Research article

Variation of serum serotonin values under specific peloidotherapy in patients with degenerative pathology of the lumbar spine

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Abstract: Serotonin is well known to be involved in the mediation of cognitive processes, but also in the regulation of multiple distinct physiological processes, such as pain. It is also involved in the modulation of nociception of the endogenous analgesic system. Among the monoamine neurotransmitters, serotonin plays an important role in signaling chronic pain, hence the importance of its monitoring in lumbar pain due to degenerative pathology, one of the common cause of this kind of pain. The aim of our study is to evaluate the impact of peloidotherapy on the variation of serum serotonin levels in patients with degenerative low back pain. In our study, conducted in Balneal and Rehabilitation Sanatorium of Techirghiol, we evaluated 130 patients who performed balneal and physical treatments for a period of 2 weeks. The patients were divided into 3 groups: 51 patients were enrolled into the hot mud baths group (HMB), 48 in the cold mud baths (CMB) group and 31 in the control group (CG). Each patient performed physiotherapy treatments which includes electrotherapy, massage and kinetotherapy, patients from HMB group had also hot mud therapy and patients from CMB group had cold mud therapy. Serum serotonin was dosed at admission and at discharge, for each patient, and was determined using ELISA method with kits from Demeditec Diagnostics GmbH for human serotonin. All the data from the study were statistically analized using the SPSS 22.0 program, values were interpreted as mean value and standard deviation, and we used ANOVA and t tests. The statistically significant value considered was $p < 0.05$.

1. Introduction

Balneotherapy is used for treatment of chronic degenerative low back pain with satisfactory results [1]. The use of peloid therapy dates back to antiquity [2] and the effects are divided into mechanical, thermal and chemical effects [3]. The sapropelic mud can be used in several forms: as cold baths, warm baths, mud packing or as cataplasm. The Balneal and Rehabilitation Sanatorium of Techirghiol is an important balneal unit, situated near the Black Sea, in South-Eastern area of Romania. In the sanatorium, patients benefit from complex therapies, in addition to natural factor therapies (mud and the salty water of Techirghiol Lake), they can do electrotherapy, thermotherapy, massage, kinetotherapy and hydrokinetotherapy in the pool with salt water from Techirghiol Lake, or they can do hydrokinetotherapy directly in Lake Techirghiol [4]. The benefits of

rehabilitatation treatments have multiple effects, which are still intensively studied [5, 6]. Degenerative pathology of the lumbar spine affects patients off all ages, but in recent years this changes occur even in young patients. It is an important health problem with negative effects on the quality of life of this patients, it also has an impact on socio-professional life and on the health system, raising costs [7].

Serotonin is known to be involved in the mediation of cognitive processes [8], but also in the regulation of multiple distinct physiological processes, such as pain [9].

It is also involved in the modulation of nociception of the endogenous analgesic system [10]. Among the monoamine neurotransmitters, serotonin plays an important role in signaling chronic pain. It has two effects: in peripheral nervous system it has a pro-nociceptive action, and in the central nervous system it has an anti-nociceptive action. There are several subtypes of serotonin receptors, which explains this dual action, different in peripheral than in central nervous system, practically the inhibitory effects can be exerted by activating different receptors [11]. Majority of serotonin is present in peripheral nervous system and here it acts together with other pro-inflammatory mediators, that contributes to signaling the pain produced by inflammation and other injuries.

The neurons that contain serotonin are located in raphe nuclei in the midbrain and in the brain stem. A group of neurons from the raphe nuclei descends in the posterior horn of the spinal cord to ensure the descending serotoninergic pathway. Serotonin thus acts through descending pathways to modulate pain signals in the spinal cord. Pain transmission depends on the type or subtype of active receptor, but also on environmental factors or pathological conditions [12].

