

Investigations of ocular changes, extraocular muscle thickness, and eye movements in Graves' ophthalmopathy

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Key words: Graves' ophthalmopathy; ocular changes; extraocular muscles; echography; eye movements.

Summary. The aim of this study was to evaluate ocular changes, to measure the thickness of extraocular muscles, and to assess eye movements in patients with active Graves' ophthalmopathy.

Material and methods. We examined 27 patients (18 women and 9 men) with Graves' ophthalmopathy. Their age ranged from 17 to 59 years; mean age was 42.7 ± 2.9 years. The control group consisted of 30 healthy persons aged 43.6 ± 2.6 years. All patients underwent a complete ophthalmic examination including best-corrected Snellen visual acuity testing, measurements of proptosis using Hertel exophthalmometer, echography using A/B mode Mentor™ Advent ultrasonic diagnostic imaging system, ocular motility, slit-lamp and ophthalmoscopic examination.

Results. The examination showed a significant increase of proptosis, periorbital edema in 66.67%, chemosis in 59.26%, injection of conjunctiva in 45.15% of patients. The majority of patients with infiltrative form of Graves' ophthalmopathy had a significant enlargement of medial rectus muscle (from 5.0 to 5.9 mm in 46.3%, from 6.0 to 6.9 mm in 22.22% of eyes) and inferior rectus muscle thickness (from 5.0 to 5.9 mm in 33.33%, from 6.0 to 6.9 mm in 24.07% of eyes), disturbances in upward (less than 30° in 62.96%) and lateral eye movements (from 30 to 50° in 77.78%).

Conclusions. The results of ocular examination showed an increase of proptosis, periorbital edema, chemosis and injection of conjunctiva in patients with Graves' ophthalmopathy. Ultrasound investigations showed a marked increase in the volume of medial and inferior eye muscle. In patients with Graves' ophthalmopathy, the changes in ocular motility (upward and lateral gaze) were detected.

Introduction

Graves' ophthalmopathy (thyroid ophthalmopathy, thyroid eye disease, thyroid-related ophthalmopathy, orbitopathy) is an autoimmune disorder and is often associated with thyroid pathology (1, 2). Usually it appears in patients with active or treated Graves' disease. Graves' ophthalmopathy can cause eyelid retraction, lagophthalmos, periorbital and lid edema, injection and edema of the bulbar conjunctivae, proptosis (exophthalmos), inflamed caruncle, increased orbital pressure, corneal exposure, disturbances in ocular motility, diplopia, and optic neuropathy (3). Proptosis and optic neuropathy can be explained mechanically by the edema and enlargement of retrobulbar tissue and extraocular muscles. These changes result because of lymphocytic infiltration, activation of fibroblasts, accumulation of collagen and glycosaminoglycans (4, 5).

Careful orbital ultrasonography, computed tomography, magnetic resonance imaging analysis can help to measure the thickness of the extraocular muscles. These methods reveal the swelling of extraocular muscle involved in Graves' ophthalmopathy by showing the enlargement of the muscles and increased volume of orbital fat. The thickness of extraocular muscles and ocular motility are not frequently investigated in patients with Graves' ophthalmopathy.

The objective of the present study was to evaluate the thickness of extraocular muscles and eye movements in patients with Graves' ophthalmopathy.

Material and methods

There were 27 (18 women and 9 men, 54 eyes) patients with Graves' ophthalmopathy in the study. Their mean age was 42.7 ± 2.9 years (range from 17 to

59 years). The control group consisted of 30 healthy persons aged 22 to 62 years (the mean age was 43.6 ± 2.6 years).

Graves' ophthalmopathy was present in 14 (51.85%) hyperthyroid, 6 euthyroid (22.22%), 4 (14.81%) hypothyroid patients, and in 3 (11.11%) patients with Hashimoto's thyroiditis. The duration of the disease was less than one year in 11 patients (40.74%), one to two years in 9 (33.33%), and more than two years in 7 (25.93%).

All patients underwent a complete ophthalmic examination including best-corrected Snellen visual acuity testing, proptosis measurement by Hertel exophthalmometer, ocular motility, slit-lamp (soft tissue changes) and ophthalmoscopic examination. The diagnosis of Graves' ophthalmopathy was based on standard clinical features and the measurements of extraocular muscle thickness by echography. The measurements of extraocular muscles (medial, lateral, inferior, and superior rectus) were performed using A/B mode Mentor™ Advent ultrasonic diagnostic imaging system with a 7.5 MHz transducer. The probe was placed on the side of the globe opposite the muscle to be examined. Eye movements were examined by the method of kinetic perimetry.

