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Elevated serum fluoride levels in perimenopausal women are related to the components of metabolic syndrome

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Abstract. – OBJECTIVE: Increased fluoride levels can lead to numerous complications, including skeletal effects, cardiotoxicity, endocrine dysfunction, neurotoxicity, hepatotoxicity and nephrotoxicity. The aim of this study was to analyze the relationship between serum fluoride levels and MetS or its individual components, and to assess the diagnostic usefulness of fluoride as a factor contributing to MetS.

PATIENTS AND METHODS: The study included a group of 475 women (mean age of 52.9 years), living in the West Pomeranian Voivodeship in Poland. The study involved data collection and biochemical analysis.

RESULTS: Analysis of the relationship between the levels of fluoride and the presence of MetS or its components showed that the mean fluoride level was statistically significantly higher in patients with hypertriglyceridemia (dCohen = 0.39; 95% CI; confidence limits: 0.13, 0.63) and hypertension (dCohen = 0.25; 95% CI; confidence limits: 0.07, 0.44). Moreover, the mean fluoride level was significantly higher in women who met the diagnostic criteria for MetS than in the remaining subjects (dCohen = 0.40; 95% CI; confidence limits: 0.17, 0.64).

CONCLUSIONS: Elevated serum fluoride levels may be associated with an increased incidence of MetS among perimenopasal women, although its diagnostic value as a marker of MetS is limited.

Key Words:
Fluoride, Metabolic syndrome, Perimenopausal women.

Introduction

Metabolic syndrome (MetS) is defined as a cluster of symptoms whose coexistence significantly contributes to cardiovascular disease, type 2 diabetes, stroke, and other conditions, thus increasing the risk of premature death[1]. The definition of MetS has evolved over time into its current form, adopted in 2009. The components of this disorder include: reduced high-density lipoprotein cholesterol, and increased waist circumference, triglycerides (TG), blood pressure and fasting plasma glucose. The presence of three out of the five above-mentioned criteria qualifies for the diagnosis of MetS. Attempts are still made to define the causes of this disorder, the most important of which are lifestyle, genetic factors, insulin resistance, chronic inflammation, the disturbed circadian rhythm, and sleep disorders[2]. A high incidence of metabolic disorders in the general population, and the risk they pose, make MetS a serious public health problem[3]. Women in the perimenopausal period are especially likely to develop MetS components due to changes that then occur in their bodies. They include the changed distribution of adipose tissue, a potential increase in insulin resistance, changes in serum lipid levels, and a higher incidence of arterial hypertension[4].

The likelihood of developing metabolic disorders in perimenopausal women may be enhanced by many factors, of which nutritional factors (balanced diet, exposure to xenobiotics) appear to be of key importance. Xenobiotics include fluorides characterized by a very narrow safety range between the optimal dose (beneficial in the prevention of dental caries) and the chronic poisoning with this element, regarded as a cumulative toxin[5]. Excessive fluoride levels can lead to numerous complications, including skeletal effects, cardiotoxicity, and endocrine dysfunction[6], as well as neurotoxicity, hepatotoxicity and nephrotoxicity[7].

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Fluorides are commonly found in a wide range of concentrations in the natural environment – in soil, water, air, rocks, plants and animals[8]. They are absorbed by the human body to the greatest extent along with water, oral hygiene products, chemicals and pharmaceuticals, as well as through smoking and exposure to industrial emissions. Among all food products, tea is considered to be one of the main contributors to an increase in the daily intake of fluorides[7]. So far, neither the key role of fluoride for the human body, nor the symptoms of its deficiency in humans have been observed. Fluorides are used in prevention of dental caries. Therefore, in some countries they are added to water and food products, although there is evidence that using them locally in the form of toothpaste is a more effective method of protecting teeth[5].