2. Results

Analyzing the characteristics of our patients (Table I), the following were found: in the HMB group patients were between 29 and 70 years old, with an average age of 55.71 years; in the CMB group patients were between 42 and 70 years old, with an average age of 56.81 years; and in the CG group they were between 40 and 69 years old, with an average age of 56.97 years. The average ages of the patients in the 3 study groups are comparable, situated between 55 and 57 years. The ANOVA test reveals no statistically significant differences between the average age of the 3 groups (F = 0.309, p = 0.753 > α = 0.05).

Regarding the gender of the patients, females were predominant, in all 3 groups (62.7% - HMB, 64.6% - CMB, 54.8% - CG). Chi-square test does not show statistically significant differences between the sexes of our study patients.

Analyzing the weight of our patients – BMI values – overweight and obese patients represent 70.6% of   patients of HMB group, 81.3% of patients of CMB group and 64.5% of patients of CG group; and normal weight patients were only between 18.8% (CMB) and 35.5% (CG). ANOVA test does not reveal statistically significant differences between the average values of BMI in the 3 study groups (F = 1.400, p = 0.250 > α = 0.05), nor does the chi-quare test applied to the BMI categories in the 3 groups of patients do not reveal statistically significant differences (χ^2_{calc} =5,622, df=8, p =0,689).

In what concerns the residence of patients from our study, the majority of patients come from urban area, as following: 84.3% patients from HMB group, 87.5% patients from CMB group and 80.6% patients from CG group. Chi-square test does not show statistical differences of the origin of patients from the 3 groups studied (χ^2_{calc} =0,686, df=2, p=0,710).

Patients		Hot mud bath group	Cold mud bath group	Control group
Mean value of Age (Years)		55.71	56.81	56.97
Gender	Female	62.7%	64.6%	54.8%
	Male	37.3%	35.4%	45.2%
BMI (mean value)		27.2	29.38	27.81
BMI	Normal weight	29.4%	18.8%	35.5%
	Overweight	43.1%	39.6%	38.7%
	Grade I obesity	13.7%	22.9%	12.9%
	Grade II obesity	9.8%	14.6%	12.9%
	Grade III obesity	3.9%	4.2%	0.0%
Demographic distribution	Urban	84.3%	87.5%	80.6%
	Rural	15.7%	12.5%	19.4%

Table 1. Demographic features of our patients from study groups

More than 50% of patients enrolled in our study were diagnosed with Spondylosis (52.9% / 27 patients from HMB group, 62.5% / 30 patients from CMB group and 54.8% / 17 patients from CG group), being followed by those with Discopathy Phase III or Disc Herniation (23.5% / 12 patients from HMB group, 16.7% / 8 patients from CMB group and 29% / 9 patients from CG group), then by those with Discopathy phase II (17.6% / 9 patients from HMB group, 12% / 6 patients from CMB group and 6.5% / 2 patients from CG group) and those with Spondylolisthesis, in low percentage (5.9% / 3 patients from HMB group, 8.3% / 4 patients from CMB group and 9.7% / 3 patients from CG group) (Figure 1). Chi-square test reveals that there are no statistically significant differences between pathology of patients in the 3 groups studied (χ^2_{calc} =4,044, df=6, p=0,671).
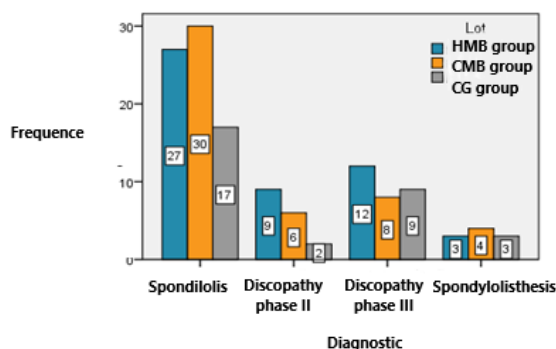

Figure 1. Diagnostic of patients from study groups

Serum serotonin values were analyzed at admission and discharge, for each patient from each group, and according to Table II and Figure 2, the values from discharge increased compared to admission. Values from HMB group registered a greater increase compared to the other two groups.

