The Role of Non-Pharmacological Treatment for Osteoporosis at Patients with High Plasmatic Concentration of ACTH

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Cushing disease is characterized by the hypersecretion of adrenocorticotropic hormone (ACTH) due to a pituitary adenoma that causes endogenous hypercortisolism by stimulating adrenal glands. Objective of the study was to analyse the benefits of the physical therapy for patients with ACTH-secreting adenomas osteoporosis.This retrospective study was performed at Craiova, Bunavestire Hospital, the patients were monitorized during 6 months and included 17 patients with ACTH-secretingadenomas. Participants in this study group exercised 3 days a week for 6 consecutive months. Each session is intended to take approximately 60 minutes to complete and will comprise of a warm-up, progressive resistance training using medium weights, moderate impact weight-bearing exercises, flexibility and also stretching exercises. Physical therapy for osteoporosis treatment in patients with ACTH-secreting adenomas improved joint mobility and reduced pain, significantly increasing BMD performed by DEXA in group I patients compared to patients included in group II. Pain relief is evident following evaluation using the VAS rating scale. The increase in joint mobility is observed following the goniometric measurement from day 1 to the end of treatment. Applying the physical therapy program the bone pain and joint mobility was improved, physical therapy can modify bone turnover in the sense of increasing the body mass.

Keywords: ACTH secreting adenomas, physical therapy, osteoporosis

ACTH-secreting pituitary adenomas (Cushing disease), one of more important causes of high plasmatic concentration of ACTH, represent 4.8%–10% of endocrine-secreting pituitary adenomas and occur more frequently in females compared with males (F:M ratio is 3:1) [1]. Cushing disease is often associated with osteoporosis(40% of cases) accompanied by vertebral compressions and spinal injuries, therefore, beside the medical treatment, is very important to include, a long-term non-pharmacological therapy based on kinetic methods [2].

The pituitary adenoma are endocrine benign tumors with the origin in the epithelial cells of adenohypophysiswhich evolute, having functional manifestations, polymorphic endocrines (hypo- or hyper-secretions symptoms) and tumoral syndrome of compression of adjacent tissues. The functioning (endocrine-active) tumors include almost 70% of pituitary tumors which produce 1 or 2 hormones, measurable in the serum and cause definite clinical syndromes, that are classified based on their secretory product(s). But non-functioning adenomas are endocrine-inactive tumors [3].

Pituitary adenomas are benign tumors from the epithelial pituitary cells and they represent 10-15%of intra-cranial tumors. They can be found at 3% up to 20% of the population, on autopsy series [4]. These tumors can be hormonally active; they clinically manifest by acromegaly (excessive secretion of growth hormone), Cushing syndrome (ACTH and secondary of cortisol excess), amenorrhoea-galactorrhea syndrome (prolactine excess) or it can be hormonally inactive (dysfunctional clinical tumors). From the historical point of view pituitary tumors are mostly benign. The adenoma secreted by PRL or prolactine is the most frequent type of secretive pituituraytumor (about 39%), followed by GH secretive adenomas and ACTH secretive tumors.[5]. Cushing's disease is considered a rare condition characterized by the hypersecretion of the adrenocorticotropic hormone (ACTH) due to a pituitary adenoma that ultimately causes endogenous hypercortisolism by stimulating the adrenal glands. The clinical signs suggesting Cushing's disease, such as obesity, moon face, hirsutism, and facial plethora, psychiatric and neurocognitive changes, decreased libido, and osteoporosis [2]. Endogenous hypercortisolism is associated with an increased risk of cardiovascular and metabolic manifestations, as well as respiratory disorders, psychiatric complications, osteoporosis and infections, leading to high rates of morbidity and mortality. Hypercortisolism causes insulin resistance and impaired glucose tolerance, leading to diabetes mellitus in patients with Cushing's disease (20–50%)[6].

