FLUORIDE CONCENTRATION IN SYNOVIAL FLUID, BONE MARROW, AND CARTILAGE IN PATIENTS WITH OSTEOARTHRITIS

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ABSTRACT: The aim of this study was to compare the concentrations of fluoride (F) in cartilage, bone marrow, and synovial fluid taken from patients with osteoarthritis (OA). We also determined the correlation between OA risk factors, including age, sex, obesity, and hypertension, and F concentrations in the studied materials. The cartilage (n=27), bone marrow (n=29), and synovial fluid (n=22) were obtained from 29 patients (21 women and 8 men) with OA during knee replacement surgery. The median concentrations of F observed in studied materials could be arranged in the following descending order: cartilage > bone marrow > synovial fluid. The examination did not show a correlation between OA risk factors and F concentrations in the analyzed materials. Based on literature data and on the results of this study, we noticed that the level of F in the bone marrow and synovial fluid in patients with OA did not exceed 1.5 mg/L and 0.5 mg/L, respectively. The present study reports the first documentation of F concentrations in the synovial fluid and bone marrow of patients with OA.

Keywords: Bone marrow; Cartilage; Fluoride; Osteoarthritis; Synovial fluid.

INTRODUCTION

Osteoarthritis (OA) is the most common human health disorder in an aging population. OA risk factors include age, sex, and obesity, and can cause events resulting in the degradation of joint tissues.[1] OA is considered to be a disease of the whole joint, comprising cartilage, bone, meniscus, and synovium.[2,3] There is evidence that bone marrow lesions (BMLs) also play an important role in the pathogenesis of OA in the knee joint.[4] BMLs are associated with radiological progression of the disease, knee pain, and cartilage loss.[4-6] Recent evidence indicates that in OA, the joint fluid may show significant changes before cartilage degeneration has occurred.[3] Pathophysiological changes occurring in a joint disease state may influence the chemical composition of the synovial fluid.[7,8]

It is assumed that F accumulates mainly in hard tissues,[9] where among the structures forming the knee joint, the highest concentration of F is observed in the cartilage.[10,11] It is suggested that with high concentrations of trace metals in the cartilage some can be released to the synovial fluid.[12] The level of F in body fluids is thought to be a good indicator of exposure to this element and is important for the control and prevention of fluorosis.[13,14] Determination of trace elements in synovial fluid has not been reported frequently in medical literature so far,[7,15,16] and we have found no data on F levels in synovial fluid. However, there are some data concerning influence of F on bone marrow. Machaliński et al.[17,18] indicated that NaF affected human hematopoietic progenitor cells (HPCs) and significantly decreased their

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clonogenic growth. Moreover, exposure to 50 mg/L NaF in drinking water induced significant apoptosis in human HPCs.[19]

The aim of the study was to compare the concentrations of F in cartilage, bone marrow, and synovial fluid taken from patients with OA following knee replacement. We also determined the correlation of age, sex, obesity, and hypertension with the F concentration in the studied materials.

MATERIALS AND METHODS

The cartilage (n=27), bone marrow (n=29), and synovial fluid (n=22) were obtained from 29 patients with OA who had undergone knee replacement surgery at the Department of Orthopaedics, Traumatology and Orthopaedic Oncology, Pomeranian Medical University in Szczecin, Poland. The study group consisted of 21 women (aged 52 to 83 years) and 8 men (aged 42 to 79 years). All patients were interviewed using a questionnaire to collect data on demographics and their health status. The research was approved by the Bioethics Committee of the Pomeranian Medical University in Szczecin (KB-0012/56/14).

The samples of cartilage were degreased with acetone and dried to a constant weight at 105ºC. The cartilage, synovial fluid, and bone marrow were dissolved in a perchloric acid solution and shaken for 60 min at 95ºC using a Thermomix. After cooling, TISAB II and sodium citrate were added. Concentrations of F were determined by potentiometric method using an Orion ion-selective electrode, according to Gutowska et al.[20] The F concentrations were expressed in the cartilage in mg/kg dw, and in the bone marrow and synovial fluid in mg/L.

