Repeated Retrobulbar Injections of Triamcinolone Acetonide for Thyroid Orbitopathy

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Abstract

Background: Thyroid associated orbitopathy (TAO) is an autoimmune disorder. It usually occurs in association with hyperthyroidism. Systemic corticosteroids provide the mainstay treatment for patients with severe and active orbitopathy, but its benefit is associated with important side effects. Attempts to reduce the systemic effects of corticosteroid by using local steroid administration by retrobulbar injection as triamcinolone acetonide.

Purpose: To identify the result of retro-bulbar triamcinolone injection in patients with thyroid associated orbitopathy.

Material and Methods: Prospective non-comparative study in 20 eyes of 10 patients who had been diagnosed as thyroid associated orbitopathy during October 2008 through October 2009. The patients received retrobulbar 40mg triamcinolone treatment for each orbit weekly, totaling 4 applications. Complete Ophthalmological examination including ocular ultrasonography were performed before and after treatment.

Results: Three months after treatment. Improvement of proptosis was observed in 16 eyes (80%). All patients had improvement of extraocular muscle function as demonstrated by EOM Movement. These results remained stable in the majority of patients at the 6 months follow-up period. No systemic side effects were observed. The only local side-effect was transitory increase in intraocular pressure in one patients was controlled with topical medication.

Conclusion: This preliminary study demonstrated the potential benefit of retrobulbar triamcinolone injection in cases of thyroid associated orbitopathy. Long-term study in these patients is required.

Key Words: Triamcinolone – Thyroid – Orbitopathy – Retrobulbar.

Introduction

THYROID associated orbitopathy (TAO) is an autoimmune disorder that is progressive but self-limited. It usually occurs in association with hyperthyroidism but the clinical course of orbitopathy seems to proceed independently of thyroid gland dysfunction and treatment. The clinical manifestation is usually accompanied by proptosis, lid retraction, orbital congestion and motility disturbance, with unpredictable severity and duration of disease. In severe cases, vision loss due to optic nerve compression or corneal exposure can be found [1,2].

There is no gold standard of treatment for the thyroid associated ophthalmopathy (TAO) in the early (inflammatory) stages of the disease. Corticosteroids reduce the transitory manifestations of TAO but their multiple adverse effects make the risk/benefit relation unsatisfactory [3,4].

Corticosteroids are used commonly in the treatment of ocular inflammatory diseases. Systemic use of corticosteroids may be associated with serious side effects. To minimize these, local routes of administration generally are preferred over systemic routes [8].

Systemic corticosteroids provide the mainstay and well-established treatment for patients with severe and active orbitopathy. Glucocorticoid therapy provides rapid relief from the inflammatory changes, but its benefit is associated with important side effects; and, tapering or discontinuation of treatment often results in disease exacerbation. There have been attempts to reduce the systemic effects of corticosteroid by using local steroid administration by retrobulbar injection [6].

Triamcinolone acetonide (TA) is a long-acting depot preparation of triamcinolone that is minimally water soluble and is injected in a suspension form. The decreased water solubility contributes to its prolonged duration of action: The anti-inflammatory potency of TA is approximately 5 times more than that of cortisol. Posterior sub-Tenon injection of TA is used for various conditions like intermediate uveitis, posterior uveitis, diffuse diabetic macular edema, reducing diplopia and the sizes of extraocular muscles in thyroid associated ophthalm-
mopathy of recent onset, macular edema associated with branch retinal vein occlusion, postoperative inflammation after uncomplicated cataract surgery, and choroidal neovascularization [7,8].

Triamcinolone acetonide was one of several long acting repository corticosteroid preparations. It appears pharmacologically to be equally effective as methylprednisolone. However, anecdotally the residual vehicle left after injections with methylprednisolone is not as well tolerated by some patients and can cause an allergic response [9].

The first use of peribulbar injection of triamcinolone in patients with TAO was recently described by Ebner. Local retrobulbar triamcinolone (20mg/wk for 4 weeks) has been associated with an increased range of motion and decreased recti thickness with minimal local side effects [10].

The objective of the present study was to identify the efficacy and safety of retrobulbar triamcinolone injection in patients with TAO.

**Patients and Methods**

This prospective non comparative pilot study included 20 eyes of 10 consecutive patients, with a diagnosis of TAO from October 2008 through October 2009 at the Ophthalmology Clinic-Kasr El-Aini Hospital.

The diagnosis of TAO was based on the presence of typical clinical features in combination with a history of thyroid disorder or abnormal thyroid function test and finding of enlarged extraocular muscles (EOM) by ocular ultrasonography.

**Inclusion criteria were:** (I) TAO patients with clinical presentation of proptosis and diplopia due to limited EOM function, (II) No current treatment for orbitopathy, regardless of the stage of dysthyroidism (no systemic corticosteroid and no other immunosuppressive drugs), and (III) All patients had at least 6 months of follow-up time. Patients were excluded if they had signs and symptoms of sight threatening conditions such as compressive optic neuropathy and/or severe exposure keratopathy.

With standard retrobulbar injection technique, each patient received retrobulbar injection of 40mg triamcinolone for each orbit. In the supine position, the eyes were anesthetized with two drops of topical anesthesia. The 25 gauge needle was introduced through the skin of the lateral one third of the lower eyelid and passed posteriorly, medially, and upward to reach the retrobulbar space.

