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SELENIUM REMOVAL STUDY IN PATIENTS WITH CHRONIC RENAL DISEASE

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Abstract. Selenium is an essential element of life. In humans, selenium is a cofactor of antioxidant enzymes, such as glutathione peroxidase and certain forms of tioredoxin - reductase. Selenium may inhibit Hashimoto's disease (in which thyroid cells are attacked by autoantibody). Patients with chronic renal failure are usually subjected to three weekly dialysis procedures. Since selenium removal is done only during the dialysis procedure, it is important to study it to determine the risk of high level of selenium in blood. For determination of selenium concentrations, authors used a Varian atomic absorption spectrometer with graphite tube atomizer, GF-AAS. We have performed a comparative study concerning selenium concentrations in blood determined on subjects in a control group versus blood selenium concentrations in subjects belonging to a group of patients undergoing dialysis procedure. In order to highlight the selenium removal dynamics in dialysate fluid, samples were collected during dialysis procedure at predetermined intervals. Statistical analysis concerning the differences between the averages selenemia in the patients group versus control group, and the Lagrange polynomial interpolation ruling the variation of selenium level in the dialysate fluid, in order to establish eliminations equation of selenium in chronic renal disease patients during the dialysis procedure, are presented in this paper.
Keywords: selenium, GF-AAS, chronic renal disease, Lagrange interpolation

General considerations

Selenium, the chemical element with the atomic number 34, is a nonmetal that appears in the form of compounds or ore and, rarely, in its elementary state.

Selenium salts are toxic in large quantities, but are necessary for life due to their cellular functions in many organisms. Selenium is a component of antioxidant enzymes - glutathione peroxidase and reductase tioredoxin which indirectly reduce certain oxidized molecules. Selenium is found in three deiodinaze enzymes that convert thyroid hormones. In plants, selenium requirements differ depending on the species [1].

In living systems, selenium is found in amino acids: selenomethionine, selenocysteine and metylselenocysteine. In these compounds, selenium plays a role analogous to that of sulfur. Another natural organoseleniate compound is dimethyl selenide [2].

Selenium is part of the essential elements of life. For humans, selenium is a nutrient that functions as a reduction cofactor of antioxidant enzymes, such as glutathione peroxidase and certain forms of tioredoxin - reductase.

The family of glutathione peroxidase enzymes

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(GSH-Px) catalyzes certain reactions to eliminate oxygen reactive species such as hydrogen peroxide and organic hydroperoxides:

$$2GSH + H_2O \xrightarrow{p_x} GSSG + 2H_2O$$

Selenium plays a role in the functioning of the thyroid gland and in every cell that uses thyroid hormone, by participating as a cofactor for three of the four known types of deiodinaze that transforms thyroid hormones, which then activate and deactivate thyroid hormones and their metabolites [4]. Selenium may inhibit Hashimoto's disease, in which one's own thyroid cells are attacked by autoantibody. A 21% reduction of Thyroperoxidase (TPO) antibodies was reported after dietary intake of selenium of 0.2 mg/day [5].

Patients with chronic renal failure are usually subjected to three weekly dialysis procedures [6]. Since selenium removal is done only during the dialysis procedure, it is important to study it to determine the risk of contamination/intoxication selenium.

Materials and method

We performed a prospective study between selenium concentrations determined in blood of subjects in the control group versus selenium concentrations determined in blood of subjects in the group of patients undergoing dialysis procedure.

To highlight the dynamics of selenium removal in the dialysate, samples were collected from the dialysate during dialysis procedure at predetermined intervals.

Materials

Study groups

(Criteria for inclusion/exclusion in the control group/patients' group)

To realize the prospective study, two groups.

a) The control group, which had the following inclusion criteria:

- normal renal function – given by the creatinine parameter, which should be less than 1.5 mg/dL;
- age between 18 and 65 years old;
- being a Bucharest citizen,
- and the exclusion criteria:
- being younger than 18 years old and older than 65 years old;
- having creatinine > 1.5 mg/dL;
- living outside Bucharest.

b) The patients' group had the following inclusion criteria:

- being diagnosed with chronic renal deficiency;
- do two/three dialysis procedures per week, in a special dialysis unit;
- being between 18 and 65 years old.

Samples

The following samples were collected:

- from the control group:

- 1 ml blood collected on anticoagulant to determine selenemia;

- 1 ml blood collected without anticoagulant to determine creatinine.

- from the patients' group:

- 1 ml blood collected on anticoagulant before starting the dialysis procedure- denoted by S1; and at the end of the procedure-denoted by S2, to determine selenemia;

- 10 ml of dialysate, collected at 30 min - denoted by LD_1, 1 h - denoted by LD_2, 2 h – denoted by LD_3, 3 h - denoted by LD_4, 4 h - denoted by LD_5;

- 10 ml of dialysate to determine the concentration of the element in the liquid that will perform the dialysis procedure, denoted by LD_0.

Analytical laboratory

To determine the selenium concentration in the collected samples from the two groups, an atomic absorption spectrometry machine with graphite furnace atomization - GF-AAS was used.

The AAS - Varian system has:

- Atomic absorption spectrometer SpectrAA 880;
- GTA 100 graphite furnace atomizer;
- Autosampler PSD 25;
- Water cooler CFT 33-Neslab;
- Nitrogen generator – Domnick Hunter (purity 99.999 %);
- Analytical balance – Precisa 40 SM – 200 A;
- Thermostat - MEMMERT - SLM 400;
- Analytical nitrogen – purity 99.999%;
- Analytical argon – purity 99.999%;
- Apparatus and common fixed tools in a toxicology laboratory;
- Reagents and consumables specific to AAS.

