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Evaluation of the clinical effectiveness of Protectorial® isotonic eye ointment

Domenico Porfido[1], Elizaveta Pozharitskaya[2]

[1]Outpatient Clinic Specialist, Ophthalmology Day Service, ASL Bari

[2]PhD, Associate Professor at the Ophthalmology Department of Federal Medical - Biological Agency, Russia; Private Ophthalmology Specialist, Bari

Introduction

The increasing prevalence and clinical importance of the various forms of dry eye disease have resulted in a greater need for new therapies for the ocular surface. In a sector that was once limited to a few alternative treatments, we now have a range of available options for patients who are refractory to conventional therapies. In this study, we examined 10 clinical cases of patients with dry eye disease previously prescribed artificial tears without obtaining a satisfactory response, whom we treated with Protectorial® isotonic eye ointment containing 0.4% sodium hyaluronate.

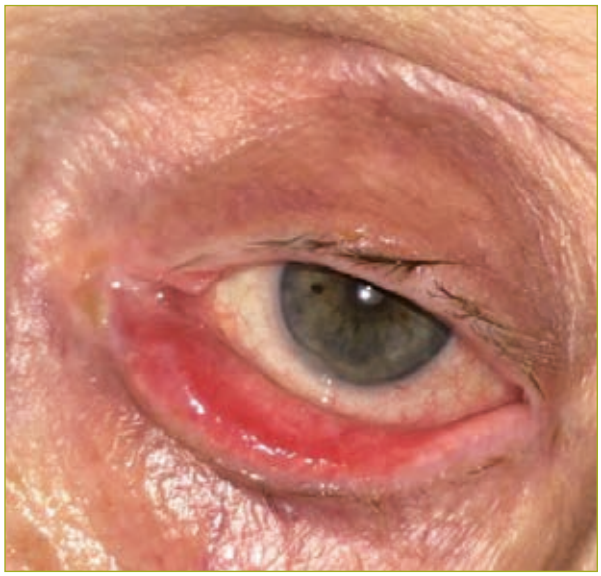
Presentation of the clinical cases

Patients 1 and 2, two women aged 47 and 51 years, came to our centre for a routine check-up complaining of periodic mild discomfort without clinically overt signs, treated as needed with a tear substitute containing sodium hyaluronate. When examined they presented a normal anterior segment, and no corneal lesions or conjunctival hyperaemia.

Patient 3, a 92-year-old woman, complained of pain, burning sensation and lacrimation in both eyes. Our examination revealed bilateral ectropion (**Figure 1**); the patient refused surgery due to systemic comorbidities (cardiovascular disease).

Patient 4, a 36-year-old male welder with subjective symptoms was referred to us complaining of difficulties opening his eye-

Figure 1. Patient 3. Long-standing ectropion.

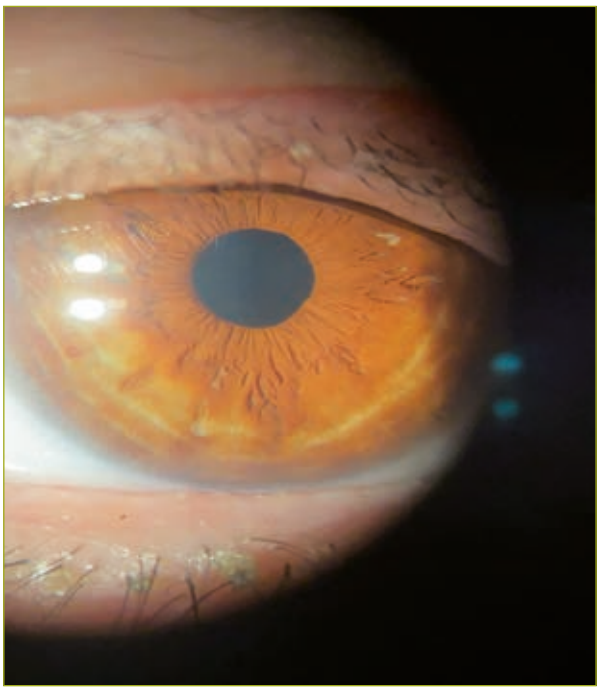


lids and dry eye sensation; he presented objective signs of mild blepharitis and rosacea, but no signs of corneal lesions or conjunctival hyperaemia (**Figure 2**).

Patients 5 and 6, two men aged 67 and 75 years, were referred to us with a foreign body sensation and photophobia secondary to facial nerve paralysis. The physical exam revealed paralytic lagophthalmos, mild conjunctival hyperaemia, and an inferior segment corneal lesion as seen on the fluorescein test, already on treatment with NSAID eye drops and artificial tears (**Figure 3**).

