FLUORIDE ION CONCENTRATIONS IN CARTILAGE, SPONGY BONE, ANTERIOR CRUCIATE LIGAMENT, MENISCUS, AND INFRAPATELLAR FAT PAD OF PATIENTS UNDERGOING PRIMARY KNEE JOINT ARTHROPLASTY

Karolina Kot,[a] Żaneta Ciosek,[a] Natalia Łanocha-Arendarczyk,[a] Danuta Kosik-Bogacka,[a] Paweł Ziętek,[b] Maciej Karaczun,[b] Irena Baranowska-Bosiacka,[c] Izabela Gutowska,[d] Elżbieta Kalisińska,[a] Dariusz Chlubek[c]

Szczecin, Poland

ABSTRACT: Despite substantial literature on the concentrations of trace elements in the human body, including the fluoride ion (F^-), their levels and effects in some parts of the osteoarticular system still remain unknown. This applies to F^- concentrations in the joint forming structures. Therefore, the aim of this study was to compare the concentrations of F^- in the spongy bone, cartilage, meniscus, anterior cruciate ligament, and infrapatellar fat pad taken from patients with osteoarthritis following primary knee surgery. The study group comprised 20 patients from north-western Poland undergoing primary knee joint arthroplasty: 15 women aged from 60 to 84 yr and 5 men aged from 57 to 82 yr. The concentrations of F^- were determined by potentiometry in dried samples and the results were expressed per dry weight (dw). The levels of F^- in examined structures ranged from 19.82 to 2223.15 mg/kg dw and the medians had the following descending order: spongy bone > cartilage > meniscus > infrapatellar fat pad > anterior cruciate ligament. Based on the results of the present study, we are of the opinion that the physiological level of F^- in connective tissue elements in patients undergoing knee arthroplasty does not exceed 200 mg/kg dw.

Keywords: Anterior cruciate ligament; Cartilage; Fluoride; Infrapatellar fat pad; Knee arthroplasty; Meniscus; Spongy bone.

INTRODUCTION

The fluoride ion (F^-) plays a significant biological role in the human body, participating in the binding of magnesium, calcium, and phosphorus, and in hard tissue mineralization.[1,2] Fluorine compounds have been used in the treatment of osteoporosis and fewer vertebral body fractures were observed following therapies of small F^- doses.[3,4] However, as early as the middle of the 20th century F^- poisonings were observed to cause bone fractures and pathological bone formation.[5] In a study conducted in populations exposed to elevated levels of F^- (drinking water concentrations higher than 3 mg/L), it was established that F^- acts as a neurotoxic agent.[6] Fluorosis is the result of chronic exposure to high levels of F^-, mostly in drinking water, dust, fumes, tea, toothpastes, drugs, and supplements.[7] Endemic fluorosis has been reported in most regions of Africa and Asia, where populations are exposed to high levels of F^- in drinking water.[8] As water fluoridation was stopped in Poland in the 1980s, and the European Union does not permit enrichment of drinking water with F^-, the main sources of F^- for

[a]Department of Biology and Medical Parasitology; [b]Department of Orthopaedics, Traumatology and Orthopaedic Oncology; [c]Department of Biochemistry and Medical Chemistry; [d]Department of Biochemistry and Human Nutrition, Pomeranian Medical University, Szczecin, Poland. For correspondence: Professor D Chlubek, Department of Biochemistry and Medical Chemistry, Pomeranian Medical University, Szczecin, Poland; E-mail: dchlubek@pum.edu.pl

the inhabitants of Central and Eastern Europe are diet and F^- pollution of anthropogenic origin.[9,10]

F^- balance depends on quantitative features of absorption and excretion. Approximately half of the absorbed fluoride is retained by uptake in calcified tissues, and the remaining half is excreted in urine.[11,12]

The highest F^- concentration is found in strongly mineralized tissues, such as teeth and bones.[11,13] Current knowledge shows a difference in the accumulation of F^- between spongy and cortical bone taken from patients following knee and hip joint surgery.[13] Cortical tissue has a lower resistance to the adverse influence of F^- than spongy bone, and in its inner part the concentration of F^- is lower than in the bone surface.[14,15,16] Importantly, there is little data on the levels of F^- in cartilage, meniscus, anterior cruciate ligament, infrapatellar fat pad, and ligament of head of femur. These structures of the knee joint are usually tested for calcium, magnesium, zinc, and iron concentrations.[17,18] In this study we wanted to fill this gap, in line with the suggestion of Kumai et al.[19] that information on age-related or site-related changes in the trace element content of tendons and ligaments could be a useful tool for supplementing, interpreting, and evaluating morphological and biochemical changes in the tissues and alterations in their mechanical properties.

