Measurement of the retention time of different ophthalmic formulation with ultra-high resolution Optical Coherence Tomography

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INTRODUCTION

The residence time of a topically applied ophthalmic preparation refers to the duration of its contact time with the ocular surface. Viscous polymer solutions have been widely used with the expectation that extended residence times permit longer interval between instillations.

Xanthan gum (XG) is a high molecular weight anionic polysaccharide (**Figure 1**) characterized by a low viscosity at low concentration (as 0.1- 0.2%) or by a "gel-like" behaviour at high concentration (as 1%). It is high hydrophilic and therefore binds high quantities of water. XG exhibits also pseudoplastic (i.e. non-Newtonian rheology) and mucoadhesive properties allowing its topical use in ophthalmic formulations (1-4)

The aim of this study was to compare the precorneal retention time of two ophthalmic formulations (eye drops and eye gel) that differ only in the presence of 1% XG, by using optical coherence tomography (OCT) (**Figure 2**).

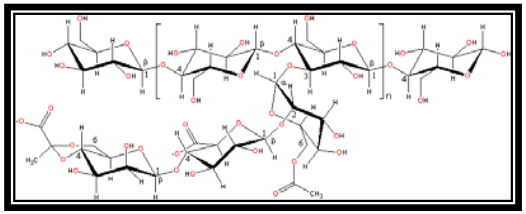

Figure 1. Structure of xanthan gum

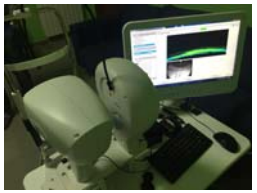

Figure 2. OCT Optovue

MATERIAL AND METHODS

Sixteen healthy subjects (5 males and 11 females) participated in the study after receiving written explanation of the procedures involved. The age of the participants was 14-78 years (46.7±18.7, mean ± SD).

One eye of each subject randomly received a single dose of a fixed steroid-antibiotic combination (FC) containing 0.1% dexamethasone and 0.3% netilmicin (Netildex, SIFI, Italy) formulated as eye drops; the fellow eye received a single dose of the same product formulated as eye gel. Both formulations were preservative-free.

Evaluation was performed using an ultra-high resolution anterior segment spectral domain OCT (Optovue Inc., Fremont, CA-USA). Central tear film thickness (CTFT) was measured before instillation (time 0=baseline value). Measurement was repeated immediately after instillation after 2 blinking and then after 10, 20, 30, 40, 50, 60 and 120 min.

The precorneal retention time was calculated by plotting CTFT in function of time. Differences between time points and groups were analyzed by Student's t test.

REFERENCES

1. Meseguer G, et al. Gamma scintigraphic comparison of eyedrops containing pilocarpine in healthy volunteers. J Ocul Pharmacol Ther. 12:481-8, 1966
2. Snibson GR, et al. Ocular surface residence times of artificial tear solutions. Cornea 11:288-93, 1992
3. Ceulemans J, et al. The use of xanthan gum in an ophthalmic liquid dosage form: rheological characterization of the interaction with mucin. J Pharm Sci. 91:1117-27, 2002
4. Mazzone MG, et al. Evaluation of mucoadhesive properties of xanthan gum hydrogels versus marketed ophthalmic gel formulations using a tensile strength method. *Invest. Ophthalmol. Vis. Sci.*. 2006; 47(13):1966.

RESULTS

Baseline CTFT was 516 ± 33 µm in the eyes to be treated with eye gel and 518 ± 30 µm (mean ± SD) in the eyes to be treated with eye drops. After the instillation of the eye gel, a significant increase of CTFT was observed (p<0.001). The maximum effect was observed immediately after instillation (532±35 µm); CTFT reduced progressively returning to baseline values 60 min after instillation. By contrast the instillation of eye drops had only a modest effect on not CTFT (**Figure 3**). Differences between two formulations were statistically significant after instillation (p<0.0001), at 10 min (p<0.001) and at 20 min (p<0.01). Representative OCT in both groups of treatment are shown in **Figure 4 and 5**.

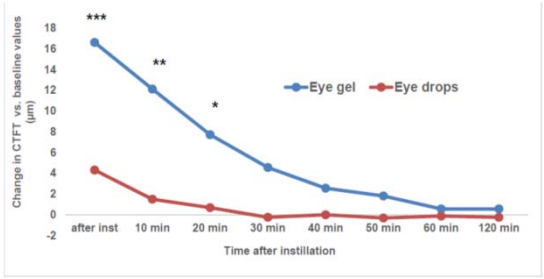

Figure 3

Changes in CTFT after instillation of a single dose of a FC containg 0.1% dexamethasone and 0.3% netilmicin formulated as eye drops or eye gel

***p<0.0001, **p<0.001, *p<0.01

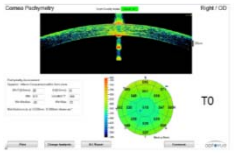

Figure 4. Representative OCT: eye drops

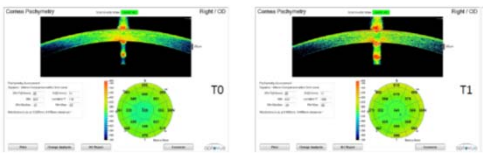

Figure 5. Representative OCT: eye gel

CONCLUSIONS

These data indicates that a FC containing 0.1% dexamethasone and 0.3% netilmicin, formulated as eye gel, is able to increase the CTFT, for as long as 1 hour, in comparison to the corresponding eye drop solution. This may suggest to extend the interval between instillations. In addition the study confirm that an ultra-high resolution anterior segment spectral domain OCT may be a useful tool for measuring precorneal residence time of any compounds on the ocular surface.

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