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Research article

The impact of specific balneotherapy on the endocrine physio-pathological mechanism in obesity

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Abstract: Obesity is a complex, multifactorial metabolic pathology, within the path of modification of the endocrine system plays a significant role. Changes in growth hormone (GH) and in-sulin growth factor (IGF) have been associated with obesity in various ways, mainly through changes in GH-binding proteins, insulin and ghrelin levels. The balneal treat-ment with Techirghiol Romanian sapropelic mud has an important impact on the endo-crine system, primarily through the action on the hypothalamic-pituitary-adrenal axis. We investigated the secretory changes of the IGF-1 hormone that appeared after the balne-al treatment. It was a total number of 52 patients, divided into two groups: 1 group who performed the treatment with Techirghiol sapropelic mud at thermoneutrality tempera-tures - warm mud baths, and the second group who followed treatment with the balneal therapeutic factor in a thermal contrast regime - cold mud baths. We studied whether there are correlations between the body mass index (BMI) and the secretion of this hormone. We also determined the serum levels of blood glucose at admission and discharge. In the cold mud baths- thermal contrast therapy, can be observed a statistically significant increase in IGF-1 values during the balneal treatment ($p = 0.044 < \alpha = 0.05$). Comparative-ly, in the warm mud baths, the increase in serum IGF-1 reached values close to statistical significance at the end of the treatment ($p = 0.067 > \alpha = 0.05$). There were no statistically significant correlations between BMI and IGF-1 hormone secretion at admission and at discharge. The results showed a statistically significant decrease in blood glucose values determined at admission and discharge in the group that performed warm mud baths. The balneal treatment with sapropelic mud of Techirghiol lake, from Romania, through the impact on the endocrine system, on the hypothalamic-pituitary-adrenal axis, can be registered as a treatment with a natural therapeutic factor with an impact on obesity, therapy carried out within the parameters of metabolic safety, and the conduct of future re-search in this direction it will help develop new concepts and approaches to obesity.

Keywords: obesity, endocrine system, IGF-1, mud therapy, balneotherapy

1. Introduction

Obesity, an important metabolic pathology, is defined by the World Health Organization as an excess accumulation of body fat and has recently been receiving special attention from specialists involved in medical research, primarily due to the negative impact on the patient's quality of life, but also because abdominal obesity is a mandatory criterion for metabolic syndrome, also a pathology that has been on the rise recently [1,2].

Although the molecular mechanisms regulating the body's energy balance are fairly well known, the causes of obesity still remain unclear, as it is a complex pathology with a

heterogeneous component of the pathophysiological mechanism, with biological, social and behavioral factors being involved in addition to energy imbalances. Complications and morbidity risk generally increase with increasing body mass index (BMI) [3].

Decreased growth hormone (GH) levels and increased plasma levels of growth hormone-binding protein (GHBP) are secretory changes that commonly occur in people with obesity.

Some studies show that although GH secretory levels are reduced, there are no significant differences between insulin growth factor (IGF-1) levels in patients with BMI within the parameters for a diagnosis of obesity, compared to normal weight patients. In other studies, patients with visceral obesity, even if they did not have positive diagnostic criteria for the metabolic pathology that is the subject of this study, showed low serum IGF-1 levels [4,5].

Clinical situations have also been reported in which serum free IGF-1 concentration is elevated in obese patients, who also show elevated GHBP, which raises the hypothesis that low GH levels may demonstrate increased peripheral sensitivity to this hormone. The mechanism of increased sensitivity may be due to the hyperinsulinemia that frequently occurs in obese patients. As a result, insulin-like growth factor binding protein-1 (IGFBP-1) levels decrease and IGF-1 increases, but within physiological parameters, even though serum GH levels are low in obesity. Within this mechanism, there is a hypothesis of negative feedback, whereby increased IGF-1 levels lead to decreased GH secretion. This is a possible peripheral mechanism and not a central one [6].

Other hypotheses that may explain the abnormal GH response in obesity include increased fatty acids and leptin [5]. Changes in growth hormone - GH secretion and plasma GH concentrations decrease with age, both basally and in response to provocative stimuli, and there is a parallel decrease in serum IGF-1 concentrations [7,8].

In obesity, glucose metabolism shows changes, supported by the presence of hyperglycemia and a statistical correlation between BMI and glycemia in the obese patient. The involvement of the pancreas, through quantitative dysfunction of insulin synthesis and decreased insulin sensitivity, are at least two important mechanisms by which the above changes are scientifically explained [2, 9].