The aim of this study was to compare the concentration of F^- in the cartilage, spongy bone, anterior cruciate ligament, meniscus, and infrapatellar fat pad taken from patients with osteoarthritis following primary knee surgery.

MATERIAL AND METHODS

Patients: The study was performed on the structures of the knee joint from patients (n=20) who had been hospitalized at the Department of Orthopaedics, Traumatology and Orthopaedic Oncology, at the Pomeranian Medical University in Szczecin in 2014. The study group comprised 15 women aged 60 to 84 yr (70±10.3), and 5 men aged 57 to 82 yr (66.3±11.6), undergoing primary knee joint arthroplasty. The use of this tissue in the research was approved by the Bioethics Committee of the Pomeranian Medical University in Szczecin (KB-0012/56/14).

Preparation of material for analysis and determination of the fluoride ion concentrations: In total, 100 samples were collected, comprising 20 samples of spongy bone, cartilage, meniscus, anterior cruciate ligament, and infrapatellar fat pad. After removal of the soft tissues, the sampled spongy bone and cartilage were degreased with acetone and dried to a constant weight at 105ºC. After preparation of a 10 mg test portion, the sampled material was dissolved in a perchloric acid solution and shaken. After cooling, sodium citrate and TISAB II were added to the sample. F^- concentrations were determined by potentiometric method using a fluoroselective electrode (Orion, USA), and expressed in mg/kg dry weight (dw); more details of the analytical procedures are given by Łanocha-Arendarczyk et al.[13]

Statistical analysis: The arithmetic means (AM), standard deviations of AM (SD), medians (Med), and coefficients of variation (CV) were calculated for each studied group. The median was chosen to compare the results because it is not sensitive to outliers. Mann-Whitney non-parametric *U*-test was used for statistical analysis. The results were processed using the statistical program Statistica for Windows, version. 10.0.

RESULTS

The median concentrations of F^- found in the studied materials from the patients after knee arthroplasty had the following descending order: spongy bone > cartilage > meniscus > infrapatellar fat pad > anterior cruciate ligament, and ranged from ~62 mg/kg dw in the infrapatellar fat pad to ~421 mg/kg dw in the spongy bone (Table).

Table. Fluoride concentrations in the joint forming structures (mg/kg dw) of the patients after knee arthroplasty (AM: mean, SD: standard deviation, Med: median, CV: coefficient of variation)

Gender	Parameter	Spongy bone	Cartilage	Anterior cruciate ligament	Meniscus	Infrapatellar fat pad
Female (n=15)	AM±SD	514.84 ±341.28	661.96 ±549.36	71.90 ±68.75	338.55 ±586.47	203.30 ±375.43
	Med	458.99	457.91	60.28	72.81	66.98
	CV	66.29	83.99	95.62	173.23	184.65
	range	64.60–1105.46	34.61–1770.78	23.53–310.00	30.70–2223.15	31.48–1222.28
Male (n=5)	AM±SD	225.37 ±187.13	278.58 ±184.08	125.99 ±197.71	344.27 ±595.48	74.52 ±55.83
	Med	198.10	275.45	48.20	75.88	43.74
	CV	83.03	66.08	156.93	172.97	74.92
	range	53.86–513.16	46.12–554.51	19.82–478.60	31.98–1404.84	23.80–155.50
Female + male (n=20)	AM±SD	442.47 ±331.26	566.12 ±508.45	85.42 ±110.86	339.98 ±572.79	171.10 ±328.31
	Med	421.36	354.46	56.20	74.20	62.14
	CV	74.87	89.81	129.79	168.48	191.88
	range	53.86–1105.46	34.61–1770.78	19.82–478.60	30.70–2223.15	23.80–1222.28

The median F^- in the meniscus, the anterior cruciate ligament, and the infrapatellar fat pad did not exceed 75 mg/kg dw. In two of the patients, high levels of F^- were observed (>1000 mg/kg dw) in the spongy bone; in one of those patients F^- levels were 1021.26 mg/kg dw in the infrapatellar fat pad and 2223.15 mg/kg dw in the meniscus (Table).

The highest median F^- concentration was observed in the cartilage of women being 1.67 times higher than in men. An even greater difference in F^- concentration was noticed in the spongy bone which was 2.31 times higher in women than in men, but the difference was not statistically significant. The concentration of F^- in the anterior cruciate ligament ranged from 19.82 to 478.60 mg/kg dw, and again was 1.25 times higher in women than in men. In the meniscus, the F^- concentration was similar in both women and men, and did not exceed 76 mg/kg dw. The median F^- in the infrapatellar fat pad did not exceed 67 mg/kg dw in the female patients or 44 mg/kg dw in the male patients, and the difference between the genders was not statistically significant (Table).

