



### Original Research Article

## Use of Plasma Rich in Growth Factors (PRGF) for the Treatment of Dry Eye in Patients Attending in Tertiary Care Hospital at A.N.M.M.C.H. Gaya

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### Abstract

**Objective:** Present study was undertaken to evaluate the efficacy of plasma rich in growth factors (PRGF) for the treatment of dry eye.

**Material and Methods:** A total of 62 patients suffering from dry eye problems were included in the study. These patients did not respond previously to other standard treatments. PRGF treatment was given topically in these patients. We quantified several growth factors present in the PRGF of each patients and record the data of the symptoms (modified score dry eye questionnaire), both before and after PRGF treatment.

**Result:** Out of 62 patients, 48 (77.41%) patients treated with PRGF have no further treatment been required, whereas in the remaining 14 patients (22.59%) other ocular treatments could be reduced. Significant improvement in score of dry eye questionnaire value was observed after PRGF treatment.

**Conclusion:** PRGF treatment led to improvement in the symptoms in patients with moderate or severe dry eye.

**Keywords:** Dry eye, Plasma growth factors, Symptoms, treatment.

### Introduction

The dry eye is among the most common diseases in ophthalmology. The prevalence is between 5% and 34%. Dry eye frequently motivates patients to seek clinical advice. However, despite advances in our understanding of its pathophysiology and in therapeutic options, the treatment of the dry eye continues to be somewhat unsatisfactory because of the multifactorial etiology of dry eye like the lack of correspondence between symptoms

reported, observed clinical parameters and Unavailability of ideal tear substitute commercially.

Tears have antimicrobial, nourishing, mechanical and optical properties. They contain components like growth factors, fibronectin and vitamins to support proliferation, migration and differentiation of corneal and conjunctival epithelium.

The use of eye drops made from autologous serum was first described by forx et al in 1984 in their

search for a tear substitute free of potentially harmful preservatives. Later Tsubota et al realized that because of the presence of growth factors and vitamins serum eye drops might also have a true epitheliotropic potential for the ocular surface. In recent years, further progress has been made by including factors derived from platelets in the composition of a novel blood derivative that is plasma rich in growth factors (PRGF). This product is being successfully applied in a variety of medical areas such as maxillofacial surgery, traumatology and so on. More recently, its application in ophthalmology for the treatment of persistent epithelial defects has been reported.

Our study represents a new approach to evaluate the efficacy of PRGF for the treatment of dry eye in terms of resolution of symptoms which were evaluated subjectively by means of questionnaire about dry eye symptoms. We also measured the efficacy in terms of improvements in specific clinical parameters.

### Materials and Methods

Present study was conducted in the Department of Ophthalmology, A.N.M.M.C.H., Gaya, during the period of January 2014 to December 2014. A total of 62 patients (55 women and 7 men) who presented with symptoms of moderate or severe dry eye were included in the study. The mean age of population was 61.5 years. All the patients were clinically examined. All these patients had never given or no response to standard treatments previously.

### PRGF Preparation

By venopuncture under sterile condition, whole blood was collected (30 ml) in 5 ml sterile tubes containing 0.5 ml of 3.8% sodium citrate. Samples were centrifuged at 460g for 8 minutes at room temperature. The resultant plasma was recovered, at platelets were activated with 22.8 mm calcium chloride as reported elsewhere. After the formation of a clot and the release of growth factors, the supernatant was recovered and diluted to 20% with 0.9% sodium chloride. This diluted PRGF (2.5 ml) were transferred into 5ml sterilized

eye drop bottles. All procedure was done under highly sterile condition, operating inside a laminar airflow hood.

Patients were instructed to keep the bottles at -20°C for a maximum period of 3 months, before start of treatment. The bottle in use was to be stored at 4°C and is used for maximum 5 to 7 days. The solutions in the drop form were to be applied for 4 times per day.

### Clinical Follow-up of Patients

Our study evaluated patient discomfort using a questionnaire based on the score dry eye questionnaire (SDEQ) modified according to the demographic characteristics of the region, both before PRGF treatment and three months later.

In this questionnaire, the patient evaluated each of the following dry eye symptoms using a scale of 0 to 4; dryness, foreign body sensation, stinging, pain, itchiness, photosensitivity, blurred vision and redness (Total 32 points).

We have defined moderate/severe dry eye based on SDEQ (Score > 10) and on the absence of improvement with conventional previous treatments (unpreserved artificial tears, punctal plug, lid hygiene, systemic tetracycline and or topical steroid).

We also performed a biomicroscopic exploration including staining with Lissamine green and the Jones test both at the beginning and end of the first treatment with PRGF.

### Result

Out of 62 patients, 48 (77.41%) patients treated with PRGF have no further treatment been required, whereas in the remaining 14 patients (22.59%) other ocular treatments could be reduced. We observed an improvement in the symptoms of dry eye in the majority of patients. Significant improvement in score of dry eye questionnaire value was observed after PRGF treatment.

These patients had reduced scores in the modified SDEQ 3 months after PRGF treatment, indicating symptom improvement after treatment. The mean questionnaire score before treatment was

significantly different from the mean score after treatment from the mean score after treatment.