The arithmetic means (AM), standard deviations of the AM (SD), medians (Med), and coefficients of variation (CV) were calculated for each group. Nonparametric Mann-Whitney U-test was used for statistical analysis. The results were processed using Microsoft Excel 2016 and Statistica StatSoft 10.0.

RESULTS

The median concentrations of F observed in the studied materials from OA patients could be arranged in the following descending order: cartilage > bone marrow > synovial fluid (Table). We found no differences in F concentration in the analysed materials according to patient sex. However, we found statistically significant differences in the concentration of F between the studied materials ($F_{SF}F_{BM}$: U=482, p=0.002; $F_{SF}F_{C}$: U=594, p<0.001; $F_{BM}F_{C}$: U=783, p<0.001) (SF=synovial fluid, BM=bone marrow, C=cartilage).

Cartilage F level in the younger group of patients (≤65 years of age, n=10) was 447.45 mg/kg dw, about 7% lower than in the group of patients >65 years of age (n=17) (480.41 mg/kg dw). Bone marrow F in the younger group was 39% higher than in the older group of patients, 1.27 mg/L compared to 0.91 mg/L. F concentrations in the synovial fluid in patients ≤65 years of age and >65 years of age were similar (0.44 mg/L and 0.41 mg/L, respectively). We found no significant differences in F concentration in the cartilage, bone marrow, and synovial fluid between patients ≤65 years of age and >65 years of age (Figure 1).

Table. Fluoride concentrations in the synovial fluid, bone marrow, and cartilage of osteoarthritis patients. (AM: mean, SD: standard deviation, Med: median, CV: coefficient of variation)

Sex	Parameter	Fluoride concentration		
		Synovial fluid (mg/L)	Bone marrow (mg/L)	Cartilage (mg/kg dw)
Female	n	16	21	20
	AM±SD	0.44±0.27	1.19±1.06	499.49±328.43
	Median	0.40	0.92	469.84
	CV	61.31	89.05	65.75
	Range	0.12–1.22	0.17–4.02	67.16–1433.72
Male	n	6	8	7
	AM±SD	0.38±0.16	0.67±0.46	376.06±207.55
	Median	0.37	0.52	365.49
	CV	40.93	69.03	55.19
	Range	0.20–0.67	0.03–1.64	69.77–653.05
Female+Male	n	22	29	27
	AM±SD	0.42±0.25	1.05±0.96	469.86±309.06
	Median	0.39	0.82	450.18
	CV	57.82	92.00	65.78
	Range	0.12–1.22	0.03–4.02	67.16–1433.72

Overweight patients had a higher concentration of F in the cartilage (519.22 mg/kg dw) than patients with normal weight (450.66 mg/kg dw). However, patients with normal body mass index (BMI) had 2 times higher bone marrow F (1.20 mg/L) than overweight patients (0.58 mg/L). F levels in the synovial fluid in overweight patients and patients with correct BMI were similar (0.45 mg/L and 0.42 mg/L, respectively). We found no influence of BMI on F concentration in the cartilage, bone marrow, and synovial fluid (Figure2).

Cartilage F level in the patients with hypertension (HT) was about 35% higher than in healthy patients (non-HT) (495.47 mg/kg dw and 367.44 mg/kg dw, respectively). However, higher bone marrow F was found in the non-HT group (1.27 mg/L) than in the HT group (0.96 mg/L). F concentrations in the synovial fluid in HT and non-HT patients were similar (0.43 mg/L and 0.41 mg/L, respectively). We found no

significant differences in F concentration in the cartilage, bone marrow, and synovial fluid between HT and non-HT groups of patients (Figure 3).

