POSTMENOPAUSAL OSTEOPOROSIS – AN EXPLORATIVE LITERATURE REVIEW

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Abstract

The "osteoporosis" domain is changing, and if in the past the focus was more on the bone, now the field is evolving and focusing more on the risk of fracture. Such a change is necessary because fragile fractures are common and can have devastating effects on quality of life.

Osteoporosis and low bone mass are considered a major public health problem. Osteoporosis is a complex, multifactorial chronic disease that can progress silently for decades until characteristic fractures result late in life. Because symptoms are rare until a fracture occurs, few people are diagnosed in time to receive effective therapy

The purpose of the research

The purpose of this paper is to highlight important issues regarding postmenopausal osteoporosis.

Methods

We searched Science Direct, Springer Link, Web of Science and PubMed for articles and reviews in the English language pusblished between 2000 and 2020, although older references were also used when appropriate. The following terms were used to give as broad range of studies as possible: ,,osteoporosis", ,,bone density", ,,bone mass", ,,postmenopausal", ,,elderly women", ,,osteopenia", ,,bone physiology".

Results

We limited the search to the following study designs: controlled clinical trials, guidelines, meta-analyses, systematic reviews and

randomised controlled trials. Of all the articles found, we selected 73 scientific articles from which we selected the most conclusive information.

Bone anatomy and physiology

The skeleton of the human body provides protection to the vital organs, serving as the insertion point of the muscles and hosting the bone marrow. Bones contain approximately 99% of the body's total calcium and play an important role in homeostasis (maintaining internal homeostasis), serving as a reservoir from which calcium ions can be transported. If the calcium absorbed in the intestine does not meet the needs of the body, bone lysis covers the calcium requirement and maintains serum calcium between normal or as close to normal intervals (Rizzoli, 2010, p. 1), (Tortora & Derrickson, 2012, pg. 182-207), (Marieb, Wilhelm, & Mallatt, 2014, pg. 123-149).

There are three types of bone cells called osteoblasts, osteoclasts and osteocytes. Osteoblasts form new bone (osteogenesis), and osteoclasts participate in bone resorption (osteolysis) (Villiers, 2009), (Yang, et al., 2012), (Cheng, et al., 2013).

Osteoblasts are derived from pluripotent stem cells, and their principal role is to synthesize the osteoid (bone matrix) and to regenerate bone tissue (Monzur, Dympna, Jose, Marc, & Gerard, 2005), (Thompson, Rubin, & Rubin, 2012).

Osteoclasts are cells that play a role in bone resorption, and they derive from hematopoietic cells of monocytes / macrophages. Osteoclasts are multinucleated, hard-membrane, bone-oriented cells that secrete specific acid and enzymes required for bone matrix dissolution / digestion (Sevgi & Duong, 2008), (Lau & Guo, 2011).

Osteocytes are differentiated osteoblasts that are embedded within the mineralized bone matrix. Osteocytes make up about 90% - 95% of the bone cells in the skeleton of an adult person (Rochefort, Pallu, & Benhamou, 2010). They are connected to each other, but also to the osteoblast cells on the surface of the bone through a network of canaliculi that contain the extracellular fluid of the bone. Osteocytes behave like mechanosensors in the bone, which feel the physical (mechanical) stress and microtrauma, preparing in response the subsequent bone modeling or remodeling (Bonewald, 2007).

What is osteoporosis?

Osteoporosis is a systemic skeletal disorder characterized by decreased bone mass and deterioration of bone tissue microarchitecture (Costa, et al., 2016), (Hou, et al., 2018), (Phipps, Mitlak, Burr, & Allen, 2019, p. 389) .

Osteoporosis is the most common disease that affects adults, especially the elderly. It is different from osteomalacia because it results from the diminution of the bone matrix and not due to deficient calcification. In the case of osteoporosis, the activity of cells called osteoblasts is lower than normal, and as a consequence the rate of bone formation decreases (Guyton & Hall, 2006, pg. 992-993), (Chen, et al., 2014), (Li, et al., 2015), (Li, et al., 2015).

Bone loss occurs in "quiet" and progressive. Often, there are no symptoms until the first fracture occurs (International Osteoporosis Foundation, 2015), (Henriquez & Romero, 2018).

Osteoporosis affects millions of people worldwide, being most common among women, where the incidence is much higher after the onset of menopause (Burge, Dawson-Hughes, Solomon, Wong, King, & Tosteson, 2007), (Kanis, et al., 2008), (Lai, et al., 2013), (Weber-Rajek, Mieszkowski, Niespodzinski, & Ciechanowska, 2015).

The WHO (World Health Organization) diagnostic categories of bone mass deficiency: a T-score of -1.0 or above is normal bone density; a T-score between -1.0 and -2.5 means you have low bone density or osteopenia; a T-score of -2.5 or below is a diagnosis of osteoporosis (Carmen, 2005, p. 109).

