Chapter

Analysis of Occurrence of Elements in Tissues of the Knee Joint

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Abstract

The mineral structure of bones is never static, it is a living structure, reacting and adapting to load and having the ability to remodel. Skeletal cells work continuously to maintain the remodelling process therefore they are in a constant state of dynamic balance both in the sense of composition and structure, and they react to external mechanical forces. The remodelling processes that occur in the bone tissue allow for a proper functioning of this tissue, as well as for inclusion of additional elements, toxic ones included, in the remodelled bone, and they affect the metabolic processes occurring therein. This may result in disturbances in the osteoarticular system, manifested by changes in the bone tissue and within other organs. The influence of tobacco smoking on the content of strontium, lead, calcium, phosphorus, sodium and magnesium has not been confirmed. Non-smokers showed a high iron content in knee joint tissues compared to smokers. There were no statistically significant differences in the content of cadmium, nickel, copper and zinc in women and men in the studied knee joint components. With age, an increase in the content of chromium in knee joint tissues was observed, while gender, place of residence and occupational exposure had no effect.

Keywords: knee joint tissues, structural and trace elements, environmental hazards

1. Introduction

Many joints can be distinguished in the human body, but one of them stands out in terms of function and size. It is the knee joint [1]. It belongs to a group of complex joints and connects the femur and the tibia together. This largest joint, apart from the mentioned elements, is formed by the sesamoid bone in the form of the kneecap, and two pieces of meniscus, which allow to match the joint surfaces to each other during movement. The knee joint allows making straightening and flexion movements, but also rotational movements possible only in incomplete joint flexion [2]. The entire structure of the knee joint is strengthened by strong internal and external ligaments. The afore-mentioned joint is the second most strained joint in the human body, after the ankle joint. Due to the powerful force that the quadriceps exerts on the kneecap (max. 300 kg), the knee joint is exposed to overload. Taking into account the functions of the knee joint, it must be both mobile and flexible, as well as resistant to pressure [3, 4].

The mineral structure of bones is never static, it is a living structure, reacting and adapting to load and having the ability to remodel. Skeletal cells work continuously to maintain the remodelling process therefore they are in a constant state of dynamic balance both in the sense of composition and structure, and they react to external mechanical forces. The remodelling processes that occur in the bone tissue allow for a proper functioning of this tissue, as well as for inclusion of additional elements, toxic ones included, in the remodelled bone, and they affect the metabolic processes occurring therein. This may result in disturbances in the osteoarticular system, manifested by changes in the bone tissue and within other organs. Maintaining all the characteristics of the knee joint is possible thanks to the balance of many elements of the bone tissue that are responsible for individual properties of bones, which in turn create separate joints. Elements occurring in large quantities, e.g. calcium, magnesium, phosphorus, and those with low content - the so-called trace elements, e.g. Strontium, can be found in the bone tissue. Regardless of the amount of elements contained in the bone tissue, all of them are important and play significant roles. Mostly, calcium and phosphorus are part of bone hydroxyapatite. However, during the mineralisation process, metal ions present in the blood plasma may be built into the bone tissue, and their uptake will depend on the affinity of a given metal for mineral and extracellular matrix, as well as the concentration of metal ions in the blood plasma, and the degree of skeletal mineralisation. Strontium present in the knee joint is a trace element, although it plays a special role in the bone remodelling process of the human body [5, 6]. It is accumulated mainly in bones due to the high similarity to calcium [7] but unlike it, it is absorbed from food much less efficiently and in a larger percentage it is excreted [8]. Previous in vivo studies demonstrate the effect of strontium on improvement of mechanical characteristics of bones [7]. These studies also proved the effectiveness of treatment with small doses of strontium in the form of strontium chloride. Their conclusion is that 9–26 week Sr. therapy activates bone building and also stops bone resorption in humans [8].

