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A Single Center Experience of Intravenous Corticosteroid Bolus Doses in Graves' Ophthalmopathy

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Abstract

Exophthalmos makes up a clinical manifestation very frequent in Graves' disease. European Group on Graves' Orbitopathy proposes intravenous glucocorticoids to treat severe, moderate-to-severe and active Graves' orbitopathy as the first line treatment.

The aim of our study is to report results obtained with patients treated for Graves' ophthalmopathy with this protocol in real life.

It is a descriptive and analytical study involving the whole patients with Graves' ophthalmopathy which activity score ≥3 or who had an optical neuropathy. Evaluated parameters before and after treatment were GO activity score, quality of life and corticosteroid therapy complications.

In total, 21 patients received corticoid boluses for Graves' ophthalmopathy. Sex ratio men/women was 3.2 with the average age of 37.4±11 years old. Graves' ophthalmopathy activity score before corticosteroid boluses were 4.5±0.8 with a slight insignificant increase (p=0.58) in smokers (score=4.64) compared with non smokers (4.43). Concerning the seriousness, 8 patients were admitted with severe exophthalmos and 13 showed a moderate-to-severe exophthalmos. Evolution under treatment has been marked by noticeable improvement. Mean activity score was significantly reduced to 1.95±0.74 (p< 0.0001) at the end of 12 boluses and kept at 1.14±0.91 (p< 0.0001) 6 months after the first bolus. Concerning the alteration impact of vision on the quality of life (Q1-8), the score changed from 56±11.5 before boluses to 82.3±11 after boluses (p< 0.0001); furthermore psychosocial impact score raised from 41.9±12 before boluses to 57.4±9.6 after boluses (p< 0.0001).

These encouraging results support the use of methylprednisolone bolus in Graves' ophthalmopathy.

Keywords: Hyperthyroidism; Graves' disease; Exophthalmos; Corticoid; Activity score; Quality of Life

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Introduction

Exophthalmos makes up a clinical manifestation very frequent in Graves' disease. Its treatment is a real genuine problem due to its potential seriousness and the patient's gene linked to functional and aesthetic risks. European Group on Graves' Orbitopathy (EUGOGO) proposes intravenous glucocorticoids to treat severe, moderate-to-severe and active Graves' Orbitopathy (GO) as the first line treatment [1]. The aim of our study is to report results obtained with patients treated for Graves' ophthalmopathy with this protocol in real life.

Materials and Methods

It is a descriptive and analytical study involving the whole patients with Graves' ophthalmopathy which activity score ≥3 or that had an optical neuropathy from December 2012 to May 2016. Graves' disease or Basedow disease was defined as hyperthyroidism associated with a clinical vascular goiter and/or with positive anti-TSH receptor antibodies and/or scintigraphic signs. EUGOGO recommended methylprednisolone with a starting dose of 0.5 g once a week during 6 weeks, followed by 0.25 g once a week during 6 weeks (4.5 g cumulative dose) in most cases of moderate-to-severe and active GO. Patients underwent systematic clinical check up and consultation in ophthalmology; they had also benefited before treatment an assessment including fasting blood glucose, blood count, liver enzymes, renal assessment, urine culture, serology for hepatitis B and C, tuberculin skin test to suspicious radiological image or history of tuberculosis. Moreover adjuvant treatment with dietary measures has been established and regular clinical and biological monitoring has been advocated. The parameters evaluated before and after treatment have been the score's activity, the quality of life and corticosteroid therapy complications.

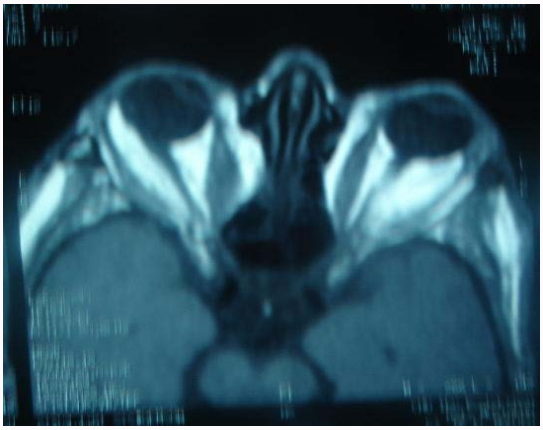

Figure 1: Bilateral exophthalmos Grade III.

Quality of life was assessed by Graves' Ophthalmopathy-Quality of Life (GO-QoL) questionnaire recommended by EUGOGO and available in 8 languages [1]. This questionnaire includes 16 questions Weighted 0 to 100. Statistical analysis was made by SPSS 20.0 software.

Results

In total, 21 patients with Graves' ophthalmopathy were candidate to a corticosteroid protocol during the study's period. Sex ratio man/woman was 3.2 with the average of 37.4±11 years old. Exophthalmos life was about 2.35±1 years old. Nineteen patients were having carbimazol and two benefited therapy for recurrence. An active smoking was noticed in 14 men (67%). Graves' ophthalmopathy activity score before corticosteroid boluses were 4.5±0.8 with a slight insignificant increase (p=0.58) in smokers (score=4.64) compared with non smokers (4.43). The score's activity was 4.63 in men against 4.4 in women (p=0.6). Concerning the seriousness, 8 patients were admitted with severe exophthalmos and 13 showed moderate to severe exophthalmos. From the view of biology, at the inflammatory thrust time, four patients had hypothyroidism with low free thyroxine (6±2.5 pmol/l), two patients had hyperthyroidism with increased free thyroxine (29±17 pmol/l) and fifteen patients were in euthyrodism. Dosage of anti-TSH receptor antibodies was not systematic due to the lack of financial resources. Thus, 5 patients could perform them with positive results (35±19 ui/l). Tomodensitometry was carried out in 8 patients having severe exophthalmos and in 11/13 patients showing moderate-to-severe from one. The main anomalies were: thickness of intra orbitary fats, hail optic nerve and protrusion of ocular globe from grade I to grade III (Figure 1). There was no compression of optic nerves.