DISCUSSION

F^- may cause toxicity, with a negative impact on cellular structure and many enzymes, and its levels depend on the daily dose, exposure time, and biological factors such as age, gender, metabolic changes, and the concomitant diseases of bones and kidneys.[20] It has been reported that the physiological F^- concentration in bones of people living in Poland is <550 mg/kg dw.[13] Toxic concentrations of F^- in bones, i.e., above 1000 mg/kg dw, may weaken these tissues and increase their susceptibility to fractures.[21]

In the spongy bone, F^- causes an increase in bone volume and thickness without a concomitant increase in connectivity, which reduces bone quality.[22] In the present study, F^- concentrations in the spongy bone of the knee joint were in the range of the physiological F^- level, but in patients with osteopathy bone F^- levels varied significantly (50–9680 mg/kg dw). In our previous study, the F^- concentrations in spongy bone of the femoral head removed during arthroplasty in the West Pomerania and Lubuskie voivodeships were 542.13 mg/kg dw and 387.16 mg/kg dw, respectively.[13] Higher F^- levels in the spongy bone were observed by Bohatyrewicz in bone samples of patients from Szczecin undergoing hip replacement than in our research, 762 mg/kg dw vs. 421.36 mg/kg dw, respectively.[14] It may have been associated with the cessation of water fluoridation in Szczecin in the 1980s and modernization of the nearby chemical plant in Police.[13]

Skeletal fluorosis is caused by abnormally high levels of bone F^-. Wolff and Kerr found F^- concentrations of 1800–2900 mg/kg in the long bones of persons with chronic fluorosis.[23] In the present study, two patients from north-western Poland had F^- concentrations above 1000 mg/kg dw in the spongy bone. One of these patients also had F^- concentrations above 1000 mg/kg dw in the meniscus and infrapatellar fat pad. These values may be associated with supplementation and the use of certain drugs containing F^-, including steroids, anti-androgens, antibiotics, and/or antitumor drugs.

F^- takes part in mineralization of the cartilage, thus increasing its mass.[1,2] Abnormalities in the cartilage structure can appear when the F^- concentration in this tissue is above 500 mg/kg dw.[24] In our study, seven patients from north-western Poland had cartilage F^- concentrations higher than 500 mg/kg dw. This can be suggested as the reason of cartilage degeneration and the qualifying factor for the knee joint alloplasty. In addition, most of the patients had osteoarthritis, which is accompanied by cartilage calcification, increasing its affinity to F^-.[25]

The ligaments, meniscus, and infrapatellar fat pad are rarely analyzed in research about the concentration of trace elements in the human body, and therefore their optimum values are not known; if used, they are not representative for healthy individuals. In the current scientific literature, we found no data on F^- concentration in the connective elements of the knee joint.

The anterior cruciate ligament is one of the most important ligaments of the knee joint because of its function, structure and localization. The abnormal structure of the ligament can predispose it to degenerative changes in the knee joint. F^- is responsible for binding calcium and phosphorus, which accumulate in the ligaments with age,[18] and this process can cause changes in the ligament structure. In the present study, the median F^- concentration in the anterior cruciate ligament was the lowest, at 56.20 mg/kg dw. In addition, F^- concentration in this ligament was not higher than 500 mg/kg dw.

The meniscus is directly connected with the anterior cruciate ligament, jointly participating in the amortization phase. In the present study, the median F^- concentration in the meniscus was 74.20 mg/kg dw. Apparently, F^- has a higher affinity to a more gelatinous tissue, as in the present study a higher F^- concentration was observed in the meniscus than in the anterior cruciate ligament.

The infrapatellar fat pad is a fatty element in the knee joint. It plays a role in preventing injuries and in the biomechanics of the knee joint. In the present study, the median concentration of F^- in this structure of the knee joint was 62.14 mg/kg dw. Two women had F^- concentration above 1000 mg/kg dw. One of these patients also had high levels of F^- in two other parts of the knee joint, while in the second patient the F^- levels in the other parts of knee joint were below 550 mg/kg dw.

We observed a difference in the F^- concentration between men and women in spongy bone and cartilage, but it was not statistically significant. Łanocha-Arendarczyk et al. also found no difference between men and women in the knee spongy bone.[13] In contrast, Palczewska-Komsa et al. noted a significant difference in bone F^- concentration between men and women >65 years of age.[26] Also, Ishiguro et al. found increased bone content of F^- in males and females over the age of 55 years.[27]

Due to the lack of publications on F^- concentrations in the joint forming structures, more research on this topic is necessary.

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