	HMB group		CMB group		CG group	
	S1 (ng/ml)	S2 (ng/ml)	S1 (ng/ml)	S2 (ng/ml)	S1 (ng/ml)	S2 (ng/ml)
Mean	121.53	213.06	118.49	159.65	114.63	125.47
Median	103.00	220.30	103.30	152.55	101.20	120.10
Standard deviation	42.72	37.75	38.51	43.72	37.13	48.97
Minimum value	75.20	116.00	76.30	90.20	77.70	70.50
Maximum value	240.80	269.50	196.90	252.20	201.60	265.30
Interval	165.60	153.50	120.60	162.00	123.90	194.80
Interquartile index	59.00	50.83	61.18	78.80	46.00	67.76

Table 2. Statistical indicators for serotonin serum values at admission(S1) and discharge (S2) for each group
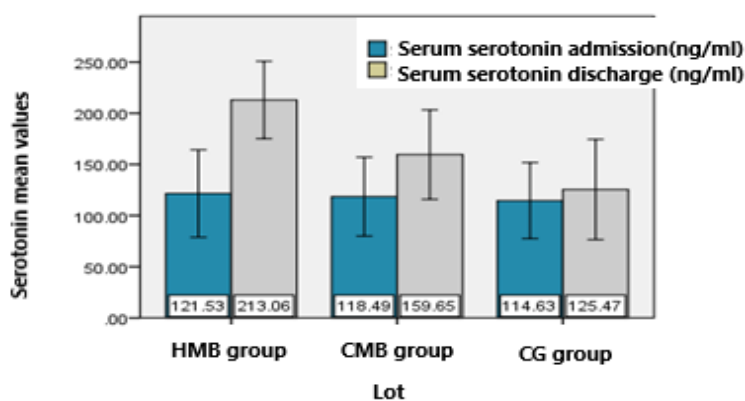
Figure 2. Box-Plot representation of serotonin serum values for each group

The increased values were statistical significant, for all 3 groups, according to table III.

Lot	Paired Samples t-Test (dependent samples)		
	t	df	p
HMB	-14.726	50	.000
CMB	-7.737	47	.000
CG	-2.109	30	.043

Table 3. Statistical indicators of t-test applied to serotonin serum values for the 3 groups.

Serum serotonin values were analyzed in patients under 50 years old and over 50 years old, and was found that the median values of serum serotonin in patients under 50 years old are higher at admission (HMB group – 189ng/ml, CMB group – 185ng/ml, CG – 196.10ng/ml) compared to the values recorded in patients over 50 years old (HMB group – 94.74ng/ml, CMB group, CG – 99.7ng/ml). The same is maintained at discharge (median values of serum serotonin in patients under 50 years old: HMB group -   251.30ng/ml, CMB group – 201.90ng/ml, CG group – 210.50ng/ml, median values of patients over 50 years old: HMB group - 217.49ng/ml, CMB group - 146ng/ml and CG group – 100.70ng/ml) (Table IV).

Age (years)		HMB		CMB		CG	
		S1 (ng/ml)	S2 (ng/ml)	S1 (ng/ml)	S2 (ng/ml)	S1 (ng/ml)	S2 (ng/ml)
(…-50)	Mean	191.57	233.74	179.57	198.67	195.68	220.33
	Median	189.00	251.30	185.00	201.90	196.10	210.50
	Standard deviation	23.24	34.98	14.30	17.54	5.26	33.05
	Minimum value	160.30	182.10	158.60	174.30	188.90	195.00
	Maximum value	240.80	269.50	196.90	221.50	201.60	265.30
	Interval	80.50	87.40	38.30	47.20	12.70	70.30
	Interquartile index	31.90	71.10	31.50	40.20	9.97	59.98
[50-…)	Mean	102.27	207.37	100.33	148.04	102.63	111.42
	Median	94.79	217.49	95.90	146.00	99.70	100.70
	Standard deviation	20.92	36.87	19.97	42.51	20.67	32.43
	Minimum value	75.20	116.00	76.30	90.20	77.70	70.50
	Maximum value	153.25	267.30	149.20	252.20	149.60	187.20
	Interval	78.05	151.30	72.90	162.00	71.90	116.70
	Interquartile index	26.23	47.79	22.70	47.92	26.30	52.75