Improvements, as measured in questionnaire, could be classified as minimal (< 25% score reduction), moderate (score reduction between 25% and 50%) or substantial (reduction > 50%). The improvement was minimal or no change in 10% of patients, moderate in 40% and substantial in 50%.

We found no cases of poor intolerance or undesirable effect that could be attributed to the use of PRGF.

We found that, reduced symptoms reported by patients were associated with a reduction in the grade of squamous metaplasia after PRGF treatment.

### Discussion

Dry eye is a multifactorial disease of tears and surface of the eye which leads to symptoms, visual disturbances and instability of tear film with possible changes in the ocular surface. They are accompanied by an increase in the osmolarity of tear film and inflammation of the ocular surface.

Objective tests that are currently available frequently do not establish a correlation between damage to the ocular surface and symptoms. Thus both of these parameters should be kept in mind during the diagnosis and when deciding the optimal therapeutic approach. Regardless of the cause, all dry eye patients have the almost same symptoms.

All these patients have in common abnormal or insufficient tears. This leads to reduced tear clearance, increased osmolarity, ocular surface irritation, and the infiltration and production of proinflammatory cytokines. The end result is inflammation. Once inflammation starts, damage can occur to ocular structures that perpetuate and intensify a cycle of signs, symptoms and further inflammation.

Because different type of dry eye often present with the same symptoms, it is necessary to correctly identify the principal etiopathogenic

factors involved, to administer the most appropriate treatment. Thus, the use of tear plugs, topical steroids and immunosuppressors, mucolytics, secretagogues, and so on will be more or less appropriate, depending upon the nature of each case, but the essence of therapy, common to all cases, will always be the substitution of defective tear with a product that is as similar as possible to the natural tear. However, such an ideal substitute for the tear does not exist.

A number of artificial tear-related pharmaceutical products are available (carboxy methyl cellulose, hyaluronic acid, polyvinyl alcohol and so on). Despite the fact that currently these products are preservative free, another class of compound known as conservation stabilizers is invariably present, making them potentially toxic for the ocular surface. In addition tissue growth and repair factors and antimicrobial properties are absent from these artificial tears.

The principal revolution in the search for a substitute for the natural tear came when Fox et al. in 1984 reported the application of eye drops made from autologous serum for treatment of dry eye. Later Tsubota et al realized that because of the presence of growth factors and vitamins serum eye drops might also have a true epitheliotrophic potential for the ocular surface. Subsequent publications motivated more extensive use of autologous serum as a therapeutic agent for cases of severe dry eye as well as for cases of persistent epithelial defects and other pathologies of the ocular surface. These studies revealed the superior capacity of autologous serum to maintain the integrity of the corneal and conjunctival epithelial cells as well as to regenerate the ocular surface because of its constituent growth factors whose presence in these ocular surface diseases is very much decreased.

In early 2000, a deeper understanding of platelets as a principal source of growth factors present in plasma promoted interest in elaboration of autologous blood derivatives, which are rich in platelet factors. In vitro studies revealed that the growth of corneal epithelial cells is stimulated

more by such derivatives than by autologous serum. PRGF is one of such derivative which is liberated from platelets during the process of preparation of preparation of the plasma.

PRGF is now being successfully applied in multiple fields of regenerative medicine especially maxillofacial surgery and traumatology.

In light of all this, we evaluate the potential application of PRGF as a treatment of dry eye. We studied a group of patients with dry eye of various etiologies in whom previous conventional treatments had not been efficacious. The prevalence of non-sjogren-type aqueous tear deficient dry eye syndrome is higher in this group because of the symptom severity and the absence of beneficial response of these patients to conventional treatments. Thus, the data we present here could reasonably be extrapolated to the general population of patients with moderate to severe dry eye who do not respond to conventional treatment.

The results indicate that PRGF is an effective therapeutic agent for the treatment of patients who present with moderate to severe dry eye, not only because we observed symptom improvement in most of the patients but also because of the improvements in the signs of squamous metaplasia the efficacy and good tolerance of PRGF are also confirmed by the fact that patients often request continued use of PRGF.

In fact, in many cases, PRGF treatment not only leads to symptom improvement and reduced squamous metaplasia but also leads to the reduction of associated therapies such as topical steroids and cyclosporine. This is likely because of an indirect reduction of inflammation on reducing tear osmolarity and the dilution of proinflammatory factors, which are present in the ocular surface. It also may be because of the presence in PRGF of potential inhibitors of inflammation, such as the interleukin- 1 receptor antagonists and inhibitors of metalloproteinases and other important growth factors, which are known to participate in corneal re epithelialization, such as epidermal growth factor.

## Conclusion

PRGF is an interesting therapeutic alternative for the treatment of moderate to severe dry eye. Because experience with the application of this blood derivative is limited, more specific guidelines regarding the concentrations and treatment protocols will be required. However, there are some limitations in the study. In this preliminary study we included patients with different pathologies. Further studies are required for the role of topical PRGF in the treatment of the specific types of dry eye.

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