BONE FLUORIDE CONTENT IN PATIENTS AFTER HIP AND KNEE JOINT SURGERY

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SUMMARY: The aim of this study was to compare the concentration of fluoride ions (F^-), in bones taken from patients with osteoarthritis following knee and hip joint surgery from different parts of Poland (West Pomerania voivodship – WV and Lubuskie voivodship – LV). The study included patients subject to arthroplasty of the femoral head (n=49) and the knee (n=34). The concentrations of F^- were determined by potentiometry in dried bone and the results were expressed per dry weight (dw). Cortical bone F^- level correlated with age, and in patients <60 years was 455.7 mg/kg dw, about 10% higher than in patients >60 years. The median cortical bone F^- following hip and knee replacement, did not exceed 510 mg/kg dw in the female patients or 450 mg/kg dw in the male patients. Comparisons of bone F^- levels between patients from WV and LV showed statistically significant differences (U=484.5, p<0.001). Despite many studies on the concentration of trace elements (including F^-) in the human body, knowledge of their concentration in bone and their effects on the osteoarticular system is still incomplete. It seems very likely that the concentrations of elements in bone are strongly associated with environmental conditions, diet, geographical range, occupational exposure, and health status of populations. As in Europe there is a lack of comparative data on the concentration of these elements in the bones of the knee and hip against the place of residence and environmental exposure, it is necessary to conduct wider and more numerous studies in this field.

Keywords: Bone; Fluoride; Hip replacement; Knee replacement; Poland.

INTRODUCTION

Trace elements in human bones are increasingly often studied in Europe, including Poland,[1,2] in order to monitor human health and prevent various diseases caused by an imbalance in the content of trace elements in the body.[3] However, few papers focus on the mineral composition of the knee joint in patients with osteoarthritis (OA), despite the high incidence of this disease in Europe. In Poland, OA affects more than 8 million patients, of which 40% suffer from changes in the hip and 25% in the knee.[4]

Due to the long-term nature of bone remodeling processes, bone tissue can be a good model for studying long-term accumulation of trace elements, including fluoride (F^-). In 2008, global production of fluorine amounted to 5840 kt.[5] Fluorine compounds are commonly used in the metallurgical industry, mainly in the production of aluminum, and in the manufacture of glass, ceramics and

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phosphate fertilizers. Until recently, F^- had been added to drinking water; water fluoridation started in 1950 in the United States and then in Europe and other countries in the world. Currently, F^- is mainly used in toothpastes, as protection against dental caries.[6,7]

Although fluorine compounds in drinking water are the main source of this element in the human diet, concentrations of F^- in bottled and tap water are low in the European Union (0.21 mg/l and 0.09 mg/L, respectively).[8] Endemic fluorosis occurs more in dry and hot climates where natural water F^- levels can reach 8 mg/L, for example in some parts of India (reaching 10–20 mg/L of F^- in natural water).[9] F^- ingestion from food in individuals over the age of twelve has remained constant at approximately 0.4 mg/day, while, according to various sources, daily intake ranges from 0.3 to 5 mg/day.[7] The most notable sources include fish, and other marine products such as seafood, and tea.[10]

It is assumed that approximately 93–97% of F^- in the body is accumulated in hard tissues. F^- stimulates the proliferation of osteoblasts, while inhibiting osteoclast activity, which induces an increase in bone mass.[6] Fluorine compounds have been used in the treatment of osteoporosis due to their role in improving the calcium balance. They replace hydroxyl groups by converting hydroxyapatite into less soluble fluorohydroxyapatite, thereby increasing the resistance of bone to resorption processes.[11]

Chronic exposure to F^- has been shown to result in bone fluorosis. Furthermore, F^- excess has also been associated with the possibility of hyperparathyroidism, fertility disorders, and damage to the central nervous system.[12,13] Prolonged exposure to large amounts of fluorine in the inhaled air or diet results in the deposition of F^- in bone tissue, mainly cancellous bone. These changes are seldom found in people living in areas with trace F^- levels in the environment.[11,14] Although bone with F^- accumulation becomes harder and more resistant to compression, the change in the structure of hydroxyapatite may lead to disturbances in the mineralization process.[15] Intake of excessive amounts of F^- and a reduced intake of calcium can lead to impaired mineralization of newly formed osteoid, outbreaks of osteomalacia, and microfractures of trabecular bone.[16] In addition, bone fluorosis is associated with pain in the spine and large joints, as well as leading to restricted mobility.