Table 4. Statistical indicators of serum serotonin values at admission (S1) and discharge (S2) for the 3 groups of study, according to age of patients under and over 50 years old.
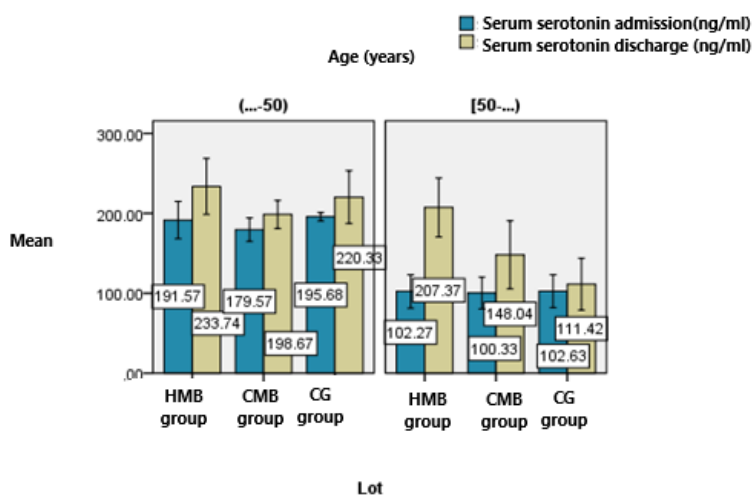

Figure 3. Box plot representation of serum serotonin values according to age of patients

Comparison between study groups		ANOVA	
		F	p
(…-50)	Admission	1.719	.201
	Discharge	4.218	.028
[50-…)	Admission	.125	.883
	Discharge	55.067	.000

Table 5. ANOVA test values for serum serotonin for patients from our study

Following the application of ANOVA test (Table V) and according to Figure 3, we had statistically significant values at discharge, for both groups of patients according to age (under 50 years old and over 50 years old) ($p<0.05$).

In the following table (Table VI and Figure 4), serum serotonin values are analyzed in comparison between female and male patients in each group. We found comparable values between the 2 genders, slightly higher values at discharge were recorded in women compared to men in HMB group, in CMB group higher values were recorded at discharge in men compared to women, and in CG group values recorded in female patients were slightly higher than male patients, both at admission and discharge.

Gender		HMB		CMB		CG	
		S1 (ng/ml)	S2 (ng/ml)	S1 (ng/ml)	S2 (ng/ml)	S1 (ng/ml)	S2 (ng/ml)
F	Mean	120.22	218.98	118.28	153.70	122.65	141.62
	Median	104.20	229.14	103.20	149.30	101.80	122.60
	Standard deviation	41.63	38.96	38.30	44.48	43.54	55.73
	Minimum value	75.20	116.00	76.30	90.20	79.30	70.60
	Maximum value	210.20	267.30	196.90	252.20	201.60	265.30
	Interval	135.00	151.30	120.60	162.00	122.30	194.70
	Interquartile index	57.51	59.17	62.90	68.03	61.97	100.05
M	Mean	123.74	203.07	118.88	170.48	104.90	105.87
	Median	103.00	193.90	104.00	165.30	92.35	95.05
	Standard deviation	45.59	34.32	40.08	41.39	25.72	30.92
	Minimum value	78.00	153.17	78.40	98.30	77.70	70.50
	Maximum value	240.80	269.50	190.80	231.90	149.60	154.50
	Interval	162.80	116.33	112.40	133.60	71.90	84.00
	Interquartile index	63.05	49.97	71.80	66.80	48.07	55.48