It is essential for public health to understand the impact of relatively low levels of fluoride (mainly from food and oral care products) on bodily function and the reasons behind the sharp increase in the incidence of metabolic disorders in humans. Hence, the aim of this study was to analyze the relationship between serum fluoride levels and MetS or its individual components, and to assess the diagnostic usefulness of fluoride as a factor contributing to MetS.

Patients and Methods

The study included a group of 475 perimenopausal women, living in the West Pomeranian Voivodeship in Poland. They were recruited through the dissemination of information in the local community. Information posters with an invitation to participate in the study were put up in public places, such as schools, offices, health care clinics and others, and published in the local press. People with neoplastic, infectious and psychiatric diseases were excluded from the study.

Ethics Statement

The investigation was conducted in compliance with ethical standards, the Declaration of Helsinki, and national and international guidelines. The protocol of the study was approved by the Bioethical Commission of the Pomeranian Medical University of Szczecin, Poland (permission number KB-0012/181/13). The participants' informed consent has been obtained.

Description of the Research Procedure

The research procedure consisted of three stages. The first of them involved a structured interview conducted to collect basic information on age and pharmacotherapy for hypertriglyceridemia, a low level of high-density lipoprotein (HDL), hyperglycemia, hypertension, as well as neoplastic, psychiatric, and inflammatory diseases. Then, the blood pressure was measured in a sitting position, using a hand-held manometer in accordance with the principles of correct measurement. Waist circumference was measured using a sewing tailor's ruler in a standing position between the lower rib margin and the upper margin of the iliac crest at the end of a gentle exhalation. Furthermore, the analysis of the body composition was carried out using the MC780 MA P analyzer by the bioelectrical impedance method, which provides reliable data on body weight and its individual components. The last part of the study was venous blood collection. This procedure was performed according to the binding principles, on an empty stomach between 7.00 and 9.30 a.m., using Vacutainer tubes (Sarstedt, Germany). The blood was collected into tube for biochemical serum analysis (7 mL). In this material, fasting glycemia, the levels of triglycerides, HDL cholesterol, and fluorides were determined.

After collecting the necessary data, the study sample was divided into two groups: the first group included women who met the diagnostic criteria for metabolic syndrome (MetS+), and the second group included those who did not meet these criteria (MetS-). The study adopted the MetS diagnostic criteria based on the 2009 International Diabetes Federation (IDF) guidelines: 1. waist circumference $\geq$ 80 cm; 2. fasting blood glucose $\geq$ 100 mg/dl or treatment for diabetes; 3. hypertriglyceridemia $\geq$ 150 mg/dl or related pharmacotherapy; 4. low HDL cholesterol $\leq$ 50 mg/dl or related pharmacotherapy; 5. elevated blood pressure: systolic blood pressure $\geq$ 85 mmHg and/or diastolic blood pressure $\geq$ 130 mmHg or pharmacotherapy for hypertension.

Potentiometric Analysis of Serum Fluoride Levels

The patients' serum (n = 475) was checked for the content of fluoride ions. The determinations were made by potentiometric analysis using a fluoride ion-selective electrode (9609BNWP, Thermo Fisher Scientific, Germany). To measure fluoride levels, 0.5 mL of 5% TISAB III buffer solution was added to 0.5 mL of the serum por-

Table I. Characteristics of the study sample.

Parameter	M	SD	Min	Maks	CV [%]
F- [mg/L]	0.087	0.112	0.005	0.908	130.01
Age [years]	52.86	5.38	37.00	68.00	10.17
Weight [kg]	72.00	14.21	42.50	160.30	19.74
Body Mass Index [kg/m^2]	26.56	4.84	17.50	51.70	18.21
Body Fat Mass [kg]	24.28	8.94	8.50	80.80	36.81
Percent of Body Fat [%]	32.76	5.90	16.50	50.40	18.00
Visceral adipose tissue	7.07	2.44	3.00	19.00	34.49
Components of MetS					
Fasting glucose [mg/dl]	85.55	17.18	97.0	310.90	20.08
HDL [mg/dl]	68.18	17.19	28.50	142.30	25.21
Triglycerides [mg/dl]	105.63	54.70	35.10	379.60	51.78
Systolic blood pressure [mmHg]	117.75	16.92	67.00	260.00	14.37
Diastolic blood pressure [mmHg]	77.17	10.60	50.00	160.00	13.73
Waist circumference [cm]	87.05	12.51	57.00	148.00	14.37

