ORIGINAL ARTICLE

Gamma Linolenic Acid in Dry Eye

Ashok K. Sharma, Hans Raj, Archana Pandita, Vishal R. Tandon*, Annil Mahajan**

Abstract

In this prospective study to evaluate the role of gamma linolenic acid in the management of dry eye, 100 patients of dry eyes were studied by dividing randomly into two groups of 50 each. In the test group, all the 50 patients were put on medication which consisted of cap gamma linolenic acid - 120 mg once daily dose, artificial tears solution/ointments 4-6 times daily with a topical mild steroid (loteprednol etabonate 0.5%) thrice daily. In the control group all the 50 patients were put on artificial tear solution/ointments and topical mild steroid (loteprednol etabonate 0.5%) thrice daily. All the patients were subjected to slit lamp examination, schirmer test, and fluorescien stain for tear film break up time (TBUT). In the test group symptomatic relief was shown by all 50 (100%) patients after one week of treatment. There was not much improvement in the schirmer test and TBUT results at 1 week. At 1 month follow up the result showed improvement and at 6 months there was definite increase in the schirmer test & TBUT values. The results were not influenced by the age & gender of the patients. In the control group though there was definite symptomatic relief in all the patients, but there was no change in the major study parameters i.e. tear film meniscus height; schirmer test and TBUT. At six month of the study there was marginal improvement of the major parameters but there was a lot of difference between the test and control groups. Thus gamma linolenic acid has a definite role in the management of dry eye.

Key Words

Dry eye, Gamma linolenic acid, Loteprednol etabonate.

Introduction

Dry eye is a clinical condition of ocular discomfort caused by deficient tear production and or excessive tear evaporation (1). The incidence of the condition is 9.8% among US women above 50yrs (2). There has been increase in the incidence of the condition in the previous years. It has been more than 50 yrs since Henrik Sjogren's described a disease he called keratoconjunctivitis sicca (KCS), which is characterized by autoimmune damage to the lacrimal gland tissue, decreased tear secretion and ocular surface disease(3). It is now recognized that so called dry eye syndrome is a variety of conditions with the common feature of an absolute or relative deficiency of the aqueous component of the tear film, due to any condition that decreases aqueous tear production, interferes with its distribution on the ocular surface (mucin-abnormalities) or increases its evaporation (meibomian gland dysfunction) (4,5).

Successful management of the dry eye has been constant challenge for ophthalmologists all over the world. The aim of therapy is to relieve symptoms and improve vision. Various treatment modalities are being tried. Conventionally, therapy of dry eye follows a staged concept including topical normal saline(NS) or normal saline with high molecular weight polymers, tear replacement in the form of cellulose esters (methyl cellulose hydroxypropyl methylcellulose) or polyvinyl

From the Postgraduate Department of Ophthalmology, Pharmacology & Therapeutics* and General Medicine, GMC, Jammu.**
Correspondence to Dr. Ashok Sharma, Incharge Cornea Services, PG Deptt. of Ophthalmology Govt. Medical College, Jammu (J&K).

alcohol & saline artificial tears, serum eye drops, punctum plugs, novel anti-inflammatory drugs (cyclosporin A), and surgical procedures. Interdisciplinary care, especially of patients with autoimmune disease, is recommended and is best provided in a specialized dry eye outpatient clinic (6). Other modalities like increased room humidity, moist chambers, swim goggles and in desperate cases tarsorrhaphy is done. Laser-assisted subepithelial keratomileusis in dry eyes and keratoconjunctivitis associated with complicated soft contact lens wearing is equally safe and efficacious (7).In spite of the proved efficacy and safety of these agents in dry eye (8-11), every conventional therapy is associated with some or other limitations (5,6,12).

Hence, continuous search is on to explore new modalities in dry eye. Role of corticosteroids like loteprednol etabonate (13-15) and more recently gamma linolenic acid in the management of dry eye is being tried with great success (16-17).The data do exist from other part of the world claiming role of gamma linolenic acid in the management of dry eye but it remain scanty from this region. Hence, the present study was planned to evaluate the efficacy of gamma linolenic acid in dry eye.