To determine creatinine, a VITROS 950 machine was used.

Methods

Statistic comparing method between the control group and the patients' group

For the analysis of selenium, selenemia averages were compared statistically, before and after the dialysis procedure, with those of the control group. Statistical analysis was performed based on gender. In the group of patients, selenium averages obtained from the dialysate in the subgroup of women to those obtained in the subgroup of men were compared.

Student test

For statistic analysis, the Student test was used, its result revealing whether the averages of analyzed groups significantly differ statistically or not and the probability for which the statement is made.

Appreciation of selenium removal dynamics through the dialysis procedure

Selenium is eliminated from the organism only during the dialysis procedure. Its removal must be performed depending on both quality and quantity.

Calculation of removed selenium quantity during the dialysis procedure

Calculation of removed selenium quantity during the dialysis procedure is performed with the trapeze method.

The trapeze is the tetragon with two paralleled sides and the other two unparalleled, Fig. 1.

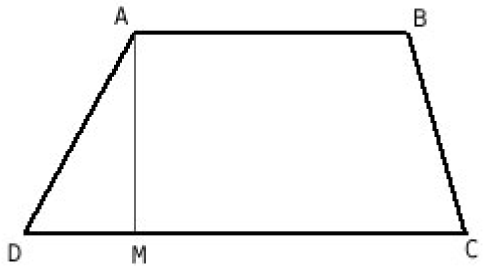

Figure 1. The trapeze

The trapeze's area is calculated with the following formula (1):

$$A = \frac{(AB + DC) * AM}{2}$$

Selenium elimination curve in the dialysate of patients with chronic renal disease can be in Fig. 2.

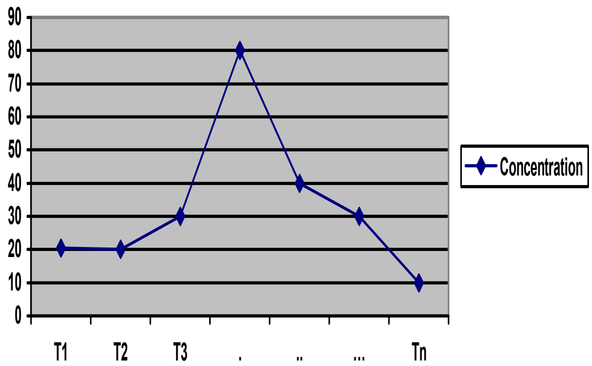

Figure 2. Variation curve of an element's concentration in the dialysate

The area below the curve (AUC) is the sum of all trapezoids formed from moment t_0 to t_n, relation (2)

$$AUC_{element} = \sum_{i=1}^{n} \frac{C_{i-1} + C_i}{2} (t_i - t_{i-1})$$

The total selenium quantity eliminated through the dialysis procedure is given by relation (3)

$$Q = AUC_{element} * D_{LD}$$

The average clearance of selenium is given by relation (4)

$$CL_{element} = \frac{Q}{T}$$

Where:

Q - represents the total amount of removed element during the dialysis session

CLelement - represents the average clearance of the element during the dialysis process

DLD - dialysate debit during the dialysis procedure

C (i) - concentration of the element in the dialysate at the moment the sample is collected

T – the duration of the dialysis session

ti – time at which the sample was collected

n- number of samples collected from the dialysate

Lagrange interpolation

In numeric analysis, the Lagrange polynomials are utilized for polynomial interpolation. Thus, for a certain set of distinct points a_i, b_i shown in Fig. 3. The Lagrange polynomial will have its degree equal to the maximum number of points taken into calculation for interpolation.

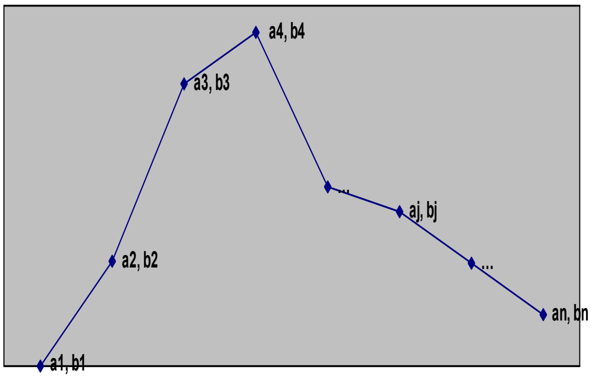

Figure 3. Data set a_i, b_i

The Lagrange interpolation formula is the following relation: (5)

$$P(x) = b_1 * \frac{(x-a_2)(x-a_3)\cdots(x-a_n)}{(a_1-a_2)(a_1-a_3)\cdots(a_1-a_n)} +$$

$$+ b_2 * \frac{(x-a_1)(x-a_3)\cdots(x-a_n)}{(a_2-a_1)(a_2-a_3)\cdots(a_2-a_n)} +$$

$$+ b_3 * \frac{(x-a_1)(x-a_2)\cdots(x-a_n)}{(a_3-a_1)(a_3-a_2)\cdots(a_3-a_n)} +$$

$$+ \cdots$$

$$+ b_n * \frac{(x-a_1)(x-a_2)\cdots(x-a_{n-1})}{(a_{1n}-a_{21})(a_n-a_2)\cdots(a_n-a_{n-1})} +$$

The AAS method for determining selenium concentration

The analytical method used for determining selenium concentration, from the analyzed matrices is the atomic absorption spectrometry method with atomization in graphite furnace GF-AAS (Graphite Furnace Atomizer – Atomic Absorption Spectrometry) [7].

