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Original Research Article

# Clinical Study of Efficacy and Safety of Oral Pilocarpine in the Treatment of Severe Dry Eye Disease

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**Abstract**

**Introduction:** Dry eye disease is a multi-factorial disease with varied presentation of foreign body sensation with or without visual disturbance. When its presentation is severe and refractory to conventional tear substitution treatment, it maybe it can lead to compromised quality of life. **Aim & Objective:** The purpose of this study is to effectively treat aqueous deficient, severe dry eyes with oral Pilocarpine, which is conventionally refractory to conventional tear substitute ocular instillation. **Material & methods:** 32 continuous cases of bilateral dry eye disease with severe symptoms, refractory to the conventional tear film substitute treatment and fitted in our inclusion criteria. All the patients were given oral Pilocarpine tablet of 5 mg once a day. **Results:** There were mean improvement of 4.37 mm in Schirmer's value and mean improvement of 3.03 seconds in TBUT. The result was analysed by using two tailed t- test and found to highly significant ($p<0.001$) for both TBUT and Schirmer's test. A few patients complained of sweating after taking the medicine which was relieved in few minutes. **Discussion:** Pilocarpine is widely used as sialagogue. Oral Pilocarpine is approved for management of dry eye in Sjögren's syndrome and has been ascertained to be effective in dry eye (6-11). Our study shows similar effect of improvement who were otherwise refractory to tear film substitutes without significant adverse effects. Though we do not rule out that many of them may be cases of Sjögren's syndrome. **Conclusion**: Oral Pilocarpine (5 mg OD) is safe and effective in otherwise healthy individuals in relieving symptoms of severe dry eye disease in cases who are refractory to various tear film substitutes.

**Key words:** Oral Pilocarpine, Severe dry eye, Keratoconjunctivitis sicca, Sjögren's syndrome.



## Introduction

Dry eye disease (DED) is a multifactorial disease characterized by unstable tear film causing a variety of symptoms and/ or visual impairment, potentially

accompanied by ocular surface damage [1]. Concept of tear deficiency was first proposed by Schirmer's in 1903. Sjogren proposed a term Keratoconjunctivitis sicca in 1933.[2] Dry Eye Workshop (DEWS) and Tear Film And Ocular Surface Society (TFOS) described DED with discomfort, visual disturbance, tear film abnormality with increased osmolarity and inflammation of ocular surface. [3] The National Eye Institute/Industry Workshop headed by Lemp concluded that "dry eye is a disorder of tear film due to tear deficiency or excessive evaporation, which cause damage to the interpalpabral

ocular surface and is associated with symptoms of ocular discomfort". [4] Most of the treatment regimen for DED is based on tear film substitution, amelioration of inflammation and meibomitis. Still some of the patients are refractory to the treatment. Sjogren syndrome is a condition where there is secretory disorder, and which leads to diminished salivary secretion as well as tear deficiency. Oral Pilocarpine improves the symptoms and signs of dry mouth and dry eye in those patients [5].

**Aim of the study:**

To evaluate the efficacy and safety of oral Pilocarpine tablet (5mg) once day in improving the Schirmer's and Tear Break Up Time (TBUT) and global symptoms of dry eye.

**Material & methods:**

The study was prospective and in which pretreatment Schirmer's value, TBUT value and global subjective response were compared with those of post intervention with oral Pilocarpine tablet once a day after weeks. The study was conducted at a tertiary center and private clinic in Bihar from August 2018 to December 2019. Inclusion criteria were, patients of severe dry eye having Schirmer's below 5 mm with disabling foreign body sensation and compromised quality of life. The patients with allergy to Pilocarpine, bradycardia, bundle branch block, gastritis and dyspepsia, diabetes mellitus, glaucoma, peripheral myopic degeneration with extensive lattice and atrophic hole, pregnant and lactating mother were excluded. After taking an informed consent, a total of 32 patients were included in the study.

All enrolled patients underwent general examination, fasting blood glucose level, and ECG. A base line Schirmer's (Figure 1), tear break up time (TBUT) (Figure 2)were recorded.[6] A subjective overall symptoms were recorded on a scale of 1 to 4, 4 being the worst disabling symptom and 1 being mild symptom. Fluorescein staining was done to see superficial epithelia erosion, if any. [6] Infrared photo graphs of Meibomian glands were also taken to look for any damage to the glands. Same were repeated at the end of four week. We did not stopped the tear substitutes and other treatment, which the patients were already taking. One tablet of Pilocarpine (5mg) was given orally under supervision on day one at 11 AM. Patients were directed to report any discomfort. Schirmer's test, TBUT, and global response were recorded sixty minutes after oral Pilocarpine. Then patients were prescribed same dose of Pilocarpine for four weeks. Patients were asked to follow up after 1 week to see any untoward effect, if any. At the fourth week follow up, Schirmer's, TBUT and global subjective response were recorded (Table 1). Its summary is given in Table 2