Results were statistically analyzed by using Student's t-test. P values less than 0.05 were considered statistically significant.

Results

The majority of patients had corrected visual acuity of 1.0. The mean visual acuity was 0.97 ± 0.28 .

In patients with Graves' ophthalmopathy, the mean of exophthalmos was 20.83 ± 0.64 mm ($p < 0.001$). We found that overall patients with Graves' ophthalmopathy had a greater degree of proptosis. The mean value of ocular protrusion in healthy persons was 15.62 ± 0.58 mm. Asymmetry of exophthalmos was present in 14.81% of patients. Periorbital edema was found in 66.67% of patients, chemosis – in 59.26%, conjunctival injection was noted in 48.15% of patients. Diplopia was found in 6 (22.22%) patients. Ultrasono-

graphic investigations showed that in healthy persons, the thickness of medial rectus was 3.83 ± 0.08 mm, superior rectus – 3.5 ± 0.09 mm, lateral rectus – 3.67 ± 0.08 mm, inferior rectus – 3.58 ± 0.07 mm. The amplitude of movement to the lateral side was $51.4 \pm 0.26^\circ$, downward – $58.7 \pm 0.17^\circ$, medial – $49.3 \pm 0.24^\circ$, upward – $38.3 \pm 0.23^\circ$.

The majority of patients with infiltrative form of Graves' ophthalmopathy had a significant enlargement of medial rectus (from 5.0 to 5.9 mm in 46.3%, from 6.0 to 6.9 mm in 22.22% of eyes) and inferior rectus thickness (from 5.0 to 5.9 mm in 33.33%, from 6.0 to 6.9 mm in 24.07% of eyes). The thicknesses of extraocular muscles are shown in Table 1 and Fig. Medial rectus thickness was 5.1 ± 0.12 mm, inferior rectus – 5.5 ± 0.13 mm ($p < 0.001$). Inferior and medial recti were the most affected muscles, although the superior and lateral muscles were involved too. The thickness of superior rectus (from 5.0 to 5.9 mm in 31.48% of eyes) and lateral rectus (from 5.0 to 5.9 mm in 44.44% of eyes) was enlarged also.

Ultrasonography is a useful tool to assess the degree of extraocular muscle thickening, which indicates the need for very careful monitoring of eye movements.

In patients with Graves' ophthalmopathy, a statistically significant decrease in the amplitude of upward ($34.22 \pm 0.66^\circ$, $p < 0.001$) and lateral movements ($45.44 \pm 0.83^\circ$, $p < 0.001$), reflecting the impairment of inferior and medial rectus, was observed. The disturbances of upward movement (less than 30°) were present in 34 (62.96%) eyes, lateral movement (from 30 to 50°) – in 42 (77.78%) eyes (Table 2). Limitation of inward and downward movements also was noted. Limitation to the medial side (less than 30°) was present in 39 (72.2%) eyes and to the inferior side (30 to 50°) – in 10 (37.04%) eyes.

Discussion

In Graves' ophthalmopathy, the inflammatory cells are present within the orbital tissues and surrounding extraocular muscles (6–11). Graves' ophthalmopathy represents frequent inflammatory state of the orbital

Table 1. The thickness of extraocular muscles in patients with Graves' ophthalmopathy

Rectus muscle	The thickness of extraocular muscle			
	<5.0 mm eyes, n (%)	5.0–5.9 mm eyes, n (%)	6.0–6.9 mm eyes, n (%)	>6.9 mm eyes, n (%)
Inferior	22 (40.74)	18 (33.33)	13 (24.07)	–
Medial	13 (24.07)	25 (46.30)	12 (22.22)	4 (7.41)
Lateral	22 (40.74)	24 (44.44)	8 (14.81)	–
Superior	33 (61.11)	17 (31.48)	4 (7.41)	–