The evolution under treatment has been marked by noticeable improvement (Figure 2). Exophthalmos became inactive in 76% and 87% of the patients respectively at the end of the bolus and six months later. Group mean activity score was significantly reduced to 1.95±0.74 (p< 0.0001, IC 95%) at the end of 12 boluses and kept at 1.14±0.91 (p< 0.000, IC 95%) 6 months after the first bolus. This activity score was 2 in smokers against 1.86 in non smokers at 3 months (p=0.68) and 1.21 in smokers against 1 in non smokers at 6 months (p=0.62). According to gender, the score of activity was 1.19 in men against 1 in women (p=0.69). At the end of boluses we found a change of severe forms to moderate-to-severe category (8 cases) and a change of moderate-to-severe forms to minor category (3 cases). Quality of life score has been significantly improved. So, concerning

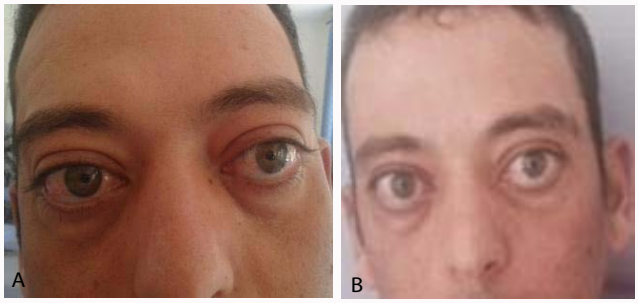

Figure 2: Ocular signs evolution from patient (P12).
2a: Before boluses.
2b: After boluses.

the alteration impact of vision, on the quality of life (Q1-8), the score changed from 56±11.5 before boluses to 82.3±11 after boluses (p< 0.0001); furthermore psychosocial impact score (Q9-16) raised from 41.9±12 before boluses to 57.4±9.6 after boluses (p< 0.0001) (Table I).

As far as side effect is concerned we have found a case of diabetes corticosteroid adverse (one case), weight gain over 3 kilograms (two cases). We also found before bolus, one case of glaucoma which was balanced under treatment before starting bolus with close monitoring twice a week by ophthalmologist.

Discussion

The average age of our patients was 37.4±11 years comparable to what was found in the meta-analysis carried out by Gao Guohong et al. [2]; over 8 studies they found the average age varying from 32 years to 56 years. Male gender was predominant in our series which was also found by Aktaran et al [3]. Sixty seven per cent (67%) of our patients were active smokers against 50% found by Guia Vannucchi et al [4]. Smoking could account for male predominance in our series as the whole smokers were men. A significant decrease of activity score was noticed as well as the change in severity. So mean activity score was significantly reduced from 4.5±0.8 to 1.95±0.74 (p< 0.0001, IC 95%) at the end of 12 boluses and kept at 1.14±0.91 (p< 0.000, IC 95%) 6 months after the first bolus. These results were similar to those found by several authors. Thus Guia Vannucchi et al. [4] found the score decrease from 4.4±0.9 to 2.2 ±1.5 (P< 0.03), 1.8±1.5 (P< 0.001), 1.9±1.7 (P< 0.03) respectively at 6–8 weeks, 12–16 weeks and at 24 weeks; Gao Guohong et al. [2] also reported the significant improvement of activity score after boluses. Smoking being one of the mains factors of supervention and worsening of Graves' ophthalmopathy [5-7]. A comparison of the activity score of smokers allowed us to notice an increase of those scores before and after boluses in smokers compared to non smokers but the difference was not significant. Rate of inactive exophthalmos in our study was respectively 76% at the end of 12 boluses and of 87%, six months after; which was comparable to several studies with percentages varying between70 and 80% [1,4,8,9]. The Quality of life has been improved after boluses as shown by the GO-QoL score which increased from 56±11.5 before boluses to 82.3±11 after boluses (p< 0.0001) and from 41.9±12 to 57.4±9.6 after boluses (p< 0.0001) respectively for visual and psychosocial impacts. These improvements of quality of life after corticosteroid boluses are noted in certain studies [3,10]. On the other hand, let's notice that whatever the selected treatment, 12% and 13% of patients will always keep quality scores below 50 respectively for visual and psychosocial scores [11]. In our study 10% of patients had scores below 50 after treatment regarding psychosocial impact

and none of them had a score below 50 on visual score. One case of diabetes corticosteroid-induced and two cases of weight gain have been observed as complications which were similar to the results of Gao Guohong et al. [2] who had objectified one case of diabetes and 2 cases of weight gain. This low number of side effects in our study could be explained by our doses of methylprednisolone which does not exceed 500 mg per week.

Conclusion

These encouraging results support the use of methylprednisolone bolus in Graves' ophthalmopathy according EUGOGO indications. However, protocol of administration requires close monitoring to prevent complications of corticosteroid therapy.

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