M – mean, SD – standard deviation, CV – coefficient of variation, Min – minimum value, Max – maximum value, MBF – mass of body fat, PBF – percent body fat.

tion. After mixing, the difference of each sample potential was measured for 10 minutes: 5 minutes before and 5 minutes after the addition of the appropriate standard. The fluoride content in the sample was calculated on the basis of measured difference in sample potential, the sample weight, and the concentration of the added standard[9].

Characteristics of the Study Sample

The study included perimenopausal women, whose mean age was 52.9 years. Of all measured parameters, special attention should be paid to BMI and waist circumference. The average values of these parameters, analyzed collectively for all women included in the study, exceeded the normal range (Table I).

The most common abnormalities regarded as the components of MetS were a large waist circumference (70.1%) and elevated blood pressure (37.7%). The basis for the diagnosis of MetS is the coexistence of at least three out of the five components discussed. 18.1% of the studied women met this criterion (Table II).

Comparative assessment of the mean fluoride levels in the groups singled out according to MetS diagnostic criteria revealed statistically significant differences in two criteria: triglycerides and blood pressure. The mean fluoride levels were higher in the group which met these two criteria for MetS diagnosis (Table III).

Results

Analysis of the odds of MetS and its components depending on serum fluoride levels demonstrated that an increase in fluoride levels by one standard deviation raises the odds of developing hypertriglyceridemia by almost 13 times (OR = 12.9; 95% CI; confidence limits: 2.1, 79.3). Moreover, an increase in the level of fluoride by one standard deviation raises the odds of elevated blood pressure by nearly nine times (OR = 9.1; 95% CI; confidence limits: 1.7, 49.5). The odds of meeting the diagnostic criteria for MetS (minimum three out of the

Table II. Characteristics of the study sample with regard to the components of MetS.

Symptom	The 2009 IDF criteria for MetS diagnosis	N	%
Waist circumference	[≥ 80 cm]	333	70.1
Fasting glycemia	[≥ 100 mg/dl or pharmacotherapy for diabetes]	42	8.8
Triglycerides	[≥ 150 mg/dl or related pharmacotherapy]	73	15.4
HDL cholesterol	[≤ 50 mg/dl or related pharmacotherapy]	70	14.7
Blood pressure	[≥ 85 mmHg and/or ≥ 130 mmHg or pharmacotherapy]	178	37.5

M – mean, SD – standard deviation, CV – coefficient of variation, Min – minimum value, Max – maximum value, MBF – mass of body fat, PBF – percent body fat.

Table III. Comparative analysis of the mean fluoride (F-) levels [mg/L] in the groups singled out according to MetS diagnostic criteria.

	F- [mg/L]				
	M	SD	$t_{df = 473}$	*p*-value*	d (95% CI)
Waist circumference [≥ 80 cm] N = 333	0.087	0.115	0.237	0.813	-
Waist circumference [< 80 cm] N = 142	0.085	0.106			
Fasting glycemia [≥ 100 mg/dl or pharmacotherapy for diabetes] N = 43	0.080	0.094	-0.405	0.686	-
Fasting glycemia [< 100 mg/dl] N = 432	0.087	0.114			
Triglycerides [≥ 150 mg/dl or related pharmacotherapy] N = 72	0.122	0.182	2.954	0.003	0.38 (0.12; 0.63)
Triglycerides [< 150 mg/dl] N = 403	0.080	0.094			
HDL cholesterol [≤ 50 mg/dl or related pharmacotherapy] N = 69	0.094	0.116	0.586	0.558	-
HDL cholesterol [> 50 mg/dl] N = 406	0.085	0.112			
Blood pressure [≥ 85 mmHg and/or ≥ 130 mmHg or pharmacotherapy] N = 179	0.104	0.128	2.680	0.008	0.25 (0.06; 0.44)
Blood pressure [< 85 mmHg and/ or < 130 mmHg] N = 296	0.076	0.101			

