

ASSESSMENT OF EFFICACY OF TEAR SUBSTITUTES BY SCHIRMER'S TEST

Kawtikwar PS*, Kshirsagar SN and Vibhute SK

S.N. Institute of Pharmacy, Nagpur road, Pusad- 445 204, Maharashtra, India.

Received on : 14.10.2009

Revised : 21.01.10

Accepted : 27.01.10

ABSTRACT

The objective of this work was to carry out Schirmer's test to assess the lubricating efficacy of the tear substitutes; by using test preparation (containing 0.1% CMC + 0.1 % HPMC) and standard preparation- GlyTears (containing 0.5% HPMC). The study was conducted using healthy New Zealand albino rabbits. From the study it is evident that both the preparations- test as well as standard provides ophthalmic lubrication for quite a long period of time. The test preparation; although containing less amount of polymers as compared to the standard has shown slightly more lubricating efficacy; which is due to the synergistic effect of two polymers.

Keywords: *Schirmer's test; tear substitute; CMC; synergistic effect.*

INTRODUCTION

Dry eye syndrome (also known as *Keratoconjunctivitis sicca*) occurs when there is a problem with the tear film that normally keeps the eye moist and lubricated¹. The causes of dry eye include: aging, medication, illness increased evaporation of tears, blepharitis and other unknown causes². The symptoms of dry eyes are – eye irritation, slight blurring of vision and dislike towards bright lights. The symptom for a contact lens wearer is discomfort. Possible complications of dry eyes are inflammation of the conjunctiva or the cornea at the front of the eye (keratitis)^{3, 4, 5}. In severe cases, small ulcers may develop on the cornea. If left untreated, loss of vision may occur⁶. The prevalence of dry eye is more in developed countries than in the developing or the underdeveloped countries. A dry eye affects about 7 % people in their 50s, and about 15 % people in their 70s^{7, 8}. It is estimated that approximately 12 million Americans are suffering from dry eye syndrome. However, the data of Indians is not available. Women are more affected by this than men⁹.

The goals of treating dry eyes are to control the dryness of the eye, relieve symptoms, improve quality of life, minimize risk factors and prevent ocular damage. Though there is no absolute cure for dry eye syndrome, treatment includes symptomatic relief. Tear substitutes, eye ointment and other medications are generally used. Tear substitutes or artificial tears enjoy significant advantages over other measures used in the treatment of dry eye. Various viscosity enhancing agents like HPMC, sod CMC, PVA, PVP-K30, PEG-400, propylene glycol etc. are used in composition of tear substitutes. HPMC and sod CMC show synergistic effect¹⁰. Sodium CMC also acts as modulator of corneal epithelial wound healing¹¹.

MATERIAL AND METHOD

Schirmer's test-I was performed on nine healthy New Zealand albino rabbits. The permission for this work was obtained from Institutional Animal Ethical Committee. The animals were provided by animal house department of Sudhakar Naik Inst. of Pharmacy, Pusad, Maharashtra (India). Schirmer's tear strips (Contacare Ltd.) were provided by Dr. Rewanwar M.S. (Ophth), Pusad. Atropine sulphate (1%) drops were purchased from market. The polymers; CMC and HPMC were received as gift samples from Ajanta Pharma, Mumbai. GlyTears containing 0.5% sodium CMC (Sun Pharma) were purchased from market. The 'test preparation' was prepared using sodium CMC (0.1%) and HPMC (0.1%) and GlyTears was used as 'standard preparation'.

