Retrobulbar Injection of Triamcinolone in Thyroid Associated Orbitopathy

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Objective: *To identify the result of retrobulbar triamcinolone injection in patients with thyroid associated orbitopathy*

Material and Method: *Prospective noncomparative pilot study in 27 eyes of 19 patients who had been diagnosed as thyroid associated orbitopathy during October 2000 through April 2002. The patients received retrobulbar 40 mg triamcinolone treatment for each orbit weekly, totaling 4 applications.*

Results: *Three months after treatment, most of the patients demonstrated no significant change in visual acuity and visual field. Improvement of proptosis was observed in 15 eyes (56%) and stable in 10 eyes (37%). Seven patients (41%) had improvement of extraocular muscle function as demonstrated by Hess test. These results remained stable in the majority of patients at the 6 months follow up period. No systemic side effects were observed.The only significant local side-effect was intraocular pressure elevation which was found in 8 eyes and responded to antiglaucoma therapy.*

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.*

Keywords: *Triamcinolone, Thyroid, Orbitopathy, Retrobulbar*

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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[1,2]. 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.

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. Favorable results have been reported in some published literature. Although soft tissue signs may improve, the efficacy of retrobulbar methylprednisolone injection compares perhaps less favorably with systemic corticosteroids[3,4].

Triamcinolone acetonide was one of several long acting repository corticosteroid preparations. It appears phamarcologically 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[5]. Periocular injection of triamcinolone by retrobulbar or subtenon's technique has been used for many ophthalmic indications such as refractory cystoid macular edema[6], intermediate uveitis[7] and chorioretinitis. The first use of peribulbar injection of triamcinolone in patients with TAO was recently described by Ebner. Local retrobulbar triam-

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cinolone (20 mg/wk for 4 weeks) has been associated with an increased range of motion and decreased recti thickness with minimal local side effects[8]. The objective of the present study was to identify the efficacy and safety of retrobulbar triamcinolone injection in patients with TAO. The dosage used in our study was 40 mg per eye based on previous data of methylprednisolone[3,9].

Material and Method

This prospective noncomparative pilot study included 27 eyes of 19 consecutive patients, with a diagnosis of TAO from October 2000 through April 2002 at the neuro-ophthalmology clinic, Ramathibodi Hospital. The diagnosis of TAO was based on the presence of typical clinical features as NOSPEC[10] signs in combination with a history of thyroid disorder or abnormal thyroid function test or abnormal thyroid antibody and finding of enlarged extraocular muscles (EOM) on computed tomography scan of the orbits. 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 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 40 mg triamcinolone for each orbit. In the supine position, the eyes were anesthetized with two drops of 0.4% oxybuprocaine HCl. The 25 gauge 1 " 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. Aspiraton was first attempted to rule out reflux of blood into the syringe. One ml of 40 mg triamcinolone (Kenacort A) was slowly injected and the needle was then withdrawn. After injection, gauze was applied to compress the eye for 1 to 2 minutes and the patient lay recumbent with both eyes closed for 5 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 an injection. At follow up examinations, several measurements were made: visual acuity assessment by using ETDRS chart, intraocular pressure (IOP) measurement by applanation tonometry and degrees of proptosis by Hertel exophthalmometer. Ocular movement and binocular function were tested by orthoptic examination and Hess's screen test. Visual field was tested with Goldmann perimetry or Humphrey automated static perimetry (program 30-2). 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 Hess test and improvement of visual acuity of 2 lines or more.

Patient gave their written informed consents to the present study, and the protocol of study was approved by the Medical Ethics Committee of Ramathibodi Hospital, Mahidol University. Mean and range were presented to describe patients' characteristics. The mean changed of proptosis and EOM involvement and IOP after 3 and 6 months of treatment were analyzed by paired t test. P-value < 0.05 was considered significance.

Results

During 2 years of study, there were 19 patients who met the inclusion criteria. Of these, there were 9 males and 10 females. The mean age at study entry of all patients was 39.4 years, ranged from 20-53 years. Eight patients had bilateral ocular involvement and 11 patients had unilateral involvement: 6 cases on the right side and 5 cases on the left side. The median duration of ocular symptoms of TAO was 12 months, ranged from 2 months to 3 years. The follow-up time ranged from 6 to 16 months, with an average of 12 months.

