Osteoporosis and Environmental Substances

Subjects: Others
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Osteoporosis is a disease having adverse effects on bone health and causing fragility fractures. Osteoporosis affects approximately 200 million people worldwide, and nearly 9 million fractures occur annually. Evidence exists that, in addition to traditional risk factors, certain environmental substances may increase the risk of osteoporosis.

Keywords: Osteoporosis ; Environmental Substances

1. Introduction

The World Health Organization (WHO) defines osteoporosis as a systemic skeletal disease including reduced bone mass and micro architectural degrading of bone tissue, which causes an increase in bone frailty and susceptibility to fractures [1]. Women suffer from osteoporosis more commonly than men. Women start losing bone mass younger, have a fourfold higher rate of osteoporosis and a twofold higher rate of osteopenia at the age of 50 or above, and have fractures 5–10 years younger than men [2]. However, the density and trabecular architecture of bones are equivalent in both genders. The fracture rates in men are lower than in women, mainly because men lose less porous (trabecular) bone compared to women [3]. The risk of fractures can be assessed with a variety of techniques. Two prominent categories exist: clinical assessment of risk factors and physical measurement of skeletal mass. Various different types of bone mineral density (BMD) assessments can be applied. The most common method is dual-energy X-ray absorptiometry (DXA). Quantitative ultrasound (QUS) is regarded as a possible non-invasive alternative using sound waves to examine the velocity, attenuation, or reflection of ultrasound in the bone. Ionizing radiation is not needed, and ultrasound gives information concerning the structural organization of bone in addition to bone mass or density [1].

A total of 200 million people throughout the world are estimated to be affected by osteoporosis and furthermore, more than 8.9 million fractures take place annually. Of the global fractures, one-third takes place in Europe [4][5][6]. The osteoporosis prevalence in the European Union (EU) (based on the 27 countries) was estimated at 27.6 million in 2010 with 22 million being women and 5.6 million men. At the same time period, 3.5 million new fragility fractures occurred [6]. In the EU, the economic burden of osteoporosis and former fragility fractures was approximately €37 billion in 2010. Of this cost, incident fractures accounted for 66%, fracture care for long-term 29%, and pharmacologic prevention 5%. Prior and incident fractures caused 1,180,000 quality-adjusted life years (QALYs) lost in 2010. These costs are predicted to increase by 25% in 2025 [6].

Vulnerability to fractures is heightened by high age, menopause at an early age, a maternal incident of hip fracture, a fracture after the age of 40 years, low body weight levels, or particular diseases and treatments [4]. Ensuring a nutritious diet with sufficient calcium and vitamin D consumption, engaging in steady weight-bearing activities and refraining from under-nutrition, smoking, and heavy drinking are the cornerstones of building and maintaining healthy bone mass [7]. Also, environmental substances such as Cd, Pb, phthalates, and PFASs are expected to have adverse effects on BMD and therefore increase the risk of osteoporosis [8]. In this study, only the substances showing the strongest epidemiological evidence on humans according to the current search are selected, and therefore e.g., heavy metals such as arsenic (As) and mercury (Hg) are excluded.

2. Impact of Environmental Substances on Osteoporosis

There is evidence that among other adverse health effects of environmental substances, the effects on human bones are also occurring. The evidence suggests that exposure to Cd, Pb, phthalates, and PFASs can cause alterations to bone metabolism and can lead to osteoporosis. Also, according to the literature, the substances such as bisphenols, As, Hg, and PAHs are supposed to cause harmful effects on bone health, but the epidemiological evidence is still to be completed. BMD is widely used as an endpoint to investigate the association of chemical exposure and osteoporosis. In many studies an inverse association of chemicals and BMD is discovered [9][10][11][12][13][14][15][16]. Women, especially at perimenopausal and post-menopausal stage, have a greater risk of adverse effects. Reasons are e.g., that total hip and femur neck BMDs are drastically reduced with age and there is an accelerated post-menopausal bone loss when the protective effect of estrogen is lost [1][7][17][12][13][15]. Nevertheless, the relation between chemical exposure and bone metabolism in humans is yet widely understudied, and thorough conclusions of the causality and temporal sequence of the associations are difficult to draw. Some studies show inconsistent and even contradictory results. The level of chemical exposure often varies between the studies, and the study sizes are sometimes too small to draw a generally valid conclusion. In order to come up with accurate conclusions, the threshold values of BMD and standardized diagnostic methods of osteoporosis should be used.

Furthermore, there is a controversy over the starting point for the bone effects and more research is needed to identify the causal relation between e.g., low-level Cd exposure and bone effects. It is hoped that this low-level exposure threshold can be specified in the future with additional data.

