

Response of Autologous Serum Supratarsal Injection in Patients of Vernal Keratoconjunctivitis in Longterm Followup

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Abstract

Purpose: To study the response of 0.1 ml autologous serum supratarsal injection in patients of vernal keratoconjunctivitis in their long term followup.

Materials and Methods: This prospective, nonrandomized study was carried out in 50 patients of either sex and any age suffering from vernal keratoconjunctivitis. Previous medications were discontinued for period of 15 days before commencing serum injection. 0.1 ml of autologous serum was injected in each eye supratarsally. Injection was repeated every week for 8 weeks and follow up of all patients was done at one month, three months, six months and one-year interval.

Results: Significant improvements in symptoms and some of the signs were achieved. Improvement was significant even after discontinuation of treatment. No additional medications were required.

Conclusions: 0.1 ml supratarsal injection of autologous serum is an effective alternative treatment in vernal for long term and without any adverse effects.

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Keywords: Vernal Keratoconjunctivitis, autologous serum, long term

Introduction

Vernal keratoconjunctivitis is a bilateral inflammatory disorder of conjunctiva and cornea,¹ commonly in first and second decade.²

Topical corticosteroids are the mainstay of therapy. However prolonged use may result in glaucoma, cataract, dry eye and secondary infections.³ Therefore serious side effects with steroids, incomplete amelioration of symptoms with other drugs and requirement of long term instillation of drugs, necessitated the study of other therapeutic agents.

In vernal keratoconjunctivitis increase of Th2 occurs, that leads to overactivation of Th2 cells giving rise to hypersensitivity reaction and autologous serum acts mainly by shifting of the Th2 cytokine profile to Th1.⁴

Material and Methods

This quasi experimental study was carried out in 50 patients of either sex and any age suffering from vernal keratoconjunctivitis. VKC was diagnosed on the basis of the presence of itching, ropy discharge, photophobia, papillae on upper tarsal conjunctiva and limbal changes. Previous oral or topical medications were discontinued for period of 15 days

before commencing autologous serum injection. Complete ophthalmic examination was performed including details of symptoms, visual acuity and slit lamp biomicroscopy. Family or personal history of allergic disorders was taken. Symptoms were recorded and graded according to [Table-1] (Tahir Masaud et al, 2011).⁵

Table 1: Grading of symptoms

	Grade 0	Grade I	Grade II	Grade III
Symptoms	No	Mild	Moderate but does not interfere with daily routine activities	Severe-disrupt daily routine activities

Ocular clinical signs were graded according to [Table-2] (Tahir Masaud et al, 2011).⁵

Patients were informed of the aim and informed consent was taken before procedure. Autologous serum was prepared by withdrawing 5 ml of the venous blood from antecubital vein and centrifuging it at 2000 rpm for 10 min. The supernatant serum was removed and 1 ml of serum was taken. Supratarsal injection was given under topical anaesthesia using 26 G

Table 2: Grading of signs

Signs	Grade 0	Grade I	Grade II	Grade III
Conjunctival hyperaemia	Absent	Mild bulbar hyperaemia	Moderate bulbar hyperemia	Severe bulbar hyperemia
Papillary hypertrophy	Absent	Mild papillary hypertrophy	Moderate papillary hypertrophy (edema of the palpebral conjunctiva with hazy view of the deep tarsal vessels)	Severe papillary hypertrophy where the papillary hypertrophy was in more than 50% of the surface
Limbal changes	Absent	Less than 90 degree of limbal infiltration	Less than 180 but more than 90 degree of limbal infiltration	More than 180 degree of limbal infiltration.
Horner Tranta dots	Absent	1 to 2 dots	3 to 4 dots	More than 4 dots.
Superficial punctate keratopathy	Absent	One quadrant of punctate keratitis	Two quadrants of punctate keratitis	Three or more quadrants of punctate keratitis

needle and 0.1 ml of autologous serum was injected in each eye. Injection was repeated every week for 8 weeks and follow up of all patients was done at one month, three months, six months and one-year interval.

Results

Our observations are based on 1 year follow up study of 50 patients diagnosed as cases of vernal keratoconjunctivitis. There was male predominance with male:female ratio 7.3:1. Mean age was 12.34 years and SD was 4.98. The minimum age was 4 years and maximum age was 25 years. Most common in summer months of April-June, however disease was seen throughout the year. Symptoms such as itching, redness and watering were present in all the cases, photophobia was present in 52% cases and ropy discharge in 34% of patients. Signs such as conjunctival hyperaemia was present in 72% of patients, papillary hypertrophy at superior tarsus in 48%, gelatinous limbal ring in 98%, horner trantas dots in 26% and corneal involvement in form of superficial punctuate keratopathy was seen in only 4% of patients.