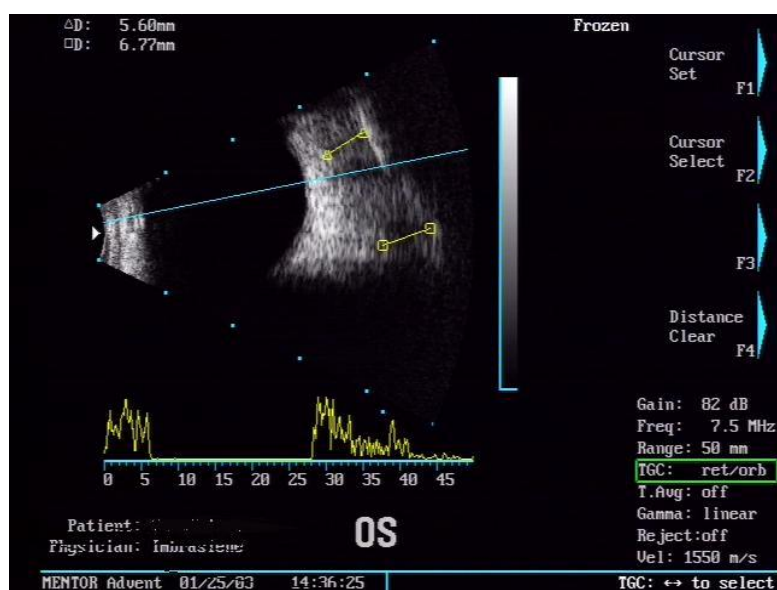


Fig. The thickness of rectus medial muscle in patient with Graves' ophthalmopathy

Table 2. Disturbances of movements in patients with Graves' ophthalmopathy

Movement	The amplitude of ocular movements		
	<30° eyes, n (%)	30–50° eyes, n (%)	>50° eyes, n (%)
Upward	34 (62.96)	20 (37.04)	–
Outward	2 (3.7)	42 (77.78)	10 (18.52)
Inward	2 (3.7)	39 (72.22)	13 (24.08)
Downward	–	21 (38.89)	33 (61.11)

tissues and extraocular muscles. The disturbances in eye movements may be with or without diplopia (1, 3, 12, 13). Diplopia is caused by external eye muscle dysfunction, either due to the presence of lymphocytic infiltration and edematous swelling in active Graves' ophthalmopathy or fibrosis in inactive disease of the muscles. Marked swelling of the extraocular muscles may be demonstrated by ultrasonography, computed tomography, and magnetic resonance imaging (12–16). The enlarged extraocular muscles can be detected by A-scan or B-scan ultrasonography or by computerized tomography and magnetic resonance imaging (14–16).

The examination showed a significant increase of proptosis, periorbital edema, chemosis and injection of conjunctiva.

We have found the swelling of extraocular muscles, especially of medial and inferior rectus muscles in patients with Graves' ophthalmopathy. Ultrasound alone or in combination with clinical or laboratory parameters, however, is not sufficient and often mis-

leading in the assessment of extraocular muscle diameter and thickness (12). The most common abnormality of extraocular motility in Graves' ophthalmopathy in our study was the limitation of upward and lateral gaze. It may be due to fibrosis of the inferior and medial rectus muscles, which often results in diplopia on upward and lateral gaze.

Conclusions

1. Ocular examination showed an increase of proptosis, periorbital edema, chemosis and injection of conjunctiva.

2. The results of ultrasound examination showed a marked increase in the volume of the medial and inferior rectus muscle in patients with Graves' ophthalmopathy.

3. In patients with Graves' ophthalmopathy, the changes in ocular motility (especially upward and lateral gaze) were detected.

4. These findings showed the impairment of the inferior and medial rectus muscles.

Sergančiųjų Greivso oftalmopatija akių pakitimų, išorinių akių raumenų storio ir akių judesių tyrimai

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Raktažodžiai: Greivso oftalmopatija, akių pakitimai, judesiai, akių tiesieji raumenys, ultragarsinis tyrimas.

Santrauka. Darbo tikslas. Įvertinti akių pokyčius, išmatuoti išorinių akių tiesiųjų raumenų storį ir įvertinti akių judesius ligoniams, sergantiems Greivso oftalmopatija.

Tyrimo medžiaga ir metodai. Ištyrėme 27 ligonius (18 moterų ir 9 vyrus), sergančius Greivso oftalmopatija. Jų amžius – nuo 17 iki 59 metų; amžiaus vidurkis – 42,7±2,9 metų. Kontrolinę grupę sudarė 30 sveikų asmenų, kurių amžius – 43,6±2,6 metų. Visiems ligoniams atliktas oftalmologinis tyrimas: regėjimo aštrumo įvertinimas, biomikroskopija ir oftalmoskopija, išverstakumo ir akių judesių tyrimai, ultragarsinis A/B skenavimas.

Rezultatai. Sergančiųjų Greivso oftalmopatija tyrimai parodė ryškų išverstakumą, junginių paburkimą (59,26 proc.) ir paraudimą (48,15 proc.), akiduobės audinių paburkimą (66,67 proc.), tiesiųjų akių raumenų sustorėjimą (vidinio nuo 5,0 iki 5,9 mm – 46,3 proc., nuo 6,0 iki 6,9 mm – 22,22 proc., apatinio nuo 5,0 iki 5,9 mm – 33,33 proc., nuo 6,0 iki 6,9 mm – 24,07 proc.), akių judesių sutrikimą (į viršų mažiau nei 30° – 69,96 proc., į šoną nuo 30° iki 50° – 77,78 proc.).