Epidemiology of osteoporosis

Osteoporosis affects about 40% of women and 20% of men at some point in life (Riggs, et al., 2004), (Cooper, et al., 2011). Osteopenia and osteoporosis are two of the most common disorders in the elderly. Half of people over the age of 50 suffer from one of the two conditions mentioned above (David, Jackie, & Lewis, 2012, pp. 131-132).

The prevalence of osteoporosis in the coxofemoral joint and spine in nine industrialized countries in North America, Europe, Japan and Australia is between 9% and 38% among women and between 1% and 8% among men. In these countries, osteoporosis affects up to 49 million jealousy. Prevalence among women (based on bone mineral density in the hip or spine) ranges from 9% in the UK to 15% in France and Germany and from 16% in the United States to 38% in the United States.

Japan. Among men, prevalence was lower, respectively between 1% in the UK and 4% in Japan (bone mineral density was measured at the hip level) and from 3% in Canada to 8% in France, Germany, Italy and Spain (Wade, Strader, Fitzpatrick, Anthony, & O`Malley, 2014).

Osteogenesis and osteolysis according to age

During life, the bones are constantly remodeling, as a result of the balance between osteogenesis and osteosynthesis. During growth, the rate of bone formation is higher than the rate of bone destruction. The bone mass continues to grow until the age of 20-30 years. The peak of bone mass is reached at the age of 20 - 25 years in the case of women, and in the case of men up to the age of 20 (Heaney, et al., 2000), (Gauthier, et al., 2011).

Then the rate of formation (osteogenesis) and destruction (osteolysis) is kept in balance until the age of 40-50 years. After this age, the rate of bone formation decreases, the rate of bone resorption increases excessively, and the bone mass gradually decreases (Li, et al., 2009), (Gauthier, et al., 2011), (Chen, et al., 2014), (Li, et al., 2015), (Li, et al., 2015).

This imbalance leads to a loss of bone mineral density by 1% - 2% or more each year (Gauthier, et al., 2011). Increased remodeling rate is responsible for the rapid changes that occur in osteoporosis, and the imbalance between resorption and bone formation is responsible for long-term effects (Phipps, Mitlak, Burr, & Allen, 2019, p. 393).

Bone mineral density in the spine decreases throughout life (Riggs, Wahner, Dunn, Mazess, Offord, & Melton, 1981), and other authors have found that at least 50% of women's trabecular bone mass is lost before menopause (Riggs, Wahner, Dunn, Mazess, Offord, & Melton, 1981).

Etiopathogenesis of postmenopausal osteoporosis

With increasing life expectancy and aging worldwide, osteoporosis has become a major concern for public health, affecting millions of individuals, especially postmenopausal elderly women (Shen, Chyu, & Wang, 2013), (Jaul & Barron, 2017).

Postmenopausal osteoporosis appears as a consequence of osteoclast resorption in the presence of estrogen deficiency and exaggerated inflammation, being associated with vertebral and hip fractures (Black & Rosen, 2016), (Alejandro & Constantinescu, 2018).

It is worth noting that more and more research has come to the same conclusion, namely that early menopause, prior to its normal onset, is often associated with postmenopausal osteoporosis and its associated complications (Svejme, Ahlborg, Nilsson, & Karlsson, 2012), (Svejme O., Ahlborg, Nilsson, & Karlsson, 2013), (Qiu, et al., 2013).

In the first 10 years after menopause, bone mass suffers significant losses (Riggs, Khosla, & Melton, 2002).

The rate of bone deterioration decreases by 0.3% every year, and in addition, women experience a decrease of about 3% - 7% in bone mineral density after the menopause (Heaney, 2000).

Bone mass loss is more accelerated in menopausal women because the rate of bone remodeling increases in favor of osteolysis, as a consequence of estrogen deficiency. Estrogen causes the lifespan of osteoclasts to increase, and that of osteoblasts to decrease (Ego, 2003), and as estrogen production decreases and calcium absorption decreases in the intestines, as a consequence of reduced calcitonin production, a hormone that inhibits bone demineralization (Lanzillotti, Lanzillotti, Trotte, Dias, Bornand, & Costa, 2003), (Silva, Mendonca, Conceicao, Zahar, & Farias, 2007).

During the intense activity of osteoclasts, the formation of osteoblasts also increases, which indicates that these processes are coupled with each other. RANKL (Receptor activator of nuclear factor kappa-B ligand) was discovered and helped to understand the mechanism by which osteoblasts regulate osteoclast activity (Suda, Takahashi, Udagawa, Jimi, Gillespie, & Martin, 1999), (Hofbauer, Khosla, Dunstan, Lacey, Boyle, & Riggs, 2000), (Arron & Choi, 2000), (Nakashima, et al., 2011), (Phipps, Mitlak, Burr, & Allen, 2019, p. 393).