The method involves setting the working conditions of the spectrometer, graphite furnace, sample dispenser and those for automatic control of analysis quality [8].

Working parameters

To determine Se concentration in the collected samples from the two groups, the following method was used:

- pipeting mode - automixing;
- injected sample quantity - 10 μl;
- measurement mode - peak height;
- calibration - in concentration;
- smoothing - 9 points;
- number of replicates - 2 for standard and sample;
- lamp current - 10 mA;
- wavelength - 196 nm;
- slit width - 1 nm;
- background correction - none;
- drying - 80 - 110 ^{0}C
- calcination - 300 - 1000 ^{0}C
- atomization - 2700 ^{0}C
- cleaning - 2700 ^{0}C
- 3 - point calibration curve - 0, 50 and 100 μg/L;
- recalibration rate - 20;
- method detection limit < 1 μg/L.
- machine detection limit < 0.06 μg/L.

The automatic quality control - dispersion < 10%; correlation coefficient of the calibration curve > 0.998.

Selenium calibration curve, absorbance in relation to concentration, is calculated with relation (6):

$$A / C = a + b * A + cA^2$$

Where:

A- the sample's absorbance

C- sample's concentration

a, b, c, d- are the coefficients of the calibration curve

Results and discussions

Selenium concentration values in the control group are shown in Table I. For each patient, gender and variables (age and creatinine) are being shown as well.

The control group in which selenemia was determined was composed of 27 patients: 17 men and 10 women.

The age averages of 41.47 for men's subgroup and 41.0 for women's subgroup. The averages of the two subgroups do not significantly differ statistically, for a probability of p= 0.91.

The average values of creatinine in men's subgroup (0.9 mg/dL) and women's subgroup (0.99 mg/dL). The averages do not significantly differ statistically for a probability of p = 0.35.

The averages of selenemia in men's subgroup (23.57 μg/dL) and women's subgroup (15.83 μg/dL). The averages of the two subgroups do not significantly differ statistically for a probability of p = 0.298.

Although the standard deviations of age for the subgroup of women= 8.06 years and that of men= 14.23 years, standard deviations of the averages are small, 2.55 years for women and 3.45 years for men. For selenemia, standard deviation of the subgroup of women is 15.26 μg/dL and the subgroup of men is 22.45 μg/dL, standard deviations of averages of 4.83 μg/dL for women and 5.44 μg/dL for men.

For creatinine, women's subgroup standard deviation is 0.24 mg/dL and in the subgroup of men it is 0.2 mg/dL, standard deviations of averages being of 0.8 mg/dL in women 0.05 mg/L in men.

Thus, variable averages of: age, creatinine and selenemia in the subgroup of men did not differ significantly from the subgroup of women in the control group. Low values of standard deviations of the average, compared to its value, shows that the control group is homogeneous in terms of: age, selenemia and creatinine.

In Table II, age and gender variables are being shown in addition to S_1, S_2, LD_0, LD_1, LD_2, LD_3, LD_4 and LD_5 of the group of patients the study was made for.

The patients' group in which selenemia was determined was made of 29 patients: 18 men and 11 women.

The dispersions of age averages for the two groups for selenium were 12.03 years for the control group and 14.01 years for the patients' group, differing by 1.02 (7.3 %).

The average of the control group, 41.3 years, significantly differs statistically from the average of the patients' group, 58.45 years, for a probability of p < 0.0001.

Standard deviations of the subgroups' age: control group women = 8.6 years and patients' group women= 11.48 years, differ by 2.88 (25.09 %); control group men= 14.23 and patients' group men = 14.01 years, differ by 0.22 years (1.55 %). Standard deviations of the average selenemia in subgroups: control group women = 2.55 and patients' group women = 3.46 years, have a difference of 0.91 (26.3 %) and control group men = 3.45 with patients' group men= 3.3 years differ by 0.15 years (4.3 %) .

Nr.	Patient code	Age (years)	Gender	Se (µg/dL)	Creatinine (mg/dL)
1.	M1	29	M	2.68	0.8
2.	M2	44	M	2.05	0.9
3.	M3	23	M	6.34	0.7
4.	M7	60	M	16.87	0.9
5.	M9	23	M	1.68	0.95
6.	M10	60	M	16.95	0.8
7.	M11	57	M	5.6	1.4
8.	M15	60	M	58.62	0.8
9.	M17	56	M	43.95	0.6
10.	M19	23	M	60.36	0.9
11.	M20	30	M	29.2	0.9
12.	M21	32	M	11.13	0.7
13.	M22	43	M	22.77	0.7
14.	M25	41	M	8.6	1.1
15.	M26	53	M	4.82	1.1
16.	M28	44	M	66.69	0.9
17.	M31	27	M	42.44	1.2
18.	M4	41	W	2.37	0.6
19.	M5	42	W	8.95	1.2
20.	M12	42	W	14.3	1.2
21.	M13	45	W	5.43	1.3
22.	M16	27	W	18.7	0.7
23.	M18	51	W	50.06	1.2
24.	M24	33	W	31.06	1
25.	M27	51	W	20.78	0.8
26.	M29	46	W	13.17	0.9
27.	M30	32	W	7.79	1
M.G		**41.2963**	**17M/10W**	**21.2356**	**0.93519**
A.S.G		**12.1301**	**58.6%M/41.8%W**	**19.7486**	**0.21654**
A.S.M.G		**2.334441**		**3.80**	**0.041672**
MM		**41.4706**		**23.5735**	**0.90294**
A.S.M		**14.2308**		**22.4481**	**0.20346**
A.S.M.M		**3.451468**		**5.444472**	**0.049347**
MW		**41**		**17.261**	**0.99**
A.S.W		**8.05536**		**14.2464**	**0.23781**
A.S.M.W		**2.54733**		**4.505098**	**0.075203**