Išvados. Akių tyrimų duomenys rodo ryškų išverstakumą, akiduobės aplinkinių audinių paburkimą ir paraudimą sergant Greivso oftalmopatija. Ultragarsiniai tyrimai parodė tiesiųjų raumenų sustorėjimą (ypač vidinio ir apatinio). Sergantiejiems Greivso oftalmopatija nustatyta akių judesių (ypač į viršų ir šoną) pokyčių.

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References

1. Jankauskienė J, Imbrasienė D, Jankauskaitė D. Investigation of extraocular muscles thickness and eye movements in Graves' ophthalmopathy. Zabolevanija, opukholi i travmaticheskie povrezhdenija orbity: sbornik nauchnikh trudov mezhdunarodnogo simpoziuma. Moskva; 2005. p. 169-73.
2. Jankauskienė J, Paunksnis A, Bluzienė A, Saulgozis J. The effect of pulsed electromagnetic field in patients with endocrine ophthalmopathy. Eur J Ophthalmol 1998;8:253-7.
3. Yamada M, Li AW, Wall JR. Thyroid-associated ophthalmopathy: clinical features, pathogenesis and management. Crit Rev Clin Lab Sc 2000;37:523-49.
4. Mourits MP, Koornneef L, Wiersinga WM, Prummel MF, Berghout A, van der Gaag R. Clinical criteria for the assessment of disease activity in Graves' ophthalmopathy: a novel approach. Br J Ophthalmol 1989;73:639-44.
5. Aniszewski JP, Valyasevi RW, Bahn RS. Relationship between disease duration and predominant orbital T cell subset in Graves' ophthalmopathy. J Clin Endocrinol Metab 2000;85:776-80.
6. Kiljanski JI, Peele K, Stachura I, Pickeral J, Stolarski C, Kennerdell JS, Wall JP. Antibodies against striated muscle, connective tissue and nuclear antigens in patients with thyroid-associated ophthalmopathy: should Graves' disease be considered a collagen disorder? J Endocrinol Invest 1997;20:585-91.
7. Bahn R S, Gorman CA, Johnson CM, Smith TJ. Presence of antibodies in the sera of patients with Graves' disease recognizing a 23 kilodalton fibroblast protein. J Clin Endocrinol Metab 1989;69:622-8.
8. Bahn RS, Heufelder AE. Pathogenesis of Graves' ophthalmopathy. New Eng J Med 1993;329:1468-75.
9. Hatton MP, Rubin PAD. The pathophysiology of thyroid-associated ophthalmopathy. Ophthalmol Clin North Am 2002; 15:113-9.
10. Joffe BI, Panz VR, Yamada M, Wall JR. Thyroid-associated ophthalmopathy in black South Africans with Graves' disease: relationship to serum antibodies reactive against eye muscle and orbital connective tissue autoantigen. Endocrine 2000;13:325-8.
11. Wakelkamp IM, Gerding MN, Van Der Meer JW, Prummel MF, Wiersinga WM. Both Th1- and Th2-derived cytokines in serum are elevated in Graves' ophthalmopathy. Clin Exp Immunol 2000;121:453-7.
12. Wiersinga WM, Prummel MF. Pathogenesis of Graves' ophthalmopathy: current understanding. J Clin Endocrinol Metab 2001;86:501-3.
13. Nagy EV, Toth J, Kaldi I, Damjanovich J, Mezosi E, Lenkey A, et al. Graves' ophthalmopathy: eye muscle involvement in patients with diplopia. Eur J Endocrinol 2000;142:591-7.
14. Gerding MN, Prummel MF, Wiersinga WM. Assessment of disease activity in Graves' ophthalmopathy by orbital ultrasonography and clinical parameters. Clin Endocrinol 2000;52:641-6.
14. Kahaly GJ. Imaging in thyroid-associated orbitopathy. Eur J Endocrinol 2001;145:107-18.
15. Schenome M, Polizzi A, Buono C, Ciurlo C, Ciurlo G. Graves' disease: measurement of the extraocular muscle thickness with the echobiometer. Ophthalmologica 1998;212:104-6.
16. Scott IU, Siatkowski MR. Thyroid eye disease. Semin Ophthalmol 1999;14:52-61.

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