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"MYROSLAVA" AND "KHRYSTYNA" DRINKING MINERAL WATERS MODULATE THE STATE OF NEUROENDOCRINE-IMMUNE COMPLEX AND METABOLISM IN PATIENTS OF TRUSKAVETS' SPA

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Background. Earlier in an experiment on rats we showed that newly created sulfate-chloride sodium-magnesium drinking mineral waters "Myroslava" and "Khrystyna" of Truskavets' spa has a significant modulating effects on the parameters of metabolism and the autonomic nervous, endocrine and immune systems. Adhering to the principle "Ex experimento ad clinic", we continued research in this direction with the participation of patients of the resort. We showed that these mineral waters have favorable effects on metabolic, HRVs, EEGs, endocrine and immune parameters. This article presents an integrated assessment of previously identified effects. **Materials and Methods**. The object of clinical-physiological observation were 34 men aged 23-70 years, who underwent rehabilitation treatment of chronic cholecystitis and pyelonephritis in remission in the Truskavets' spa. The examination was performed twice, before and after a 7-10-day course of balneotherapy. All patients received bioactive water Naftussya, however, 11 men additionally drank water "Khrystyna", and the other 11 men water "Myroslava". The subject of the study were the parameters of the neuroendocrine-immune complex and metabolism. **Results**. The complex balneotherapy by interval use of sulfate-chloride sodium-magnesium mineral waters with Naftusya water causes significant changes in the constellation of EEGs, HRVs, endocrine, metabolic and immune parameters, which are different from the effects of Naftusya water monotherapy. Own effects of mineral waters are estimated by modeling. In general, the effects are physiologically favorable and have a normalizing nature. **Conclusion**. The newly created sulfate-chloride sodium-magnesium drinking mineral waters of Truskavets' spa have favorable neuroendocrine, metabolic and immune effects on patients with chronic cholecystitis and pyelonephritis.

Keywords: sulfate-chloride sodium-magnesium drinking mineral waters, Truskavets' spa, EEG, HRV, hormones, metabolism, immunity.

INRODUCTION

Earlier in an experiment on rats, carried out in line with the concepts of neuroendocrine-immune complex [4,16,17,19,20] and functional-metabolic continuum [3], we showed that newly created sulfate-chloride sodium-magnesium drinking mineral waters "Myroslava" (5 g/L) and "Khrystyna" (10 g/L) of Truskavets' spa has a significant modulating effects on the parameters of metabolism and the autonomic nervous and endocrine systems [5-7,18] as well as immunity [1]. Adhering to the principle "Ex experimento ad clinic", we continued research in this direction with the participation of patients of the resort. We showed that these mineral waters have favorable effects on metabolic, HRVs, EEGs, endocrine and immune parameters [8,9]. This article presents an integrated assessment of previously identified effects.

MATERIALS AND METHODS

The object of clinical-physiological observation were 34 men aged 23-70 years, who underwent rehabilitation treatment in the Truskavets' spa of chronic cholecystitis and pyelonephritis in remission with of neuroendocrine-immune complex dysfunction. The examination was performed twice, before and after a 7-10-day course of balneotherapy. All patients received bioactive water Naftussya (3 ml/kg one hour before meals three times a day), however, 11 men in half an hour additionally drank water "Khrystyna", and the other 11 men - water "Myroslava" in the same dose.

The subject of the study were the EEGs [9], HRVs, endocrine, metabolic and immune [8] parameters.

RESULTS AND DISCUSSION

Following the accepted algorithm, the method of discriminant analysis [10] revealed 35 parameters, according to which the conditions of patients before and after the two balneotherapy regimens differ significantly. Characteristic were 14 EEGs, 2 HRVs, 2 endocrine, 4 immune and 13 metabolic parameters (Tables 1 and 2).

Table 1. Summary of the analysis of discriminant functions in relation to the parameters of EEG

Step 35, N of vars in model: 35; Grouping: 3 grps; Wilks' Λ: 0,0072; approx. $F_{(71)}=9,5$; $p<10^{-6}$

