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RESEARCH ARTICLE

HOW OSTEOPOROSIS IN POSTMENOPAUSAL WOMEN IS RELATED TO HEARING LOSS?

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Abstract

Osteoporosis is a very common medical condition that may cause bone resorption and deposition in auditory structures. The aim of the study is to assess the relationship between osteoporosis in postmenopausal women and hearing loss. According to published papers on osteoporosis leading to hearing loss, the pathophysiology and manifestations of the problems of the inner ear are related to bone metabolic diseases such as osteoporosis. To be exact, demineralization of the bone tissue and bone resorption, which are typical procedures of osteoporosis, affect the bone structures of the hearing system and lead to hearing loss in postmenopausal women.

Introduction:-

Osteoporosis affects over 5% of the global population. It is a common skeletal disease that is characterized by low bone mineral density (BMD) and poor bone quality, resulting in reduced bone strength and increased risk of fractures [1].The World Health Organization (WHO) defines osteoporosis in postmenopausal women as BMD with T score over 2.5 standard deviations below the mean value of young healthy adults, while BMD between 1.0 and 2.5 standard deviations below the mean value (*T* score = −1.0 to −2.5) is classified as osteopenia [2].

Methods:-

Published papers regarding the mechanism of osteoporosis which leads to hearing loss were sought through MEDLINE, PUBMED and GOOGLE SCOLAR searches.

Results:-

Normal bone remodelling is modulated by local and systemic regulators. Bone resorption and formation are normally in balance, enabling the repair of minor damages and the maintenance of calcium homoeostasis and bone mass. Bone is constantly remodelled by the interaction of osteoclasts, which resorb the existing bone and osteoblasts, which form new bone matrix. These two cell types cooperate with resident bone osteocytes in the basic multicellular units (BMUs) that conduct bone remodelling. Bone loss and structural damage occur when the extent of bone resorption within a BMU exceeds that of bone formation. This condition is characterized as negative bone balance [3].

An important cause of negative bone balance is menopause: reduced estrogen production leads to increased RANKL secretion by osteoblasts and osteocytes. Receptor activator of nuclear factor kappaB ligand (RANKL) is a cytokine member of the tumor necrosis factor (TNF) superfamily. RANKL is expressed on the surface of osteoblasts and in soluble form after cleavage from the cell surface or secretion from T-cells and acts as an essential mediator of

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osteoclast formation, survival and function. When RANKL binds to receptor activator of nuclear factor kappaB (RANK) on the surface of osteoclasts and preosteoclasts, it promotes osteoclast differentiation, activity, and survival, thereby increasing bone resorption [4]. In other words, the increased RANKL secretion in postmenopausal women leads to activation of osteoclast precursors and mature osteoclasts [5,6] and longer lifespan of osteoclasts, which are responsible for increased rate of bone remodeling and osteoporosis[7] .

Osteoprotegerin (OPG), also known as tumor necrosis factor receptor superfamily member 11b (TNFRSF11B), is a key regulator of bone remodeling. It is a soluble non signaling decoy receptor that binds to RANKL, preventing its interaction with RANK. In this way OPG inhibits osteoclastogenesis and decreases the survival of the existing osteoclasts. An increase in the RANKL:OPG ratio has been implicated in the pathogenesis of osteoporosis in both women and men [7].

Regarding the hearing mechanism, the temporal bone contains three highly mineralized bones: malleus, incus and stapes. The malleus firmly attaches to the tympanic membrane and transmits vibration to the incus and stapes, which consequently vibrates the fluid in the inner ear through the oval window [8]. These auditory ossicles are arrayed in the tympanic cavity of the middle ear. Disturbances in sound transmission in the middle ear result in conductive hearing loss, whereas impairment of the internal ear or the auditory nerve causes sensorineural hearing loss.

Discussion:-

While bones develop through endochondral and intramembranous ossification-bone modeling-, osteoclastic bone resorption is usually balanced by osteoblastic bone formation through “coupling” mechanisms, which maintain bone integrity -bone remodeling- .The otic capsule and auditory ossicles participate in the ossification of the temporal bone [9].In patients suffering from osteoporosis this procedure is disturbed. Osteoporotic auditory ossicles dysfunction and therefore the hearing ability impairs.

A common cause of osteoporosis is menopause, which is implicated with low estrogen levels. Estrogens contribute to bone protection since they decrease the response of osteoclasts to RANKL and induce osteoclast apoptosis.

Additionally, estrogens regulate prolactin release. A decrease of estrogens levels leads to increased secretion of prolactin [10]. Prolactin affects calcium metabolism and BMD. Recent data show that prolactin decreases OPG and increases RANKL [10]. OPG has been shown to be expressed at high levels in the cochlea and OPG knock-out mice have indeed abnormal remodeling of the otic capsule and resorption of the auditory ossicles [11].

Osteoprotegerin (OPG) functions as a soluble, neutralizing antagonist that competes with receptor activator of NF-κB (RANK) on preosteoclasts and osteoclasts for RANK ligand (RANKL), which is produced by osteoblasts, and impairs osteoclast formation and function [12] .

Genetic variation at the OPG locus is considered to be a risk factor for osteoporosis. Furthermore, neutralizing autoantibodies against OPG cause the development of high-turnover osteoporosis in celiac disease, which is an autoimmune mal absorptive disorder of the small intestine associated with hearing loss [12].

The ability of nerves to secrete OPG, which promotes their survival and inhibits bone remodeling, may be advantageous because nerves within the central nervous system are surrounded by bone and pass through osseous foramina to reach their distal targets. Antiapoptotic properties of OPG are also thought to limit immune-mediated damage in the nervous system. Therefore, the OPG knock-out mice develop skeletal abnormalities very similar to human osteoporosis. A detailed examination of their temporal bone, which houses the inner ear, includes abnormal bony remodelling, cavitation within some remodelling foci, and thickening of middle ear mucosa. Besides, OPG deficiency inhibits proliferation and promotes apoptosis of auditory stem cells. Therefore, the OPG knock-out mice are known to have progressive hearing loss due to resorption of ossicles in the middle ear [11].

Conclusion:-

RANKL, OPG and estrogens are strongly related to osteoporosis in postmenopausal women. The combination of increased RANKL:OPG ratio and decreased estrogen levels has been implicated in the pathogenesis of osteoporosis. Once osteoporosis is established, the process of demineralization of the bone tissue affects the otic capsule, the auditory ossicles and the internalacoustic meatus. Furthermore, the decrease of OPG causes immune-mediated

damage in the nervous system. Osteoporosis in postmenopausal women leads to conductive hearing loss, due to impaired conduction of sound to the inner ear, or sensorineural, due to damage of delicate mechanosensory structures in the inner ear, the cochlear nerve, or higher order auditory centers.

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