Proptosis

Pretreatment baseline proptosis of all patients, ranged from 15 to 32 mm, with an average of 23.4 mm. The average proptosis significantly decreased from 23.4 mm to 22.4 mm and later to 22.5 mm at 3 and 6 months respectively. Three months after treatment, 15 of 27 eyes (56%) had a decrease in proptosis of 1 mm or more. The average reduction of proptosis in these eyes was 1.7 mm, ranged from 1 to 4 mm. Ten eyes (37%) had no change in proptosis and only 2 eyes had further progression of proptosis. These results remained stable in the majority of patients at the

6-month follow-up period (Table 1). For the proptotic patients who did not respond to treatment and had cosmetic concern, 5 patients underwent orbital fat removal and 1 patient needed orbital decompression.

Extraocular muscle function

Seventeen patients (89.5%) had abnormal EOM function, as demonstrated by limited EOM movement and abnormal Hess test at study entry. At 3 months after treatment, EOM function improved in 7 patients (41%), and worsened in 2 patients (12%); there was no change in 8 patients (47%). At 6-month follow-up period, these results also remained stable in the majority of patients (Table 1). After completion of the study, 2 patients needed strabismus surgery.

Visual acuity and visual field

Pretreatment best corrected visual acuity ranged from 20/20 to 20/160. After 6 months, visual acuity remained stable in 74% of patients (20 eyes). Nineteen percent (5 eyes) of patients experienced some improvement of visual acuity but both eyes of one patient had worsening of visual acuity because of deteriorating keratopathy. No significant changes of visual fields were recorded among all patients throughout the present study.

Intraocular pressure

Baseline IOP ranged from 13 to 22 mm Hg, with average of 16.6 mm Hg. Glaucoma (IOP 22 mm Hg or more with glaucomatous cupping or visual field defect) was diagnosed in 6 eyes of 4 patients before receiving any injection. Among these patients, IOP was well controlled by timolol eyedrop.

In most patients, the ocular tension was normal on the first examination and remained normal throughout the study. The overall mean IOP rising was 1.9 ± 2.4 and 2.2 ± 3.4 mmHg at 1 and 2 months after first injection respectively. During 3 months after injection, 8 eyes of 5 patients had IOP of 22 mm Hg or more. Highest IOP of each paitent in this group ranged from 23 to 28 mm Hg. The mean different between highest and baseline IOP was 5.8 ± 4.6 mmHg. The interval between the first injection and development of rising IOP ranged from 3 to 10 weeks. Two of these 5 patients (4 eyes) had previously diagnosed glaucoma. The IOP were medically controlled with 1 or 2 antiglaucoma drugs in most patients and pressure returned to normal within several weeks, with no further therapy. However, one patient developed further increased IOP bilaterally despite full antiglaucoma medical therapy and finally underwent trabeculectomy.

Other minor complications

No major adverse effects and no systemic side effects of retrobulbar triamcinolone were observed, with the exception of 3 cases of ecchymosis, 2 cases of subconjunctival hemorrhage and 1 case that had transient hirsutism.

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. Proptosis and ophthalmoplegia also may improve but to a lesser degree and with a greater likelihood of exacerbation after discontinuation of treatment[1,12,13]. A favorable response has been reported in about two-thirds of patients treated by high dose oral corticosteroid[13-15]. Treatment seems to be more effective in association with orbital radiotherapy[3,16,17]. However, it may be difficult to wean such patients off corticosteroids, and the disease often gets worse

Table 1. Effects of retrobulbar triamcinolone treatment in patients with thyroid associated orbitopathy

Type of abnormality	Total number	Improvement	No change	Worsening
Proptosis				
3 months	27 eyes	15 (56%)	10 (37%)	2 (7%)
6 months	27 eyes	14 (52%)	10 (37%)	3 (11%)
EOM involvement				
3 months	17 patients	7 (41%)	8 (47%)	2 (12%)
6 months	17 patients	7 (41%)	8 (47%)	2 (12%)

when the dose has been reduced or stopped. The dosage necessary to achieve and maintain the desired result is usually accompanied by severe side effects which may necessitate withdrawal of the corticosteroids.