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Experimental part

Materials and methods

This retrospective study was performed at Craiova, Bunavestire Hospital, the patients were monitorized during 6 months.

The morning serum hypercortisolism measured by immunoassay test and plasma ACTH high levels detected on patients confirm the biochemical diagnosis of Cushing disease with a pituitary source and excluding other ectopic sources.

The present study includes 17 patients with Cushing disease who have muscular and joint pain were divided in 2 groups:

-group I - 9 patients with Cushing disease diagnosed with secondary osteoporosis receiving analgesic and anti-resorptive medication as well as physical therapy programme;

-group II - included 8 patients with same characteristics as group I, which didn't received the physical therapy programme.

The physical therapy treatment improve the posture and the alignment of the body segments, ameliorate balance and coordination, increasing the strength and the muscle resistance and joint mobility.

Participants in this study group exercised 3 days a week for 6 consecutive months. Each session is intended to take approximately 60 minutes to complete and will comprise of a warm-up, progressive resistance training using free weights, moderate impact weight-bearing exercises, flexibility and also stretching exercises.

Results and discussions

It is well accepted that the incidence of Cushing disease is higher among women than among men, with new cases diagnosed at the ratio of 3–8 : 1[7], but in this study we registered 11 women and 6 men with ACTH secreting adenomas.

The average distribution of patients by age has revealed that osteoarticular pathology is more frequent between 30 – 50 years. In our study we found 8 cases (5%) with ages between 30 – 39 years, 6 cases (8,75%) with ages between 40 – 49 years, and only 3 cases (3.75%) with ages between 20 – 29 years.

As for the 17 patients diagnosed with Cushing disease there has been performed serum ACTH dosing and as a result there were higher values than the upper limit (over 37,23pg/ml). At the Cushing disease patients the ACTH average was 88,62pg/ml, with a minimum of 62.08pg/ml and a maximum of 115,24pg/ml and serum cortisol was higher values than the upper limit (31.52mcg/dl) with an average levels by 49.91mcg/dl.

Physical therapy for osteoporosis treatment in patients with ACTH-secreting adenomas improved joint mobility and reduced pain, significantly increasing BMD performed by DEXA in group I patients compared to patients included in group II. Pain relief is evident following evaluation using the VAS rating scale. The increase in joint mobility is observed following the goniometer measurement from day 1 to the end of treatment.

Clinical and functional evaluation was performed using the VAS pain rating scale and goniometer measuring from day 0 to the last day of kinetic program. The parameter studied was the visual analogue scale (VAS) for pain, used to assess the antialgic effect of therapy. Patient pain assessment was performed using VAS scales from day 1 to the end of the proposed kinetic program. Evaluation of knee joint mobility was done using the goniometer measuring all degrees of motion, analysing knee flexion and extension from day 1 to the end of treatment. Thus we calculated the average value of the initial and final score of the scale showed by a graphical comparison of the obtained results (Figs. 1,2, 3).

Table 1
VAS SCALE FOR STUDY GROUP

Current No	Name	Initial VAS	Final VAS
1.	B.N	8	3
2.	A.F	9	4
3.	N.A	7	2
4.	S.N	6	1
5.	T.P	8	2
6.	V.C	9	3
7.	Z.N	9	2
8.	F.O	10	4
9.	D.N	6	1
10.	A.L	4	0
11.	I.P	10	4
12	G.R	6	2
13	C.L	6	1
14	I.I	4	0
15.	A.X	10	6
16	Z.V	7	4
17	A.C	8	3
Average Value		**7.5**	**2.5**

