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GENERAL ARTICLE

GRAVES OPHTHALMOPATHY –TERAPEUTICAL ALTERNATIVES

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Abstract

Graves disease associates thyroid and non-thyroid symptoms and signs with autoimmune pathogeny, including the ophthalmopathy. The treatment of Graves ophthalmopathy consists of medical immunosuppressive therapy, retrobulbar injections and general treatment. Recently, Somatostatin injections have proved their efficiency.
Keywords: ophthalmopathy, hyperthyroidism, Somatostatin

Objective

The study indented to compare therapeutic effects of classic treatment with cortisone derivates in separated or associated both general (Prednisone) and local periocular administration (Diprophos), and effectiveness of neurohormonal treatment, less known, with Somatostatin subcutaneously [**1,2**].

Materials and methods

The study included 63 patients (50 women - 79.3% and 13 men - 20.7%), with Graves ophthalmopathy rated according to clinical-paraclinical evaluation indices which compose the ophthalmopathy score [**3**]. Patients had various degrees of ophthalmopathy depending on the severity of the lesions, rated from 0 to 6, according to the American Thyroid Association [**4**].

The patients were differently treated, with Somatostatin subcutaneously, one vial per day for 14-21 days or cortisone derivates following one of the next regimens:

- The general route: orally, Prednisone tablets of 5mg, 40-150 mg/ day;
- Local injection, parabulbary: Diprophos 2 vials/ week, 10-12 seepage;
- Combined both oral and periocular steroids.

Following a period of three months, the severity of Graves ophthalmopathy was again evaluated according to clinical and paraclinical assessment indices, aiming to score the ophthalmopathy evolution in patients treated with steroids and those treated with Somatostatin.

Table 1. Ophthalmopathy grades in Graves disease

THE DEGREE OF DAMAGE	SCORE
Periocular soft tissues damages:	
• Mild	1
• Moderate	2
• Severe	3
Exophthalmos (mm):	
• 16	0,2
• 17	0,4
• 18	0,6
• 19	0,8
• 20	1
• 21	2
• 22	3
• ≥23	4
Differential intraocular pressure (mm Hg):	
• 1	0,1
• 2	0,2
• 3	0,3
• 4	0,4
• 5	0,5
• 6	0,6
• 7	0,7
• 8	0,8
• 9	0,9
• 10	1,0
Diplopia:	
• Intermittent	1
• Inconstant	2
• Constant	3
Cornea:	
• Initial injury	1
• Ulceration	2
• Opacification/perforation	3
Optic neuropathy:	
• Evoked visual potentials - abnormal	3
• Visual acuity = 0,5- 0,9	5
• Visual acuity = 0,1 – 0,4	7
• Visual acuity < 0,1	9

Table 2. Ophthalmopathy grades in Graves disease

DEGREE	SIGNS AND SYMPTOMS
0	Without signs and symptoms. Without symptoms, just signs.
1	Objective: • Retraction of upper eyelid • Fixed gaze • Oculo-palpebral asynergy • Proptosis until 22mm.
2	Impairment of soft tissue (conjunctival congestion, chemosis, eyelid edema).
3	Exophthalmos (proptosis) over 22 mm was measured with exophthalmometer: Normal • Caucasian ≤ 20 mm • Yellow race ≤ 18 mm • Black race ≤ 22 mm Pathological: • +3 – 4 mm = mild exophthalmos • +5 – 7 mm = medium exophthalmos • +8 and more = severe exophthalmos CT scan can estimate the size of the eyeball and the dynamic of retroocular intraorbital space.
4	Impairment of external eye muscles (with diplopia, limitation of the eyeballs motricity).
5	Corneal damage (ulceration, opacity, necrosis, perforation).
6	Loss of vision (optic nerve damage).

Table 3. Distribution of patients according to the degree of Graves ophthalmopathy (G.O.)

G.O. DEGREE	I	II	III	IV	V	VI
Number of patients	9	25	20	9	-	-
% patients	14%	40%	32%	14%	-	-
Number of men	-	6	4	1	-	-
% men	-	9 %	7%	2%	-	-
Number of women	9	20	15	8	-	-
% women	14%	32%	24%	12%	-	-
No. patients treated with PREDNISON	4	6	1	9	-	-
No. patients treated with DIPROPHOS	-	3	3	-	-	-
No. patients treated with Prednisone + Diprophos	-	3	6	3	-	-
% patients treated with PREDNISON	7%	10%	2%	5%	-	-
% patients treated with DIPROPHOS	-	5%	5%	-	-	-
% patients treated with Prednisone + Diprophos	-	5%	10%	5%	-	-
No. Patients treated with SMS	4	12	9	3	-	-
% patients treated with SMS	7%	19%	14%	5%	-	-