Table 6. Statistical indicators of serum serotonin values in patients from the 3 groups according to their gender (female – F and male - M)
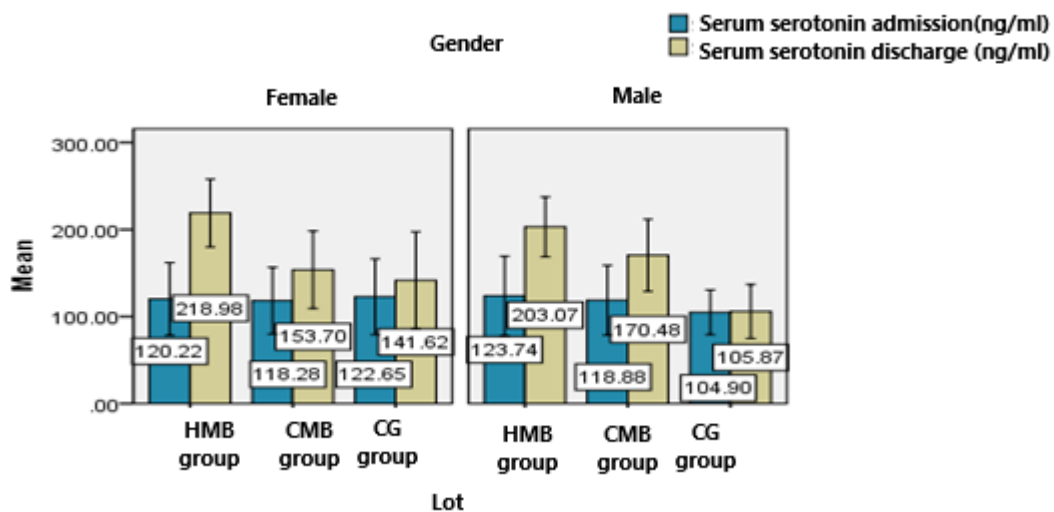
Figure 4. Box plot representation of serum serotonin values according to gender of patients

Differences recorded between values at discharge and admission are statistical significant for both genders in all patients from our study ($p<0.05$) (Table VII).

Comparison between study groups		ANOVA	
		F	p
Feminin	Admission	.064	.938
	Discharge	23.308	.000
Masculin	Admission	.974	.385
	Discharge	29.645	.000

Table 7. ANOVA test values for serum serotonin for patients from our study

Furthermore, analyzing the variation of serum serotonin values depending on the patient's weight, we noticed that normal weight patients had mean (HMB – 134,76 ng.ml and 215,53ng/ml, CMB– 140,72ng/ml and 162,23ng/ml, CG – 120,15ng/ml and 135,96 ng/ml) and median values (HMB – 108,20ng/ml and 229,60 ng/ml, CMB – 158,60 ng/ml and 176,70ng/ml, CG -101,80 ng/ml and 141,50ng/ml) higher than overweight patients (mean values: HMB – 116,02 ng/ml and 212,03 ng/ml, CMB – 113,36 ng/ml and 159,05 ng/ml, CG – 111,60ng/ml   and 119,71ng/ml, meadian values: HMB – 99,80 and 207,87 ng/ml , CMB – 102,90 ng/ml   and 152,20 ng/ml, CG – 100,70 ng/ml and 104,35 ng/ml) at admission and discharge as well.

