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Review article

Increased Risk of Osteoporosis in Postmenopausal Women: Review

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ABSTRACT

Osteoporosis is more common in females over the age of 50, as estrogen's chemical effect on bone density fades with the start of menopause. Pathological fractures and an upsurge in incidence and death in menopausal women result from subtle changes in bone form, quality, and density. Osteoporosis is a disorder that affects bone to deteriorate because they become brittle and losing density. Weaker bones are unstable and more liable to shatter. This disease is more frequent in menopausal women. Lower estrogens levels are connected to menopausal women bone loss. This hormone is important in hormone metabolism and regulates specialized bone cells termed osteoclasts, osteoblasts, and osteocytes. Because osteoporosis has few visible signs, it can grow without a person's knowledge. Data was collected from electronic databases such as Google Scholar, PubMed, and Springer publications. A total of three studies were included, based on various study groups and inclusion and exclusion criteria. Data regarding menopause was collected by taking detailed menstrual history and Bone mineral density data of these postmenopausal women was analyzed. Therapy aims to slow or delay the occurrence of osteoporosis, promote healthy bone density and bone strength, prevent broken bones, ease pain, and maximize the woman's potential to survive with their everyday life. People who are at risk of osteoporosis and fractures can achieve these goals through preventive lifestyle measures, diet modification along, and certain medications.

Key Words – Osteoporosis, menopause, women, Lifestyle modification

INTRODUCTION

The World Health Organization (WHO) considers spontaneous menopausal as being at least twelve months of no menstrual cycle that is not caused by physiological or pathological factors. According to research, the average age of normal menopause in industrialized countries is 51 years, contrasted to 48 years in impoverished and unindustrialized countries. Having a life expectancy of 70 years, majority women will live more than 33 percent of their lives past menopause. Furthermore, the number of menopausal women is increasing as the ageing population grows fast (1).

As a result, the heath of menopausal women has become a major issue across the world. Menopause is a normal biological process caused by ovarian failure caused by apoptosis, or programmed cell death. With ageing, ovarian function reduces. Menopause begins with a decrease in estradiol synthesis and an increase in follicle-stimulating hormone levels (FSH). Women will encounter a variety of annoying symptoms throughout the menopausal transition phase, including heartburn, excessive sweating, and genital atrophy and drying, sexual dysfunction, sleep difficulty, and mood changes.

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Aside from these symptoms, this condition of porous bones is by far the highly prevalent occurrence among menopausal females and is exceedingly related with degraded quality of life; postmenopausal osteoporosis is mainly focused in this (2).

Osteoporosis is a complex systemic skeletal condition characterized by weak bones (BMD) and micro-architectural bone tissue degradation, culminating in fracture risk. The criterion for diagnosing osteoporosis is BMD assessed by dual X-ray densitometry. The WHO defines osteoporosis as having a T-score of less than 2.5 and Osteopenic as having a T-score within 1.0 and 2.5. The anatomical area of attention is recommended to be the femur neck and lumbar spine. Since BMD decreases with age, initial osteoporosis primarily affects women 15–20 years following menopausal and aged men approximately 75–80 years old (3). With an ageing population, osteoporosis and pathological fractures are rapidly becoming significant public health challenges that place a significant cost strain on health-care resources. Bone density is crucial for bone health and plays a key role in avoiding osteoporosis and resultant fractures later life. Hip fractures might be decreased by 30% with a 10% rise in peak bone mass, according to research. 2 Peak bone mass can be obtained in the mid-twenties for the spine along with hip, however other joints, for example the radius, reach highest at the age of 40. Following that, bone mass often falls. Bone mass has dropped by 30–40% by the age of 70. Genetic factors are the most important determinants of peak bone mass. Several genetic variations associated with bone mass, particularly low-density, have been discovered in studies (4).

Constant remodeling is required for healthy bone, which is critical for bone mineral density (BMD) maintenance. It is thought that this process updates roughly 10% of the bone every year. Osteoclasts (bone resorbing cells) and osteocytes (bone creating cells) are two types of cells that work together to keep a balance of bone resorption production. The resting phase, activation phase, resorption phase, reversal phase, and formation phase are the five stages of normal bone remodeling. To begin, osteoclasts are drawn to the bone's surface, where they create an acidic microenvironment between the cell and the bone's surface, disintegrating and resorbing the nutrient levels of the bone (5).