Table I. Parameter and variables' values for selenium in patients in the control group

Legend:

M.G – represents the group average

A.S.G – represents the standard deviation of the group

A.S.M.G – represents the standard deviation of the group's average

M.M – represents the average for men's subgroup

A.S.M - represents the standard deviation of men's subgroup

A.S.M.M – represents the standard deviation of men's subgroup's average

M.W - represents the average for women's subgroup

A.S.W - represents the standard deviation for women's subgroup

A.S.M.W – represents the standard deviation of women's subgroup's average

The age averages of 41.47 years for men's subgroup and 41 years for the subgroup of women, in the group of patients. The averages of the two subgroups did not differ significantly for a probability of p = 0.46.

This data shows that the two groups can be considered homogenous from the age variable's point of view. Selenemia dispersion of the patients' group compared to that of the control group, at coupling and restitution.

Groups' dispersions: control = 20.13 µg/dL and patients' at coupling = 100.39 µg/dL and 101.1 µg/dL at restitution, differing by 80.26 µg/dL (79.9%) at coupling and 80.97 µg/dL (80.1%), and standard deviations of averages: control = 3.87 µg/dL and patients' at coupling = 18.97 µg/dL and 19.1 µg/dL at restitution, have a difference of 14.84 µg/dL (78.2%) at coupling and 15.23 µg/dL (79.7%).

				Blood			Urine				
Nr.	**Cod**	**Age** (years)	**Gender**	**S_1** μg/dL	**S_2** μg/dL	**LD_0**	**LD_1** μg/L	**LD_2** μg/dL	**LD_3** μg/L	**LD_4** μg/L	**LD_5** μg/L
1.	P6	31	M	25.26	107.2	0	25.26	107.	53.6	53.6	107.2
2.	P23	70	M	285.6	223.5	0	30.34	26.1	26.85	23.62	27.94
3.	P26	58	M	243.5	224.6	0	105.7	33.9	34.68	33.94	34.92
4.	P27	70	M	181.7	176.0	0	33.44	34.3	43.68	45.1	47.02
5.	P28	68	M	231.5	194.1	0	42.39	43.9	48.95	47.24	47.45
6.	P29	62	M	39.6	20.2	0	32.8	24.3	19.95	20.23	17.53
7.	P30	30	M	20.86	19.12	0	39.55	45.3	26.26	34.59	26.95
8.	P31	67	M	21.2	22.13	0	6.76	6.69	6.1	11.25	10.13
9.	P32	71	M	3.83	3.5	0	48.19	96.9	48.66	63.32	55.09
10.	P33	69	M	80.1	27	0	54.9	46.9	22.6	26.9	36.9
11.	P38	67	M	4.86	11.31	0	29.5	47.5	30.83	24.44	27.05
12.	P39	84	M	0.6	0.6	0	45.37	55.7	52.63	49.41	57.32
13.	P40	68	M	1.09	3.31	0	55.59	55.2	47.41	53.38	46.09
14.	P41	47	M	0.6	0.6	0	10.26	9.54	8.85	20.89	15.22
15.	P42	64	M	10.32	7.27	0	27.23	24.2	23.4	21.51	42.22
16.	P44	63	M	10	9.89	0	31.6	29.8	33.29	38.22	26.21
17.	P45	51	M	57.01	21.41	0	47.42			37.26	36.25
18.	P50	73	M	109.7	84.78	0	26.57	48.5	33.64	33.45	32.83
19.	P22	45	F	253.1	269.9	0	39.98	41.0	37.24	34.85	30.15
20.	P24	61	W	183.4	127.0	0	27.43	20.9	22.77	34.58	44.53
21.	P25	67	W	299.5	385.3	0	41	33.6	34.54	34.79	65.34
22.	P34	55	W	87.97	67.4	0	22.71	42.8	36.63	41.44	32.49
23.	P35	47	W	25.26	53.6	0	25.26	72.2	36.7	50.53	25.26
24.	P36	63	W	81.24	7.65	0	35.97	62.3	29.08	27.69	31.11
25.	P37	55	W	154.0	29.29	0	31.8	25.7	18.84	32.97	41.31
26.	P46	63	W	0.6	0.6	0	49.68	17.1	22.02	10.88	10.47
27.	P47	35	W	18.87	67.52	0	40.71	56.6	64.71	36.03	47.45
28.	P48	58	W	5.29	0.6	0	60.73	59.4	50.82	59.68	36
29.	P51	33	W	0.6	0.6	0	41.53	28.2	41.78	56.59	40.94
M.G		**58.45**	**18M**	**85.6**	**76.6**	**0**	**37.08**	**42.70**	**34.16**	**36.5**	**37.9**
A.S.G		**13.39**	**11W**	**100.4**	**101.1**	**0**	**14.1**	**23.26**	**13.95**	**13.8**	**18.81**
A.S.M.G		**2.49**	**62 % M**	**18.97**	**19.10**	**0**	**2.62**	**4.396**	**2.635**	**2.571**	**3.493**
MM		**61.83**	**48 % W**	**75.75**	**66.8**	**0**	**36.59**	**43.28**	**33.02**	**35.5**	**38.57**
A.S.M		**14.01**		**97.9**	**84.5**	**0**	**15.94**	**26.41**	**14.6**	**14.2**	**21.61**
A.S.M.M		**3.302**		**23.75**	**20.48**	**0**	**3.76**	**6.4060**	**3.535**	**3.348**	**5.094**
MW		**52.91**		**100.1**	**91.8**	**0**	**37.89**	**41.8**	**35.9**	**38.2**	**36.8**
A.S.W		**11.48**		**107.**	**125.6**	**0**	**11.12**	**18.53**	**13.4**	**13.7**	**13.955**
A.S.M.W		**3.46**		**32.26**	**37.87**	**0**	**3.352**	**5.587**	**4.039**	**4.138**	**4.208**