Little is known about the concentrations of F^- in different bones of patients with OA of the hip and knee. Trace element compositions of cortical and cancellous bone differ due to different tissue remodeling rates and metabolic activity (i.e., cancellous bone is more metabolically active and remodels more quickly than cortical tissue). In our previous studies, concentrations of some heavy metals (Cd, Pb) were significantly depleted in cortical bone relative to cancellous bone.[2] The aim of this study was to compare the concentration of F^- in bones taken from patients with OA following knee and hip joint surgery from different parts of Poland.

MATERIALS AND METHODS

Patients: The patients (n=83) were divided into two groups. The first study group comprised women (n=35) aged from 35 to 85 years (66.9±12.6) and men (n=14) aged from 40 to 81 years (58.6±11.3) who had been hospitalized due to degeneration of the hip or femoral fractures, and following total hip arthroplasty. The second study group comprised women (n=23) aged from 54 to 83 years (67.0±8.0) and men (n=11) aged from 48 to 79 years (64.5±10.3) after knee joint arthroplasty. The study included patients who had been treated with arthroplasty of the femoral head (n=49) and the knee (n=34). These patients were hospitalized at orthopedic clinics in the West Pomerania (WV) and Lubuskie (LV) voivodships in 2013–2014. The analysis excluded patients who had been treated with preparations containing fluorine. All patients were interviewed using a questionnaire to collect data on demographics, health status, and occupational exposure to fluoride. The study was approved by the Bioethics Committee of the Pomeranian Medical University in Szczecin (KB-0012/78/13).

Preparation of material for chemical analysis and determination of fluoride: Cortical and cancellous tissues were obtained from the femoral head, while only cortical bone was taken from the tibial plateau. The samples were obtained from the bones removed during hip replacement and knee replacement. In total, 132 samples were collected, comprising 49 samples of cancellous bone and 83 samples of cortical bone. After removal of the soft tissues, the sampled bones were degreased with acetone, dried to a constant weight at 105ºC so that water content could be determined (gravimetric method), and then crushed in an agate mortar. After preparation of a 10 mg test portion, the sampled bones were dissolved in a perchloric acid solution and shaken. After cooling, sodium citrate and TISAB II were added to the sample. Fluoride concentrations were determined by potentiometric method using an Orion fluoroselective electrode, according to Gutowska et al.[17] The F^- concentrations were expressed in mg/kg dry weight (dw); more detail of the analytical procedures is given by Palczewska et al.[18]

Statistical analysis: The arithmetic means (AM), standard deviations of the AM (SD), medians (Med) and coefficients of variation (CV) were calculated for each studied group. Mann-Whitney nonparametric *U*-test was used for statistical analysis. In determining the correlation between F^- content and age we used a Spearman's rank correlation coefficient (r_S). The results were processed using the statistical program Statistica for Windows ver. 10.0.

RESULTS

Table 1 shows F^- levels in the studied bone samples from the femoral head and tibial plateau of patients following hip replacement and knee replacement, respectively, taking into account the gender of the patients. The highest median F^- level, 501.04 mg/kg dw, was found in the femoral head spongy bone in men while for men and women combined the highest level, 497.44 mg/kg dw, was in the cortical bone of the tibial plateau of patients after total knee replacement.

Cortical bone F^- level correlated with age (r_S=0.48, p<0.01). Cortical bone F^- level in the group HS1 (<60 years) was 455.7 mg/kg dw, about 10% higher than in HS2 (>60 years) (412.93 mg/kg dw). Cancellous bone F^- in the HS1 group was 1.5 times higher than in the HS2 group, 519.46 compared to 350.39 mg/kg dw (U=38; p<0.05)

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Table 1. The fluoride concentration (mg/kg dw) in the bones of the patients after arthroplasty of the femoral head and knee arthroplasty by gender (AM: mean; SD: standard deviation; Med: median; CV: coefficient of variation in percentage; F: female, M: male)

Arthroplasty of the femoral head

Gender	Parameter	Cortical bone	Spongy bone
F (n=35)	AM±SD	485.12±220.07	473.84±235.2
	Med	447.01	435.45
	CV	45.3	49.6
	Range	220.80–1046.3	170.03–1031.8
M (n=14)	AM±SD	404.80±185.77	593.13±319.8
	Med	393.99	501.04
	CV	45.9	45.6
	Range	127.20–774.6	189.5–1093.8
F+M (n=49)	AM±SD	462.17±212.13	510.48±266.41
	Med	428.26	436.82
	CV	45.9	52.2
	Range	127.20–1046.3	170.03–1093.8