Iron is a cofactor in many enzymes and cells in redox reactions. Low levels of iron ions can be detrimental to cells, while an excess of iron ions can lead to the production of reactive oxygen species through the Fenton reaction. The cellular iron content is strictly regulated by homeostatic mechanisms to maintain the right amount of iron in cells. Nickel ions and other divalent metals can compete with iron ions to enter the cell through DMT1 (divalent metal transporter 1) because they have similar ionic radii. Therefore, metal ions can affect many other processes dependent on the presence of iron in cells. As an enzymatic cofactor, iron is involved in bone matrix synthesis (activation of lysyl hydroxylase) and in 25-hydroxy-cholecalciferol hydroxylase synthesis. What is more, thanks to active vitamin D, iron ions stimulate the absorption of calcium ions in the intestine. Iron deficiencies in rats led to poor mineralisation of skeletons and pathological changes in the micro-architecture of the spongy substance. In turn, administration of estrogens' increases the accumulation of iron in hamsters and facilitates the uptake of iron ions by lymphocytes in culture. The deficiency of iron ions in young rats leads to a decrease in the mechanical strength of femurs and the cortical bone. In severe iron deficiency, both bone strength and mineral density decrease. Excessive iron ion content in mice leads to increased oxidative stress. Oxidative stress mediates in bone loss through changes in bone remodelling. In rats with severe anaemia due to iron deficiency, the concentration of the N-terminal pro-collagen type I was low, which reduced bone formation and mineralisation [9]. These parameters returned to normal values after a diet with a normal iron content. There is no data, given the importance of iron for bone health in humans. Whereas, osteopenia was observed in patients with genetically determined hemochromatosis, and a very high iron content in tissues. Thus, the protective or destructive effects of iron on bones depend on its concentration. Iron deficiency related anaemia is still important for public health. Deficiencies of iron ions in women of childbearing age and in adolescents may also have an effect on bone health at a time when peak bone mass is achieved [9, 10].

Chromium in living organisms occurs as a trace element, yet its presence is extremely important. According to research on osteoblasts, chromium suppresses the level of osteocalcin the too high levels of which may accompany the osteoporosis process. It does not inhibit collagen production [11]. Reduced bone resorption in postmenopausal women has also been observed, and thus the prevention of osteoporosis together with an adequate level of chromium replenishment [12]. Due to its properties, chrome has been used in the production of orthopaedic implants. There are still concerns about local toxicity of chromium contained in prostheses, many studies address this issue [13–15]. Trace elements have a significant effect on the growth, development and condition of bone tissues. Changes in the mineral composition of bone tissues may cause degenerative changes and fractures. According to recent epidemiological data, the incidence of osteoarthritis around the world varies between 2 and 15% of the population. In Poland, this disease affects approximately 7–8 million people; in 40% of cases, degenerative changes are located within the hip joint and in 25% in the knee joint [8]. Trace elements have a significant effect on the growth, development and condition of bone tissues. Changes in the mineral composition of bone tissues may cause degenerative changes and fractures. The deficiency of some trace elements such as zinc, selenium, copper may increase the risk of bone resorption, inhibiting bone growth.

Environmental exposure to lead and cadmium is associated with the risk of a number of chronic diseases related to ageing, cardiovascular diseases, chronic renal failure and osteoporosis. The deficiency of some trace elements such as zinc, selenium, copper may increase the risk of bone resorption, inhibiting bone growth. Among metals that can affect the skeleton, there is no significant distinction between cellular effects and effects caused by the accumulation in the mineral or extracellular matrix. A given metal will undergo significant accumulation in the mineral and cause changes in its properties. Therefore, by studying specific mechanisms of the accumulation of metal ions, more information about bone mineralisation processes can be obtained. From a practical point of view, the influence of metal ions is often studied in relation to applied implants and prostheses.

2. Research goal

The goal of the manuscript was to determine the content of trace elements (Cd, Ni, Fe, Cr, Sr., Cu, Zn, Pb) and structural elements (Ca, P, Mg) in knee joint tissues. A diversified content of elements was determined in particular elements of the knee joint: tibia, femur and meniscus. Differences in the content of selected elements in the studied tissues between particular groups: women and men, smokers and non-smokers, inhabitants of cities and villages, people at risk of exposure and not exposed, patients operated on due to degenerative changes, and depending on age were considered in the research. The next stage of the research was a correlation analysis in the occurrence of elements, taking into account antagonistic and synergistic changes. For this purpose, various statistical methods were used to determine the dependence between the content of elements in bone tissues, e.g. main factors analysis and group similarity analysis.

Tissues that were examined were acquired intraoperatively during knee arthroplasty procedures based on the consent of the Bioethical Commission 2/2013 of 18.06.2013. The studied population consisted of women (n = 36) and men (n = 14) from 41 up to 82 years of age. Those people lived mainly in the areas of southern Poland, with the largest number of people coming from Upper Silesia.