Variables currently in the model	Groups (n) and Means±SE			Parameters of Wilks' Statistics					
	Before therapy (34)	After Naftussya (12)	After SW and N (22)	Wilks' Λ	Partial Λ	F-remove (2,31)	p-level	Tolerancy	Norm Cv
Phosphates Excretion, mM/24 h	18,2 1,2	16,8 1,8	42,4 3,8	0,013	0,538	13,3	10^{-4}	0,187	25,2 0,294
Calcitonin, ng/L	6,95 0,62	6,16 1,11	10,48 1,21	0,009	0,778	4,41	0,021	0,404	13,95 0,493
Killing Index vs Staph. aur., %	48,2 1,5	45,2 1,9	57,7 1,4	0,011	0,631	9,04	0,001	0,286	58,9 0,142
Testosterone, nM/L	18,5 1,6	9,0 1,0	15,3 2,1	0,013	0,568	11,8	10^{-4}	0,286	14,8 0,400
Magnesium Urine, mM/L	2,40 0,11	2,14 0,23	2,22 0,13	0,011	0,655	8,16	0,001	0,055	2,93 0,256
Creatinine Plasma, µM/L	92,6 2,6	81,9 2,8	87,4 2,0	0,011	0,657	8,10	0,001	0,352	79,5 0,167
Laterality β, %	-3 5	-33 10	-4 4	0,008	0,925	1,25	0,301	0,286	-6 *28*
Sodium Plasma, mM/L	141,5 1,5	146,7 2,1	142,3 2,0	0,012	0,613	9,79	0,001	0,254	145,0 0,034
LD Cholesterol Plasma, mM/L	3,54 0,18	3,43 0,32	3,25 0,21	0,010	0,729	5,77	0,007	0,269	3,44 0,192
Interleukin-6, ng/L	4,45 0,36	3,67 0,56	4,58 0,33	0,011	0,673	7,52	0,002	0,146	4,25 0,324

F7-θ PSD, %	7,1 0,7	9,8 1,0	8,8 1,3	0,010	0,748	5,23	0,011	0,128	7,9 0,568
VLF HRV PS, msec²	969 99	869 141	1238 168	0,010	0,730	5,72	0,008	0,259	1250 0,572
Entropy Fp2	0,817 0,024	0,797 0,036	0,705 0,048	0,008	0,948	0,84	0,440	0,208	0,799 0,180
Sodium Urine, mM/L	119 5	114 8	89 7	0,009	0,759	4,93	0,014	0,017	110 0,211
Chloride Urine mM/L	102 3	127 14	96 10	0,009	0,814	3,54	0,041	0,023	120 0,172
Phosphate Plasma, mM/L	1,04 0,03	1,13 0,06	0,91 0,04	0,007	0,997	0,05	0,949	0,306	1,20 0,167
$CD3^+$ active T-Lymphocytes, %	28,3 0,8	31,3 0,9	26,1 1,1	0,009	0,824	3,32	0,050	0,508	30,0 0,167
Lithogenicity Urine	0,86 0,03	0,83 0,03	0,95 0,03	0,010	0,750	5,17	0,012	0,358	0,73 0,300
T4-θ PSD, μV²/Hz	34 7	22 4	19 3	0,009	0,819	3,42	0,045	0,210	32 2,582
Laterality θ, %	-4 7	-24 10	-35 10	0,011	0,670	7,65	0,002	0,096	-3 *32*
C3-α PSD, %	35,5 3,2	30,1 4,8	38,9 3,4	0,012	0,588	10,9	10^{-3}	0,089	35,3 0,510
P3-α PSD, %	42,1 3,6	37,7 5,5	49,5 3,8	0,010	0,731	5,71	0,008	0,089	40,8 0,480
Sodium Excretion, mM/24 h	225 18	179 11	238 19	0,009	0,821	3,39	0,047	0,011	154 0,211
Magnesium Excretion, mM/24 h	4,40 0,29	3,43 0,36	5,98 0,43	0,012	0,613	9,78	0,001	0,022	4,10 0,256
Chloride Excretion, mM/24 h	186 13	197 15	259 27	0,008	0,874	2,23	0,124	0,020	167,5 0,172
HF HRV PS, msec²	354 75	407 262	541 100	0,008	0,854	2,65	0,087	0,266	350 0,713
Glucose Plasma, mM/L	4,77 0,17	4,68 0,33	4,59 0,18	0,008	0,883	2,06	0,145	0,441	4,70 0,160
F8-δ PSD, %	38,8 4,7	50,2 8,8	28,3 7,3	0,007	0,987	0,21	0,816	0,316	38,3 0,700
Fp2-β PSD, μV²/Hz	74 8	50 7	74 10	0,009	0,793	4,05	0,027	0,130	61 0,629
T5-δ PSD, μV²/Hz	395 200	85 21	234 111	0,008	0,916	1,42	0,258	0,252	174 3,737
F4-β PSD, μV²/Hz	86 9	68 11	92 12	0,008	0,923	1,29	0,290	0,106	73 0,612
Entropy T6	0,790 0,031	0,834 0,026	0,710 0,046	0,009	0,801	3,86	0,032	0,126	0,761 0,249
Microbian Count for St. aur., B/Ph	62,8 1,2	66,0 2,0	60,2 2,3	0,009	0,847	2,81	0,076	0,478	61,6 0,160
Laterality α, %	-1 6	-23 9	-18 5	0,008	0,854	2,64	0,087	0,129	-4 *27*
Entropy F7	0,704 0,039	0,851 0,024	0,724 0,054	0,008	0,911	1,52	0,235	0,127	0,751 0,282

Note. In each column, the first line is the average, the second – SE for variables and Cv or ***SD*** for Norm.