Table II. Values of parameters and variables for the patients' group for selenium

Legend:

M.G - represents the group average

A.S.G - represents the standard deviation of the group

A.S.M.G - represents the standard deviation of the group's average

M.M - represents the average for men's subgroup

A.S.M - represents the standard deviation of men's subgroup

A.S.M.M - represents the standard deviation of men's subgroup's average

M.W - represents the average for women's subgroup

A.S.W - represents the standard deviation for women's subgroup

A.S.M.W - represents the standard deviation of women's subgroup's average

Note: In case a sample is missing, no value is being shown in the table

Dispersions of selenemia values for the women's subgroup compared to the men's subgroup at coupling and restitution are being shown in Fig. 4.

Selenemia averages in the subgroup of men of 75.75 μg/dL and in subgroup of women 100.1 μg/dL at coupling, and 66.84 μg/dL in men and 91.78 μg/dL in women at restitution.

The averages of the two subgroups differ sig-

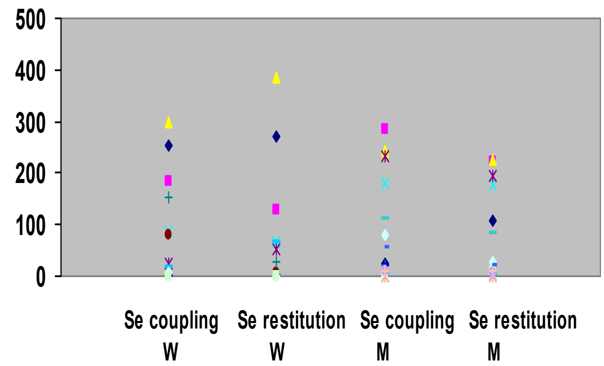

Figure 4. Selenemia dispersions in women's subgroup and men's subgroup at coupling and restitution

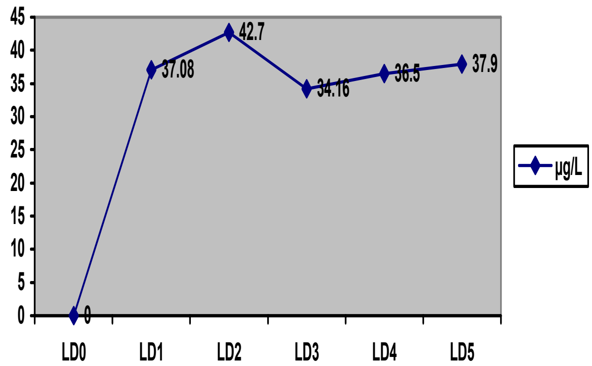

Figure 6. Variation of selenium elimination in the dialysate in the group of patients

nificantly both at coupling for a probability of p = 0.0024 and at restitution for p = 0.008 compared to the averages of selenemia in the control group.

In the group of patients, although selenemia average at restitution is lower by 9.21 μg/dL, this difference is not statistically significant for a probability of p = 0.739714.

This data shows that selenemia in the patients' group is significantly higher from a statistic point of view, compared to the control group's, both at coupling and restitution.

Dispersion of selenemia concentrations determined in the dialysate during the following time intervals: 0, 0.5, 1, 2, 3 and 4h, is shown in Fig. 5, where T_0 is not presented since the selenium concentration value in the dialysate was = 0 μg/L.

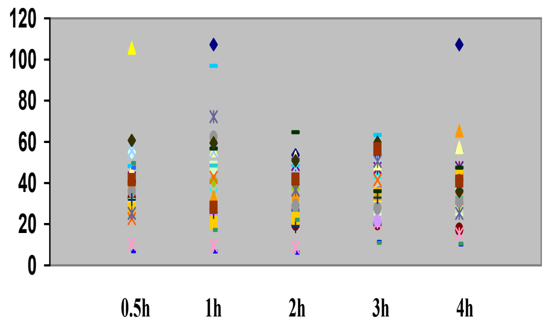

Figure 5. Dispersion of selenium concentrations in the dialysate in the patient's group at 0.5, 1, 2, 3 and 4h

Standard deviations of concentrations determined in the dialysate are high: LD_1 = 17.98 μg/L, LD_2 = 23.26 μg/L, LD_3 = 13.95 μg/L, LD_4 = 13.85 μg/L and LD_5 = 18.81 μg/L, and standard deviations of the averages of selenium concentrations in the dialysate are relatively high: LD_1 = 3.34 μg/L, LD_2 = 4.4 μg/L, LD_3 = 2.64 μg/L, LD_4 = 2.57 μg/L and LD_5 = 3.49 μg/L.