Knee arthroplasty

Gender	Parameter	Cortical bone
F (n=23)	AM±SD	600.8±371.19
	Med	508.15
	CV	61.78
	Range	238.4–1815.2
M (n=11)	AM±SD	596.09±300.92
	Med	449.31
	CV	52.88
	Range	229.85–1153.6
F+M (n=34)	AM±SD	590.54±345.72
	Med	497.44
	CV	58.54
	Range	229.85–1815.2

The median cortical bone F^- following hip and knee replacement, did not exceed 510 mg/kg dw in the female patients or 450 mg/kg dw in the male patients (Table 1), and the differences between genders were not statistically significant. F^- in both groups combined ranged from 127.2 to 1815.2 mg/kg dw (Table 1). The Mann-Whitney test showed no statistically significant differences between patients following hip replacement and those following knee replacement, although median F^- levels (in all bone samples) were greater in the cortical bone of patients after total knee replacement, 497.44 mg/kg dw, compared to the median levels after femoral head arthroplasty of 436.82 mg/kg dw in spongy bone and 428.26 mg/kg dw in compact bone

Comparison of bone F^- levels between patients from north-western Poland (West Pomerania voivodship - WV: Szczecin, Police, Barlinek, Nowe Warpno, Trzebież) and western Poland (Lubuskie voivodship - LV: Międzyrzecz, Świebodzin, Skwierzyna) showed statistically significant differences ($U=484.5$, $p<0.001$) (Tables 2 and 3).

Table 2. The fluoride concentration (mg/kg dw) in the bones of the patients after arthroplasty of the femoral head from West Pomeranian voivodeship (WV) and Lubuskie voivodeship (LV) (AM: mean; SD: standard deviation; Med: median; CV: coefficient of variation in percentage; F: female, M: male)

		Arthroplasty of the femoral head			
Gender	Parameter	West Pomerania voivodeship (n=29)		Lubuskie voivodeship (n=20)	
		Cortical bone	Spongy bone	Cortical bone	Spongy bone
F	n	21	21	14	14
	AM±SD	540.93 ±250.07	530.83 ±263.85	414.88 ±133	378.78 ±146.13
	Med	456.91	464.42	401.42.77	370.62
	CV	46.30	49.70	33.23	39.42
	Range	239.44–1046.3	178.91–1031.8	220.79–642.69	170.03–774.9
M	n	8	8	6	6
	AM±SD	461.11 ±223.59	837.27 ±318.59	331.06 ±172.34	425.73 ±190.29
	Med	456.56	765.36	321.67	398.94
	CV	47.86	41.62	22.49	44.69
	Range	127.20–774.6	189.50–1093.8	222.71–412.93	202.75–774.9
F+M	n	29	29	20	20
	AM±SD	520.56 ±241.44	595.53 ±294.08	377.50 ±122.58	396.08 ±157
	Med	456.91	542.13	359.23	387.16.52
	CV	46.38	49.38	22.49	40.68
	Range	127.20–1046.3	178.91–1093.8	220.79–642.69	170.03–774.58

Table 3. The fluoride concentration (mg/kg dw) in the bones of the patients after knee arthroplasty from West Pomeranian voivodeship (WV) and Lubuskie voivodeship (LV) (AM: mean; SD: standard deviation; Med: median; CV: coefficient of variation in percentage; F: female, M: male)

Gender	Parameter	Knee arthroplasty: West Pomerania voivodeship (n=11) Cortical bone	Knee arthroplasty: Lubuskie voivodeship (n=23) Cortical bone
F	n	9	14
	AM±SD	911.13±421.60	420.57±119.40
	Med	893.84	401.30
	CV	46.27	29.75
	Range	323.30–1815.18	238.40–578.40
M	n	2	9
	AM±SD	1099.95±75.89	451.12±162.37
	Med	1099.95	438.34
	CV	75.88	35.99
	Range	1046.29–1153.61	229.85–716.14
F+M	n	11	23
	AM±SD	945.46±385.50	420.79±136.49
	Med	897.83	438.34
	CV	40.77	32.43
	Range	323.30–1815.18	229.85–716.14

The highest mean and median F^- concentration (1099.95 mg/kg dw) was observed in the cortical bone of two men following knee arthroplasty living in the northern part of the West Pomerania. F^- levels in the femoral cortical and cancellous bone from all patients from WV and LV (n=49) ranged from 127.20 to 1046.3 and from 170.03 to 1093.8 mg/kg dw, respectively (Table 2). Median F^- levels in the cortical bones of all patients after knee surgery in the north-western and western Poland were 897.83 and 438.34 mg/kg dw, respectively, and these differences were confirmed statistically ($p<0.05$) (Table 3).