BMI interval		HMB		CMB		CG	
		S1 (ng/ml)	**S2 (ng/ml)**	**S1 (ng/ml)**	**S2 (ng/ml)**	**S1 (ng/ml)**	**S2 (ng/ml)**
Normal weight	Mean	134.76	215.53	140.72	162.23	120.15	135.96
	Median	108.20	229.60	158.60	176.70	101.80	141.50
	Standard deviation	45.00	37.69	45.29	44.19	43.77	48.94
	Minimum value	86.90	116.00	83.90	105.20	77.70	70.50
	Maximum value	210.20	255.00	196.90	221.50	201.60	225.00
	Interval	123.30	139.00	113.00	116.30	123.90	154.50
	Interquartile index	93.10	49.60	92.30	87.50	64.60	75.80
Overweight / Obesity	Mean	116.02	212.03	113.36	159.05	111.60	119.71
	Median	99.80	207.87	102.90	152.20	100.70	104.35
	Standard deviation	41.13	38.26	35.48	44.18	33.78	49.27
	Minimum value	75.20	129.40	76.30	90.20	79.30	70.60
	Maximum value	240.80	269.50	190.80	252.20	197.00	265.30
	Interval	165.60	140.10	114.50	162.00	117.70	194.70
	Interquartile index	44.53	57.01	48.90	77.11	32.50	51.69

Table 8. Statistical indices for serum serotonin values at admission and discharge depending on patient's weight

Comparison between study groups		ANOVA	
		F	p
Normalweight	Admission	.586	.562
	Discharge	11.506	.000
Overweight	Admission	.099	.906
	Discharge	31.854	.000

Table 9. ANOVA test values applied to serum serotonin values according to patient's weight

Differences registered at discharge were statistically significant in both categories of patients, for all patients from our study ($p < 0.05$) (Table IX and figure 5).
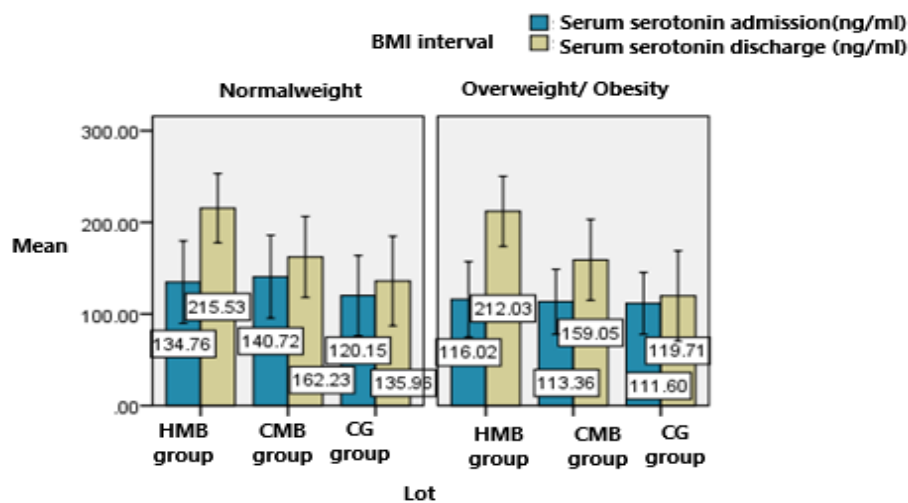
Figure 5. Box-plot representation of serum serotonin values of patients from study groups depending on their weight (normal weight or overweigh

3. Discussion

Although we evaluated a relatively small number of patients suffering from carpal tunnel syndrome, this pathology has a high incidence and prevalence worlwide[7]. In our study, it was observed that serum serotonin values increased at discharge compared to admission, alter 2 weeks of therapy. The values were higher in patients who also benefited from mud therapy, compared to patients from control group, and values at discharge from the group that performed hot mud baths were higher than values at discharge from the group that performed cold mud baths. The differences recorded in the 3 groups of patients were statistically significant, $p<0.05$. There are few studies to establish how serum serotonin evolves in patients with chronic degenerative lumbar pain. There are some studies that have highlighted the role of physical exercise in modulating serum serotonin, and also reducing chronic pain [13 - 15], or the effects of yoga-exercises which increased the serum level of serotonin [16]. Beside this kind of exercise program, there is a study that analyzed a spinal stabilization exercise program and changes in serotonin values in chronic low back pain patients, and this kind of specific exercises increased the values of serotonin [17]. Another recent study observed that magnetotherapy increase serotonin serum [18]. There are some studies that highlights the effect of peloidotherapy (hot mud bath therapy) and exercises on patients with chronic low back pain on reducing the pain [19 - 22]. However, until now, no study has been carried out to analyze the influence of complex rehabilitation treatment, which combine not only specific programs of kinetotherapy and balneal therapy with natural factors, but also electrotherapy and massage, on serum serotonin in patients with chronic lumbar degenerative pathology.