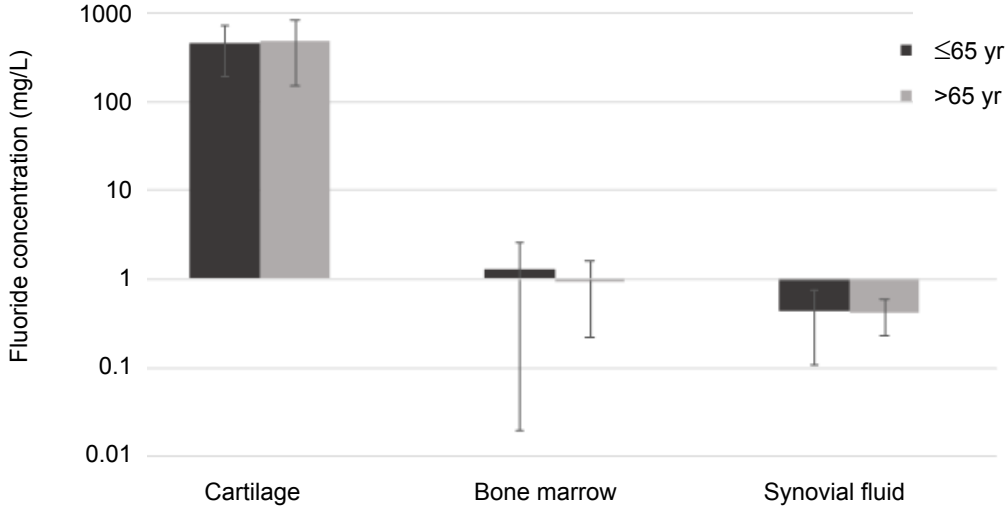

Figure 1. Concentration of fluoride ions in the cartilage (mg/kg dw), bone marrow (mg/L), and synovial fluid (mg/L) in patients ≤65 years of age and >65 years of age (logarithmic scale).

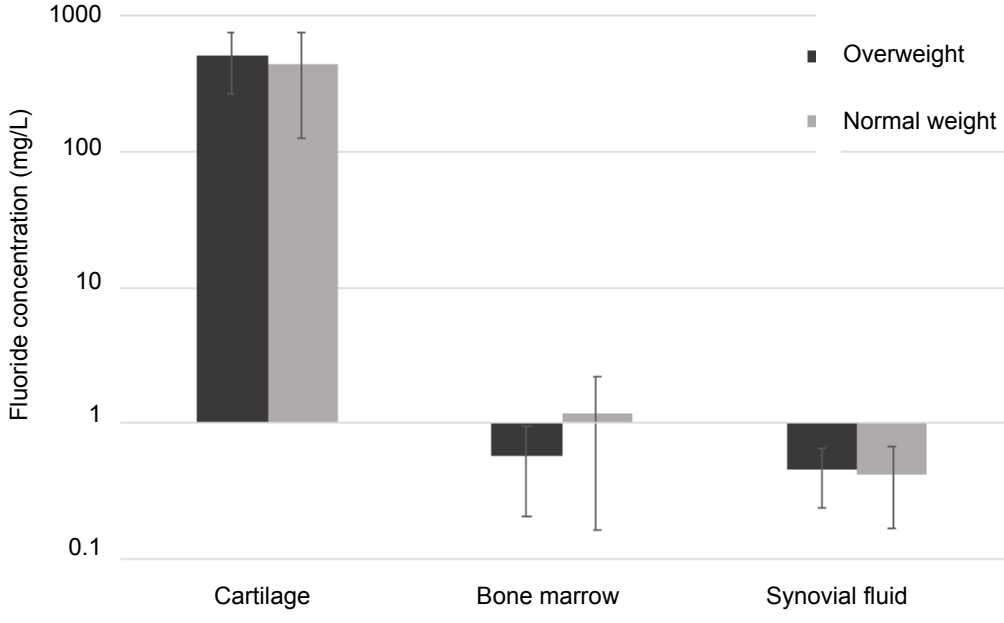

Figure 2. Concentration of fluoride ions in the cartilage (mg/kg dw), bone marrow (mg/L), and synovial fluid (mg/L) in overweight patients and in patients with normal weight (logarithmic scale).