5 patients (3 male and 2 female) lost subsequent follow ups after first injection.

Symptoms [Table-3] - There was highly significant improvement in the symptoms after 8 supratarsal autologous serum injections and in long term follow up till 1 year.

Table 3: Improvement in the symptoms after 8 supratarsal autologous serum injections and in long term follow up till 1 year

Symptoms	1 month	3 months	6 months	1 year	P value
Itching	40 (88.9%)	40 (88.9%)	35 (77.8%)	35 (77.8%)	<0.001
Redness	37 (82.2%)	37 (82.2%)	32 (71.1%)	32 (71.1%)	<0.001
Watering	40 (88.9%)	40 (88.9%)	36 (80.0%)	36 (80.0%)	<0.001
Photophobia	12 (46.2%)	12 (46.2%)	8 (30.8%)	8 (30.8%)	<0.01
Ropy discharge	10 (58.8%)	10 (58.8%)	8 (47.1%)	8 (47.1%)	0.01

On day 0, 45 patients complained of itching, redness and watering, after 3 months of treatment with supratarsal autologous serum injection, improvement was seen in 88.9%, 82.2% and 88.9% of patients respectively but recurrence of itching and redness was seen in 11.1% and of watering in 8.9% of patients at 1 year, but still improvement was highly significant (p<0.001).

Initially, 26 patients complained of photophobia, after 3 months of treatment improvement was seen in 46.2% of patients, but recurrence of photophobia was seen in 15.4% and at 1 year, still improvement was significant (p<0.01).

Initially, 17 patients had ropy discharge, after 3 months of treatment improvement was seen in 58.8% of patients but recurrence seen in 11.8% of patients at 1 year, still improvement was significant (p=0.01).

Signs [Table-4] - Significant improvement was found only in conjunctival hyperemia and gelatinous limbal ring [Figure-1]. Improvement in other signs of vernal keratoconjunctivitis were not significant.

1. On day 0, 32 patients had conjunctival hyperaemia, after 3 months of treatment with supratarsal autologous serum injection improvement was seen in 27 (84.4%) patients, but recurrence was seen in 2 (6.3%) patients at

1 year, still improvement was highly significant in long term (p<0.001).

2. On day 0, 22 patients had papillary hypertrophy, after 3 months of treatment improvement was seen in 4 (18.2%) patients, recurrence seen in 1(4.5%) patient at 1 year, improvement was not significant .
3. On day 0, 44 patients had gelatinous limbal ring, after 3 months of treatment improvement seen in 20 (50%) patients, but recurrence noted in 5 (12.5%) patients at 1 year, still improvement was highly significant in long term (p<0.001).
4. 13 patients had horner trantas dots, improvement was seen in 3(23.1%) patients after months but recurred in all at 1 year.
5. No improvement was seen in superficial punctuate keratopathy.

Table 4: Improvement in the signs after 8 supratarsal autologous serum injections and in long term follow up till 1 year

Signs	1 month	3 months	6 months	1 year	P value
Conjunctival hyperaemia (32)	27 (84.4%)	27 (84.4%)	25 (78.1%)	25 (78.1%)	<0.001
Papillary hypertrophy (22)	4 (18.2%)	4 (18.2%)	3 (9.4%)	3 (9.4%)	0.31
Gelatinous limbal ring (44)	20 (45.5%)	20 (45.5%)	15 (34.1%)	15 (34.1%)	<0.001
Horner trantas dots (13)	3 (23.1%)	3 (23.1%)	0	0	0.31
Superficial punctuate keratopathy (2)	0	0	0	0	0.61

Discussion

VKC is a chronic, bilateral, seasonally exacerbated, allergic inflammation of the tarsal conjunctiva, bulbar conjunctiva, or both. More common in children and young adults with known atopy. The age incidence is more commonly between 6 to 20 years with a peak incidence between the ages of 11 and 13 years. There is stronger predilection for men being affected two or three times more frequently than women. Typically presents with itching, hyperaemia, photophobia, watering and ropy discharge. Itching was the most common symptom.