Aspiratlon was first attempted to rule out reflux of blood into the syringe. One ml of 40mg triamcinolone was slowly injected and the needle was then withdrawn. After injection, gauze was applied to compress the eye for 1 to 2 minutes. No hospitalization was required. The injected eye was not covered. The injection was given at one-week intervals, totaling 4 applications per orbit.

Demographic data recording included age and gender. The activity of orbitopathy was assessed before making the injection. At follow-up examinations, several measurements were made: Visual acuity assessment by using snellen chart, intraocular pressure (IOP) measurement by applanation tonometry and degrees of proptosis by Hertel exophthalmometer.

Data was collected at study entry and follow-up visits at 2 weeks, 4 weeks, and then one-month intervals for 6 months. Progression or improvement of orbitopathy was defined by changing in one of these following criteria: Decrease of proptosis by 1 millimeter or more, increase of EOM function as demonstrated by EOM movement and improvement of visual acuity of 2 lines or more. Patient gave their written informed consents to the present study. Mean and range were presented to describe patients’ characteristics. The mean changed of proptosis and IOP after 3 and 6 months of treatment were analyzed by paired t test. p-value <0.05 was considered significance.

**Results**

During the study period, there were 10 patients who met the inclusion criteria. Of these, there were 4 males and 6 females. The mean age at study entry of all patients was 36.5 years. All patients had bilateral ocular involvement. The duration of ocular symptoms of TAO ranged from 2 months to 1 year. The follow-up period was 6 months.

**Proptosis:** Pretreatment baseline proptosis of all patients, ranged from 15 to 32mm, with an average of 23.4mm. The average proptosis significantly decreased from 23.4mm to 22.4mm and later to 22.5mm at 3 and 6 months respectively. Three months after treatment, 16 of 20 eyes (80%) had a decrease in proptosis of 1mm or more. The average reduction of proptosis in these eyes was 1.7mm, ranged from 1 to 4mm. Four eyes (20%) had no change in proptosis. These results remained stable in the majority of patients at the 6-month follow-up period.
Extraocular muscle function:

All patients had abnormal EOM function, as demonstrated by limited EOM Movement at study entry. At 3 months after treatment, EOM function improved in all patients. At 6-month follow-up period, these results also remained stable.

The only local side-effect was transitory increase in intraocular pressure in one patients and was controlled with topical medication.

Discussion

Management of TAO especially in severe cases remains a difficult task, and many patients are not satisfied with the effects of treatment. Corticosteroid therapy is one of the most established and used treatment for the orbitopathy. Glucocorticoids have anti-inflammatory and immunomodulatory effects, and they may directly inhibit glycosaminoglycan synthesis and release from fibroblasts [11].

Corticosteroid therapy provides rapid amelioration of the pain, conjunctival injection and edema associated with the inflammatory soft-tissue changes in orbitopathy. Treatment seems to be more effective in association with orbital radiotherapy. However, it may be difficult to wean such patients off corticosteroids, and the disease often gets worse when the dose has been reduced or stopped [12].

Periocular injection of triamcinolone acetonide has been reported to benefit in variety of chronic inflammatory ocular diseases. Similar to previous publication, the present result also indicated that retrobulbar triamcinolone injection was effective on management of patients with TAO [10].

Triamcinolone is a synthetic glucocorticoid with a potency that equals five times that of cortisol, is metabolized in the liver (tetrahydrocortisol), and excreted as a soluble compound in the urine. It is fluorated in position 9 of the second ring giving it a marked glucocorticoid activity, and a reduced mineralocorticoid activity due to a OH substitution at C16 [13].

The administration by a peribulbar injection in the inferior lateral quadrant of the orbit allows its diffusion in the retrobulbar fat to the extraocular muscles [14].

Most of the patients in the study experienced improvement of orbital congestive symptoms. Proptosis appeared to be the most responsive sign, also improvement was obtained on the change of ocular motility. The safety of retrobulbar steroid injection is illustrated by many reports. Absence of major ocular and systemic side effects implies that this technique is safer than systemic steroid administration [14].

In agreement with previous reports, the author did not find any serious systemic side effects in the presented patients. Mild local side effects were found such as local discomfort, ecchymosis and subconjunctival hemorrhage, but these effects were transient without long-term sequelae [10,14].

Lee and Brazis 1998 warn against their use, based on the lack of studies that demonstrate an improvement in Graves’ ophthalmopathy by local steroids. They are concerned by the increase in volume produced by an injection in a congested orbit [15].

In our study the only local side-effect was transitory increase in intraocular pressure in one patients and was controlled with topical medication. Thach, et al. [14] and Ebner, et al. [10] observed that the final IOP measurement was not significantly higher than the pretreatment measurement. In contrast, another study investigated significant rise of IOP which required additional treatment, developed in 40% of patients with previously controlled glaucoma, perhaps this might have been related to different doses of triamcinolone or higher number of injections [6]. The author suggest that a long-term controlled study is required to identify the optimal dose and duration of treatment.

In conclusion, the present study demonstrated the potential benefit of retrobulbar triamcinolone injection in patients with TAO. This local treatment can effectively be used instead of systemic steroid, especially when systemic therapy is contraindicated.

References

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