*Student's *t*-test, M – mean, SD – standard deviation, df – degrees of freedom, d – Cohen's d coefficient, CI – confidence interval.

five components) raises by 16 times if fluoride levels are increased by one standard deviation (OR = 16.4; 95% CI; confidence limits: 2.8, 95.9) (Table IV).

Table IV. Analysis of the relationship between the level of fluoride (F-) [mg/L] and the odds of the development of MetS and its components.

	b	Wald's statistics	*p*	OR	-95% CI	95% CI
Glucose						
Intercept	-2.254	122.332	0.000	0.105	0.070	0.157
F-	-0.637	0.164	0.685	0.529	0.024	11.499
HDL						
Intercept	-1.828	125.050	0.000	0.161	0.117	0.221
F-	0.627	0.343	0.558	1.872	0.230	15.254
Triglycerides						
Intercept	-1.972	146.001	0.000	0.139	0.101	0.192
F-	2.557	7.621	0.006	12.898	2.099	79.250
Blood pressure						
Intercept	-0.698	32.747	0.000	0.498	0.392	0.632
F-	2.211	6.557	0.010	9.123	1.680	49.547
Waist circumference						
Intercept	0.834	43.305	0.000	2.302	1.796	2.951
F-	0.215	0.056	0.812	1.240	0.209	7.350
MetS diagnosis (minimum 3 out of 5 components)						
Intercept	-1.780	134.851	0.000	0.169	0.125	0.228
F-	2.795	9.605	0.002	16.364	2.794	95.850

Table V. Analysis of differences in the levels of fluoride (F-) [mg/L] with regard to MetS and its components.

	M MetS-	M MetS+	*t*	df	*p*	N MetS-	N MetS+	SD MetS-	SD MetS+
Glucose									
F-	0.0872	0.0799	0.4051	473	0.6856	432	43	0.1142	0.0939
HDL									
F-	0.0853	0.0938	-0.5863	473	0.5579	406	69	0.1120	0.1155
Triglycerides									
F-	0.0801	0.1223	-2.9544	473	0.0033	403	72	0.0938	0.1818
Blood pressure									
F-	0.0758	0.1042	-2.6803	473	0.0076	296	179	0.1009	0.1277
Waist circumference									
F-	0.0846	0.0873	-0.2369	473	0.8128	142	333	0.1060	0.1152
MetS diagnosis (minimum 3 out of 5 components)									
F-	0.0784	0.1230	-3.3629	473	0.0008	389	86	0.09548	0.1652

Analysis of the relationship between fluoride levels and the presence of MetS or its components showed that the mean fluoride level was statistically significantly higher in patients with hypertriglyceridemia (d_{Cohen} = 0.39; 95% CI; confidence limits: 0.13, 0.63) and hypertension (d_{Cohen} = 0.25; 95% CI; confidence limits: 0.07, 0.44). Moreover, the mean fluoride level was significantly higher in women with MetS than in the remaining subjects (d_{Cohen} = 0.40; 95% CI; confidence limits: 0.17, 0.64) (Table V).

As the next step, we assessed the value of serum fluoride levels as a diagnostic marker for MetS and found that it has poor diagnostic properties ($p > 0.05$, Table VI).

The relationship between the sensitivity and specificity of a fluoride-based diagnostic test for MetS detection indicates that the most optimal cut-off point may be the level of 0.071 with the Youden index of 0.17 (Figure 1).