Table 2. Summary of step-by-step analysis of discriminant variables ranked by criterion Λ

Variables currently in the model	F to enter	p-level	Λ	F-va-lue	p-level
Phosphates Excretion, mM/24 h	33,0	10^{-6}	0,496	33,0	10^{-6}
Calcitonin, ng/L	7,42	0,001	0,403	18,4	10^{-6}
Killing Index vs Staph. aureus, %	6,14	0,004	0,337	15,2	10^{-6}
Testosterone, nM/L	5,86	0,005	0,283	13,6	10^{-6}
Magnesium Urine, mM/L	5,57	0,006	0,240	12,7	10^{-6}
Creatinine Plasma,μM/L	6,31	0,003	0,198	12,5	10^{-6}
Laterality β, %	6,32	0,003	0,163	12,4	10^{-6}
Sodium Plasma, mM/L	4,61	0,014	0,141	12,1	10^{-6}
LD Cholesterol Plasma, mM/L	3,61	0,033	0,125	11,6	10^{-6}
Interleukin-6, ng/L	4,05	0,023	0,109	11,4	10^{-6}
F7-θ PSD, %	4,09	0,022	0,095	11,2	10^{-6}
VLF HRV PS, msec^2	2,99	0,058	0,085	10,9	10^{-6}
Entropy Fp2	3,84	0,028	0,075	10,8	10^{-6}
Sodium Urine, mM/L	3,43	0,040	0,066	10,7	10^{-6}
Chloride Urine mM/L	2,49	0,094	0,060	10,5	10^{-6}
Phosphate Plasma, mM/L	2,81	0,069	0,054	10,3	10^{-6}
CD3$^+$ active T-Lymphocytes, %	1,76	0,183	0,050	9,96	10^{-6}
Lithogenicity Urine	2,51	0,092	0,046	9,82	10^{-6}
T4-θ PSD, μV^2/Hz	2,33	0,109	0,042	9,66	10^{-6}
Laterality θ, %	4,06	0,024	0,035	9,94	10^{-6}
C3-α PSD, %	2,03	0,144	0,032	9,76	10^{-6}
P3-α PSD, %	2,36	0,106	0,029	9,70	10^{-6}
Sodium Excretion, mM/24 h	1,58	0,218	0,027	9,46	10^{-6}
Magnesium Excretion, mM/24 h	4,18	0,022	0,023	9,86	10^{-6}
Chloride Excretion, mM/24 h	2,95	0,063	0,020	10,0	10^{-6}
HF HRV PS, msec^2	2,62	0,085	0,018	10,1	10^{-6}
Glucose Plasma, mM/L	2,97	0,063	0,015	10,3	10^{-6}
F8-δ PSD, %	1,73	0,191	0,014	10,1	10^{-6}
Fp2-β PSD, μV^2/Hz	1,62	0,211	0,013	9,98	10^{-6}
T5-δ PSD, μV^2/Hz	1,48	0,241	0,012	9,82	10^{-6}
F4-β PSD, μV^2/Hz	1,78	0,184	0,011	9,75	10^{-6}
Entropy T6	1,73	0,192	0,010	9,69	10^{-6}
Microbian Count for St. aureus, B/Ph	1,60	0,218	0,009	9,59	10^{-6}
Laterality α, %	2,02	0,149	0,008	9,64	10^{-6}
Entropy F7	1,52	0,235	0,007	9,55	10^{-6}

A number of variables despite their recognizable properties, were outside the discriminant model, apparently due to duplication and/or redundancy of information (Table 3).