**Results:**

**Table 1:**

| Sr. No. | AGE | SEX | TBUT Pre-treatment | TBUT Post-treatment | Schirmer's Pre-treatment | Schirmer's Post-treatment | Subjective Response Pre treatment | Untoward response reported |
|---|---|---|---|---|---|---|---|---|
| 1 | 32 | F | 3 | 7 | 0 | 12 | 4 | Salivation, mild pain abdomen |
| 2 | 31 | F | 1 | 3 | 1 | 4 | 4 | |
| 3 | 35 | F | 4 | 8 | 5 | 10 | 4 | |
| 4 | 40 | F | 3 | 6 | 8 | 4 | 3 | |
| 5 | 32 | F | 5 | 9 | 0 | 4 | 4 | Sweating, salivation |
| 6 | 36 | F | 1 | 5 | 0 | 8 | 4 | |
| 7 | 46 | M | 4 | 6 | 6 | 8 | 4 | |
| 8 | 50 | F | 6 | 6 | 5 | 16 | 3 | |
| 9 | 42 | F | 1 | 3 | 12 | 12 | 4 | |
| 10 | 58 | F | 4 | 7 | 6 | 12 | 4 | |
| 11 | 52 | F | 5 | 6 | 5 | 15 | 4 | |
| 12 | 48 | F | 2 | 5 | 8 | 10 | 4 | |
| 13 | 62 | F | 1 | 5 | 5 | 12 | 4 | |
| 14 | 41 | F | 3 | 6 | 7 | 12 | 4 | |
| 15 | 72 | F | 3 | 7 | 8 | 18 | 4 | Dizziness |
| 16 | 58 | M | 4 | 8 | 10 | 14 | 3 | |
| 17 | 55 | F | 2 | 6 | 10 | 12 | 3 | |
| 18 | 57 | F | 3 | 10 | 10 | 13 | 4 | |
| 19 | 54 | F | 6 | 6 | 10 | 10 | 4 | |
| 20 | 48 | M | 4 | 7 | 5 | 8 | 4 | |
| 21 | 47 | F | 3 | 5 | 5 | 10 | 4 | |
| 22 | 46 | F | 2 | 6 | 5 | 6 | 4 | |
| 23 | 50 | F | 5 | 6 | 0 | 4 | 4 | |
| 24 | 38 | F | 5 | 7 | 8 | 10 | 4 | Salivation |
| 25 | 44 | M | 4 | 8 | 8 | 12 | 3 | |
| 26 | 60 | M | 3 | 8 | 10 | 14 | 3 | |
| 27 | 65 | F | 2 | 5 | 10 | 16 | 4 | |
| 28 | 63 | F | 2 | 5 | 5 | 7 | 4 | |
| 29 | 68 | F | 3 | 6 | 3 | 10 | 4 | |
| 30 | 61 | F | 3 | 6 | 5 | 8 | 4 | |
| 31 | 62 | F | 3 | 6 | 5 | 7 | 4 | |
| 32 | 60 | F | 3 | 6 | 8 | 11 | 3 | |

Results were analyzed statistically by using two tailed t- test and found to be highly significant ($p<0.001$) for both TBUT and Schirmer's test.

**Summary of Post intervention improvement:**

**Table 2:**

| | TBUT improvement | Schirmer's improvement |
|---|---|---|
| Range | 7.00 | 12.00 |
| Mean | 3.03 mm | 4.37 mm |
| Standard deviation | 1.40 | 3.00 |
| Standard error | 0.2479 | 0.53 |

Overall subjective improvement was seen in all the patients (figure 3 and figure 4).