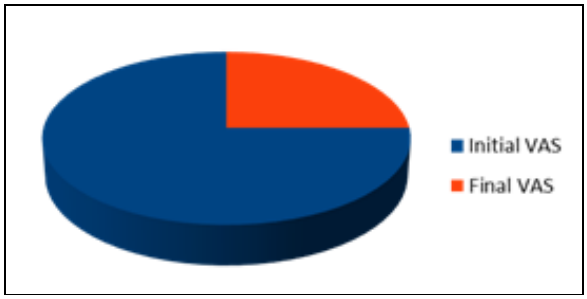

Fig.1. Average value of VAS scale

Table 2
VALUES OF KNEE FLEXION

Current No	Name	Initial Flexion	Final Flexion
1.	B.N	90˚	112˚
2.	A.F	110˚	121˚
3.	N.A	105˚	125˚
4	S.F	94˚	118˚
5.	T.P	87˚	110˚
6	V.C	85˚	105˚
7	Z.N	93˚	110˚
8.	F.O	72˚	97˚
9.	D.N	103	120
10.	A.L	110˚	120˚
11.	I.P	70˚	96˚
12.	G.R	100˚	124˚
13.	C.L	107˚	117˚
14.	I.I	108˚	119˚
15.	A.X	69˚	96˚
16	Z.V	81˚	105˚
17	A.C	97˚	110˚
Average Value		**93˚**	**112˚**

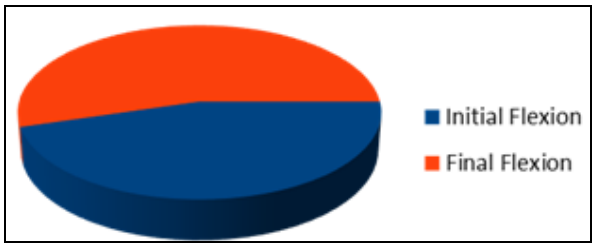

Fig.2. Average value of flexion

Table 3
VALUES OF KNEE EXTENSION

Current No	Name	Initial Extension	Final Extension
1.	B.N	15˚	10˚
2.	A.F	18˚	5˚
3.	N.A	20˚	13˚
4	S.F	19˚	11˚
5.	T.P	18˚	9˚
6	V.C	26˚	10˚
7	Z.N	15˚	5˚
8.	F.O	16˚	0˚
9.	D.N	19˚	7˚
10	A.L	29˚	12˚
11.	I.P	21˚	5˚
12.	G.R	15˚	0˚
13.	C.L	27˚	13˚
14.	I.I	21˚	6˚
15.	A.X	17˚	8˚
16	Z.V	27˚	13˚
17	A.C	30˚	14˚
Average Value		**20.7˚**	**8.3˚**

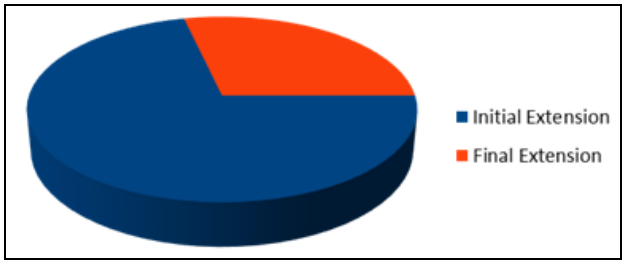

Fig.3 Average value of extension

Pathological values at Cushing disease patientswe have obtained was the following (Fig. 4):

- Systolic HTA at 8 patients (47.05%) and diasistolic HTA at 1 patient (5.88%);

-AV over 80 beats /min at 2 patient (11.76%);

-Hyperglycemia (glicemia over 110 mg/dl) at 2 patients (11.76%), with type 2 diabetes mellitus confirmed at 4 patients (23.52%);

-Hypercholesterolemia at 9 patients (52.94%);

-Hypertriglyceridemia (triglycerides over 150 mg) at 5 patients (29.41%);

- 5 patients (29.41%) had ACTH secretive macroadenoma and 12 patients (70.58%) had microadenoma (smaller than 10 mm diameter);

-hepatic steatosis and increased visceral adipose tissue was detected on 3 patients (17.64%).