Balneotherapy with therapeutic factors specific to the Techirghiol area, the sapropelic mud and salty lake water with mineral content, has a stimulating effect on the activity of the hypothalamic-pituitary-adrenal axis, with modulation of cellular metabolic activity [10].

Under the action of mud and/or mud extract, a harmonic stimulation is produced in all endocrine glands in the sense of increasing enzymatic and synthetic activity, but preserving the specificity of each. The general reactivity of the organism is thus modulated and directed towards optimal parameters. This natural therapy does not act selectively on a single system of the body, but its action takes place simultaneously improving several dysfunctions and imbalances of the metabolism [10, 11].

The aim of the paper is to demonstrate the importance of the natural therapeutic factor, the sapropelic mud of Techirghiol in the therapeutic management of obesity.

2. Results

2.1 Distribution of patients included in the research in the two study groups: cold mud baths (CMB) and warm mud baths (WMB), according to the age ranges considered

The study included 52 patients divided into two groups: the CMB group (15 patients, 28.8%) and the WMB group (37 patients, 71.2%). 11 patients aged 50-65 years (73.3%) and 4 patients aged 65-80 years (26.7%) belonged to the CMB group; 32 patients aged 50-65 years (86.5%) and 5 patients aged 65-80 years (13.5%) belonged to the WMB group (Table 1).

Table1. Distribution of patients included in the research distributed in the two study groups according to the age ranges considered

Group * Age ranges (years)

			Age ranges (years)		Total
			[50-65)	[65-80)	
Group	CMB	Number	11	4	15
		% in Group	73,3%	26,7%	100,0%
		% Age ranges (years)	25,6%	44,4%	28,8%
		% from Total	21,2%	7,7%	28,8%
	WMB	Number	32	5	37
		% in Group	86,5%	13,5%	100,0%
		% Age ranges (years)	74,4%	55,6%	71,2%
		% from Total	61,5%	9,6%	71,2%
Total		Number	43	9	52
		% in Group	82,7%	17,3%	100,0%
		% Age ranges (years)	100,0%	100,0%	100,0%
		% from Total	82,7%	17,3%	100,0%

2.2. Distribution of patients included in the research according to the predominant type of activity carried out

The study followed 52 patients distributed according to the predominant type of activity: physical activity (29 subjects, 55.8%), intellectual activity (23 subjects, 44.2%) (Table 2).

Table 2 Distribution of patients included in the research according to the predominant type of activity carried out

Activity		Frequency	Percentage	Valid Percentage	Cumulative Percentage
Valid	Physical	29	55,8	55,8	55,8
	Intellectual	23	44,2	44,2	100,0
	Total	52	100,0	100,0	

2.3. Distribution of patients included in the research according to their background

52 patients were followed up in the study distributed according to their background: urban (44 subjects, 84.6%), rural (8 subjects, 15.4%) (Table 3).

Table 3. Distribution of patients included in the research according to their background

Background		Frequency	Percentage	Valid Percentage	Cumulative Percentage
Valid	Urban	44	84,6	84,6	84,6
	Rural	8	15,4	15,4	100,0
	Total	52	100,0	100,0	

2.4. Distribution of the patients included in the research from the both groups analyzed in comparison to admission and discharge, according to their clinical and paraclinical features: IGF-1, glycemia (Table 4,5,6,7)

Tabel 4 - Statistical analysis of the patients included in the research from the CMB group analyzed compared to admission and discharge according to the variation in IGF-1 levels

Pair	Differences Pair						t	Df	Sig. (2-tailed) (p)
	Average	SDA	SDD	Standard error of the mean	95% Confidence interval for differences				
					Minimum	Maximum			
IGF-1 (A) [ng/mL] - IGF-1 (D) [ng/mL]	-22,16	33.61	52.70	10,00	-43,61	-0,71	-2,21	14	0,044

SDA- standard deviation admission, SDD- standard deviation discharge

For the CMB group patients: at admission the mean value of IGF-1 is MAdmission = 129.22 ng/mL and the standard deviation of SDAdmission = 33.61 ng/mL; at discharge the mean value of IGF-1 is MDischarge = 151.38 ng/mL and the standard deviation of SDDischarge = 52. 70 ng/mL. Significant differences exist between the mean values of the IGF-1 variable measured at the two time points: MDif = -22.16 ng/mL; t = 2.21; df = 14; p = 0.044 < α = 0.05; 95%ICDif = (-43.61, -0.71) ng/mL.