3. Discussion of research results

Bone tissue has the ability to accumulate chemical elements and incorporate them into its structure, which is why it is often used to determine the impact of not only environmental but also occupational exposure.

Some metals such as zinc, iron and copper are closely related to human health because they are essential for maintaining normal physiological functions. However, heavy metal ions that are environmental pollutants show adverse health effects. Cadmium and lead can replace other elements that change the course of a number of biochemical reactions and can act as inhibitors, usually due to formation of complex compounds with sulphhydryl groups of proteins. Exposure to heavy metal compounds can affect genetic material and increase susceptibility to diseases. The World Health Organisation (WHO) classified some heavy metals such as cadmium, lead, mercury and arsenic as pollutants that need to be closely monitored [16]. The accumulation of an adequate amount of harmful heavy metal compounds in the human body changes the hormonal metabolism and narrows blood vessels. Metals are considered a risk factor for fractures and degenerative diseases in osteoporosis [17, 18].

As results from tests for the presence of elements, the average content of strontium in the entire knee joint reaches 17,50 mg/kg. There are no significant differences between Sr. depending on gender. The following strontium content can be distinguished in individual elements of the knee joint: meniscus - 1,44 mg/kg; femur - 24,60 mg/kg; while in tibia - 26,64 mg/kg. It is easy to see that the highest level of strontium in the examined knee joint is in the tibia, the lowest in the meniscus. The effect of smoking on the level of the element determined in the knee joint was also examined. The obtained results confirm a high level of Sr. in smokers compared to non-smokers, however the differences shown are not statistically significant.

Phosphorus present in the knee joint is the main component of all tissues of the human body. It plays a key role in mineralisation of the skeleton [19]. The content of phosphorus in individual bones is different. For example, in the femoral and tibial bones, the level of this element is 24 times higher than in the meniscus. The average content of phosphorus in the knee joint is 36,04 mg/kg. The obtained result is almost twice higher compared to strontium discussed above [20]. The level of phosphorus determined in the knee joint is slightly predominant among men, depending on gender groups. The differences generated in the study did not reach the statistically significant level.

In the case of Pb, Ca, P, Na, Mg content, significant statistical differences occurred in individual elements of the knee joint (Kruskal-Wallis ANOVA test, $p < 0{,}001$). The lead content in the meniscus was 0,32 mg/g, in the tibia 2,67 mg/g, and in the femur 2,64 mg/g. The highest calcium content was in the tibia – 122,57 g/kg, and in the femur – 112,45 g/kg, in the meniscus the content was about 23 times lower and was 5,08 g/kg. The phosphorus content was similar, the highest in the tibia – 55,34 g/kg and in the femur – 50,56 g/kg, and the lowest in the meniscus – 2,21 g/kg. In the case of sodium in the tibial and femoral bones, the content was 5,50 and 5,56, and in the meniscus – 2,11 g/kg. The magnesium content was as follows: tibia 1,55, femur 1,42, and meniscus 0,10 mg/kg. The highest content of Sr., Pb, Ca, P, Na, Mg was in the tibia and the smallest in the meniscus. Statistically significant differences between men and women occurred only in the tibia and related to lead content (U Mann–Whitney U test, $p = 0{,}011$).

The influence of tobacco smoking on the content of strontium, lead, calcium, phosphorus, sodium and magnesium did not cause statistically significant differences. Among those elements, only the content of strontium was greater in people who smoked tobacco. Whereas, the contents of lead, calcium, phosphorus, sodium and magnesium were higher in non-smokers. There were no differences between individual elements of the knee joint and sex and smoking.