The variation curve of average selenium concentration in the dialysate during dialysis session is shown in Fig. 6. It is noted that the elimination of selenium in the dialysate is approximately constant throughout the dialysis procedure, being only 0.94 μg/L lower in the fourth hour than at 30 minutes after the beginning of the procedure. Elimination presented a maximum elimination in the first hour from the commencement of dialysis.

Dispersion of selenium concentrations determined in the dialysate in the subgroup of women at time intervals of 0, 0.5, 1, 2, 3 and 4 h are shown in Fig. 7, where T_0 = 0 is not shown because the concentration of selenium in the dialysate was = 0 μg/L.

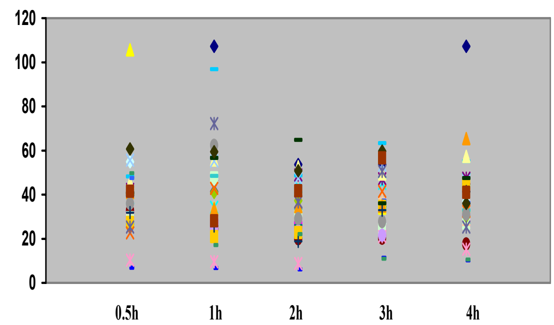

Figure 7. Dispersion of selenium concentrations in the dialysate in the subgroup of women at 0.5, 1, 2, 3 and 4h

Standard deviations of selenium concentrations determined in the dialysate are high in the subgroup of women: LD_1 = 11.1178 μg/L, LD_2 = 18.5311 μg/L, LD_3 = 13.3963 μg/L, LD_4 = 13.7367 μg/L, and LD_5 = 13.9551 μg/L and standard deviations of average selenium concentrations in the dialysate are elevated: LD_1 = 3.352133 μg/L, LD_2 = 5.58734 μg/L, LD_3 = 4.039147 μg/L LD_4 = 4.141767 μg/L and LD_5 = 4.207608 μg/L.

Dispersions of selenium concentrations determined in the dialysate at intervals of 0, 0.5, 1, 2, 3 and 4 h, in the subgroup of men are shown in Fig. 8, where T_0 = 0 was not presented because the concentration of selenium in the dialysate was = 0 μg/L.

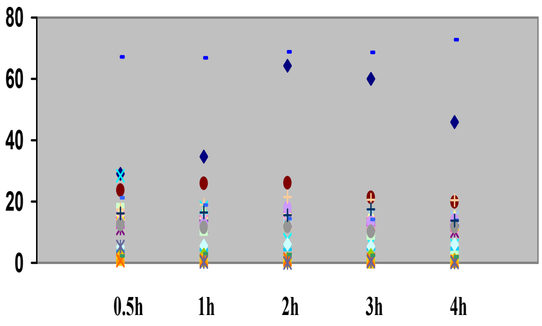

Figure 8. Dispersion of selenium concentrations in the dialysate in the subgroup of men at 0.5, 1, 2, 3 and 4h

Standard deviations of concentrations determined in the dialysate in the subgroup of men are high: LD_1 = 21.4374 µg/L, LD_2 = 26.4127 µg/L, LD_3 = 14.5769 µg/L, LD_4 = 14.2054 µg/L and LD_5 = 21.6107 µg/L; standard deviations of the average selenium concentrations are elevated in the dialysate: LD_1 = 3.76 µg/L, LD_2 = 6.406015 µg/L, LD_3 = 3.535413 µg/L, LD_4 = 3.348248 µg/L and LD_5 = 5.093684 µg/L.

Variation of average concentration of selenium in the dialysate at predetermined intervals in the subgroup of women compared to the subgroup of men is shown in Fig. 9. The averages of the two subgroups did not differ significantly in the entire study with the following probabilities: LD_1 p = 0.8, LD_2 p = 0.86197, LD_3 p = 0.594439, LD_4 p = 0.614588 and LD_5 p = 0.793055.

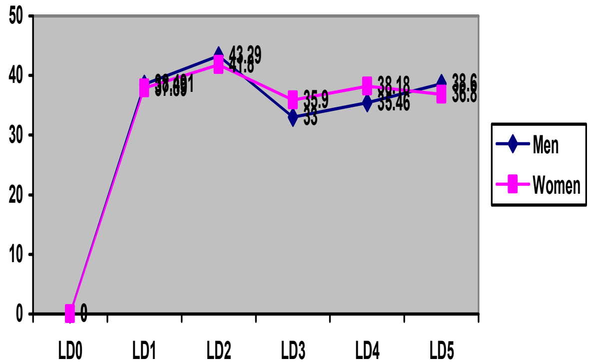

Figure 9. Variation of selenium elimination in the dialysate in the subgroup of women, compared to the subgroup of men in the group of patients

It is observed that the two subgroups have similar elimination, being almost constant throughout the dialysis procedure with a small maximum one hour after the start of the procedure.

Thus, the variables' averages: age, selenemia and selenium concentrations in dialysate collected at preset intervals during the dialysis procedure, in the subgroup of men compared to the subgroup of women in the control group, did not differ significantly. For this reason, the group of patients can be considered homogeneous.