Material and Methods

A total of 100 patients of dry eye were studied prospectively with a questionnaire. They were divided randomly into two groups of 50 each. One group was taken as test group and other as control group. The symptoms noted are shown in Table I. No patients with corneal ulcer or blephritis were included. All the patients were subjected to slit lamp examination, schirmer test, fluorescien stain for tear film break up time (TBUT). Schirmer test was done without anaesthesia. In the *test group*, all the 50 patients were put on medication which consisted of gamma linolenic acid – 120 mg once daily dose, artificial tears solution/ointments 4-6 times daily with a topical mild steroid (loteprednol etabonate 0.5%) thrice daily. In the *control group* all the 50 patients were put on artificial tear solution/ointments and topical mild steroid (loteprednol etabonate 0.5%) thrice daily. The patients were followed at weekly interval.

Statistical analysis : The data was entered in the computer and analysis with the help of computer software SPSS 12.0 for windows. Primary outcome variables like Schirmer test value in mm, TBUT in seconds and tear film height measured in quantitative terms. Mean and SD was calculated both for test and control group. Statistical significance assessed by the use of unpaired t test (two tailed). A p value of <0.5 was considered as statistically significant. All analysis was performed according to intention to treatment plan. The patients were subjected to slit lamp examination, Schirmer test and tear film break up time at each visit in addition to the questionnaire for the symptomatic relief.

Results

The age of patients in the present study ranged from (16 yrs – 62 yrs).The number of female patients was more as compared to males(68:32).Slit lamp examination showed decrease in the inferior tear meniscus height (normal height is 1 mm) in 96 (96%) patients. Some of the patients also had mucus debris in the tear film and strings of mucoid discharge. All the patients had tear strip wetting less than 10 mm after 5 min. 79 pts (79%) had results of < 1 min in either eyes. TBUT was less than 10 sec in all 100 patients. 34 patients (34%) had TBUT of less than 5 sec. On being subjecting the patients to slit lamp examination, schirmer test & tear film break up time at each visit in addition to the questionnaire for the symptomatic relief the following results were reveled.

In the test group symptomatic relief was shown by 50 (100%) patients after one week of treatment. There was not much improvement in the schirmer test and TBUT results at 1 week. At 1 month follow up the results showed improvement and at 6 months there was definite increase in the schirmer test & TBUT values. The results were not influenced by the age & gender of the patients. In the control group though there was definite symptomatic relief in all the patients, but there was no change in the major study parameters that is tear film meniscus height; schirmer test and TBUT. At the six month of the study there was marginal improvement of the major parameters but there was a lot of difference between the test and control groups as shown in the table –II.

Table 1

Symptoms	No. of patients (100)
Foreign Body/Sandy sensation	84
Itching and Excessive mucus secretion	79
Heaviness of eyelids	38
Inability to produce tears	64
Sensitivity to light	52
Pain andRedness	87
Burning sensation	63

Table-2

Tear Film Break up Time in Sec

Time interval	Mean control	Mean test	t* value
4 weeks	5.86 (1.33)	6.54 (0.99)	-5.43 p.000
12 weeks	5.66 (1.11)	8.60 (.494)	-17.00 p.000
24 weeks	6.40 (1.12)	11.32(1.09)	-22.15 p.000

Table-3

Schirmer Test in mm

Time interval	Mean control	Mean test	t* value
4 weeks	5.71 (1.43)	6.19 (1.42)	-1.68 p.096
12 weeks	5.86(1.29)	7.37(1.04)	-6.39 p.000
24 weeks	6.22(1.42)	10.74(2.52)	-11.02p.000