LITERATURE SURVEY

Many studies have been conducted to detect the impact of the risk of Osteoporosis in post-menopausal women. Meng-Xia Ji and Qi Yu et al found that the main sequelae of the osteoporosis among menopausal women is osteoporotic fractures and post 40’s the density of the bones is already declining owing to age related consequences. In addition, it found that it is linked with the decrease in hormone of estrogen, which is triggered by increasing age. The study also suggested the hormone therapy for the women who did not attained the age of 60. Damir Franic et al conducted a study to determine the odds of getting the osteoporosis post menopause each year and found that by each increasing year the odds increases by 8 percent. In addition, it linked the Body Mass Index to the prevalence of the osteoporosis as the women having BMI less than 18.5 are two times susceptible to it. Confirming the trend, it also suggested that the risk of fractures increases with increasing age and it is more among the women aged more than 50 years of age. The disease concerns with skeletal system, which can hamper the day-to-day life of the affected women, especially working women. The North American menopause society conducted research on similar topic and found out that the primary cause behind the Osteoporosis in post-menopausal women is the decrease in estrogen, which is in alignment with the previous observations. The study suggested non-pharmacological interventions, which are linked to diet and nutrition and better lifestyle. The susceptible group must ensure the intake of the nutrients such as calcium protein. In addition, the absorption of the calcium depends on the Vitamin D, which is also necessary among such women.

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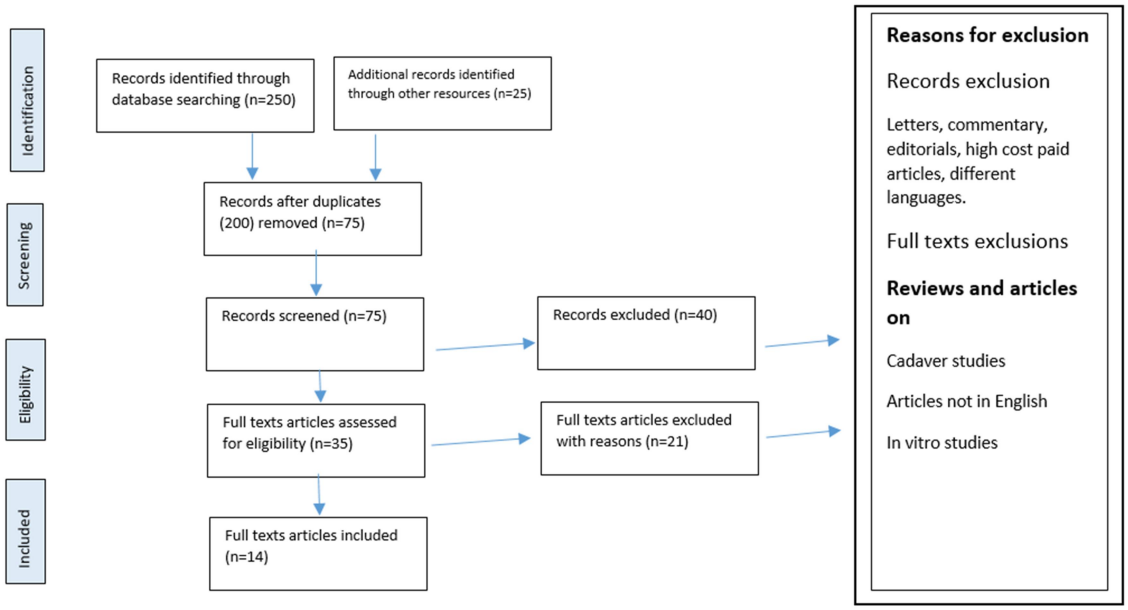

FIGURE 1: Study selection process using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines

Data was collected from electronic databases such as Google Scholar, PubMed, and Springer publications. A total of three studies were included, based on various study groups and inclusion and exclusion criteria. Data regarding menopause was collected by taking detailed menstrual history and Bone mineral density data of these postmenopausal women was analyzed. The elderly population is growing at an unprecedented rate. As the population grows, so will the number of people suffering from osteoporosis. It is anticipated that the incidence of the disease grows from one-third of adults aged 50–60 to more than half of people over the age of 80. By 2050, the worldwide osteoporosis population will be 6 million (both in men and women), with emerging nations accounting for 3/4 of the total.