Schirmer's test was described by a German ophthalmologist Otto Schirmer in 1903^{12, 13}. The Schirmer's tear strip is employed for this test which is a specialized filter paper strip having a marking or a scale in mm on it. The Schirmer's tear strip is placed in the lateral third of the lower eye lid. Schirmer's test-I (without anesthesia) determines the basic and reflex secretion^{14, 15, 16}. The general outline of Schirmer's test is as follows:

- Selection of animals
- Maintenance on healthy feed / observation
- Initial tear production assessment
- Desiccation / drying of animal eyes using 1 % atropine sulphate instillation
- Tear production assessment after atropine instillation
- Actual test using test, standard and control groups of animals

Among the available New Zealand albino rabbits; nine healthy animals having average body weight of 2.5 Kg were selected for the study. All of these animals were kept on the same healthy feed for a week. Meanwhile

*Correspondence : pskawtikwar@rediffmail.com

EFFICACY OF TEAR SUBSTITUTES

all the animals were under observation for any abnormal changes. After re-ensuring the health of animals after observation period; tear production in animals was assessed using Schirmer's tear strips. Atropine sulphate (1%) was instilled in the eyes of the animals at regular intervals until 'dry eyes' were produced¹⁴. Tear production is again assessed after atropine sulphate instillation for a week. Next all the animals with 'dry eyes' were categorized into three groups each group comprising of three animals viz. test, standard and control. Two drops of test preparation was instilled into the eyes of the test group animals. Two drops of the marketed preparation of lubricating eye drop – GlyTears containing 0.5 % sodium CMC (Sun Pharma) was instilled into the eyes of the standard group. The third group of animals was kept as a control group. Schirmer's test-I was performed as shown in Fig 1. The Schirmer's tear strip readings suggest following significance^{12, 13}.

- < 5 mm wetting in 5 min is sign of clinical dry eye
- 5-10 mm wetting in 5 min suggests borderline dry eye
- > 10mm wetting in 5 min indicates normal secretion



Fig. 1: Schirmer's test

RESULT AND DISCUSSION

Table 1 shows the tear strip readings before and after instillation of atropine sulphate (1%). Before atropine sulphate (1%) instillation the average tear strip reading was found to be 20.7 and after atropine sulphate instillation tear average strip reading was found to be 6.4 which is quite less than the required one¹⁴; and it indicates that dry eye was being produced among all the animals.

After one hour of instillation of tear substitutes in the dry eyes of animals, the lubrication was quite high; 25 mm in test group and 26 mm in standard group. Lubrication was quite less i.e. 06 mm in the control group in which no tear substitute was instilled; indicating

Table 1: Tear strip readings

| Sr. No. | Rabbit code | Tear strip reading before 1% atropine sulphate instillation (mm) | Tear strip reading after 1% atropine sulphate instillation (mm) |
|---------|-------------|--|---|
| 1 | R1 | 21 | 06 |
| 2 | R2 | 20 | 07 |
| 3 | R3 | 23 | 06 |
| 4 | R4 | 22 | 06 |
| 5 | R5 | 20 | 06 |
| 6 | R6 | 22 | 07 |
| 7 | R7 | 19 | 05 |
| 8 | R8 | 19 | 06 |
| 9 | R9 | 23 | 07 |
| Average | | 20.70 | 6.4 |

Table 2: Lubrication assessment

| Sr. No. | Time (Hr) | Tear strip reading (mm)* | | |
|---------|-----------|--------------------------|-----------|-----------|
| | | Test | Standard | Control |
| 1 | 01 | 25 ± 1.73 | 26 ± 1.55 | 06 ± 1.07 |
| 2 | 02 | 23 ± 1.94 | 24 ± 1.85 | 07 ± 1.14 |
| 3 | 03 | 20 ± 1.58 | 21 ± 1.25 | 07 ± 1.18 |
| 4 | 04 | 17 ± 1.73 | 18 ± 1.88 | 06 ± 1.15 |
| 5 | 05 | 14 ± 1.23 | 14 ± 1.57 | 07 ± 1.07 |
| 6 | 06 | 11 ± 1.35 | 10 ± 1.58 | 07 ± 1.14 |
| 7 | 07 | 09 ± 1.55 | 07 ± 1.82 | 06 ± 1.10 |

*Mean of triplicate readings; ±: Standard deviation

desiccation of the eyes of the animals. Over a period of time, the lubrication got decreased due to evaporation of tear film. But the required lubrication eⁿ10 mm^{12, 13, 14}; was maintained up to six hours (Table 2). After six hours, the tear strip reading in the test group was found to be 11 ± 1.35 mm, in the standard group it was 10 ± 1.58 mm while in the control group no significant change was observed. SEM (Standard error in mean) values observed in the different groups are as follows: Test- 2.254, Standard-2.694, Control-0.26; P value: Test>0.1. Standard> 0.01 Control = 0.06.