**Figure 1: Schirmer's test**

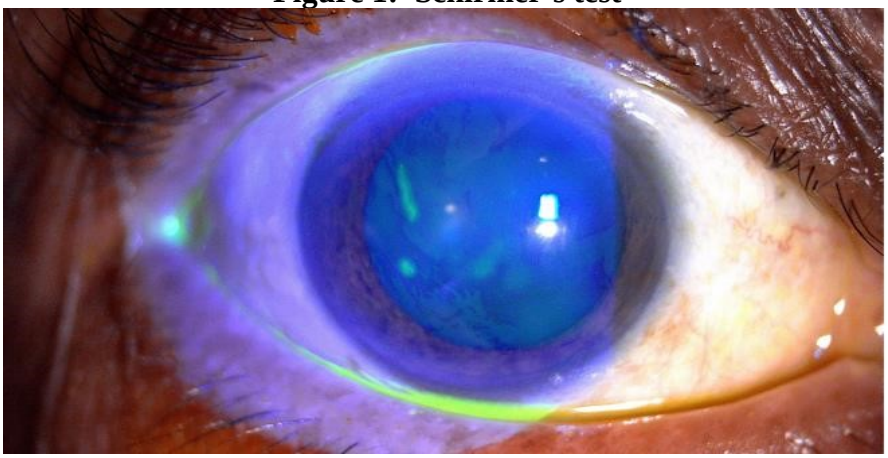

**Figure 2: TBUT measurement**

**Figure 3: Pre- Pilocarpine**

**Figure 4: Post- Pilocarpine**

**Discussion:**

On the basis of aetio-pathogenic classification dry eyes can be aqueous deficient or evaporative. On the basis of severity; dry eyes can be mild, moderate and severe. So, the effective treatment of dry eyes can be based on by categorizing it clinically on the basis of etiology or severity. Though symptoms in milder cases may vary among patients. Symptoms may include watering eyes, burning sensation, feeling of dryness in eyes, sensitivity to light, transient blurring of vision, foreign body sensations or gritty sensations.

Management of dry eyes encompasses three basic strategies: Conservation of the available tears, replacement with artificial tears and stimulating the production of tears. Methods of conserving tears include the use of moisture chamber panels and, glasses, both of which shield the eye from wind currents and decrease tear evaporation, and the occlusion of the puncta of the lower canaliculi with silicon plugs.[7] Milder cases of dry eye can be can be controlled conventionally by lubricating eye drops. However, in daily medical practice, patients presenting with severe dry eye, that compromises patients quality of life by hampering functional visual acuity, is difficult to control satisfactorily even with best conservative ocular instillation treatment. Some kind of effective treatment modality is required in such patients. Pilocarpine is an alkaloid obtained from the leaves of plant *Pilocarpus jaborandi*, is a parasympathetic stimulant mainly with a stimulatory effect on muscarinic M3 receptors. [8] Pilocarpine is a FDA approved prescription medicine both for topical and Systemic use. Topical Eye drops has long been used for treating glaucoma. Pilocarpine hydrochloride as Oral Pilocarpine tablet, was approved for symptomatic improvement of dry mouth due to radiation treatment of head and neck cancer and also, indicated for symptomatic improvement of dry eye in Sjögren. [9] Oral Pilocarpine is widely used as sialagogue. Oral Pilocarpine is approved for management of dry eye in Sjögren syndrome and has been ascertained to be effective in dry eye.[9] Studies by various researchers in past showed that, patients with Sjögren syndrome with Keratoconjunctivitis sicca have shown improvement in salivation, lacrimation and severe dry eye associated with Keratoconjunctivitis sicca after oral Pilocarpine administration. [10, 11, 12]

The ophthalmologist may very well be the first health care provider to diagnose a systemic condition associated with dry eye. Sjögren's syndrome (SS) is particularly important consideration in the initial assessment of a patient as prevalence of primary SS may be as high as 10-11% in patients presenting with clinically significant AD-DED. [13]

Results of our study on 32 patients also showed that use of oral Pilocarpine significantly improves Shirmer's value and TBUT value in all the patents of severe dry eye presenting in OPD. Similar results were found among patients of Sjogren syndrome as shown in the study done by *Frederick B. Vivino, MD; Ibtisam et al.*[5] *Bhamra J, Wong J, Gohill J.* [12] In our study, Male : Female ratio was 5:27. Average age of the patients were 50.40 years. This type of association is also found in Sjögren's syndrome. Our patients received oral Pilocarpine 5mg once daily at 11 AM. The treatment continued for four week. There were mean improvement of 4.37 mm in Schirmer's value and mean improvement of 3.03 seconds in TBUT. The result was analysed by using two tailed t- test and found to highly significant ($p<0.001$) for both TBUT and Schirmer's test. There were significant overall global symptomatic improvement including improved visual acuity and other symptoms, and dry eye related eye pain. Though we did not tried to find out, but, many of them may be cases of Sjögren's syndrome. Adverse effects like sweating, salivation and pain abdomen were mostly due to parasympathetic over stimulation. But, none of them had to discontinue due to these adverse effects.

## Conclusion:

As per our results, oral Pilocarpine was found to be highly useful in patients with severe dry eye in terms of efficacy and safety. This treatment modality seems to have a beneficial effect on subjective eye symptoms with overall, improved TBUT, Schirmer's test and functional visual acuity in patients of severe dry eye. Oral Pilocarpine in the dose of 5mg OD is safe in otherwise healthy individuals.

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