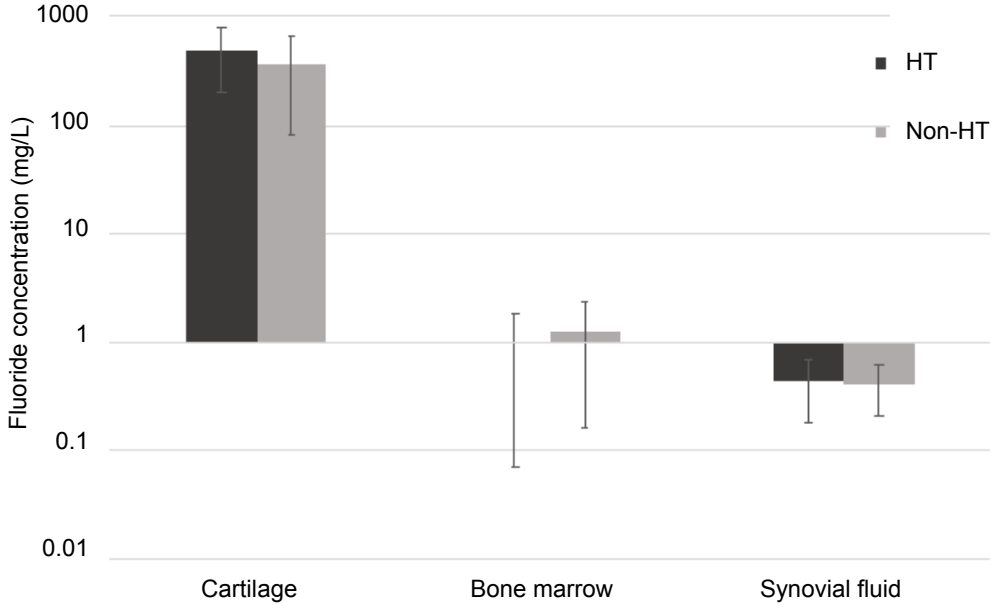

Figure 3. Concentration of fluoride ions in the cartilage (mg/kg dw), bone marrow (mg/L), and synovial fluid (mg/L) in patients with hypertension (HT) and in healthy patients (non-HT) (logarithmic scale).

DISCUSSION

Scientific literature data indicate that the joint fluid of patients with rheumatoid arthritis has increased concentrations of Cu, Fe, and Al,[7] and in patients with OA the levels of Cu and Fe in the synovial fluid are higher than in healthy patients.[21] These elements, due to their high reactivity, may promote reactive oxygen species (ROS) generation, and so their concentration in the joint fluid may increase ROS levels in that tissue. ROS activate the intracellular signaling, leading to the initiation and progression of inflammation.[22] Therefore, physiochemical analysis of joint effusions may turn out to be a potential diagnostic tool.[8,16]

Although F has been used in the treatment of osteoporosis[23,24] it is not regarded as being an essential element for human growth and development, including that of bone.[25] In osteoporotic patients treated with F (~1.1 mg/kg/day) periarticular pain and swelling were observed and have been ascribed to synovitis.[26,27] In our study, the mean concentration of F in the synovial fluid did not exceed 0.5 mg/L.

The present study did not show the influence of sex, age, BMI, or hypertension on the F concentration in the analysed materials. However, we noticed significant differences in concentrations of F between the studied materials. The highest concentration was found in the cartilage, which confirms the well-known fact that most F ions in the body accumulate in hard tissues.[24] Abnormalities in the structure of this tissue appear when cartilage F level is above 500 mg/kg dw.[28] In our study, 9 patients had cartilage F concentration higher than 500 mg/kg dw. Interestingly, both

the highest and lowest F concentrations in the synovial fluid, as well as in bone marrow, were in patients whose cartilage F concentrations were <500 mg/kg dw.

Taking into consideration the F levels in the synovial fluid and bone marrow, a higher concentration was found in the bone marrow. The most likely reason is that F stimulates the proliferation of osteoblasts, which are formed from precursor cells found in the bone marrow.[24,29] In experimental studies on mice injected intraperitoneally with different doses of NaF, a significant chromosomal aberration in mouse bone marrow cells was noticed in the higher treatment groups (5, 7.5, 15, and 30 mg NaF/kg bw) but not at 2.5 mg NaF/kg bw. Moreover, a significant level of ROS was observed in mouse bone marrow cells treated with NaF.[30] In our study, mean bone marrow F concentrations in the studied patients was ~1.0 mg/L, which we suggest has no negative influence of bone marrow cells, but a morphological analysis of bone marrow is necessary to confirm our suggestion.

CONCLUSION

The present study reports the first documentation of F concentrations in the synovial fluid and bone marrow of patients with OA. Due to the lack of publications on this topic and lack of physiological recognized values of F concentrations in the analyzed materials of patients without evidence of degenerative joint disease, more research on this topic is necessary.

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