*unpaired t test

Discussion

New innovative approaches for treating dry eye have been emerging with a hope to alleviate symptoms for the enormous number of patients affected by this disease. We tried a new approach for treating dry eye syndrome using systemic gamma-linolenic acid therapy. It was seen that gamma-linolenic acid produced statistically significant changes in the major study parameters. At 3 month follow up Schirmer score increased significantly from 1-2 mm to up to 6 mm on average. TBUT was also seen to increase significantly in these patients. The increase was up to 10±4 sec. Symptomatic relief was observed at 1 week follow up only. This could have been because of low dose steroids used along with systemic therapy. It is proven in many studies that topical steroids improve signs and symptoms of moderate to severe dry eye patients and is associated with reduction in HLA-DR+ cells and an increase in PAS+ cells in conjunctival impression cytology specimens. The use of gamma-linolenic acid is based on its efficacy in rheumatoid arthritis, a chronic inflammatory autoimmune disease characterized by symmetric polyarthritis (16). A cytokine and receptor-mediated inflammatory process has been demonstrated to affect both the lacrimal gland and ocular surface in patients with keratoconjunctivitis sicca. The ability of the immunomodular agent cyclosposin A and of therapy with local steroids to improve the signs and symptoms of moderate to severe dry eye disease unrelated to Sjogren's syndrome gives further support to hypothesis that an inflammatory process may contribute to a vicious cycle leading to chronic dry eye symptoms and signs (11).

The findings of the present study are in agreement to the studies of Barabino *et al* (16) and Macri *et al (*17). Barabino *et al* (16) suggested that therapy with systemic linoleic (LA) and gamma-linolenic acid (GLA) and tear substitutes reduces ocular surface inflammation and improves dry eye symptoms. In there study statistically significant changes in symptoms ($p < 0.005$), lissamine green staining ($p < 0.005$), and ocular surface inflammation ($p < 0.05$) occurred in the test group compared with controls. However, no statistically significant difference between groups was found for fluorescein break-up time (FBUT) and the Schirmer-1 test, which is contrary to our study.

Reduced corneal sensitivity has already been proved after photorefractive keratectomy (PRK). This could be the main reason for a decrease in tear production and for a reduced blinking rate leading to delayed tear clearance. Similarly to our results, Macri *et al (*17) suggested that linoleic acid and gamma-linolenic acid increases tear production, tear clearance and on the ocular surface after photorefractive keratectomy.

The use of topical loteprednol etabonate 0.5% 4 times a day has been suggested beneficial in patients who have keratoconjunctivitis sicca with at least a moderate inflammatory component (14, 15). However in our study loteprednol etabonate was given in both the groups (test & control) and gamma-linolenic acid produced statistically significant increase in major study parameters i.e. schirmer score and TBUT values indicating that gamma-linolenic acid definitely is effective in dry eye.

Conventional therapies, like artificial tear administration in glaucomatous patients with dry eye seems to improve significantly reliability parameters and visual field indices

(8). The results show a significant beneficial effect even with the use of sodium carboxy-methylcellulose (CMC) to improve clinical parameters in mild and moderate forms of dry eye (9). The autologous serum eye drops group similarly show prolongation of the tear BUT and a reduction in rose bengal staining score (10). However, conventional therapies focus on tear replacement or increasing tear volume but cannot affect the inflammatory process unlike corticosteroid and gamma linolenic acid (14-17).

Moreover, topical normal saline or normal saline with high molecular weight polymers give only a temporary relief from the symptoms. Cellulose esters or polyvinyl alcohol & saline create artificial tears have been shown to exert toxicity especially with the preservatives. Some people have tried rod lacrisert (propylmethyl cellulose 5 mm ×1 mm) which is placed in the inferior cul-de sac and can release the artificial tears for up to 24hrs. However it is expensive and many are not comfortable with it (5). Punctual occlusion (Silicon plugs/cautery) also is done sometimes but tear over flow has been observed (12). Artificial tear ointments coat ocular surface but give blue visions (5).