Osteoprotegerin (OPG) is a receptor with the role of inhibiting bone resorption by diminishing osteoclast activity and function. OPG prevents osteoclast formation, bone attachment, osteoclast activation and function. OPG inhibits RANKL binding to RANK (receptor activator of nuclear factor kappa-B) (Simonet, et al., 1997), (Hsu, et al., 1999), (Ha, et al., 2004), (Wada, Nakashima, Hiroshi, & Penninger, 2006), (Boyce & Xing, 2008), (Clarke & Khosla, 2010), (Hanada, Hanada, Sigl, Schramek, & Penninger, 2011), (Lau & Guo, 2011), (Weitzmann, 2013), (Phipps, Mitlak, Burr, & Allen, 2019, p. 393).

RANK is a receptor located in the membrane of osteoclasts and osteoclast precursors. Studies in animals have shown that a deficiency of OPG (osteoprotegerin) increases the activity of osteoclasts and as a result

osteoporosis occurs. In these studies, the bones of the mice on which the studies were performed were thinner, and the porosity of the cortical and trabecular area increased (Bucay, et al., 1998), (Mizuno, et al., 1998),

The relationship between RANKL and OPG has shown that it plays an important role in bone resorption, an increased level of the first mentioned and a low level of the second favors bone resorption. As long as the ration between RANKL and OPG is within normal limits, bone resorption remains under control (Kostenuik, 2005), (Phipps, Mitlak, Burr, & Allen, 2019, p. 393).

RANKL and OPG not only affect bone mineral density, but also bone geometry and strength (Ross, Bateman, Kostenuik, Ferguson, Lacey, & Dunstan, 2001), (Ichinose, Tanaka, Inoue, Mochizuki, Tsuda, & Seino, 2004).

Hormonal changes (estrogen) and the use of steroid-based drugs have been accused of destroying the balance between RANK / OPG by increasing their ration, favoring osteoporosis and osteoporotic fractures (Khosla, Atkinson, III, & Riggs, 1997).

With these menopause changes, the biochemical markers of bone formation and resorption (measured in either blood or urine) increase substantially. Although bone resorption increases by approximately 90% compared with the premenopausal period, bone formation increases by only 45%, so bone loss is significantly higher than bone formation (Garnero, Sornay-Rendu, Chapuy, & Delmas, 1996).

Along with this superior increase in bone resorption, calcium efflux is associated as a result of this process in the extracellular fluid, an effect that requires physiological compensation to prevent the occurrence of hypercalcemia. Compensatory mechanisms include decreased renal calcium uptake (Gallangher, Young, & Nordin, 1972), reduced intestinal calcium uptake (Gennari, Agnusdei, Nardi, & Civitelli, 1990) and reduced parath-hormone (PTH) secretion (Sundeep Khosla, 2011).

Collectively, these resulting changes lead to an imbalance of calcium balance throughout the body, and as a result demineralization of the skeletal bone appears. These compensatory mechanisms appear as a direct result of decreased estrogen concentration (McKane, et al., 1995).
Apart from these effects in calcium metabolism, a molecular approach to the direct effect of estrogen on bone cells (osteoblasts, osteoclasts, osteocytes) remains an area of interest (Cauley, 2015).

Estrogen suppresses the activity of RANKL. RANKL promotes the differentiation, formation and lifespan of osteoclasts, as a

consequence of binding with RANK. RANKL is on the surface of osteoblasts; RANK is on the surface of osteoclasts (Eghbali-Fatourechi, Khosla, Sanyal, Boyle, Lacey, & Riggs, 2003), (Wright, McCarthy, Middleton, & Marshall, 2009), (Streicher, et al., 2017).

In addition, estrogen increases the activity of osteoprotegerin (OPG), a receptor for RANKL, the role of OPG being to bind to RANKL and prevent its interaction with RANK, the purpose being to limit bone degradation, the RANKL / OPG ratio being the determinant of bone mass and bone resorption (Boyce & Xing, 2008).

As estrogen decreases, RANKL concentration increases and OPG concentration decreases, together with increasing RANKL / OPG ratio and as a result, osteoclastogenesis and osteoclast activity increases, because estrogen regulates osteoclast apoptosis (Nakamura, et al., 2007). Constantinescu, 2018).

Conclusion

There are several drugs that can stop bone degeneration or that can maintain or even increase bone mass and density, reducing the risk of fractures. Not only do the medicines support this condition, but also the lifestyle change, by practicing physical exercises and adopting a balanced diet.

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OSTEOPOROZA POSTMENOPAUZĂ – O RECENZIE EXPLORATIVĂ A LITERATURII

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Abstract

Domeniul „osteoporozei" se schimbă, iar dacă în trecut accentul era mai mult îndreptat spre os, acum câmpul evoluează și se concentrează mai mult asupra riscului de fractură. O astfel de schimbare este necesară, deoarece fracturile fragile sunt comune și pot avea efecte devastatoare asupra calității vieții.

Osteoporoza și masa osoasă scăzută sunt considerate o problemă majoră de sănătate publică. Osteoporoza este o boală cronică complexă, multifactorială, care poate progresa în tăcere timp de zeci de ani, până la apariția fracturilor caracteristice cu întârziere în viață. Deoarece simptomele sunt rare până la apariția unei fracturi, puține persoane sunt diagnosticate la timp pentru a primi o terapie eficientă