The diagnostic value of fluoride levels in the detection of MetS was estimated. The assumed cut-off point for the fluoride level was 0.071. With this assumption, in the group meeting the MetS diagnostic criteria, 42 results were true positive (fluoride levels above 0.07) and 44 results were false positive (F- levels below or equal to 0.071). Among women who did not have MetS, 266 true negative results (fluoride levels below or equal to 0.071) and 123 false negative results (fluoride levels above 0.071) were obtained.

Analysis of the fluoride diagnostic properties demonstrated that its level with the diagnostic limit value of 0.071 allows to fairly accurately identify healthy people (an accuracy of 85.81%: 95% CI; confidence limits: 81.42, 89.49). However, the detection rate for people with MetS is relatively low (an accuracy of 25.45%: 95% CI; confidence limits: 19.00, 32.81). The mean Positive Predictive Value indicates the average preci-

Table VI. The area under a receiver operating characteristic curve in a diagnostic test for MetS with regard to serum fluoride levels.

AUC	SE	Lower AUC 95%	Upper AUC 95%	z	*p*-value
0.568	0.038	0.495	0.642	1.817	0.0693

AUC – area under the curve, SE – standard error.

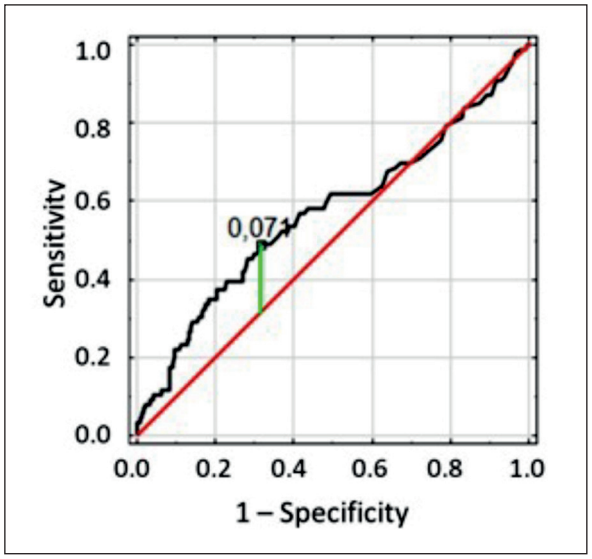

Figure 1. A receiver operating characteristic curve in a diagnostic test for MetS with regard to serum fluoride levels.

sion of the test (43%: 95% CI; confidence limits: 34, 53), while the fairly high Negative Predictive Value (73%: 95% CI; confidence limits: 71, 75) indicates a high probability that the negative result is true.

Discussion

Statistical analysis of the results confirmed the usefulness of serum fluoride levels as a marker of perimenopausal women's health with regard to the odds of metabolic disorders. This seems to be an important piece of information, especially in the context of numerous scientific publications indicating that fluorides significantly contribute to the development of metabolic disorders.

The Role of Fluorides in the Development of Carbohydrate Metabolism Disorders

The pancreas is the organ responsible for secreting insulin and glucagon – two of the most important hormones in the body's glucose control. Activating the process of glycolysis, insulin has a hypoglycemic effect, and affects the storage of nutrients and the speed of lipogenesis[10]. Glucagon increases the rate of gluconeogenesis, fatty acid oxidation, and is a hyperglycemic factor[11].

Impaired glucose tolerance has been observed in humans exposed to high doses of fluorides. Research conducted on residents of 22 states in the USA in the years 2005-2010 revealed a strong correlation between the widespread use of water fluoridation (in order to achieve the optimal level of 0.7-1.2 ppm) and the prevalence of diabetes in the society[12]. It is also noteworthy that the oral administration of sodium fluoride (NaF) caused a significant decline in plasma insulin[13], which is known to regulate glycolysis[14]. The study of 15-30-year-old patients with symptoms of endemic fluorosis demonstrated higher fasting levels of immunoreactive insulin and a lower ratio of glucose to insulin[15]. In another study, higher glucose peaks and later achievement of glucose peaks after the oral glucose tolerance test were found in patients with fluorosis compared to the control group. Moreover, a decrease in blood insulin and C-peptide levels, high fasting glucose, and abnormal glucose tolerance were observed[16].