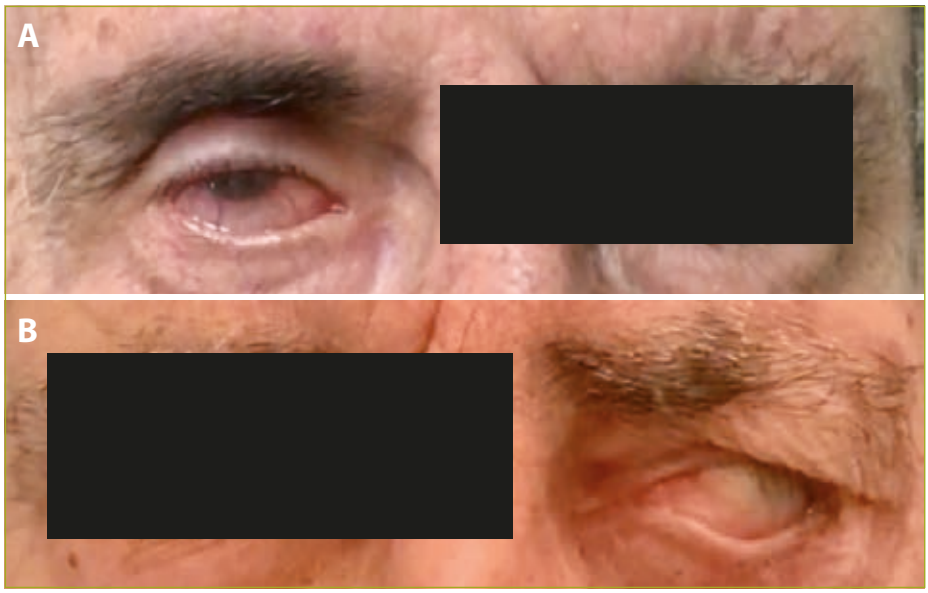
Patient 7 was a 66-year-old woman with rheumatoid arthritis on treatment with a disease-modifying anti-rheumatic drug (DMARD), in a clinical compensation phase. Her eyes were dry and painful, with heavy eyelids and itch. The physical exam revealed a classic case of early-stage Sjögren syndrome associated with discomfort, conjunctival oedema and hyperaemia, Meibomian gland inflammation with dense discharge obstructing the orifices, lacrimal alterations with the presence of mucous filaments, and corneal epithelial alterations.

Figure 2. Patient 4 presented objective signs of mild blepharitis and rosacea, but no signs of corneal lesions or conjunctival hyperaemia.



Patient 8, a 30-year-old man, was referred to our centre complaining of mild dry eye, and discomfort when driving, as well as increased blinking, and blurred vision in the evening.

Figure 3. Patient 5 (**A**) and patient 6 (**B**), with paralytic lagophthalmos, mild conjunctival hyperaemia, and an inferior segment corneal lesion.



Patient 9, a 79-year-old man with a history of left eye cataract, was referred for a consultation for reduction of visual acuity and mild photophobia. The physical exam revealed corneal oedema, epithelial damage, corneal thickness of 635 µm, and an endothelial count of 1600 cells/mm.

Patient 10, a 44-year-old woman, previously treated with endocrine therapy and chemotherapy for breast cancer, presented complaining of lacrimation, redness, foreign body sensation and difficulties opening her eyes in the morning during the previous 2 months. The physical exam revealed conjunctival hyperaemia, and corneal epithelial damage in the inferior segment on the fluorescein test, with multiple punctiform erosions.