Tabel 5 - Statistical analysis of the patients included in the research from the WMB group analyzed compared to admission and discharge according to the variation in IGF-1 levels

Pair	Differences Pair						t	df	Sig. (2-tailed) (p)
	Average	SDA	SDD	Standard error of the mean	95% Confidence interval for differences				
					Minimum	Maximum			
IGF-1 (A) [ng/mL] - IGF-1 (D) [ng/mL]	-9,52	34,26	34,24	5,04	-19,76	0,70	-1,88	36	0,067

SDA- standard deviation admission, SDD- standard deviation discharge

For the WMB group patients: at admission the mean value of IGF-1 is MAdmission = 141.70 ng/mL and the standard deviation of SDAdmission = 34.26 ng/mL; at discharge the mean value of IGF-1 is MDischarge = 151.23 ng/mL and the standard deviation of

SDDischarge = 34. 24 ng/mL. There are NO significant differences between the mean values of the IGF-1 variable measured at the two time points: MDif = -9.52 ng/mL; t = -1.88; df = 36; p = 0.067 > α = 0.05; 95%ICDif = (-19.76, 0.70) ng/mL.

Tabel 6- Statistical analysis of the patients included in the research from the CMB group analyzed compared to admission and discharge according to the variation in glycemia levels

Pair	Differences Pair						T	df	Sig. (2-tailed) (p)
	Average	SDA	SDD	Standard error of the mean	95% Confidence interval for differences				
					Minimum	Maximum			
Glycemia (A) [mg/dl] – Glycemia (D) [mg/dl]	6,79	17.68	23.46	3,64	-1,02	14,60	1,86	14	0,083

SDA- standard deviation admission, SDD- standard deviation discharge

For the patients of the CMB group: At admission the mean value of Glycemia is MAdmission = 107.73 mg/dL, and the standard deviation of SDAdmission = 17.68 mg/dL; at discharge the mean value of Glycemia is MDischarge = 100.94 mg/dL, and the standard deviation of SDDischarge = 23. 46 mg/dL. There are NO significant differences between the mean values of the Glycaemia variable measured at the two time points: MDif = 6.79 mg/dL; t = 1.86; df = 14; p = 0.083 > α = 0.05; 95%ICDif = (-1.02, 14.60) mg/dL.

Tabel 7 - Statistical analysis of the patients included in the research from the WMB group analyzed compared to admission and discharge according to the variation in glycemia levels

Pair	Differences Pair						t	Df	Sig. (2-tailed) (p)
	Average	SDA	SDD	Standard error of the mean	95% Confidence interval for differences				
					Minimum	Maximum			
Glycemia (A) [mg/dl] – Glycemia (D) [mg/dl]	7,04	18.72	9.11	2,88	1,20	12,89	2,44	36	0,020

SDA- standard deviation admission, SDD- standard deviation discharge

For patients of the WMB Group: On admission the mean value of Blood Glucose is MAdmission = 102.37 mg/dL and the standard deviation of SDAdmission = 18.72 mg/dL; on discharge the mean value of Blood Glucose is MDischarge = 95.32 mg/dL and the standard deviation of SDDischarge = 9. 11 mg/dL. Significant differences exist between the

mean values of the Glycemia variable measured at the two time points: MDif = 7.04 mg/dL; t = 2.44; df = 36; p = 0.020 < α = 0.05; 95%ICDif = (1.20, 12.89) mg/dL.

2.5. Correlation of IGF-1 levels and BMI of patients in the two groups at admission and discharge (Table 8 and Table 9)

Table 8. Statistical analysis of the correlation between the Body Mass Index (BMI) of the patients included in the research in the CMB group at the time of admission (A) and discharge (D) according to the variations in IGF-1 levels.

	IGF-1 (A) [ng/mL]	IGF-1 (D) [ng/mL]	BMI [Kg/m2] (A)	BMI [Kg/m2] (D)
Pearson correlation (r)	1	1	0,210	-0,109
Sig. (2-tailed) (p)			0,453	0,698
N	15	15	15	15

The two variables (IGF-1/ BMI) for CMB group at admission and discharge are NOT correlated (r = 0.21; p = 0.453 > α = 0.05) – A, (r = -0.109; p = 0.698 > α = 0.05) – D.

Table 9. Statistical analysis of the correlation between the Body Mass Index (BMI) of the patients included in the research in the WMB group at the time of admission (A) and discharge (D) according to variations in IGF-1 levels.

	IGF-1 (A) [ng/mL]	IGF-1 [ng/mL (D)	BMI [Kg/m2](A)	BMI [Kg/m2] (D)
Pearson correlation (r)	1	1	-0,004	-0,195
Sig. (2-tailed) (p)			0,983	0,248
N	37	37	37	37

The two variables (IGF-1/ BMI) for WMB group at admission and discharge are NOT correlated (r = 0.004; p = 0.983 > α = 0.05) – A, (r = 0.195; p = 0.248 > α = 0.05) – D.