One-way Analysis of Variance (ANOVA): The P value is 0.0030, considered very significant. Variation among column means is significantly greater than expected by chance.

CONCLUSION

The results of the study suggest that the marketed preparations of tear substitute (GlyTears) as well as the test preparation; both are capable of providing desired ocular lubrication for six hours. That means these preparations need less frequency of instillation; 2 to 3 times a day to provide relief from dry eye syndrome. The test preparation has shown slightly better lubricating efficacy than standard preparation even in less concentration of polymers. This is due to the fact that sodium CMC and HPMC have synergistic effect¹⁰; in enhancing viscosity and thus prevent the tear film evaporation by coating the eye ball for a longer period of time.

EFFICACY OF TEAR SUBSTITUTES

ACKNOWLEDGEMENT

The authors are thankful to Principal, Sudhakarrao Naik Inst. of Pharmacy, Pusad, for providing facilities for the work. The gift samples from Ajanta Pharma, Mumbai and tear strips from Dr. Rewanwar, Pusad, are greatly acknowledged. The authors feel in-debted for Dr. Susi Burgulassi, Italy for valuable guidance in the work.

REFERENCES

1. Anzaar F, Foster C, Ekong A. Dry eye syndrome. eMedicine. August 2006, www.patientpharmacy.co.uk.
2. Mackie I, Seal D. The questionably dry eye. Br J Ophthalmol. 1981;65: 2.
3. Keratoconjunctivitis sicca, eMedicine. WebMD, Inc. (21/042006) www.patient-pharmacy.co.uk. Retrieved on 11/12/2006.
4. Wilson S. Inflammation: A unifying theory for origin of dry eye syndrome - A peer reviewed compendium of formulary consideration, P&T Digest. 2003; 28 (12):14.
5. Brewitt H, Sistani F. Dry eye disease: The scale of problem, Surv. Ophthalmol. 2001; 45(2): S199-202.
6. Dalzell M, Dry Eye: Prevalence, utilization and economic implications: A peer reviewed compendium of formulary consideration, P&T Digest. 2003; 28 (12): 9.
7. Lee AJ, et al, Prevalence and risk factors associated with dry eye symptoms: A population based study in Indonesia. Br J Ophthalmol. 2002; 86: 1347.

Kawtikwar PS et al

8. Dry eyes, MedlinePlus Medical Encyclopedia. U.S. National Library of Medicine (10/04/2006). Retrieved on 16/11/2006
9. Daniel NJ. Dry eye, Br J Ophthalmol. 1997; 81: 426.
10. (WO/2005/089715): Ophthalmic solution comprising carboxymethylcellulose and hydroxypropylmethyl cellulose. 29/09/2005.
11. Garrett Q, Simmons P, Xu S, Vehige J, Willcox M. Carboxymethylcellulose binds to corneal epithelial cells and is modulator of corneal epithelial wound healing. Inves Ophth and Vis Science. 2007; 48:1559.
12. Schirmer O. studien zur physiology and pathology der tranenabsonderung und tranenabfuhr. Arch Klin Exp Ophthalmol. 1903;56:197.
13. Schirmer's test, Wikipedia, the free encyclopedia, www.wikipedia.com, accessed 26/9/2008.
14. Burgalassi S, Panichi L, Chetoni P, Saettone MF, Boldrini E. Development of a simple dry eye model in the albino rabbits and evaluation of some tear substitutes. *Ophthalmic Res.* 1999; 31:229.
15. Slatter H, Piek J, Costan N. Lack of lacrimotoxicity to phenazopyridine in rabbits J Vet Pharmacol Ther. 2008; 5 (3):209.
16. Didem S, Safak K, Gursov A. A Simple approach to the repeatability of the Schirmer test without anesthesia: Eyes open or closed? *Cornea.* 2007; 26(8):903.