Hence gamma linolenic acid may have definite advantage over the conventional treatment modalities and it may help to alleviate the symptoms and probably the pathogenesis of chronic dry eye condition. However, the present study have some limitations as it is small trial and no scale was used to asses the symptomatic relief, thus the result of the present study need to substantiated by conducting larger adequately powered clinical trial taking into consideration the limitation of present study.

References

1. Stephen DR. Dry Eye; Cornea and External Diseases in Ophthalmology. Myron Yanoff and Jay S Duker (edts): Mosby London 1999.pp.85-89.
2. Debra AS, David AS. Epidemiology of dry eye. *Am J Ophthalmol* 2003; 136:2,318-26.
3. Sjogren H. Keratoconjunctivits sicca. In: Ridley F, Sorsby A.(eds). Modern Trends in Ophthalmology. London: Butterworh, 1940:403-13.
4. Gilbard JP. Dry eye disorders. In: Jacobiec FA, (ed). Principles and practice of Ophthalmology: Clinical Practice. Philadelphia: Saunders, 1994: 257-76.
5. KF Tabbara, Wagoner MD. Diagnosis and management of Dry-Eye Syndrome. *Int Ophthalmol Clins*1996; 36(2); 61-62.
6. Cursiefen C, Jacobi C, Dietrich T, Kruse FE. Current treatment for dry eye syndrome. *Ophthalmologe* 2006; 103(1):18-24.
7. Chen KH, Hsu WM, Lee SM, Lai JY, Li YS. Laser-assisted subepithelial keratectomy for dry eye associated with soft contact lenses. *J Cataract Refract Surg* 2005;31(12):2299-305.
8. Yenice O, Temel A, Orum O. The effect of artificial tear administration on visual field testing in patients with glaucoma and dry eye. *Eye* 2006; [Epub ahead of print]
9. Bruix A, Adan A, Casaroli-Marano RP. Efficacy of sodium carboxymethylcellulose in the treatment of dry eye syndrome. *Arch Soc Esp Oftalmol* 2006;81(2):85-92
10. Noda-Tsuruya T, Asano-Kato N, Toda I, Tsubota K. Autologous serum eye drops for dry eye after LASIK. *J Refract Surg* 2006;22(1):61-6
11. Sall KN, Cohen SM, Christensen MT, Stein JM. An evaluation of the efficacy of a cyclosporine-based dry eye therapy when used with marketed artificial tears as supportive therapy in dry eye. *Eye Contact Lens.* 2006 ;32(1):21-6
12. Eiki Goto, Yukiki Yagi, Minaki K. Improved Functional Visual Acuity after punctual Occlusion in Dry Eye Patients. *Am J Opthal* 2003; 135:704-05.
13. Lee HK, Ryu IH, Seo KY, Hong S, Kim HC, Kim EK. Topical 0.1% prednisolone lowers nerve growth factor expression in keratoconjunctivitis sicca patients. *Ophthalmol* 2006;113(2):198-205.
14. Avunduk AM, Avunduk MC, Varnell ED, Kaufman HE. The comparison of efficacies of topical corticosteroids and nonsteroidal anti-inflammatory drops on dry eye patients: a clinical and immunocytochemical study. *Am J Ophthalmo*l. 2003;136(4):593-602.
15. Pflugfelder SC, Maskin SL, Anderson B, *et al*. A randomized, double-masked, placebo-controlled, multicenter comparison of loteprednol etabonate ophthalmic suspension, 0.5%, and placebo for treatment of keratoconjunctivitis sicca in patients with delayed tear clearance. *Am J Ophthalmol* 2004; 138(3):444-57.
16. Barabino S, Rolando M, Camicione P *et al*. Systemic linolenic and Gama linolenic acid therapy in Dry-Eye Syndrome with inflammatory component. *Cornea* 2003; 22:97-201.
17. Macri A, Giuffrida S, Amico V, Iester M, Traverso CE. Effect of linoleic acid and gamma-linolenic acid on tear production, tear clearance and on the ocular surface after photorefractive keratectomy. *Graefes Arch Clin Exp Ophthalmol* 2003; 241(7):561-66.