Clinical and instrumental investigations and diagnosis

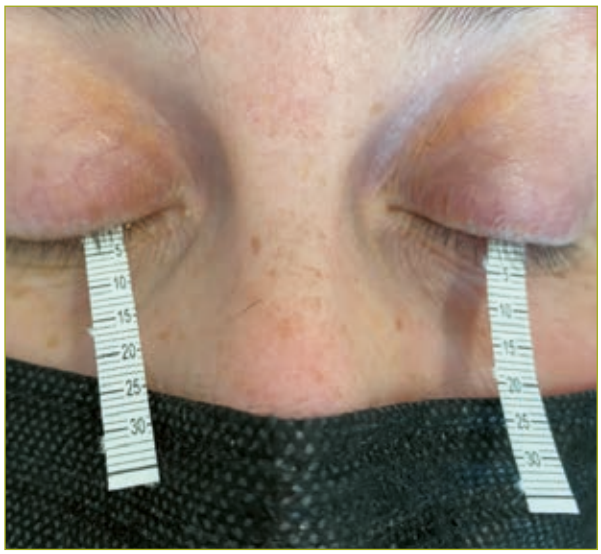
In addition to the conventional diagnostic investigations – anterior and posterior segment biomicroscopy, measurement of intraocular pressure (IoP) with the air puff test and best corrected visual acuity (BCVA) measurement – the patients also underwent lacrimal function and corneal surface assessments with the Schirmer test, tear film break-up time (TFBUT) and fluorescein staining; these tests were performed in the sequence described below to avoid impairing results and repeatability, and requiring a total time of approximately 20 minutes. Symptoms were subjectively assessed using the OSDI (Ocular Surface Disease Index) questionnaire, accompanied by an open-answer questionnaire to evaluate the degree of acceptability and tolerability of the therapies used.

It should be pointed out that due to the complexity of the tear film, the number of structures involved and the great variety of signs and symptoms that characterise dry eye disease, at the current time there is no single gold standard test for diagnosis and follow-up. This calls for the need to conduct a number of tests and compare the results. The diagnosis can be formulated on the basis of the symptoms, the characteristic signs, or a combination of both[1].

Schirmer test

The Schirmer 2 test (with anaesthesia) consists in positioning a Schirmer filter paper in the conjunctival lower temporal fornix and evaluating how many millimetres of the filter are wetted by lacrimation after 5 minutes (**Figure 4**). During this time, the patient must keep his/her eyes closed. Values equal

Figure 4. Schirmer test.



to or lower than 10 mm in 5 minutes are to be considered pathological.

Tear film break-up time (TFBUT)

Immediately after removing the Schirmer filter, a drop of 0.5% fluorescein is applied and the patient is instructed to blink. Two minutes later, the TFBUT is evaluated using a slit lamp with a cobalt blue light. The patient is instructed to blink once and then keep his/her eyes open; the clinician then counts the seconds until the appearance of dark spots interrupting the tear film and the mean of three measurements gives the TFBUT value. A value of under 10 seconds is considered pathological.

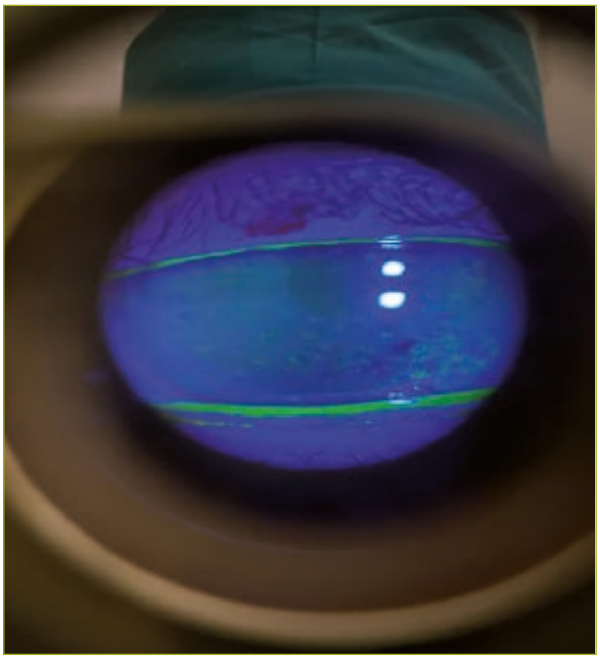
Fluorescein staining

Corneal staining with fluorescein is a method used to observe and quantify the severity of linear epithelial defects or the possible presence of superficial punctate keratopathy (**Figure 5**)[2,3].

OSDI questionnaire

The OSDI questionnaire allows rapid and precise evaluation of the severity of symptoms, their daily trends and the impact of dry eye on the patient's normal occupational activities and activities of daily living and is based on the answers to 3 panels of questions with a score of between 1 and 4, where 4 is the worst score: 0 = none of the time,

Figure 5. Corneal staining with fluorescein.



1 = some of the time, 2 = half of the time, 3 = most of the time, 4 = all of the time (see **Annex**). The OSDI is calculated using the formula: OSDI = sum of the score obtained on the test x 100 divided by the number of questions answered x 4.

If the result is:

- between 0 and 12 – normal eye condition;
- between 13 and 22 – eye condition consistent with mild dry eye;
- between 23 and 32 – eye condition consistent with moderate dry eye;
- between 33 and 100 – a clinical condition consistent with severe dry eye.