To avoid the side effects of high dose systemic corticosteroids, the use of injectable steroid preparations, usually methylprednisolone (injected subconjunctivally or into the retrobulbar space) has been attempted by some researchers. Yet the results of many reports have been conflicting. Nevertheless favorable results, especially on soft tissue changes and improved EOM movements have been published[9,18]. On the other hand, minor improvement or no perceptible changes have been reported[19]. Marcocci et al suggested that the combination of orbital irridation with retrobulbar corticosteroids may be used in the treatment of severe TAO, but this appears to be less effective than orbital irridation used with systemic corticosteroids[3]. Although favorable results in the absence of major side effects have become evident in some instances, this particular treatment has not gained wide acceptance.

Periocular injection of triamcinolone acetonide has been reported to benefit in variety of chronic inflammatory ocular diseases. Similar to previous publication[8], the present result also indicated that retrobulbar triamcinolone injection was effective on management of patients with TAO. Most of the patients experienced improvement of orbital congestive symptoms. Proptosis appeared to be the most responsive sign, whereas a lesser improvement was obtained on the change of ocular motility. Self assessment of ocular changes by the patients was in good agreement with the objective clinical responses such as decreased fullness in the orbit and improvement of diplopia, pointing to a more favorable outcome of treatment. No significant change in visual acuity and visual field was found during the 6-month follow-up periods.

The safety of retrobulbar steroid injection is illustrated by many reports[6,9]. Absence of major ocular and systemic side effects such as cushingoid, gastrointestinal irritation and no change of blood pressure, serum glucose, calcium and cortisol[8] implies that this technique is safer than systemic steroid administration. In agreement with previous reports, the authors 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. However, the ocular side effects that occurred in the presented patients and should be of some concern is the rising of intraocular pressure. Significant rising of IOP which required additional treatment was developed in 40% of patients with previously controlled glaucoma. In contrast to the authors' reports, the final IOP in another studies[6,8] was not significantly higher than the pretreatment IOP; perhaps this might have been related to a lower dose of triamcinolone[8] or fewer injections[6]. The authors 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.

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การรักษาภาวะความผิดปกติของเบ้าตาที่สัมพันธ์กับโรคไทรอยด์โดยการฉีดไตรแอมซิโนโลน

อนุชิต ปุญญทลังค์, พิศิษฐ์ ปรีชาวัฒน์, วรางคณา เจริญกุล, ภิรดี ตั้งตระกูล

วัตถุประสงค์*: เพื่อศึกษาผลการรักษาในผู้ป่วยที่มีความผิดปกติของเบ้าตาที่สัมพันธ์กับโรคไทรอยด์โดยการฉีดยาไตรแอมซิโนโลนเข้าไปในเบ้าตา*

วัสดุและวิธีการ*: ได้ทำการศึกษาในผู้ป่วยที่ได้รับการวินิจฉัยว่ามีเบ้าตาผิดปกติจากโรคไทรอยด์ จำนวนทั้งหมด 19 ราย 27 ตา ตั้งแต่ ตุลาคม 2543 ถึง เมษายน 2545 โดยผู้ป่วยจะได้รับการฉีดยาไตรแอมซิโนโลนขนาด 40 มิลลิกรัม เข้าไปในเบ้าตาแต่ละข้าง สัปดาห์ละครั้งติดต่อกัน 4 สัปดาห์*

ผลการศึกษา*: ที่ระยะเวลา 3 เดือนหลังการรักษา พบว่าอาการตาโปนดีขึ้น 15 ตา (56%) ไม่มีการเปลี่ยนแปลง 10 ตา (37%) และผู้ป่วยมีการทำงานของกล้ามเนื้อตาดีขึ้น 7 ราย (41%) ผู้ป่วยส่วนใหญ่ไม่พบว่ามีการเปลี่ยนแปลงของระดับการมองเห็นและลานสายตา ผลการรักษานี้คงที่ภายหลังการรักษาไปแล้ว 6 เดือน ผลข้างเคียงเฉพาะที่ที่สำคัญ คือ มีการเพิ่มของความดันลูกตาและจำเป็นต้องได้รับการรักษาด้วยยา โดยไม่พบผลข้างเคียงต่อส่วนอื่นของร่างกาย*

สรุป*: ผลการศึกษาในเบื้องต้นแสดงให้เห็นถึงประโยชน์ของการฉีดยาไตรแอมซิโนโลนเข้าในเบ้าตาในผู้ป่วยที่มีความผิดปกติของเบ้าตาที่สัมพันธ์กับโรคไทรอยด์ อย่างไรก็ตามการศึกษาในระยะยาวยังเป็นสิ่งจำเป็น*