Table 3. Variables not included in the model

Variables	Groups (n) and Means±SE			Parameters of Wilks' Statistics					
	Before therapy (34)	After Naftussya (12)	After Salt Waters and N (22)	Wilks' Λ	Partial Λ	F to enter	p-level	Tolerancy	Norm Cv/σ
Deviation δ, Hz	0,73 0,05	0,71 0,10	0,57 0,04	0,007	0,979	0,33	0,725	0,364	0,66 0,405
Fp2-θ PSD, %	9,7 1,5	8,9 0,8	6,7 1,3	0,007	0,994	0,09	0,911	0,173	8,3 0,588
Fp2-θ PSD, μV^2/Hz	29 7	18 3	20 4	0,007	0,999	0,02	0,983	0,150	25 1,186
F4-α PSD, %	31,4 3,4	22,0 3,8	31,5 3,1	0,007	0,959	0,65	0,530	0,100	32,7 0,564
F7-δ PSD, μV^2/Hz	342 169	84 26	870 621	0,007	0,992	0,12	0,887	0,153	319 4,542
F8-α PSD, μV^2/Hz	37 4	37 13	23 2	0,007	0,955	0,71	0,499	0,222	40 0,957
T4-β PSD, %	29,0 2,4	33,6 4,7	37,3 4,6	0,007	0,974	0,40	0,676	0,256	27,9 0,591
T4-α PSD, %	28,0 2,9	23,0 3,2	32,6 3,9	0,007	0,997	0,04	0,963	0,113	29,2 0,628
Entropy T4	0,819 0,022	0,843 0,029	0,736 0,030	0,007	0,960	0,62	0,545	0,326	0,790 0,215
T4-θ PSD, %	9,5 1,2	9,1 0,8	6,4 0,7	0,007	0,996	0,06	0,943	0,171	8,7 0,539
C4-δ PSD, %	28,6 3,5	34,8 6,5	22,9 4,0	0,007	0,994	0,10	0,908	0,221	29,9 0,617
T6-δ PSD, μV^2/Hz	174 73	53 11	279 136	0,007	0,994	0,09	0,910	0,075	276 4,53
Entropy P3	0,797 0,024	0,851 0,032	0,771 0,025	0,007	0,975	0,38	0,687	0,261	0,804 0,155
P3-δ PSD, %	27,3 3,3	27,5 4,9	19,8 3,4	0,007	0,966	0,53	0,595	0,121	26,5 0,672
Entropy O2	0,769 0,028	0,798 0,027	0,669 0,037	0,007	0,981	0,30	0,746	0,163	0,727 0,242
O2-δ PSD, μV^2/Hz	272 117	104 19	624 338	0,007	0,942	0,93	0,407	0,200	181 2,438
Potassium Urine, mM/L	39,5 3,2	41,5 3,6	30,5 1,7	0,007	0,957	0,67	0,519	0,386	46,4 0,269
Cholecystokinetic Activity, units	553 22	584 24	675 28	0,007	0,973	0,42	0,661	0,437	624 0,131
$(Ca/K)^{0,5}$ as S/V balance	0,728 0,012	0,729 0,014	0,708 0,010	0,007	0,972	0,43	0,654	0,410	0,710 0,104
Interleukin-1, ng/L	4,94 0,19	4,36 0,37	5,17 0,30	0,007	0,987	0,19	0,825	0,428	4,51 0,173
Aldosterone, pM/L	225 5	236 10	229 4	0,007	0,982	0,27	0,764	0,516	238 0,187
ULF HRV PS, $msec^2$	73 15	139 56	110 34	0,007	0,967	0,52	0,602	0,276	122 0,892

The identifying information contained in the 35 discriminant variables is condensed into two roots. The major root contains 71% of discriminatory opportunities (r*=0,971; Wilks' Λ=0,0072; $\chi^2_{(70)}$=237; p<10^{-6}), while minor root 29% only (r*=0,934; Wilks' Λ=0,127; $\chi^2_{(34)}$=99; p<10^{-6}).

Calculating the values of discriminant roots for each patient by coefficients and constants given in Table 4 allows visualization of each patient in the information space of roots (Fig. 1).

Table 4. Standardized and raw coefficients and constants for discriminant variables

Coefficients	Standardized		Raw	
Variables	Root 1	Root 2	Root 1	Root 2
Phosphates Excretion, mM/24 h	1,447	-0,749	0,124	-0,064
Calcitonin, ng/L	0,760	-0,067	0,172	-0,015
Killing Index vs Staph. aureus, %	1,123	-0,334	0,148	-0,044
Testosterone, nM/L	-0,771	-1,043	-0,089	-0,120
Magnesium Urine, mM/L	1,093	-2,423	1,649	-3,655
Creatinine Plasma,µM/L	-0,989	-0,241	-0,078	-0,019
Laterality β, %	-0,305	-0,445	-0,012	-0,018
Sodium Plasma, mM/L	0,135	1,313	0,015	0,149
LD Cholesterol Plasma, mM/L	-0,894	0,543	-0,857	0,521
Interleukin-6, ng/L	-0,368	-1,556	-0,192	-0,813
F7-θ PSD, %	0,512	1,407	0,124	0,342
VLF HRV PS, msec^2	0,936	0,496	0,0015	0,0008
Entropy Fp2	-0,111	-0,520	-0,762	-3,557
Sodium Urine, mM/L	-3,648	-1,215	-0,120	-0,040
Chloride Urine mM/L	0,173	3,030	0,005	0,085
Phosphate Plasma, mM/L	0,052	0,099	0,279	0,527
CD3$^+$ active T-Lymphocytes, %	-0,603	0,072	-0,130	0,016
Lithogenicity Urine	0,673	-0,558	4,746	-3,934
T4-θ PSD, µV^2/Hz	-0,476	-0,863	-0,017	-0,032
Laterality θ, %	-0,389	1,942	-0,011	0,054
C3-α PSD, %	-2,167	-0,498	-0,139	-0,032
P3-α PSD, %	1,787	-0,101	0,101	-0,006
Sodium Excretion, mM/24 h	3,994	1,081	0,043	0,012
Magnesium Excretion, mM/24 h	-3,408	2,714	-1,950	1,553
Chloride Excretion, mM/24 h	0,528	-2,613	0,0056	-0,0278
HF HRV PS, msec^2	-0,758	-0,079	-0,0014	-0,0001
Glucose Plasma, mM/L	0,514	0,136	0,537	0,142
F8-δ PSD, %	-0,192	0,087	-0,007	0,003
Fp2-β PSD, µV^2/Hz	-0,996	-0,870	-0,026	-0,022
T5-δ PSD, µV^2/Hz	-0,532	-0,275	-0,0007	-0,0003
F4-β PSD, µV^2/Hz	0,857	0,181	0,0188	0,0040
Entropy T6	-0,298	-1,309	-1,901	-8,342
Microbian Count for St. aureus, Bac/Phag	-0,126	0,592	-0,015	0,071
Laterality α, %	0,159	-1,125	0,006	-0,042
Entropy F7	-0,085	0,892	-0,450	4,748
		Constants	4,70	-8,79
		Eigenvalues	16,7	6,86
		Cumulative Proportion	0,708	1