DISCUSSION

Bone F^- levels depend on biological and environmental factors, including age, gender, renal function, duration of residency, remodeling state, genetic susceptibility, geographic location, treatment with fluoride, and exposure to occupational and environmental pollution.[19-21] In the bones of people living in a temperate climate, including Poland, the level of physiological F^- is <550 mg/kg dw, at F^- level in tap water not exceeding 0.9 mg/L and F^- permissible level in drinking water at 1.5 mg/L.[22,23] In the present study, 14 residents of the West Pomeranian province who were subject to water fluoridation in the 1990s, had bone F^- not exceeding 550 mg/kg dw.

Skeletal fluorosis is associated with abnormally high levels of bone F^-. Endemic fluorosis can develop under anthropogenically altered conditions or artificially fluoridated water. Samples of bone from two cryolite workers in a study by Roholm[24] had F^- levels of 2015 to 6420 and 4940 to 8515 mg/kg per dry fat-free weight. Wolff and Kerr[25] found F^- at 1800 to 2900 mg/kg in the long bones and 7000 mg/kg in vertebral samples of persons with chronic fluorosis. These values were eight times higher than the bone F^- in patients from north-western and western parts of Poland who did not have documented fluorosis, with the exception of 5 patients in whom the concentration of F^- exceeded 1000 mg/kg dw.

More recent publications have determined appropriate F^- levels for the head of the femur, iliac crest, and long bones in individuals unexposed to fluoride.[19,26] There is a certain tendency visible, showing the greatest F^- concentrations in the head of the femur and iliac crest (100–643 mg/kg dw) and lower in the long bones (100–300 mg/kg dw). This may be related to the fact that bones such as the human iliac crest have a predominantly cancellous structure.[27]

Diseases such as osteoporosis, osteoarthritis, coxarthrosis, and bone cancers may be accompanied by normal, reduced, or elevated concentrations of trace elements, including F^-. In patients with osteopathies, bone F^- levels may vary significantly (50–9680 mg/kg dw). The lowest reported F^- concentration in cortical bone was in a patient with osteoarthritis (54 mg/kg dw,)[28] i.e., more than 8.5 times less than in the bones of patients following hip surgery from WV in our study. The highest reported F^- levels (up to 9000 mg/kg dw) were in patients with skeletal fluorosis resulting from occupational exposure, including cryolitic workers[27] or with osteoporosis (more than 4000 mg/kg dw).[28] Elevated bone F^- in patients with osteoporosis may be associated with supplementation and the use of certain drugs containing F^-, including steroids, anti-androgens, antibiotics and/or antitumor drugs. A similar regularity was observed by Bohatyrewicz [16] in osteoporotic patients from the West Pomeranian province, who, similar to our research, were not treated with F^- containing drugs, yet cortical bone F^- in menopausal patients was very high at 919.6 mg/ kg dw. Even higher F^- content in cancellous bone was observed by Bohatyrewicz[11] in bone samples from patients following hip replacement carried out in the 1990s, with F^- levels about 74% higher (762 mg/kg dw) than in our research where the median spongy bone femoral head F level, in men and women combined, was 436.82 mg/kg dw (Table 1). In a study conducted by Palczewska-Komsa et al.[29] in patients hospitalized in Szczecin in 2009, cortical bone F^- in the femoral head was lower than in our study (479.4 and 520.6 mg/kg dw, respectively). Much higher F^- levels reported by Bohatyrewicz[11,16] in the West Pomeranian province in the 1990s, may have been associated with the cessation of water fluoridation in Szczecin in 1990 and the modernization of the nearby chemical plant in Police (early 1990s), which restricted the emission of F^- to the environment in this area.

