Efficacy and safety of hypertonic 0.18% sodium hyaluronate solution (Vismed®) in patients with moderate dry eye - A study of the osmolality of the tear film

A. Rapisarda 1, F. Battaglia 1, L. Bossy 2
1 Department of Ophthalmology, " Umberto I" Hospital, Syracuse, Italy,
2 TRB Chemedica International SA, Geneva, Switzerland.

Introduction
The new definition of dry eye by the International Dry Eye Workshop (DEWS) emphasises the hyperosmolality of tear film as a core mechanism of dry eye disease.

The osmolality of normal tear fluid is about 300 mOsmol (isotonic), but in patients with dry eye it may be as high as about 150 mOsmol (hypertonic). It is believed that the main cause of the clinical symptoms and signs of tear deficit is the hyperosmolality of the tears which would increase ocular irritation.

Vismed® is a unique formulation that contains sodium hyaluronate (SH) and ions namely calcium, magnesium, potassium, sodium and chloride naturally present in the tear fluid to maintain the physiology of the cornea. It has been formulated to be hypertonic (150 mOsmol), in order to compensate the hypertonicity of tears in patients experiencing dry eye syndrome.

Study objectives
The aim of this study was to compare the efficacy and safety of a hypertonic 0.18% sodium hyaluronate solution (Vismed®) vs. isotonic 0.3% hydroxypropylmethylcellulose (HPMC) eye drops and to evaluate their effects on tear osmolality.

Methods
Study design
Randomised (1:1), controlled, open parallel group, phase III trial.

Patient selection
120 patients diagnosed with moderate dry eye syndrome to:
- Sjogren syndrome (primary or secondary), or
- Keratoconjunctivitis sicca (KCS)

Main inclusion criteria
- Male and female patients aged 18 years and over, with
- Sjogren’s syndrome or KCS,
- Schirmer test I ≤ 5.5 mm wetting/5 min for each eye,
- Tear film BUT ≤ 7 s for each eye,
- Positive and typical corneal-conjunctival staining with rose Bengal,
- Positive and typical corneal-conjunctival staining with fluorescein

Products and treatment
Sodium hyaluronate 0.18% (Vismed®) or HPMC 0.3% (Dacron®)

Statistical analysis
The Student t-test was used for comparison of BUT, Schirmer I test, staining with fluorescein and rose Bengal, corrected visual acuity, and the osmolality of the tear film. The chi-squared test was used for signs and symptoms, compliance to treatment and the global clinical judgment expressed by the investigator.

Procedures and assessments
Table 1: Efficacy parameters and schedule of assessments

Results
Patients
Patient disposition is shown in Table 2 and demographic and baseline characteristics are summarised in Table 3.

Table 2: Disposition of patients

Efficacy
Osmolality of the tear film
Vismed® caused a significant decrease in tear film osmolality values, compared with HPMC. At each study visit, there was a statistically significant difference (p<0.001) between the 2 treatments in favour of Vismed®, both at 30 min (figure 1A) and 90 min (figure 1B) following the instillation of the eye drops.

Figure 1: Mean (± SD) values for the osmolality of the tear film (mOsmol/l) at baseline and after 15, 30 and 60 days of treatment with Vismed® or HPMC; 20 min (A) or 90 min (B) after instillation of the eye drops

Burning sensation
Vismed® caused a significantly (p=0.001) greater decrease of burning sensation compared to HPMC (figure 2A).

Foreign body sensation
At the Day 60 visit, 21% of the patients in the Vismed® group reported foreign body sensation in the eye, whereas 46% of the patients in the HPMC group reported this symptom. There was a statistically significant difference between the 2 groups in favour of Vismed® (figure 2B).

Ocular pain
After 60 days of treatment, ocular pain was present in 4% of patients in the Vismed® group and in 22% of the patients in the HPMC group. There was a statistically significant difference between the 2 groups (p<0.0001) in favour of Vismed® (figure 3).

Safety
Both treatments were well tolerated. The instillation of 1 drop of Vismed® or HPMC (0.3%) 6 times per day for 60 days did not induce blurred vision or adverse reactions.

Conclusions
In contrast with HPMC (0.3%), Vismed® significantly decreased values of tear osmolality. This would explain the significant reduction of ocular symptoms and signs and the significant improvement of tear film BUT and tear volume (Schirmer test) compared to HPMC. Both products were well tolerated and no adverse reaction was reported in any group.

References