Following the accepted algorithm, Table 5 collects the Z-scores of discriminant variables together with those that are not included in the model, but still reflect the specifics of the water used.

Pseudo-staining visualizes a combination of **neuroendocrine**, **metabolic** and **immune** parameters in the structure of each root (Table 5), consistent with previously identified neuroendocrine-immune and neuroendocrine-metabolic linkages [11-17,19,21-23].

Table 5. Correlations between variables and roots, centroids of clusters and Z-scores of clusters

Variables	Correlations Variables-Roots		Before therapy (44)	After Naftus-sya (12)	After Salt Waters and N (22)
Root 1 (70,8 %)	**Root 1**	**Root 2**	-3,27	-1,11	**+5,66**
Calcitonin	**0,094**	-0,055	-1,02	-1,14	**-0,51**
Triiodothyronine			-0,85	-0,55	**-0,46**
VLF HRV PS	**0,050**	-0,039	-0,36	-0,47	**-0,01**
P3-α PSDr	**0,035**	-0,048	+0,07	**-0,15**	**+0,45**
HF HRV PS	**0,038**	0,002	-0,04	-0,03	**+0,82**
Cholecystokinetic Activity			-0,86	-0,30	**+0,62**
Killing Index vs Staph. aureus	**0,148**	-0,104	-1,28	-1,64	**-0,15**
Phosphates Excretion	**0,240**	-0,093	-0,94	-1,14	**+2,31**
Magnesium Excretion	**0,111**	-0,115	+0,29	-0,64	**+1,79**
Chloride Excretion	**0,087**	-0,011	+0,62	+1,02	**+3,16**
(UA•Ca)/(Cr•Mg)^{0,25}Lithogenicity Urine	**0,072**	-0,058	+0,59	+0,43	**+0,98**
Potassium Plasma			-0,72	-0,64	**-0,25**
Calcium Urine			-1,18	-1,09	**-0,13**
Phosphates Urine			-1,41	-1,36	**-0,42**
Laterality θ	**-0,063**	-0,052	-0,04	-0,66	**-0,98**
Entropy Fp2	**-0,060**	0,004	+0,13	-0,02	**-0,66**
T4-θ PSDa	**-0,042**	-0,043	+0,03	-0,12	**-0,16**
(Ca/K)^{0,5} Plasma as Symp/Vagal balance			+0,24	+0,23	**-0,05**
Phosphate Plasma	**-0,081**	0,096	-0,82	-0,36	**-1,43**
Potassium Urine			-0,56	-0,40	**-1,27**
Sodium Urine	**-0,111**	0,010	+0,39	+0,17	**-0,90**
Uric Acid Urine			+0,30	-0,24	**-0,65**
LD Cholesterol Plasma	**-0,031**	-0,006	+0,16	-0,11	**-0,28**
Glucose Plasma	**-0,021**	-0,007	+0,09	-0,02	**-0,15**
Root 2 (29,2 %)	**Root 1**	**Root 2**	-1,47	**+5,49**	-0,72
Laterality β	0,007	**-0,167**	+0,10	**-0,95**	+0,08
Laterality α	-0,045	**-0,096**	+0,12	**-0,71**	-0,52
Fp2-β PSDa	0,004	**-0,085**	+0,35	**-0,26**	+0,35
F4-β PSDa	0,013	**-0,060**	+0,30	**-0,11**	+0,43
C3-α PSDr	0,020	**-0,055**	+0,01	**-0,29**	+0,20
T5-δ PSDa	-0,013	**-0,049**	+0,34	**-0,14**	+0,09
Testosterone	-0,029	**-0,148**	+0,84	**-0,82**	+0,24
Parathyroid activity			-0,03	**-0,22**	+0,19
Interleukin-6	0,013	**-0,062**	+0,14	**-0,42**	+0,24
Interleukin-1			+0,50	**-0,24**	+0,78
VLD Cholesterol Plasma			+0,32	**-0,21**	+0,09
Creatinine Plasma	-0,037	**-0,111**	+0,99	**+0,18**	+0,60
Urea Plasma			+0,83	**+0,45**	+0,63
Sodium Excretion	0,022	**-0,076**	+2,17	**+0,78**	+2,58
Magnesium Urine	-0,027	**-0,047**	-0,71	**-1,05**	-0,95
Entropy F7	0,003	**0,106**	-0,22	**+0,47**	-0,13
F7-θ PSDr	0,029	**0,078**	-0,11	**+0,51**	+0,29