3. Discussion

The results showed in the group that performed cold mud baths a statistically significant increase (p = 0.044) of IGF-1, the variation of this hormone demonstrating the positive effect of balneotherapy with contrasting factors in patients with grade 1 obesity, correlating with those studies in the literature, where the presence of low values of IGF-1 in obesity is demonstrated [4]. It should also be mentioned that the patients included in the study were over 50 years of age, and there is also an association between age and low hormonal activity on the endocrine GH-IGF-1 axis, associated with significant morbidity in adulthood, with an increased risk of developing cardiovascular disease, obesity, diabetes, osteoporosis and neurodegenerative diseases, with definite implications in modulating aging. Metabolic regulation, including energy metabolism, in these patients depends on tight regulation of the GH-IGF axis and maintenance of optimal IGF-1 action [12]. Optimal activity of this hormonal axis is involved in both increased lifespan, with metabolic changes within physiological limits, and increased resistance to oxidative stress [13].

The results showed in the group that performed warm mud baths an increase close to statistical significance (p=0.067) of IGF-1. The trend of quantitative increase at discharge, but not at the statistically significant values observed in thermal contrast peloid therapy underlines overall the general positive effect of balneotherapy in obesity, if we

refer to studies in the literature in which the increase of IGF-1 secretory values has a positive effect on this pathology. [14]. I believe that further studies including a larger number of participants are needed for statistical validation.

It should be noted that in both study groups the hormonal variation is within physiological limits, consistent with most studies in the literature that clearly emphasize altered parameters in obesity, but within optimal physiological limits in terms of hormonal changes in IGF-1 [14,10]. Increased IGF-1 levels have been linked in some studies to cancer risk, given the role of this hormone in mediating normal and malignant tissue growth [12].

In both study groups there were no statistically significant correlations between IGF-1 secretory levels and BMI, both in terms of values recorded at admission and at discharge. There is insufficient data in the literature to show statistical associations between these hormone values and BMI determination [15].

There are studies attesting that both variables, serum hormone values and BMI determination are correlated with age-dependent pathologies, with statistical correlation and BMI varying with age [16]. There is a negative correlation, but without statistical significance, between BMI and age 58-86 years, but a positive correlation between age group 87-110 years and BMI [16]. Age over 50 years was the inclusion criterion in the present study. The data from the statistical analysis show that all 52 patients were in the age group 50-80 years, which indicates the need in the future to widen the age range to patients over 80 years. However, it should be mentioned that this age group, due to the comorbidities that may be associated with them, may fall under exclusion criteria, not being able to perform complex treatment with natural healing factors [10]. The association of age, obesity, can lead to other concomitant metabolic pathologies [13].

Physical activity is a determining factor in maintaining body mass within normal limits, appropriate to age and sex, and an important component in the therapeutic management of the patient with obesity [17]. Individual behaviors are important risk factors [18]. It is noted that the patients enrolled in this study, patients with stage 1 obesity, were professionally engaged in 55.8% of physical activity, compared to the rest of the patients whose profession required intellectual activity, with less physical effort, compared to the first category.

The prevalence of obesity and metabolic syndrome is in most studies higher in the urban population of developing countries compared to the Western population, primarily due to increased consumption of rapidly processed, high calorie foods but with decreased quality of ingested food nutrients and decreased physical activity due to industrialization, mechanization and sedentary form of leisure and profession [19]. However, there are also studies showing that obesity, a major public health problem, affects both developed and developing societies. The urban environment appears to be an important individual risk factor in the recent epidemiological literature on obesity, but scientific evidence still requires future studies for scientific validation [18]. The data from the current study correlate with the literature, with 84.6% of the patients subjected to statistical analysis being from urban areas. There may also be the problem of lower addressability of rural patients to medical rehabilitation services, either due to poor infrastructure, financial situation or intellectual possibility of understanding the importance of attending regular medical check-ups.

Blood glucose levels showed a decrease in both study groups within physiological limits statistically significant in the warm mud bath group ($p=0.020$) and consistent with data from the medical literature: stress-induced increase in cortisol secretion rate accelerates glucose metabolism and reactive oxygen species production [20]. Thus, balneotherapy is useful in controlling blood glucose by activating the adaptive, energy-consuming antioxidant process in the obese patient. It should be noted that the patients included in the study did not present blood glucose values indicating serum hyperglycemia level. Clinical studies show the frequent existence of altered glucose metabolism, through the presence of elevated blood glucose values, without specific reference to grade 1 obesity [2,9].