The most serious health risk of osteoporosis is pathological fractures, which happens at a location linked with low BMD (usually in the spine, hip, or wrist, although occasionally the humerus or ribs are similarly implicated), and it becomes more common beyond the age of 50. Postmenopausal osteoporosis fractures occur in a sequential way, with the initial indicator ensuing fractures of the distal half of the radius beginning at the age of 50, followed by fractures at the ages of 60–75, and bone fractures originated in the late 70s. 9 Fractures pertaining to osteoporosis can result in a loss of range of motion and autonomy, a decrease in quality of life, and the development of major consequences such as pneumonia or venous thromboembolism illness, which imposes a significant health and economic cost on society.

Albright and Reifenstein discovered that estrogens might prevent osteoporosis as early as the 1940s. The link among menopausal and osteoporosis was discovered in the 1960s, and estrogens therapy was taken to avoid osteocytic degradation. A great amount of conclusions have now shown that estrogens is essential in the treatment of osteoporosis, and hormone therapy is still a first-line treatment option for postmenopausal women (6).

Menopausal Hormone Treatment (MHT) has for very long time been acknowledged to enhance BMD considerably. A meta-analysis of 57 studies (including preventative and therapy trials) involving approximately ten thousand women concluded that the difference in bone density is considerably larger in the MHT category (together controlled and uncontrolled estrogens) at all measurement locations. Following a year, the MHT group had an annual growth of 5.4 percent in bone mass at the lumbar spine, and 3.0 percent and 2.5 percent in the elbow and femoral neck,

respectively. After two years of therapy, the percentage shift in favour of MHT rose by around 1.5 percent across the board, with increases of 6.8 percent, 4.5 percent, and 4.1 percent at the lumbar spine, forearm, and femoral neck, respectively(7).

MHT can also help avoid fractures. In a pooled analysis of 22 randomized trials, there was a 27 percent decrease in favour of MHT groupings in non-vertebral fractures (RR = 0.73, 95 percent CI, 0.56–0.94, P = 0.02). MHT appeared to be more beneficial for hip and wrist fractures alone (RR = 0.60, 95 percent CI, 0.40–0.91, P = 0.02) (8) .

The HOPE experiment included 822 competent postmenopausal women aged 40–65 who were randomly assigned to daily compounded equine estrogen therapy of 0.3 mg, 0.45 mg, or 0.625 mg with or without continued everyday medroxy progesterone acetate at 1.5 mg or 2.5 mg. All individuals, including the placebo group, received a 600 mg calcium supplement. Women allocated to all active therapy groups experienced substantial increases from baseline (P 0.001) in spine or hip BMD after two years of therapy, with the difference being roughly 3–5 percent for spine BMD and 1–3 percent for total hip BMD(9) .

It is important to note that estrogen removal causes fast bone loss, with most of the prior enhanced BMD gained over 3–4 years disappearing within a year. MHT enhanced BMD by 5%–6% in a randomized trial of early postmenopausal women aged 55 years. However, 4 years after therapy was discontinued, there was a 7% decline in spine BMD in the MHT group. Another comparable study found that hip fractures rose by 50% after two years and by 77% after five years. It is thus suggested that women who quit MHT find other osteoporosis prevention medications.

RESULTS

Findings from MHT studies show that there are two groups of postmenopausal women that respond differentially to MHT. The reaction to MHT varies according to age or months menopause. When MHT is begun in women under 60 years old and/or or less 10 years postmenopausal, CHD events and total mortality are reduced, and the advantages exceed the dangers. When MHT is begun in women over the age of 60 and/or more than 10 years following menopause, there is no impact and sometimes a harmful effect. That is the hypothesis of the window of opportunity.

Data from the DOPS research, which was just published, support the concept that MHT can lower cardiovascular outcomes in women if begun immediately after menopausal, which occurs to be the era of rapid bone loss. As a result, while administering hormone to prevent postmenopausal osteoporosis, we should keep the timing theory in mind. As previously noted, bone resorption is quickest during first 3–4 years following menopause, hence it is prudent to begin hormone therapy soon after menopause. During this stage, the response to therapy may be the strongest because preventing resorption causes immediate filling of the dissolution or remodeling space, which promotes bone growth and leads in a higher increase in bone mass.