The study carried out in the C57BL6 mice also confirmed the hyperglycemic effect of fluorides on the body. Additional tests on mouse pancreatic βTC-6 cells incubated with NaF (1.35 and 2.26 mM) and glucose (2.8 and 16.6 mM, respectively) demonstrated lower expression of mRNA for insulin, which was associated with decreased insulin secretion despite glucose stimulation. Moreover, the decreased activity of superoxide dismutase (SOD) and increased production of O2- were reported[17].

The literature also provides publications showing a negative effect of fluoride on the structure of pancreatic cells and on the secretory functions of this organ. In their study conducted in rats, Matsuo et al[18] (2000) observed the formation of numerous granules in the pancreas, which appeared after subcutaneous administration of 20 mg NaF / kg bw given twice a day for a long period of time. The presence of numerous autophagosomes within exocrine cells with double or multiple membranes and dense cytoplasmic organelles has also been reported. According to the authors, it may indicate the disturbed export of zymogens from the rough endoplasmic reticulum.

In rat-based studies, an immediate decrease in serum insulin levels and an increase in glycemia were observed after a single oral fasting administration of NaF (40 μmol/100 g bw[19]; 1 mg F/kg bw[20]). The parameters studied did not return to the baseline values until after 4-5 hours, which may have been associated with the removal of fluorides from the body with urine[19]. On the other hand, chronic (one month) administration of NaF (5 mmol/L) with drinking water to rats resulted in incorrect values obtained in glucose tolerance

tests and an increase in plasma fluoride levels. At the same time, treatment of pancreatic islets of Langerhans cells isolated from the animals with NaF (2, 5, 10 and 20 μmol/L) inhibited insulin secretion[21]. In addition, long exposure of animals to this compound (rats, 42 days, 4 mg/kg bw daily) decreased insulin receptor substrate 1 (IRS-1) tyrosine phosphorylation, thus reducing the muscle and white adipose tissue insulin sensitivity (which was not observed with single administration). It also caused a decrease in the levels of TNF-alpha and resistin in plasma[22].

Influence of Fluorides on Lipid Transport and Metabolism

The relationship between fluorides and lipid metabolism has so far been studied mainly in animal models. *In vivo* and *in vitro* studies provided considerable evidence that not only exposure to very high fluoride levels, but also high glycemia cause oxidative stress and lipid peroxidation in cells and tissues, disrupting tissue lipid metabolism.

The liver is the main organ involved in the metabolism of triglycerides, HDL, and low-density lipoprotein (LDL). Impaired liver function may disturb lipid metabolism due to an imbalance between the absorption of exogenous lipids and their endogenous biosynthesis, resulting in the accumulation of lipid droplets in hepatocytes[23]. A potential contributor to dysregulation of liver metabolism is oxidative stress, caused by hyperglycemia[24-26] and insulin stress[27]. Hyperglycemia also activates the process of lipogenesis in the liver by providing glucose that is the main substrate for this process, and thus increasing the fatty acid content in hepatocytes[28]. Exposure of the body to fluorides may exacerbate this state, since this element can increase the synthesis of free oxygen radicals in cells and disturb the pro- and antioxidant balance in tissues by inhibiting the activity of antioxidant enzymes[29]. However, the effect of fluorides on lipid metabolism may be different depending on the time of exposure to this element and the diet (normocaloric or rich in carbohydrates). Animal (rat) studies[30] have shown that long-term exposure to high doses of fluoride during a high-carbohydrate diet affects the lipid metabolism in the liver. It is probably related to the inhibitory effect of fluorides on the synthesis of apolipoprotein-E (Apo-E) – a protein involved in the metabolism of triglycerides, HDL, and LDL, responsible for the transport of lipids between tissues – in the liver[31,32]. On the other hand, short-term administration of low fluoride doses combined with a normocaloric diet increased serum HDL and lowered serum LDL levels in rats, thus reducing the triglyceride content in the liver. In this case, the changes were probably caused by the decreased expression of sterol regulatory element-binding protein (SREBP), and related inhibition of *de novo* lipogenesis in hepatocytes, which led to a reduction of triglyceride levels in the liver. No such changes were noted in the group of animals exposed to high doses of fluoride[30].