- after 6 month of therapy the physical performance was increased, joint and muscle activity in Cushing disease and also cardiovascular performance were improved; total cholesterol, glycemia values and systolic HTA were also decreased at the patients group who received physical therapy.

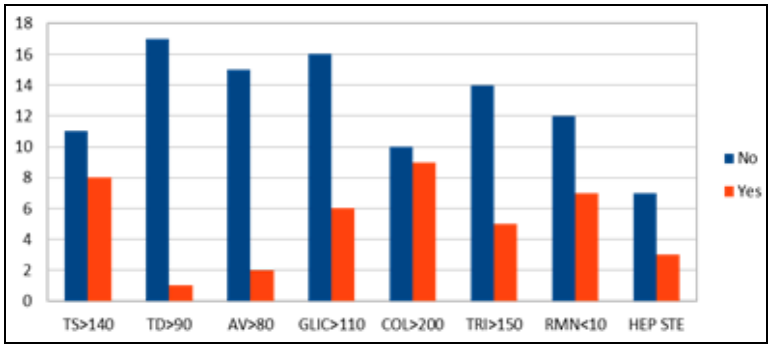

Fig. 4. Pathological values at Cushing disease patients

From the 17 patients diagnosed with Cushing disease,4 patients (23.52%) had cardiac structural and functional alterations including left ventricular hypertrophy, 7 patients (41.17%) had ischemic cardiopathy symptoms but 6 patients (35.29%) had a normal EKG.

Many cardiovascular risk factors, including hypertension, diabetes, obesity, and dyslipidaemia, are improved upon resolution of hypercortisolism, but an increased cardiovascular risk may persist and manifest in the long term [8]. Patients with Cushing's disease have severe atherosclerosis damage; persistence of metabolic syndrome, vascular damage, and atherosclerosis plaques after normalizationof cortisol levels contributes to a high cardiovascular risk despite treatment [9]. Factors contributing to the increased thrombosis risk include a long duration of uncontrolled hypercortisolism, glucocorticoid-induced hypercoagulability, and obesity [6]. This risk is thought to be already present 1–2 years before diagnosis of Cushing's disease and may remain for months after surgery [8].

Depressive disorders and other kind of disorders associated to Cushing disease were: 13% of ACTH secretive pituitary tumor had a severe depression (mania, anxiety disorders, demoralization, irritable mood), quality of life of patients with Cushing's disease is compromised at 8% while 5% present a light depression and only 2.5% didn't present any symptoms of depression.[10,11,13-16] The risk of depression at the Cushing disease patients is higher than the risk of this psychiatric manifestation at other pituitary affections. Symptoms noticed at Cushing patients were: psycho-emotional lability, physical and psychical asthenia, loss of initiative, inhibition, tendency of social isolation, amnesic difficulties, mania, psychosis, irritability, depressive ideation, panic attack, fatigue, anxiety, maladaptive personality [12,17-21].

Conclusions

Within the studied group we had 11 women and 6 men with a frequent incidence of age group 30-39 years.

47.05% of the patients had systolic HTA, 2 patients (5.88%) had HTA diastolic, diabetes mellitus type 2 was found at 4 patients and dyslipidemia was presented at 9 patients.

All patients who received exercise therapy had improvements in decreasing total cholesterol, glycemia values and systolic HTA was improved.

Physical therapy for osteoporosis treatment in patients with ACTH-secreting adenomas improved joint mobility and reduced pain, significantly increasing BMD performed by DEXA in group I patients compared to patients included in group II, ameliorating the quality of their lives, mental state and the mood of this patients.

Physical therapy can correct posture and alignment of segments by toning body muscles, especially abdominal, improving balance and coordination, protecting the vertebral spine, reducing the rate of bone degradation.

The risk of depression at the Cushing disease patients is important than the other psychiatric manifestation at pituitary affections. Quality of life of patients with Cushing's disease is compromised at 8% while 5% present a light depression and only 2.5% didn't present any symptoms of depression.

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