The results of the patients' clinical and instrumental tests before the prescribed therapy are shown in **Table 1**.

Treatment, clinical follow-up and patient counselling

As shown in **Table 1**, the patients examined presented varying degrees of lacrimal dysfunction and dry eye disease causing discomfort and tear film instability potentially able

TABLE 1. Results of the patients' clinical and instrumental tests before the prescribed therapy.

Patients	IoP (mmHg)	Schirmer (mm)	TFBUT (seconds)	Fluorescein	OSDI
1	13	9	14	No corneal alteration	23
2	15	8	11	No alteration	16
3	12	14	10	Inferior segment staining	30
4	9	8	6	Punctiform corneal epithelial erosions	55
5	10	10	8	Staining	73
6	12	7	9	Staining	64
7	14	3	6	Punctiform epithelial erosions	55
8	13	10	9	No alteration	22
9	16	8	7	Diffuse staining	90
10	15	4	6	Punctiform epithelial erosions	57

IoP, intraocular pressure; TFBUT, tear film break-up time; OSDI, Ocular Surface Disease Index questionnaire

to damage the corneal surface. In the case of patients 3, 4, 5, 6, 7, 9 and 10, the clinical decompensation and associated corneal defect was caused by predisposing factors: age-related ectropion in patient 3, occupational factors in patient 4, facial nerve paralysis in patients 5 and 6, rheumatoid arthritis with consequent sicca syndrome[4] in patient 7, phacoemulsification surgery in patient 9, and endocrine therapy and chemotherapy in patient 10. Clinical cases 1, 2 and 8 presented mild to moderate dry eye, with no corneal epithelial defects, and OSDI values at the borderline or consistent with moderate dry eye. In all the cases we examined, the patients were already on treatment with artificial tears with commercially available formulations containing sodium hyaluronate with natural antioxidants or anti-inflammatories, with poor clinical results and poor patient compliance due to a lack of awareness regarding their problem and the correct use of the product. Considering that almost all the clinical cases we examined were symptomatic and showed alterations on the functional clinical tests performed, we suggested modifying the current therapy

TABLE 2. Post-treatment test results, evaluated 2 months after the first visit.

Patients	IoP (mmHg)	Schirmer (mm)	TFBUT (seconds)	Fluorescein	OSDI
1	14	11	14	No corneal alteration	15
2	14	11	13	No corneal alteration	13
3	13	14	10	Transparent cornea	20
4	15	13	11	Transparent cornea	30
5	14	11	10	Mild inferior segment staining	25
6	13	12	13	Mild inferior segment staining	26
7	14	9	8	Punctiform erosions	25
8	13	12	13	No alteration	15
9	17	8	8	Mild staining	45
10	15	10	9	No corneal alteration	20

IoP, intraocular pressure; TFBUT, tear film break-up time; OSDI, Ocular Surface Disease Index questionnaire

by replacing the tear substitutes in use with eye drops containing 0.15% hyaluronic acid (Magenta Puro), to be applied twice a day, in combination with Protectorial® in the evening at bedtime.

Protectorial® is an isotonic ophthalmic ointment containing 0.4% sodium hyaluronate. The ointment formulation favors the permanence on the ocular surface and the sodium hyaluronate forms a protective shield on the corneal surface giving protection and hydration. The two products act simultaneously in dry eye disease by hydrating the surface of the eye and protecting the corneal epithelium from dehydration with a soothing effect on the inflammation.

Table 2 shows the post-treatment test results, evaluated 2 months after the first visit.

Conclusions

Dry eye disease is a multifactorial condition affecting lacrimation and the ocular surface that causes discomfort, has a directly proportionate impact on sight quality and visual acuity and causes tear film instability potentially able to damage the ocular surface[5,6]. The

subjective symptoms accompanying the various grades of severity of dry eye syndrome have a considerable impact on the patient's quality of life, as shown with the OSDI test.

The diagnostic tests, clinical investigations and assessments of the patient's subjective status show that the combination of eyedrops containing 0.15% hyaluronic acid applied twice daily for 2 months and isotonic eye ointment containing 0.4% sodium hyaluronate increases the TFBUT and significantly improves the Schirmer test, whilst obtaining an excellent result in the treatment of the dry eye syndrome and associated conditions such as lagophthalmos, non-specific corneal damage or corneal damage associated with predisposing conditions. A clear improvement was also observed in the OSDI thanks to the increase in sight quality and patient satisfaction resulting from the significant improvement in the TFBUT and the Schirmer test value. In all the cases we examined, at the end of the 2 months of treatment, an improvement was seen in both the quantitative data (Schirmer test and TFBUT) (**Figure 6**) and qualitative data (OSDI) (**Figure 7**).