The combined effects of exposures to multiple chemicals are scarcely studied, but researchers have observed the interactive effects of Cd and Pb on BMD in a Chinese population living in control and polluted areas [16]. They found that people living in the polluted area had markedly higher Cd and Pb levels compared to those living in the control area, and the BMDs of women from the polluted area were significantly lower than those of women from the control area. In addition, the BMD diminished with growing values of Cd and Pb. The study supports the previous evidence by strengthening the findings that Cd and Pb may adversely influence the bone [18][19], and also demonstrated that these substances may have interactive impacts on BMD. More specifically, the relative excess risks due to interaction (RERIs) of female and male study subjects with both high levels of B-Cd and B-Pb were 0.45 and 1.16, respectively. This points out that the estimated joint effect of B-Cd and B-Pb together on the additive scale is higher compared to the sum of the estimated effects of B-Cd and B-Pb alone. Consequently, the interaction was proven positive on the additive scale [16].

In the majority of the studies investigating the possible role of chemical exposures associated with BMD and osteoporosis, the traditional risk factors of osteoporosis were used as covariates and were included in the statistical models. The authors mostly acknowledged the prevalent role of these factors in osteoporosis incidences and in interpreting the results.

Human biomonitoring (HBM) studies aim to identify and quantify chemicals and their metabolites in human biological matrices. On the grounds of these findings, the rendition of the measurements is conducted to decide whether chemicals' management measures or regulation is integral. Evaluations can be conducted by comparing the measured HBM levels of a selected substance with either a reference value of the general population's background body burden or with the preferred method of an internal benchmark level on the grounds of epidemiological and toxicological data [20]. The determination of reference values of environmental chemicals is somewhat challenging since there are many pathways of exposure (e.g., occupational vs. home) and there are various different stakeholders producing the guidance value information. Some examples of these organizations setting guidance values include German Human Biomonitoring Commission (HBM Commission), European Chemicals Agency (ECHA), WHO, Centers for Disease Control and Prevention (CDC), Scientific Committee on Occupational Exposure Limits (SCOEL) set up by the European Commission and EFSA [21][22][23][24][25].

In the light of safeguarding human health and the environment, the EU has significantly developed and expanded its chemicals legislation after the acceptance of the first chemicals-related directive from the late 1960s. The legislation monitors both the chemical sector and connected industries using chemicals [26].

The regulatory measurements of Pb include the procedures of phasing out of leaded gasoline in most countries; this has successfully reduced the blood Pb concentrations of populations. However, there is still work to be done regarding the phasing out of Pb paint [27]. The Drinking Water Directive (98/83/EC) of the EU has set the health limit value regarding Pb in drinking water as 10 µg/L. Based on the EU directives (2013, 2008, 2000) the Pb concentrations in inland surface waters should be reduced to a limit of 1.2 µg/L, and 1.3 µg/L in outland surface water. The directives (2008) have also determined a regulatory limit value regarding Pb in air as 0.5 $\mu g/m^3$ per calendar year. Regulatory limit value regarding Pb in soil is 50–300 mg/kg. Pb in foodstuff is also regulated by the EU even though there has been no evidence of a threshold value for a variety of crucial outcomes such as developmental neurotoxicity and nephric impacts in adults. The Chemical Agents Directive (98/24/EC) defines regulations for occupational exposure [8].

Even today, despite heavy regulations in place, certain phthalates (i.e., their metabolites) are detected in the urine of nearly every person. Reprotoxic substances, such as the following phthalates: DnBP, DiBP, BBzP, DEHP, DMEP, DnPeP, DiPeP, DHNUP, DnHP, and DCHP are commonly not permitted to be put onto the EU market in substances or mixtures when concentrations limits are identical or surpass 0.3%. The placing on the market of items including DEHP, DnBP, DiBP, and BBzP in a concentration equal to or above 0.1% by weight individually or in any connection in any plasticized material is restricted. DiDP, DiNP, and DnOP are restricted in toys and childcare items that can be put into the mouth having a concentration limit of 0.1%. Many of them are subject or become subject to authorization in 2020, such as DEHP, BBzP, DiBP, DnBP, DMEP, DnPeP, and DiPeP, which means that they are not permitted to be put on the European market without authorizations. However, the consumer products from Asia and U.S. can contain phthalates as the authorization requirements do not apply to the goods which have been imported [8][28].

Of PFASs PFOA and PFOS are the most studied; in the EU and also elsewhere, current regulatory actions mostly involve PFOS and its derivatives. PFOA and PFOA related substances are under revision as global persistent organic pollutants (POPs). PFOS and PFOA as well as the precursory substances are subject to the EU restrictions. Strategic International Approach to International Chemicals Management (SAICM) has determined PFASs as an issue of concern [8][29].

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