The variation within physiological limits of the analyzed parameters demonstrates the metabolic safety of the application of natural factors within the Techirghiol area in patients with obesity.

It is very important that this study is continued, with the inclusion of a larger number of patients and the extension of the parameters for the classification of obesity. This would allow to study the relationship of the variables to be investigated with other categories of obesity, such as grade 2, 3 or morbid obesity.

Considering that studies in the literature have clearly shown reductions in plasma GH levels in obesity, but there is still no consensus regarding IGF-1 levels in obese compared to normal-weight individuals [4-6], the following scientific approach can be considered: study of IGF-1 hormonal variation, in parallel with GH variation, considering that the secretion of this hormone is pulsatile, even if in adults the values are more stable, the oscillations being attenuated by GHBP. It is known that a single determination of GH is of limited value [21], which is why future studies could include determinations of both basal hormone values and after stimulation tests (determinations can be made after the patient participates in an established physiotherapy program involving varying degrees of physical exertion).

4. Materials and Methods

The study presented in this scientific work is a retrospective study, carried out on patients admitted to the Techirghiol Spa and Recovery Sanatorium (SBRT), between March and August 2022, patients who meet the following inclusion criteria:

- Patients with BMI-30-34.99-Obesity grade 1;
- Patients over 50 years of age who have the correct indication for balneotherapy.

Exclusion criteria from the study:

- Patients with BMI different from inclusion in Obesity grade 1;
- Any of the situations listed as contraindications for balneotherapy; presence or appearance of inflammatory phenomena; cardiac and/or blood pressure decompensation during treatment; skin lesions; respiratory, endocrine, neurological decompensation;
- Cortisone medication or any other type of medication which could interfere with the parameters determined (diuretics, taking food supplements containing minerals or containing glucose).

The study group comprised 52 patients, in compliance with the inclusion and exclusion criteria, and the rules for the preparation of a scientific paper. The study started after obtaining the ethical advisory opinion of the Balneal and Rehabilitation Sanatorium of Techirghiol ethical board, number 15708/12.10.2022.

Subjects were divided into two groups as follows:

- Group 1 – 15 subjects (warm mud bath - WMB): performed 5 thermoneutral peloid applications - general mud baths (MB) alternating with 5 general saline baths (SB), 3 adjuvant electrical procedures per day, 1 session of regional massage therapy per day and 1 session of physiotherapy per day.
- Group 2 37 subjects (cold mud bath - CMB): carried out 10 sludge applications in a mud ointment - contrasting factor therapy regimen (progressive general heliotherapy, mud ointment, lake immersion) in the summer months, 3 adjuvant electrical procedures per day, one session of regional massage therapy per day and one session of physiotherapy per day.

In Group 1 (WMB) the endocrine secretory response of the body is studied through the variation of IGF-1, the variation of endocrine metabolic status in patients with grade 1 obesity under thermoneutral, minimally demanding peloid therapy on the body.

In Group 2 (CMB) the endocrine secretory response of the body is studied through the variation of IGF-1, the variation of the endocrine metabolic status in patients with grade 1 obesity, under contrasting peloid therapy (progressive general heliotherapy, cold mud anointing and immersion in lake water), intensely stimulating on the body.

Patients were distributed for treatment by the hospital's diagram for scheduling procedures.

Patients in the 2 groups were assessed on admission at discharge at the same time of day due to circadian variation in plasma levels of biohumoral constants: BMI, IGF-1, glycaemia.

BMI was calculated using the Body Mass Index calculator based on the weight (kg) and height (cm) of each patient.

IGF-1 values were determined by the chemiluminescence detection immunochemical (CLIA) method, taking into account that they are age and sex dependent, and limits and interferences of these determinations were also considered.

A BTS 350 semiautomatic analyzer was used for blood glucose determination.

5. Conclusions

The balneotherapy carried out with natural healing factors specific to Lake Techirghiol, Romania, by the impact it has on the harmonized functionality of the endocrine system [10], in particular through the hypothalamic-pituitary-adrenal axis, can be considered a treatment with positive impact on the patient with obesity, the therapy being carried out in conditions of metabolic safety, especially on glucose metabolism. In the future, studies involving a larger number of patients are needed so that the impact of balneotherapy on other degrees of obesity can be observed.

Further studies on natural factors are very important in today's science-based medicine, as natural products need to have all their therapeutic properties determined in the current scientific context and the existence of pathologies that are increasing in frequency in the context of the existing lifestyle worldwide, pathologies on which natural therapeutic factors can have an important therapeutic response.

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Informed Consent Statement: Informed consent was obtained from all subjects involved in the study.

Data Availability Statement: The data presented in this study are available on request from the corresponding author.

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