F8-δ PSDr	-0,034	0,072	+0,02	+0,45	-0,37
Entropy T6	-0,042	0,055	+0,15	+0,39	-0,27
ULF HRV PS			-0,45	+0,16	-0,11
Aldosterone			-0,30	-0,05	-0,19
$CD3^+$ active T-Lymphocytes	-0,063	0,110	-0,33	+0,25	-0,78
Microbian Count for Staph. aureus	-0,040	0,068	+0,12	+0,44	-0,14
Chloride Urine	-0,029	0,111	-0,85	+0,38	-1,15
Chloride Plasma			-0,26	+1,00	-0,07
Sodium Plasma	0,003	0,083	-0,71	+0,33	-0,55
Calcium Plasma			-0,66	-0,44	-0,64
Creatinine Urine			-1,69	-1,11	-2,02

The localization in the extreme right zone of the axis of the first root of the cluster of patients who received two mineral waters shows a significant increase of initially reduced or minimum for sampling parameters that are **positively** associated with the root, and reduction of initially normal or even deeper fall of initially reduced parameters correlating with the root **negatively**. Instead, in patients receiving **Naftussya** water only, these parameters remained unchanged or changed to a much lesser extent.

On the other hand, such patients are characterized by a significant **decrease**/**increase** in another number of parameters associated with the second root **negatively**/**positively**, while in combination balneotherapy their changes are insignificant or much less pronounced.

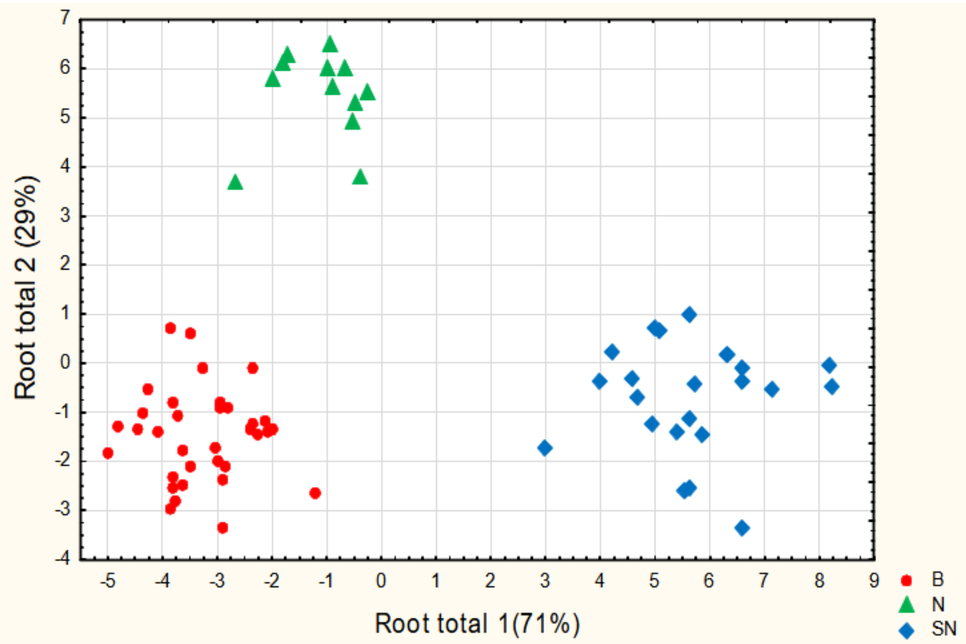

Fig. 1. Scattering of individual values of the first and second discriminant roots of patients before (circles) and after the course of drinking only water Naftussya (triangles) and in combination with water "Myroslava" or "Khrystyna" (rhombuses)

Fig. 2 illustrates that the integrated initial state of all three groups of patients was almost the same as the effect on the discriminant variables of both sulfate-chloride sodium-magnesium mineral waters.