Table 4. Distribution of treatment regimens on studied patients

TREATMENT	No. Patients	% patients	No. Men	% Men	No. Women	% Women
Steroid therapy	35	55%	27	43%	8	12%
Prednisone (P)	16	26%	16	26%	-	-
Diprophos (D)	6	10%	1	2%	5	8%
Combined (P+D)	12	19%	9	14%	3	5%
Somatostatin	28	45%	24	38%	4	7%

Table 5. Comparing G.O. score before and after the treatment with steroid therapy

G.O. Score	BEFORE STEROIDIC THERAPY						AFTER STEROIDIC THERAPY					
	No. patients	% patients	No. W	% W	No. M	% M	No. patients	% patients	No. W	% W	No. M	% M
4 – 5	-	-	-	-	-	-	3	5%	3	5%	-	-
5 – 6	-	-	-	-	-	-	3	5%	3	5%	-	-
6 – 7	-	-	-	-	-	-	8	12%	6	10%	1	2%
7 – 8	1	2%	1	2%	-	-	6	10%	5	8%	1	2%
8 – 9	1	2%	1	2%	-	-	5	8%	1	2%	3	5%
9 – 10	3	5%	3	5%	-	-	5	8%	5	8%		-
10 – 11	5	14%	8	12%	1	2%	3	5%	1	2%	-	2%
11 – 12	4	7%	3	5%	1	2%	3	5%	3	5%	1	-
12 – 13	3	5%	3	5%	-	-	-	-	-	-	-	-
13 – 14	3	5%	5	8%	1	2%	-	-	-	-	-	-
14 – 15	5	8%	1	2%	3	5%	-	-	-	-	-	-
15 – 16	3	5%	3	5%	-	-	-	-	-	-	-	-
16 – 17	1	2%	1	2%	-	-	-	-	-	-	-	-

Table 6. Comparing G.O. score before and after the treatment with SMS

G.O. SCORE	BEFORE THERAPY WITH SMS						AFTER THERAPY WITH SMS					
	No. patients	% patients	No. F	% F	No. B	% B	No. patients	% patients	No. W	% W	No. M	% M
7 – 8	-	-	-	-			-	-	-	-	-	-
8 – 9	-	-	-	-			6	10%	-	-	1	2%
9 – 10	6	10%	5	8%	1	2%	6	10%	5	8%	1	2%
10 – 11	5	8%	5	8%	-	-	5	8%	5	8%	-	-
11 – 12	5	8%	3	5%	1	2%	5	8%	5	8%	-	-
12 – 13	5	8%	5	8%	-	-	3	5%	1	5%	1	2%
13 – 14	6	10%	5	8%	1	2%	5	8%	5	8%	-	-
14 – 15	-	-	-	-	-	-	-	-	-	-	-	-
15 – 16	1	2%	1	2%	-	-	-	-	-	-	-	-
16 - 17	1	2%	1	2%	-	-	-	-	-	-	-	-

Table 7. Comparing G.O. score before and after both therapies

G.O. SCORE	STEROIDIC THERAPY				SMS			
	BEFORE		AFTER TREATMENT		BEFORE		AFTER TREATMENT	
	No. patients	% patients	No. patients	% patients	No. patients	% patients	No. patients	% patients
0	-	-	4	7%	-	-	-	-
I	4	7%	18	28%	4	7%	11	17%
II	13	21%	12	19%	12	19%	11	17%
III	11	17%	-	-	9	14%	8	12%
IV	6	10%	-	-	3	5%	-	-
V	-	-	-	-	-	-	-	-
VI	-	-	-	-	-	-	-	-

Results and discussion

1.Steroid treatment has been more effective in improving the signs and symptoms of eyes involvement in G.O., compared to the treatment with Somatostatin.
2.In the studied group, combined cortisone treatment (oral prednisone and periocular Diprophos) was proven to be more effective compared to the group treated only with oral prednisone [**5**].
3.The work points out that local anti-inflammatory and partly immunosuppressive effect provided by periocular steroid is certainly higher and safer compared to the group treated only with oral prednisone.
4.The variations of therapeutic results obtained with Somatostatin can be explained by the differences in density of periocular distributed Somatostatin receptors, due to a genetic individual program [**6**].
5.Technical possibilities of identifying the Somatostatin receptors (by indium 111-labeled Ocreotide scintigraphy) would allow a judicious selection of patients, with maximal therapeutic benefit.

Conclusions

1.Graves ophthalmopathy treatment requires a competent therapeutic approach, applied to patients at the right time.
2.General and local steroid therapy is an effective treatment, safe and fast, in controlling infiltrative processes.
3.Although effective, Somatostatin therapy is limited by individual patient response, based on the existing specific hormone retroocular receptors.

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