Another element that is significant and present in the knee joint is iron. As an enzyme cofactor, it participates in the formation of bone matrix. Iron deficiency in the human body, especially a significant deficiency, leads to a decrease in both density and bone strength. Deficiency, as well as excess of Fe adversely affects the system. Too high value of the element increases oxidative stress [21]. According to research on rats, iron deficiency leads to diseased changes in the spongy substance of discs and weakened skeletal mineralisation. For this reason, the mechanical strength of the femoral bones decreases considerably [22]. The effect of iron content on the health of human bones has not yet been studied. There are works on Fe that suggest that maintaining high levels of iron may help in the prevention of bone fractures in older women [21]. Studies concerning iron content in selected knee joint tissues are slightly different when compared to other elements studied. In the case of iron, its highest content was found in the femur, in which the level is 41,91 μg/g. The second, extreme iron value was determined at 27,04 μg/g in the tibial bone. An intermediate level was determined in the meniscus - i.e. 38,68 μg/g. There were no statistically significant differences between the tibial and the femoral bones in gender groups, but the marked values among women predominated over those marked in the opposite sex. The marked Fe content in the meniscus was different in the group of men. Differences turned out to be statistically insignificant in this case as well. The studies also included iron levels in the knee joint tissues in relation to smokers and non-smokers. In non-smokers, high Fe levels (39,11 μg/g) were determined compared to smokers (25,47 μg/g). The last examined dependence related to the iron level in knee joint tissues was the operation of knee arthroplasty. The study of this correlation shows that Fe levels are lower in patients with a knee prosthesis implanted (32,81 μg/g < 36,96 μg/g).

Chromium is found in living organisms as a trace element. Its presence is extremely important, it inhibits the level of osteocalcin the high level of which accompanies the osteoporosis process, as results from studies on osteoblasts. Reduced bone resorption in postmenopausal women has also been observed, and thus the prevention of osteoporosis together with an adequate level of chromium replenishment [23]. Thanks to its properties, Cr has been used in the production of orthopaedic implants. Nevertheless, there are many concerns about possible local toxicity of prostheses with its content. This problem has been addressed in many manuscripts [13]. As in the case of iron, the highest chromium content in the knee joint occurs in the femur (1,64 μg/g). Slightly lower levels are found in the tibial bone (1,27 μg/g), with the lowest in the meniscus (1,18 μg/g). A slightly higher level of Cr is recorded among men however without statistical significance. An interesting examined dependence is the increase in chromium levels in the knee joint along with age. Among the respondents, its highest level (1,78 μg/g) was recorded in people over 70 years of age. The Cr content of the knee joint in residents of cities is almost twice as high (2,30 μg/g) compared to inhabitants of villages (1,20 μg/g). In smokers, a higher level of some metals in the body can be seen which is due to their presence in tobacco smoke. In the case of chromium, this dependence was not confirmed. Its lower level was examined in people smoking cigarettes (1,00 μg/g) compared to non-smokers (1,47 μg/g). The content of elements in the knee joint tissues in female and male were showed in **Figure 1**.