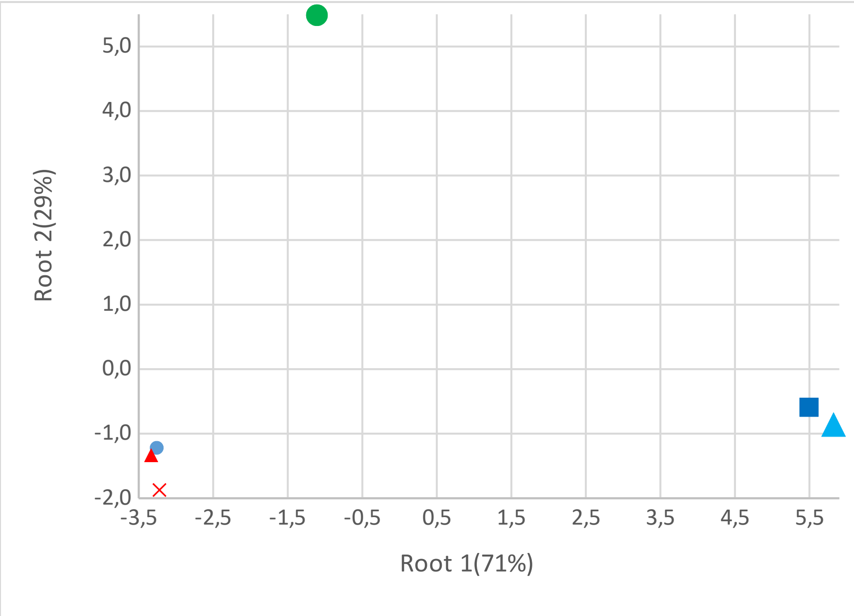

Fig. 2. Mean values (M±SD) of the first and second discriminant roots of patients before (red fill) and after the course of drinking only water "Naftussya" (circle) and in combination with water "Myroslava" (triangle) or "Khrystyna" (square)

The visual impression of a clear demarcation of the three clusters in the information field of the two roots is documented by calculating the distances of Mahalanobis (Table 6).

Table 6. Squares of Mahalanobis distances between clusters (above the diagonal) and F-criteria (df=35.3) and p-levels (below the diagonal)

Clusters	Before therapy	After Naftussya	After SW&N
Before therapy	0	53	80
After Naftussya	6,4 10^{-5}	0	84
After SW&N	14,6 10^{-6}	8,9 10^{-6}	0

Selected discriminant variables were used to identify the affiliation of a patient to a particular cluster. This goal of discriminant analysis is realized with the help of classification functions (Table7).

Table 7. Coefficients and constants of classification functions

Clusters	Before therapy	After Naftussya	After Salt W&N
Variables	p=,500	p=,176	p=,324
Phosphates Excretion, mM/24 h	-0,132	-0,310	0,929
Calcitonin, ng/L	-0,193	0,073	1,332
Killing Index vs Staph. aureus, %	1,681	1,695	2,969
Testosterone, nM/L	-1,552	-2,580	-2,434
Magnesium Urine, mM/L	-17,24	-39,09	-5,234
Creatinine Plasma, µM/L	0,956	0,654	0,243
Laterality β, %	0,346	0,195	0,223
Sodium Plasma, mM/L	6,044	7,115	6,292

LD Cholesterol Plasma, mM/L	27,72	29,49	20,46
Interleukin-6, ng/L	-15,60	-21,67	-17,92
F7-θ PSD, %	-8,705	-6,057	-7,339
VLF HRV PS, msec^2	0,036	0,045	0,050
Entropy Fp2	161,3	134,9	151,9
Sodium Urine, mM/L	0,716	0,181	-0,382
Chloride Urine mM/L	1,289	1,891	1,395
Phosphate Plasma, mM/L	159,5	163,7	162,3
CD3$^+$ active T-Lymphocytes, %	4,920	4,748	3,772
Lithogenicity Urine	135,3	118,2	174,7
T4-θ PSD, μV^2/Hz	0,758	0,501	0,579
Laterality θ, %	-0,953	-0,599	-1,010
C3-α PSD, %	2,162	1,639	0,896
P3-α PSD, %	-2,219	-2,041	-1,324
Sodium Excretion, mM/24 h	-0,041	0,132	0,349
Magnesium Excretion, mM/24 h	26,65	33,23	10,39
Chloride Excretion, mM/24 h	-0,398	-0,579	-0,368
HF HRV PS, msec^2	-0,049	-0,052	-0,061
Glucose Plasma, mM/L	22,68	24,82	27,57
F8-δ PSD, %	0,186	0,193	0,124
Fp2-β PSD, μV^2/Hz	0,506	0,295	0,260
T5-δ PSD, μV^2/Hz	0,041	0,037	0,034
F4-β PSD, μV^2/Hz	-0,399	-0,331	-0,228
Entropy T6	1,772	-60,33	-21,40
Microbian Count for St. aureus, Bac/Phag	0,501	0,962	0,420
Laterality α, %	1,040	0,759	1,062
Entropy F7	233,8	265,8	233,3
Costants	-1041	-1102	-1015

The calculation of algebraic differences between the mean Z-scores of the parameters in both groups of patients still allows us to assess the partial effects of sulfate-chloride sodium-magnesium mineral waters.