In recent years, the treatment of dry eye has evolved from tear substitutes to a rationally calculated treatment algorithm. Current research is focussing on the pathophysiology of dry eye disease, on new diagnostic techniques and new therapies.

The proposed alternative appears to be a valid option for cases of mild to moderate dry eye, subclinical inflammation, dry eye syndromes associated with predisposing factors and as a manifestation of systemic diseases (sicca syndrome in Sjögren syndrome).

Figure 6. Results based on the mean Schirmer and TFBUT test values at baseline and after 2 months of the prescribed treatment.

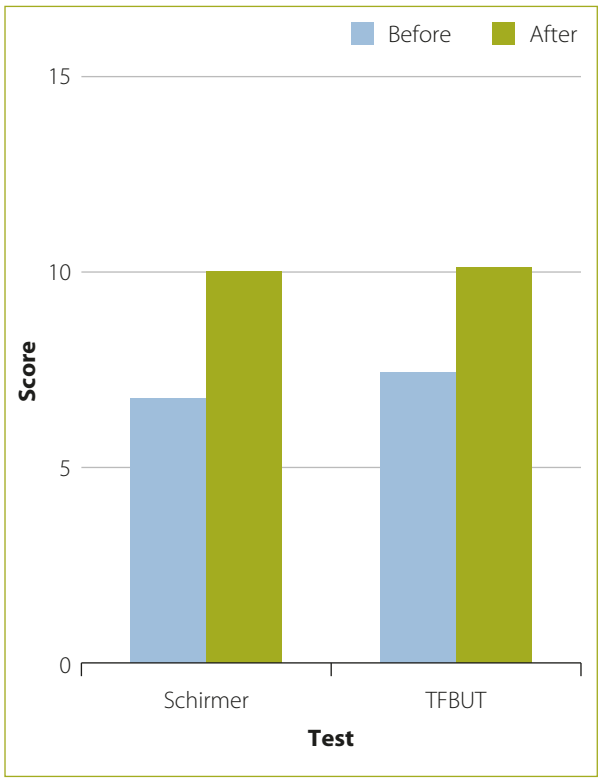
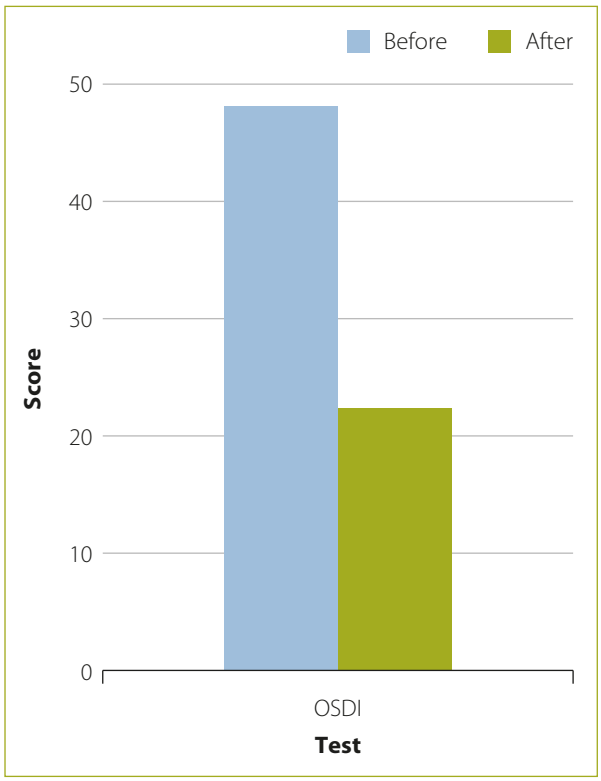


Figure 7. Results based on the mean OSDI scores at baseline and after 2 months of the prescribed treatment.



Annex

OSDI test = Ocular Surface Disease Index[7]

For each question the patient must cross the box of the answer that best represents his/her condition.

a) Have you experienced any of the following in the last week:

1. eyes that are sensitive to light
2. eyes that feel gritty
3. painful or sore eyes
4. blurred vision
5. poor vision

b) Have problems with your eyes limited you in performing any of the following during the last week:

6. reading
7. driving at night
8. working with a computer, tablet, smartphone
9. watching TV

c) Have your eyes felt uncomfortable in any of the following situations during the last week:

10. windy conditions
11. places or areas with low humidity (very dry)
12. areas that are air conditioned

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