From the published research we found that serotonin decreases with age, in both women and men [23]. In our study, values recorded in patients over 50 years old were lower compared to patients under 50 years old. Although these differences were recorded between the two age groups, the rehabilitation treatments had an effect on both categories, with statistically significant differences for all patients from all 3 groups studied. It was also observed that higher values were maintained among the patients who performed hot mud baths, compared to those who performed cold mud baths, and compared to those in the control group, without mud baths.

In our study, serum serotonin values, are approximately equal in women and men, slightly higher in female patients.

Regarding the influence of body weight on serotonin values, it was found that normal-weight patients had higher levels that obese patients, as was demonstrated in other studies [24, 25]. The fact that, although overweight patients recorded lower values both at admission and at discharge, compared to normal weight patients, after rehabilitation treatments patients with higher BMI index had increased the serum serotonin values, is encouraging, because it means that these patients experienced a decrease of pain, which was the main objective of the complex rehabilitation treatment.

4. Materials and Methods

In our prospective study carried out in the Balneal and Rehabilitation Sanatorium of Techirghiol we enrolled 130 patients divided into 3 groups: 51 patients in the hot mud bath group (HMB), 48 patients in the cold mud bath group (CMB) and 31 patients in the control group (CG). For this study was obtained the Sanatorium ethical committee approval, and all patients signed informed consent of participation to the study and they have been provided all information needed for the research. The inclusion criteria for this study were the following: patients already diagnosed with chronic degenerative pathology of the lumbar spine, both women and men, with correct indication of balneal treatment. The exclusion criteria for this study were: any decompensation of any chronic disease of the patient (cardiac, respiratory, endocrine, neurologic, hepatic, renal pathology), presence of inflammation, pregnancy or breastfeeding, trophic skin disorders, oncologic diseases or psychiatric conditions.

In the hot mud bath group, patients performed the therapy with hot mod in the bathtub inside the Sanatorium, patients from the cold mud bath group performed the cold mud therapy on the shore of Lake Techirghiol, and those form the control group did not performed any mud therapy. All 130 patients had electrotherapy, massage therapy and kinetotherapy during the 2- week hospitalization. Hot mud therapy in the tub involves diluting the mud (approximated 10-15kg of mud) in a hot water tub, the patient will stay in the hot bath at 38^0C for 20-30 minutes, with a cold compress on the forehead, and it is supervised by an assistant. The application of cold mud is carried out only in the warm season, on the shore of the Lake Techirghiol. It is a contrasting therapy, which includes general heliotherapy, application of mud and immersion into salty and mineral water of the Lake. The protocol of the study included for each patient a general examination, demographic questionnaire, and dosage of serum serotonin at admission and discharge. Serotonin was determined by ELISA method using kits from Demeditec Diagnostics GmbH for human serotonin. All the data from the study were statistically processed using SPSS 22.0 program, and values was reported as mean and standard deviation, and we used ANOVA and t tests. The level of significance was considered at $p<0.05$.

5. Conclusions

Balneal therapy along with electrotherapy, massage and kinetotherapy increase serum serotonin in patients with degenerative low back pain. Serum serotonin values are directly influenced by age, BMI index, and mud therapies. Hot mud bath therapies increase serotonin more than cold mud therapies. Patients under 50 years old and patients with normal weight registered higher values of serotonin compared with older patients and obese patients.

6. Patents

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