The Contribution of Fluorides to the Development of Hypertension

Fluoride can be a risk factor for hypertension, but the findings to date are controversial and uncertain. Research carried out in fluoride endemic areas in Iran showed that exposure to drinking water with a high fluoride content increased the risk of developing hypertension (OR 2.3, 1.03-5.14)[33]. One of Iranian studies demonstrated a statistically significant positive correlation between the mean fluoride level in groundwater resources and the incidence of hypertension in women ($r = 0.36$, $p = 0.048$)[34]. A relationship between high water fluoride levels and essential hypertension was confirmed by a Chinese study[35]. In their meta-analysis of the relationship between exposure to fluoride and hypertension, Li et al[36] (2020) did not note any statistically significant differences in blood pressure between controls and respondents exposed to NaF. However, residents of endemic fluorosis areas were found to have elevated blood pressure, which was associated with greater exposure to fluorine compounds. Our analysis of differences in fluoride levels between the MetS+ group and the MetS- (control) group showed that the mean fluoride level in hypertensive women from the MetS+ group was statistically significantly higher. Moreover, we found that an increase in the level of fluoride by one standard deviation raises the odds of elevated blood pressure by nearly nine times.

Influence of Fluorides on the Development of Overweight and Obesity

While it is known that excessive exposure to fluorides entails harmful health effects, the impact of low or moderate fluoride levels on the development of obesity remains unclear. The literature still lacks scientific studies explaining the mechanism of this linkage. A study[37] of 2,430 Chinese children aged 7-13 living in areas with low-to-moderate fluoride levels in drinking

water showed that this low-to-moderate fluoride exposure contributed to their overweight and obesity. Interestingly, the relationship between obesity and exposure to fluorides was stronger in girls than in boys. Our study also indicated a relationship between serum fluoride levels and an increase in the patients' waist circumference. This was associated with a greater amount of visceral adipose tissue, considered to be one of the factors predisposing to MetS. Probably by promoting the synthesis of free oxygen radicals and the progression of oxidative stress, fluorides enhance non-enzymatic oxidation of LDL. In this form, it can deliver unlimited amounts of fatty acids to tissues, where they are involved together with glucose metabolism products in the synthesis of triglycerides and their deposition in adipocytes. In addition, since fluorides disturb the hormonal balance in the body, they can also modify the activity of carbohydrate, lipid and protein metabolism pathways, and thus indirectly cause excessive accumulation of adipose (especially visceral) tissue[16]. However, this relationship requires confirmation.

Summary

So far, no studies have been carried out to establish the relationship between serum fluoride levels and MetS in perimenopausal women. The analysis of the influence of fluoride on individual MetS components indicates its potential role in the pathogenesis of metabolic disorders in this group of patients. It should be emphasized that the study included women representative of the general population of the West Pomeranian Voivodeship in Poland who did not live in the endemic areas and did not suffer an environmental exposure to fluorine compounds. The results of our research are therefore difficult to directly compare with the results obtained in endemic areas, characterized by a high concentration of fluoride in water and soil. Nevertheless, they indicate that long-term exposure to even low doses of this element may contribute to a faster onset and development of MetS components in perimenopausal women.

Conclusions

Elevated serum fluoride levels may be associated with an increased incidence of MetS in perimenopasal women, although its diagnostic value as a marker of MetS is limited.

Conflict of Interest

The Authors declare that they have no conflict of interests.

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