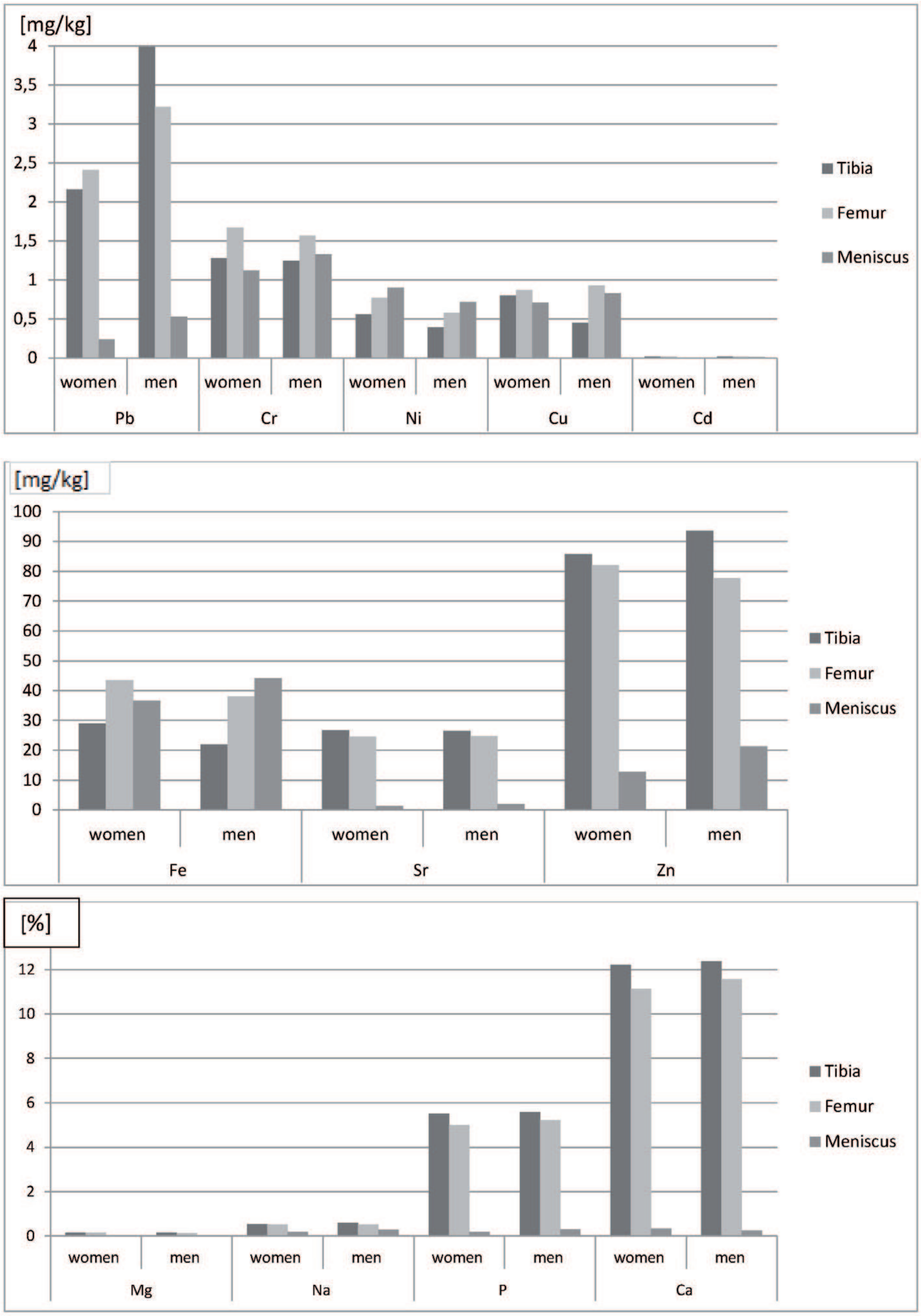

Figure 1.
The content of elements in the knee joint tissues in female and male.

Apart from the elements discussed above, the presence of nickel, cadmium, zinc and copper in the knee joint can be distinguished. Many factors affect their level. These include: the type of tissue being examined, gender, place of residence, nicotinism, age, occupational exposure. The lowest content in knee joint tissues is shown by cadmium. Nickel is characterised by a higher level in women's knee joints (tibia – 0,29 µg/g, femur – 0,36 µg/g, meniscus – 0,69 µg/g) in relation to men (tibia – 0,22 µg/g, femur – 0,28 µg/g, meniscus – 0,42 µg/g). The lowest percentage of copper in the knee joint in women concerns the femur (0,36 µg/g), and in men the tibial bone (0,31 μg/g). In the studied joint, the element that has an advantage over the others is zinc. In smokers, an increased level of cadmium in knee joint tissues is observed due to its content in tobacco smoke. Zinc affects the condition, growth and development of bone tissue. The deficiency of zinc or copper leads to an increased bone resorption and thus inhibits their growth. What is more, zinc is responsible for the activity of vitamin D. Its deficiency leads to osteoporosis.

Keeping the balance in the mineral composition of bone tissue is very important and any deviations from the norm may cause degenerative changes and fractures [24].

4. Conclusions

The results of the presented research results indicate that the bone tissue of the femur and the tibia of the knee joint can be used to determine the content of such elements as lead, cadmium, chromium, zinc, magnesium, potassium and calcium. There was 24 times more phosphorus, 23 times more calcium, 18 times more strontium, 15 times magnesium, 8 times lead, and 3 times sodium in the femur and the tibia compared to the meniscus. However, copper and nickel showed a high content in connective tissue (meniscus) compared to bone tissue (tibia and femur). High values of metals can affect the structure of bone tissue and cause a change in composition and its properties. One of the most common correlations described in the literature on the subject has been confirmed - it is a synergistic correlation between nickel and copper.

The influence of tobacco smoking on the content of strontium, lead, calcium, phosphorus, sodium and magnesium has not been confirmed. Non-smokers showed a high iron content in knee joint tissues compared to smokers. There were no statistically significant differences in the content of cadmium, nickel, copper and zinc in women and men in the studied knee joint components.

With age, an increase in the content of chromium in knee joint tissues was observed, while gender, place of residence and occupational exposure had no effect.

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