According to the Chinese menopause guidelines, menopausal transition hormone therapy is suggested for women who may be at risk of bone fractures and are younger than 60 years old; however, menopausal transition hormone treatment is not recommended for those that are older than 60 years old if it is only for the preventive medicine of osteoporotic fractures. MHT must be administered and dosed individually, and the advantages and hazards should be thoroughly evaluated during therapy. To prevent fractures, the minimum possible dose of MHT must be administered, and transdermal formulations have less adverse effects than oral medications. After quitting hormone medication, bone loss will return. Other preventative medications should be used by persons who may be at risk of osteoporotic fractures.

DISCUSSION

The incidence of osteoporosis is increasing and has become a severe public health issue of worldwide concern, particularly in postmenopausal women of advanced age, where it causes increased fracture risk at several locations. The current investigation was based on 11 randomized controlled trials with 12,013 osteoporotic or low-BMD postmenopausal women to compare the effectiveness and tolerability of denosumab versus placebo across a variety of parameters. According to the findings of this study, denosumab was associated with a large percentage change in BMD at the 1/3 radius, femur neck, lumbar spine, whole hip, trochanter, and whole body. Furthermore, denosumab significantly reduced the risk of several types of fractures, including acute fractures, non - vertebral fractures, spinal fractures, and hip fractures. The prevalence of the disease is increasing (10).

Additionally, there were no extra hazards associated with denosumab in terms of side effects,

treatment-related adverse reactions, discontinuation owing to adverse events, or mortality. Although there were substantial differences between denosumab and placebo treatments, these results will vary due to the small number of trials considered. In terms of homogeneity, the findings from trials with more weight were comparable. As a consequence, while the results of trials with reduced weight were more inconsistent, the overall results remained strong. A great number of comprehensive reviews and meta-analyses have been undertaken on denosumab for the treatment of postmenopausal women with osteoporosis or low Density. Anastasilakis et al. (2009) did a meta-analysis of 3 Randomized trials and found a substantial drop in bone markers and an increase in lumbar and hip BMD following treatment with denosumab, but no major benefits on fracture risk for infection risk were detected(11) .

Von Keyserlingk et al. (2011) did a morph based on four RCTs and found that postmenopausal women who took denosumab had a large reduction in fracture risk without an increase in adverse outcomes (12).

Zhou et al. (2014) conducted a meta-analysis of 11 Randomized trials and found that denosumab therapy resulted in a substantial reduction in the incidence of non - vertebral fractures as well as major adverse events linked to infections in osteoporotic or low-BMD postmenopausal women. Gu et al. (2015) did a meta-analysis focusing on 4 RCTs, and the results demonstrated that denosumab therapy enhanced BMD while decreasing bone turnover indicators in postmenopausal women, with no substantial risk of side events. Several RCTs on the issue have previously been completed; however the magnitude of the therapeutic efficacy of adalimumab versus placebo in postmenopausal osteoporosis or low-BMD postmenopausal women should be reevaluated (13).

Even though the trial process provides thorough efficacy data for adalimumab in postmenopausal osteoporosis or reduced density in postmenopausal women, some challenges have been identified. First, summary findings for BMD at different locations were only accessible in a few studies, causing inconsistency in the size of BMD in the denosumab subgroup. Secondly, the risk of the majority of the adverse reactions was accessible in smaller studies, and the power may not have been sufficient to distinguish between the denosumab and control subjects. Finally, because the study was based on reported RCTs and the bias towards publishing negative outcomes is well recognised, publication bias was unavoidable (14).

FUTURE SCOPE

Our study has the limitation of the pool of subjects studied as more number of subjects from different age groups through multicenter studies can give better empirical understanding. The severity and impact of Osteoporosis also varies with the age bracket and hence dedicated study to analyze particular age bracket will shed the light on nuances, which are not highlighted in the above presented study. Effectiveness of non-pharmacological interventions in the management of the osteoporosis among post-menopausal women is out of scope of this study and can be included in the future endeavors.

CONCLUSION

Osteoporosis is a frequent and quiet condition until it is worsened by frequent fractures. It is projected that 50 percent of the total of women and 20% of men over the age of 50 will experience a decreased bone fracture in their remaining lifespan. These fractures effects long-term damage, declined standard of living, and increased mortalities, putting an incredible medical and personal burden on the patient. Before fractures occur, osteoporosis can be diagnosed and treated effectively. As a result, primary care professionals should be responsible for the prevention, identification, and treatment of osteoporosis.

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