This approach suggests that sulfate-chloride sodium-magnesium mineral waters have their own (per se) more or less pronounced effect on the constellation of parameters of the neuro-endocrine-immune complex and metabolism, regardless of their initial levels (Fig. 3).

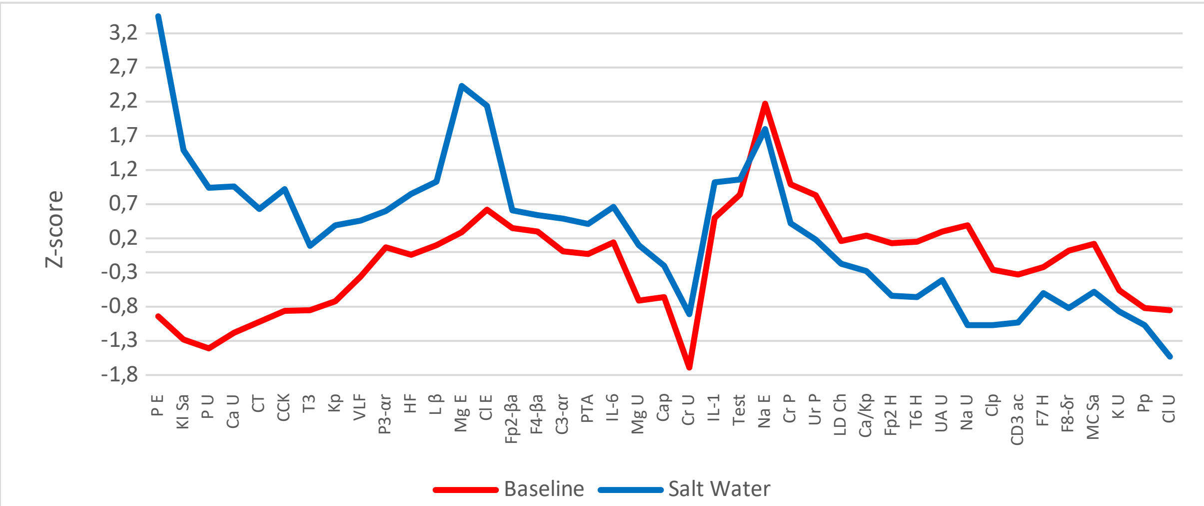

Fig. 3. Profiles of real Z-scores of initial EEG, HRV, endocrine, immune and metabolic variables and their simulated Z-scores after consumption of sulphate-chloride sodium-magnesium mineral waters

In particular, initially reduced neuroendocrine (VLF band HRV, calcitonin, triiodothyronine) and metabolic (urine concentrations of phosphate, calcium, magnesium and creatinine, phosphaturia, plasma potassium and calcium, cholecystokinetic activity) variables as well as the completion of phagocytosis of Staphylococcus aureus increase, as a rule, to the zone of norm. On the other hand, initially increased urinary excretion and concentration of sodium and plasma creatinine and urea levels are reduced. Such effects are consistent with the ancient concept of the ambivalent-balancing nature of the effects of balneal factors on the body [2].

However, there are an increase in initially normal levels of PSD of alpha rhythm in loci P3 and C3, laterality and PSD of beta rhythm in loci Fp2 and F4, vagal tone, plasma testosterone, parathyroid activity, excretion of magnesium and chloride, plasma interleukins 6 and 1, as well as a decrease in initially normal levels of EEG entropy in loci Fp2 and T6, Ca/K marker of sympathetic-vagal balance, concentration of uric acid in urine as well as LD cholesterol in plasma as well as the intensity of Staphylococcus aureus phagocytosis. The latter pattern is formed by initially reduced EEG entropy in locus F7, PSD of delta rhythm in locus F8, plasma levels of phosphate and chloride, chloride and potassium of urine, as well as active T-lymphocytes of blood, which continue to decline. Such effects do not fit into this concept, but are consistent with the known data on the diversity of responses of the neuroendocrine-immune complex and metabolism to balneal factors [15,23].

CONCLUSION

The newly created sulfate-chloride sodium-magnesium drinking mineral waters of Truskavets resort have favorable neuroendocrine, metabolic and immune effects on patients with chronic cholecystitis and pyelonephritis.

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ACCORDANCE TO ETHICS STANDARDS

Tests in patients are carried out in accordance with positions of Helsinki Declaration 1975, revised and complemented in 2002, and directive of National Committee on ethics of scientific researches. During realization of tests from all participants the informed consent is got and used all measures for providing of anonymity of participants.

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