Numerous investigations in humans and experimental animals have been carried out to assess F^- concentrations in hard tissues. This situation is complicated by the fact that F^- levels vary from one part of the skeleton to another. To some extent this is due to structural differences, cancellous bone having higher F^- concentrations than cortical bone.[11,16,22] In this study, a comparison of the concentrations of F^- between cortical and cancellous bone from patients following hip arthroplasty showed no significant differences, with the highest F^- concentration reported in cancellous bone of the femoral head. Differences in F^- levels were also recorded in cortical bone of the femoral head and tibial plateau (median values 428.26 and 497.44 mg/kg dw respectively) and were 16% higher in hard tissues obtained from knee surgery. In humans, cortical bone tissue remodels in the order of decades (25 to 30 years),[30] while estimates of trabecular bone remodeling rates are 2–3 or 2–5 years based on osteon density, which may affect the long term deposition of various trace elements (including F^-) in bone elements.

This study has demonstrated a significant age-related increase in F^- content in the cancellous bone resected from the femur head. Bone resorption apparently accelerates after the 5th decade of life[31] and since F^- levels in older bone are high, the amounts of F^- mobilized from the skeleton increase after the age of about 55. Smith[27] showed that skeletal F^- in humans reaches a plateau at about the 6th decade of life, while Suzuki[32] found that bone F^- in men and women aged 70 reveals a downward trend. Probably this process is associated with decreased bone mineral density (BMD) in the bones of people >70 years of age. In another study by Bohatyrewicz,[16] F^- levels in cortical and cancellous bones of patients with osteoarthritis from Poland did not depend on age.

In our research, F^- levels in cortical bone in two age groups (younger and older than 60 years of age) were similar and did not exceed 460 mg/kg dw, while F^- in cancellous bone of patients above 60 years of age was 1.5 times higher than in those below 60 years of age. This observation agrees with results of some studies indicating that F^- gradually accumulates in bone through life.[19] Similarly, Suzuki[32] recorded the highest F^- levels in the hip in men and women aged over 60 from Japan, which amounted to 520 and 418 mg/kg dw, respectively. Ishiguro et al.[33] found that in cortical bone of ribs in patients from Japan who had cancer surgery the F^- levels increased with age in both sexes. A similar relationship was observed in this research in cortical bone, similar to Hac et al.[34] in northern Poland, and Richards et al.[20] in Denmark.

We found no statistically significant difference in the F^- concentration in the hip and knee cortical bone of men and women following hip or knee replacement, the F^- concentrations ranging from 127.20 to 1815.2 mg/kg dw in both groups. Also Chlubek et al.[35] demonstrated that sex is not a factor which significantly influences the F^- content in skulls. In contrast, Ishiguro et al.[33] found that F^- content increased in males, and increased in females after the age of 55 years, probably not only due to F^- absorption, but also to postmenopausal and senile osteoporosis.

In this study, median F^- levels in the cortical bones of patients following knee surgery in WV and LV differed significantly ($p<0.05$) at 897.83 and 438.34 mg/kg dw, respectively. These geographical differences may result from industrial pollution in the area of Szczecin (WV). The main source of F^- contamination in West Pomeranian was the "Police" chemical plant that produces superphosphates, a potential source of hydrogen fluoride.[17,36] The highest average F^- concentration, about 1100 mg/kg dw, was observed in the cortical bone of two men from the area of Police following knee replacement. Furthermore, the nearby "Dolna Odra" power plant and the "Pomorzany" and "Szczecin" heat and power stations, are also sources of water-soluble fluoride. In contrast, in WV there are no large plants emitting F^- to the environment, which is probably the main reason for the difference between these two populations in fluoride exposure. Similarly, in Toronto, Chachra et al.[19] found F^- levels in the femoral head in patients with osteoarthritis (fluoridated water area: FA) were higher than in Montreal (non-fluoridated area: NFA). Bone F^- levels were ~1100 (FA) and 640 mg/kg (NFA), i.e., about 120% and 28% higher than in the cortical part of tibial plateau of patients with osteoarthritis from WV. Canadian patients from a fluoridated area, and patients from Poland living in range of a superphosphate production plant (WV), had significantly higher bone F^- than those from a non-fluoridated area and from western Poland with no chemical plants. The cortical bone F^- levels found in patients from Lubuskie voivodship (LV) were similar to levels observed in unexposed patients from Kuopio in Finland (not exceeding 460 mg/kg dw).[26]

Despite many studies on the concentration of trace elements (including F^-) in the human body, the knowledge of their concentration in bone and their effects on the osteoarticular system is still incomplete. It seems very likely that the concentrations of elements in bone are strongly associated with environmental conditions, diet, geographical range, occupational exposure, and health status of populations. As in Europe there a lack of comparative data on the concentration of these elements in the bones of the knee and hip against the place of residence and environmental exposure, it is necessary to conduct wider and more numerous studies in this field, including Central Europe.

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