Statistical analysis of the selenemia of the group of patients at coupling differs significantly from that of the control group for a probability of p = 0.00224, with 64.29 µg/dL (3.01 times) higher than the average of the control group. And at restitution, the average selenemia in the group of patients differs significantly from that of the control group for a probability of p = 0.008, with 55.4 µg/dL (2.6 times) higher than the average of the control group. This indicates selenium contamination risk.

The area under the elimination curve of selenium removed during the dialysis procedure is given by equation (2), where replacing gives us relation (7):

$$AUC_{Se} = .5\frac{0+37.08}{2} + .5\frac{37.06+42.7}{2} + \frac{42.7}{}$$

$$\text{AUC(Se)} = 140.175\ \mu g{*}h/L = \\ = 8445.9\ \mu g{*}min/L$$

Dialysate flow throughout the dialysis procedure was 0.5 l/min. Substituting in equation (4) we get (relation):

$$Q_{Se} = 8410.5{*}.5 = 4205.25\ \mu g = 4.2\ mg$$

The average clearance of selenium is obtained by substituting values of selenium quantity removed during dialysis session in equation (4), obtaining (10):

$$CL_{Se} = \frac{Q}{T} = \frac{4205.25}{240} = 17.52\ \mu g/min$$

The Lagrange polynomial which establishes the law of selenium removal in the dialysate is obtained by substituting the values of terms a_i, b_i in Table III, in relation (5), resulting relation (11).

$$C_{GSe}(x) = 0 + 37.08\frac{(x-0)(x-1)(x-2)(x-}{(0.5-0)(0.5-1)(0.5-2)(0.}$$
$$+42.70\frac{(x-0)(x-.5)(x-2)(x-3)(x-4)}{(1-0)(1-).5(1-2)(1-3)(1-4)} +$$
$$+34.16\frac{(x-0)(x-.5)(x-1)(x-3)(x-4)}{(2-0)(2-).5(2-1)(2-3)(2-4)} +$$
$$+36.5\frac{(x-0)(x-.5)(x-1)(x-2)(x-4)}{(3-0)(3-.5)(3-1)(3-2)(3-4)} +$$
$$+37.9\frac{(x-0)(x-.5)(x-1)(x-2)(x-3)}{(4-0)(4-.5)(4-1)(4-2)(4-3)} +$$

Solving polynomial (11) to obtain the Lagrange polynomial that approximates eliminated selenium in the dialysate in the group of patients studied, relation (12) (see next page)

Relation (12) describes the law of selenium

VARIABLE	INDEX					
	1	**2**	**3**	**4**	**5**	**6**
a (h)	0	0.5	1	2	3	4
b (µg/L)	0	**37.08**	**42.70**	**34.16**	**36.6**	**37.91**

Table III. Average selenium concentration determined in the dialysate in the patients' group

$$C_{GSe}(x) = 0.77188\,x^5 - 10.81589\,x^4 + 55.96833\,x^3 - 129.39196\,x^2 + 126.16764\,x$$

elimination in the dialysate from patients. In Fig. 10., there is a graphical representation of equation (12):

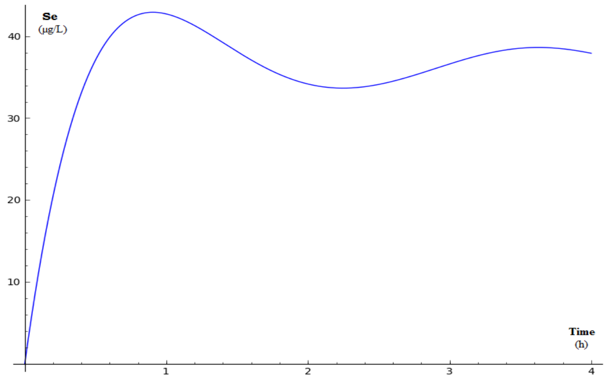

Figure 7. Graphic representation of the selenium elimination function in the group of patients

It is observed that the elimination of selenium in the dialysate in the group of patients has a maximum at about an hour and the other at 3.7 hours after the start of the dialysis. In the subgroup of women, the Lagrange polynomial is obtained by substituting values of terms a_i, b^i, from Table IV, in relation (5), resulting relation (13).

$$C_{WSe}(x) = 0 + 37.89\frac{(x-0)(x-1)(x-2)(x-}{(0.5-0)(0.5-1)(0.5-2)(0}$$
$$+41.8\frac{(x-0)(x-.5)(x-2)(x-3)(x-4)}{(1-0)(1-).5(1-2)(1-3)(1-4)}+$$
$$+35.92\frac{(x-0)(x-.5)(x-1)(x-3)(x-4)}{(2-0)(2-).5(2-1)(2-3)(2-4)}+$$
$$+38.18\frac{(x-0)(x-.5)(x-1)(x-2)(x-4)}{(3-0)(3-.5)(3-1)(3-2)(3-4)}+$$
$$+36.82\frac{(x-0)(x-.5)(x-1)(x-2)(x-3)}{(4-0)(4-.5)(4-1)(4-2)(4-3)}+$$

Solving polynomial (13) to obtain the Lagrange polynomial that approximates the elimination of selenium in the dialysate in the subgroup of women, we obtain relation (14):

Relation (14) describes the law of selenium elimination in the dialysate in the subgroup of women.

