phytoestrogen containing isoflavone has been considered as effective in increasing the bone mineral density in postmenopausal women (Table 2). Ipriflavones may also responsible for the formation of osteoblast and inhibiting the osteoclast activity and it has been measured by the urinary resorption marker detection and biochemical markers of bone resorption and bone mineral density (Valente, 1994).

**Cardiovascular Disease:** In India, there is rapid increase of CVD in postmenopausal women. Projection of around 42% of deaths by CVD only due to prevalence of metabolic syndrome which includes insulin resistance, altered glucose tolerance or diabetes, dyslipidaemia, hypertension, and central obesity (Unni, 2010). A study was done at Mamnnon Memorial Institute of Health Sciences (MMIHS) which analysed Total Cholesterol (TC), Triacylglycerol (TG), High Density Lipoprotein Cholesterol (HDL-C), and Low Density Lipoprotein Cholesterol (LDL-C) and found that lipid levels were highly significantly increased in postmenopausal women when compared to premenopausal women and hence they are more prone to CVD diseases (Pardhe, 2017).

Phytoestrogens mainly isoflavones plays a beneficial role on the cardiovascular system in reduction of LDL (bad cholesterol), increase in HDL (good cholesterol) through which it may protect from cardiovascular diseases (Clarkson TB, 2001). It has been found that 75 mg/day of soy isoflavones may cause reduction in menopausal symptoms in postmenopausal women for 1-2 years also promote beneficial role in reducing LDL cholesterol and triglycerides levels with increase in HDL cholesterol as seen in Table 3. A study revealed that 56mg and 90mg of isoflavones affects the lipid profile as they increase level of HDL cholesterol in postmenopausal women and also reported that messenger RNA level is increased in isoflavone treatment group. Although, the process of soy isoflavones to modify the lipid profile is remain unclear (Baum, 1998). As per another study soy isoflavones have antioxidant property which helps in reducing the risk of atherosclerosis and CVD. It was examined by the markers of lipid peroxidation and LDL resistance to oxidation. Atheroma is formed by the LDL oxidation and which is required for the uptake of LDL macrophage in the artery wall (Wiseman, 2000).

**Cancer:** Among postmenopausal women, most common type of cancer is breast cancer. A study showed that the risk of breast cancer increased by the presence of both hormone estrogen and progesterone in the postmenopausal women (Chlebowski, 2003). The phytoestrogens i.e., isoflavonoids and lignans plays an important inhibitory role in the initiation and progressive phase of the development of cancer (Adlercreutz et al., 1997). Many epidemiological researches suggested that diet rich in phytoestrogen plays a protective role in reducing breast cancer risk.
role in early life before puberty or during adolescence as well as in adult women to fight with the breast cancer as seen in Table 4. Further, epidemiological studies suggest that soy containing diet in adult women is protective with regard to breast cancer and it may be beneficial if consumed in early life before puberty or during adolescence (Krishna, 2004). Murkies et al., 2000 demonstrate that phytoestrogen (daidzein) has the protective role on the risk of breast cancer in postmenopausal women. In the postmenopausal phase, the estrogen and progesterone hormone level decreases but the chances of breast cancer increase with age (Simpson et al., 2005).

Conclusion

Present review article would help in creating awareness about the role of phytoestrogen to reduce the postmenopausal problems like various menopausal symptoms, osteoporosis, cancer and cardiovascular disease, so that they can improve their quality of life. Study may also help to ensure easy transition of women to old age because scarce attention is paid to post-menopausal aged women unless the condition becomes worse. Results may also help to analyze the impact of diet rich in phytoestrogens on physiological problems during post-menopausal age as well as to reduce the future complications.

References


Hodso JM, Puddey IB, Beilin LJ, Mori TA and Croft KD (1998). Supplementation with isoflavonoid phytoestrogens does not alter serum lipid concentrations:


<table>
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<th>Author</th>
<th>Study Design</th>
<th>Interventions or Diet</th>
<th>Findings</th>
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<tbody>
<tr>
<td>Aso T et al., 2012</td>
<td>Double bind placebo-controlled trial</td>
<td>10mg of natural equol</td>
<td>Effective in reduction of menopausal symptoms mainly hot flushes &amp; shoulder or neck stiffness in postmenopausal women</td>
</tr>
<tr>
<td>Cancellieri et al., 2007</td>
<td>Double bind placebo-controlled clinical trial</td>
<td>BIO, herbal supplement with 72mg/dose of isoflavones</td>
<td>Beneficial effect on postmenopausal symptoms and elements of lipid profile</td>
</tr>
<tr>
<td>Del Giorno et al., 2010</td>
<td>Randomized double blind placebo-controlled study, 12 months</td>
<td>40mg of trifolium pratense</td>
<td>No improvement in menopausal symptoms &amp; sexual satisfaction in postmenopausal</td>
</tr>
<tr>
<td>Ferrari et al., 2009</td>
<td>Randomized double blind placebo-controlled study</td>
<td>80mg of isoflavones or 60mg of genistein</td>
<td>Mainly genistein show positive effect on management of hot flushes in postmenopausal women</td>
</tr>
<tr>
<td>Nehas et al., 2007</td>
<td>Randomized double blind placebo-controlled study</td>
<td>100mg/day of soy isoflavone extract</td>
<td>Favorable effect on vasomotor symptoms mainly hot flushes</td>
</tr>
<tr>
<td>Penotti et al., 2003</td>
<td>Randomized double blind placebo-controlled study</td>
<td>72mg of soy derived isoflavones</td>
<td>No significant effect on hot flushes and endometrial thickness</td>
</tr>
<tr>
<td>Riesco et al., 2011</td>
<td>Randomized double blind placebo-controlled study</td>
<td>Four estrogen capsules containing 17.5mg of isoflavones</td>
<td>Combination of exercise and phytoestrogen supplementation beneficial to improve the postmenopausal symptoms</td>
</tr>
<tr>
<td>Van de weijer et al., 2002</td>
<td>Randomized double blind placebo-controlled study, 6 months</td>
<td>80mg/day of isoflavones from red clover (promensil)</td>
<td>Significant reduction in hot flushes</td>
</tr>
<tr>
<td>Sammartino A et al., 2006</td>
<td>Randomized double blind placebo-controlled trial</td>
<td>Combination of isoflavones, lignans, cimicifuga racemose</td>
<td>Better reduction of postmenopausal symptoms over 24-hour period</td>
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Table 2: Phytoestrogens and Osteopenia/Osteoporosis in Postmenopausal Women