Three typical forms are seen Palpebral or Tarsal, Limbal and Mixed. Palpebral form of disease is characterized by conjunctival hyperaemia and papillary hypertrophy. In limbal form wall of gelatinous thickening at the limbus, mucoid nodules and Horner-Trantas dots are characteristic findings. In mixed form both palpebral and limbal signs are observed to varying degrees. Corneal findings include pseudogerontoxon, punctuate epithelial keratitis, corneal shield ulcers and corneal ectasia rarely.^{6,7}

VKC is a manifestation of a hypersensitivity response in the conjunctiva and cornea in which exogenous allergens or autosensitisation acts as the exciting agent and in which physical factors such as warmth and light play determining part, occurring preferentially in young individuals showing an endocrine vagotonic imbalance.⁸ The imbalance between Th2 and Th1 lymphocytes leads to overactivation of Th2

cells giving rise to hyperactivity against substances that commonly comes in contact with mucosa.

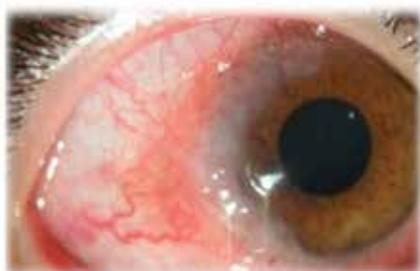
Although there is variety of drugs being used for vernal keratoconjunctivitis, none of the therapy is ideal with no or minimal side effects. However topical use of steroids is most accepted treatment of vernal keratoconjunctivitis, but it has certain disadvantages also such as rise of intraocular pressure, lenticular changes and corneal complications like keratitis.

A number of newer therapeutic agents have been attempted in treatment of vernal keratoconjunctivitis. They include topical non steroidal anti-inflammatory agents, topical mast cell stabilizers {nedocromil, lodoxamide (Caldwell 1992)},⁹ topical immunomodulators {cyclosporine}, topical antihistaminics {Levocabastine} and ganglioside derivatives {Miprogoside (Centofanti M et al, 1996)},¹⁰ supratarsal injection of steroids (Holsclaw et al, 1996).¹¹ and cyclosporine (Menna V, 2004).¹² However, most of these newer treatment modalities have been found relatively ineffective.

The pathogenesis of vernal keratoconjunctivitis suggests

that the therapy should be targeted towards reduction of Th2 activity and the major mechanism by which autologous serum acts in VKC is by shifting of the Th2 cytokine profile to Th1.^{13,14} Serum also exhibits characteristics properties which are very similar to those of tears regarding pH and osmolarity, this helps by providing symptomatic relief.¹⁵

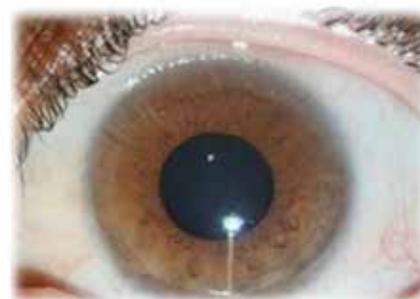
The present study was conducted to evaluate the efficacy and safety of 0.1 ml autologous serum injected supratarsally in patients of vernal keratoconjunctivitis and to see the recurrence of spring catarrh in long term follow up. The treatment was effective in alleviating the ocular symptoms of itching ($p < 0.001$), redness ($p < 0.001$), watering ($p < 0.001$), photophobia ($p < 0.01$) and ropy discharge ($p = 0.01$), even after 10 months of discontinuation of treatment. Amongst the signs, conjunctival hyperaemia and gelatinous limbal ring was reduced significantly ($p < 0.001$) [Figure 1 and Figure 2] but other signs such as papillary hypertrophy, horner trantas dots and superficial punctuate keratopathy showed little or no improvement no significant complications were observed during the trial.



Patient showing conjunctival hyperaemia and corneal limbal oedema at visit 0



Same patient at 3rd month followup with decreased conjunctival hyperaemia and corneal limbal oedema



Same patient at 1 year followup with complete resolution of conjunctival hyperaemia and corneal limbal oedema

Figure 1: Figure showing improvement in conjunctival hyperemia and corneal limbal oedema



Patient showing gelatinous limbal ring and mucoid nodules at visit 0



Same patient at 3rd month follow up with resolution of gelatinous limbal ring and mucoid nodules



Same patient at 1 year follow up

Figure 2: Figure showing improvement in gelatinous limbal ring and mucoid nodules

Conclusion

By analyzing the results of our study we have come to the conclusion that use of 0.1 ml supratarsal injection of autologous serum is an effective alternative treatment in vernal keratoconjunctivitis with decrease of signs and symptoms for long term and without adverse effects of conventional therapies.

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