It can be seen that elimination in the subgroup of women has a maximum at about an hour and another at three hours from the start of the dialysis. At the end of the session, elimination is increased.

In the men's subgroup, the Lagrange polynomial is obtained by substituting the values of terms a_i, b_i, from Table V, in relation (5), resulting equation (15).

$$C_{MSe}(x) = 0 + 36.59\frac{(x-0)(x-1)(x-2)(x-}{(0.5-0)(0.5-1)(0.5-2)(0}\quad)($$
$$+43.29\frac{(x-0)(x-.5)(x-2)(x-3)(x-4)}{(1-0)(1-).5(1-2)(1-3)(1-4)}+$$
$$+33.02\frac{(x-0)(x-.5)(x-1)(x-3)(x-4)}{(2-0)(2-).5(2-1)(2-3)(2-4)}+$$
$$+35.46\frac{(x-0)(x-.5)(x-1)(x-2)(x-4)}{(3-0)(3-.5)(3-1)(3-2)(3-4)}+$$
$$+38.57\frac{(x-0)(x-.5)(x-1)(x-2)(x-3)}{(4-0)(4-.5)(4-1)(4-2)(4-3)}+$$

)(Solving polynomial (16) to obtain the Lagrange polynomial that approximates the elimination of selenium in the subgroup of men dialysate, we obtain relationship (16):

Relation (18) describes the law of selenium elimination in the dialysate in the subgroup of men.

It can be seen that elimination in the subgroup of men has a maximum at about an hour and another 3.8 hours after the start of the dialysis. Comparison between elimination function in the subgroup of women and the group of patients is shown in Fig. 11.

It can be seen that the variation tendency of the women' subgroup selenium elimination, dictates the elimination tendency of the group, although women represent only 38 % of the group of patients.

Comparison between elimination function in the subgroup of men and the group of patients is shown in Fig. 12.

$$C_{WSe}(x) = 1.493762x^5 - 17.75345x^4 + 78.48x^3 - 157.41226x^2 + 136.99195x$$

VARIABLE	INDEX					
	1	2	3	4	5	6
A (h)	0	0.5	1	2	3	4
b (µg/L)	0	37.8909	41.7955	35.9209	38.1845	36.8227

Table IV. Average concentration of selenium determined in the dialysate in the subgroup of women

VARIABLE	INDEX					
	1	2	3	4	5	6
a (h)	0	0.5	1	2	3	4
b (µg/L)	0	36.59	43.2882	33.0224	35.4639	38.5733

Table V. Average concentration of selenium determined in the dialysate in the men's subgroup

$$C_{MSe}(x) = 0.319738x^5 - 6.460298x^4 + 41.8133x^3 - 111.793988x^2 + 119.41121x \quad (16)$$

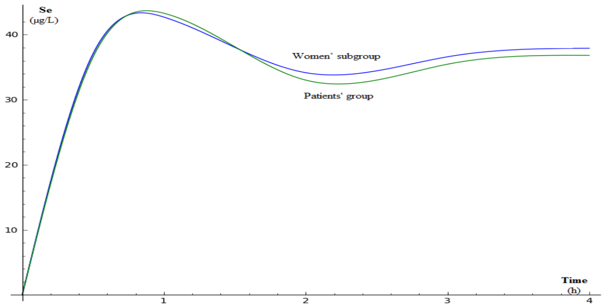

Figure 11. Graphical representation of selenium elimination function in the women's subgroup compared to the group of patients

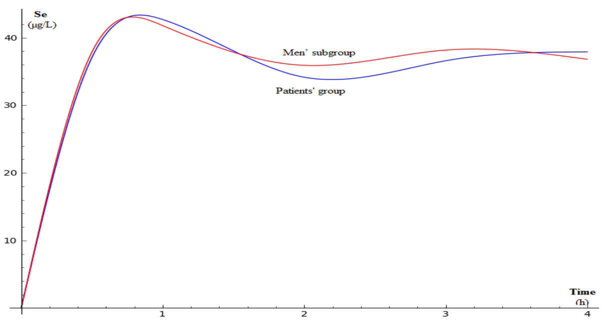

Figure 11. Graphical representation of the selenium elimination function in the subgroup of men compared to the group of patients

Conclusions

In terms of variables' statistics: age, creatinine and selenemia, the control group can be considered homogeneous.

The group of patients can be considered homogeneous too in terms of age variables, selenemia and selenium concentration in the dialysate.

Selenemia in the group of patients is significantly higher than the one in the control group both at coupling and restitution, averages in the group of patients being several times higher than the ones in the control group. These significant differences are not different by sex.

Large deviations of selenemia in the group of patients, at coupling and restitution, shows that the variation of this element must be correlated with that of other essential elements, the study should be extended regarding the characterization of elimination of the essential elements of life in the dialysate. An extensive study would also lead to a better understanding of the phenomenon of elimination and hence the possible improvement of treatment methods.

Statistically speaking there is no difference between the selenemia averages in the group at coupling compared to restitution.

Elimination of selenium in the dialysate has two peaks in women and men's subgroups. First maximum occurs at about the same time from the commencement of dialysis. The second maximum is obtained about 30 minutes earlier than that of the subgroup of men.

Unlike in the subgroup of men, by the end of dialysis procedure, elimination levels of Se in the dialysate are slightly increasing in the subgroup of women.

The law of variation of selenium in the dialysate in the subgroup of women stands out, although there are more men than women in the group.

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