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<tbody>
<tr>
<td>Kaardinaal <em>et al</em>., 1998</td>
<td>Secondary analysis</td>
<td>The isoflavonoids genistein, daidzein and equol and the lignan enterolactone</td>
<td>No difference</td>
</tr>
<tr>
<td>Clifton Bligh <em>et al</em>., 2001</td>
<td>Randomized double blind placebo-controlled trial, 6 months</td>
<td>Rimostil, red clover isoflavone containing daidzein, genistein, formononetin and biochanin</td>
<td>BMD at proximal radius and ulna increased. BMD at proximal radius and ulna increased</td>
</tr>
<tr>
<td>Potter SM <em>et al</em>., 1998</td>
<td>Double bind trial, parallel group</td>
<td>Soy protein containing concentrated isoflavones</td>
<td>Protective role on Bone maintenance</td>
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<tr>
<td>Guthrie IR <em>et al</em>., 2000</td>
<td>Population based cohort study</td>
<td>Isoflavones rich food, soy bean, milk, grits, tofu, soy and linseed breads</td>
<td>Bone mass density increases in femoral neck</td>
</tr>
<tr>
<td>Dalais FS <em>et al</em>., 1998</td>
<td>Double bind randomized over study</td>
<td>Soy and linseed diet</td>
<td>Increase in bone mineral content, but no changes in bone mineral density</td>
</tr>
<tr>
<td>Alexanderson <em>et al</em>., 2001</td>
<td>Randomized double blind placebo-controlled trial, 3 years</td>
<td>Ipriflavone</td>
<td>No difference in Bone mineral density</td>
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Table 3: Phytoestrogens and Cardiovascular disease in Postmenopausal Women

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<th>Author</th>
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<tr>
<td>Trimareo V <em>et al</em>., 2016</td>
<td>Cross over trial</td>
<td>Nutraceutics containing soy isoflavones, dry extract of Angelica sinesis, Morus alba leaf and magnesium</td>
<td>Found effective to reduce menopausal symptoms and improved Cardio vascular risk profile</td>
</tr>
<tr>
<td>Washburn <em>et al</em>., 1999</td>
<td>Randomized double cross over study, 6 weeks</td>
<td>34mg of phytoestrogen</td>
<td>Supplementation of phytoestrogen may reduce Total cholesterol and LDL levels</td>
</tr>
<tr>
<td>Wangen <em>et al</em>., 2001</td>
<td>Randomized double cross over trial, 93 days</td>
<td>Isoflavones</td>
<td>Reduction in LDL and ration of LDL/HDL levels</td>
</tr>
<tr>
<td>Author</td>
<td>Study Design</td>
<td>Interventions</td>
<td>Results/Findings</td>
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<tr>
<td>Teede et al., 2001</td>
<td>Randomized double blind placebo-controlled trial, 3 months</td>
<td>Soy supplements containing 118mg of isoflavones</td>
<td>Significant decreased in TG and LDL/HDL ratio</td>
</tr>
<tr>
<td>Howes et al., 2000</td>
<td>Randomized double blind placebo-controlled trial, 10 weeks</td>
<td>Isoflavones extract containing biochanin, formononetin, genistein and daidzein</td>
<td>No effect on TC, TG, LDL and HDL</td>
</tr>
<tr>
<td>Hodgson et al., 1998</td>
<td>Randomized double blind placebo-controlled trial, 8 weeks</td>
<td>Isoflavone tablet</td>
<td>No change</td>
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**Table 4: Phytoestrogens and Cancer in Postmenopausal Women**

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<th>Author</th>
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<tr>
<td>Den Tokelaar et al., 2001</td>
<td>Cohort Design</td>
<td>urinary genistein and enterolactone</td>
<td>Not finding any protective effects of genistein and enterolactone on breast cancer risk in our postmenopausal</td>
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<tr>
<td>Alison M et al., 2000</td>
<td>Randomized cross over</td>
<td>Soy protein powder containing genistein, daidzein and glycitein</td>
<td>Inconsistent results seen</td>
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<td>Mc Michael phillips et al., 1998</td>
<td>Randomized placebo-controlled trial</td>
<td>45mg/ day of isoflavones</td>
<td>Short term soy supplements in diet stimulates breast cancer proliferation</td>
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<td>Ingram et al., 1997</td>
<td>Case control</td>
<td>Phytoestrogens</td>
<td>Phytoestrogen rich diet may protect from breast cancer</td>
</tr>
<tr>
<td>Zheng et al., 1999</td>
<td>Case control</td>
<td>Isoflavones</td>
<td>High intake of phytoestrogens rich in isoflavones plays a protective role in breast cancer</td>
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