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Editorial Open Access

Optimization Ophthalmic Topical Antifungal Treatment

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Editorial

Currently, a significant number of ophthalmic drugs of proven efficacy have not been commercialized for economic reasons or because of stability, leaving a significant number of patients in a precarious situation and forcing ophthalmologists to seek alternative channels. At the hospital level, in order to fill this vacuum therapy has increased the use of formulations or medical products through manipulation, reformulation or adaptation to the ocular, dosage forms for administration by other routes, constituting in some hospitals over 40% of ophthalmic treatment provided, this being the case of most eye drops used for treating fungal keratitis [1].

Keratomycosis, is an infection that causes eye pain, decreased vision, despite representing only 5% of keratitis in developed countries, is often one of the main diseases causing blindness in developing countries where prevalence is far greater [2]. The filamentous fungi such as *Fusarium* and *Aspergillus spp* are the most common in temperate climates etiologic agents, being these most common infections in agricultural areas and being preceded by ocular trauma with a vegetable, although there are cases of infections *Paecylomices spp* unrelated to previous trauma. *Candida albicans* is the most common yeast is more common in cold climates and often affects patients with pre-existing corneal disease or who have received long-term corticoid therapy [3]. Usually the treatment is very complex and presents a worse prognosis than visual bacterial keratitis, probably due to lack of effective [4] treatments. Conventionally the most commonly used in the treatment of fungal keratitis treatments have been polyenes concentrations that exceed a hundred times the minimum inhibitory concentrations and more frequent yeast but currently, is booming using the new azoles, these have not shown natamycin superiority to [5].

Low investment in research and development on diseases with low incidence does not allow the development and marketing by the pharmaceutical industry of effective drugs for treatment. In countries like Spain there is currently no marketed topical ophthalmic treatment, taking responsibility processing in Hospital Pharmacy Services [6].

In the case of ophthalmic formulations, it is common to use commercial drugs intended for parenteral route for processing, by dissolving or dilution compatible with the ocular route physiological buffers. However these are not designed or adapted to this route, which can produce undesirable for ophthalmic processes level. Moreover the level of ocular penetration is unknown upon instillation and toxicity that can cause the same. In addition, the low adaptation to the road and the tendency to use very simple formulas, create systems with very low efficiency because they have a residence time on the eye surface very reduced as a result of intense precorneal clearance [7,8].

In order to maintain therapeutic concentrations, dosages prescribed based ophthalmologist frequent instillations of drops with high concentrations of drugs for long periods of time. This practice causes great discomfort to the patient, which often leads to a decrease in adherence to treatment, sometimes requiring hospitalization for proper performance and resolution of the disease. Therefore, one challenge in the ocular therapeutic design is adapted to allow an increase in the residence time of the drug at the site of application/action and control their release, thus extending the therapeutic ranges systems and improve its effectiveness. The increased therapeutic range-result in the acceptance by the patient and also significantly reduce the contact time of high concentrations of drugs and consequently, side effects [9].

Furthermore it should be noted that in ocular pharmacology, we cannot apply the same cut-off as defined by international committees to label a microorganism as sensitive or resistant to a particular anti-infective, since concentrations have nothing administered topically to do with those achieved following systemic administration [10].

It is therefore essential to make a common effort on the reinterpretation and study of cut offs for topical treatments, it being necessary to take into account the individual pharmacokinetic data and pharmacodynamics of each drug on the ocular surface, this being the first step to define the concentrations suitable for the manufacture of ophthalmic preparations [10,11].

Furthermore, the use of methods of assessing toxicity of ophthalmic preparations such as cytotoxicity studies based on bioimpedance or organotypic methods such as HET-CAM, a necessity to establish concentrations up eyedrops prepared [12-14]. Another possibility is to consider the use of high concentrations of antifungal using excipients such as cyclodextrins, to increase solubility and decrease toxicity [15]. The use of cyclodextrins also allows the opening of new therapeutic arsenal in ophthalmology, allowing the formulation of water-insoluble antifungal as econazole, which shows a broad spectrum of action against most pathogens causing fungal keratitis [16].

The availability of assets for use in ophthalmic formulation principles is conditioned by the requirement of sterility, so we use parenteral medications that are designed for other uses or routes of administration. We need more appropriate eye and adapted vehicles this route of administration, to stay longer on the corneal surface, physiologically compatible with tissues where we place that generate less tissue toxicity and more therapeutically effective doses we use

today . One of the challenges in the ocular therapeutic design is adapted to allow an increase in the residence time of the drug at the site of application/action and control their release, thus extending the therapeutic ranges and improve efficiency systems. The increased therapeutic range-result in the acceptance by the patient and also significantly reduce the contact time of high concentrations of drugs and consequently side effects. The novel ophthalmic hydrogels based manageability technology in situ gelling behave as liquids for instillation facilitating administration of precise dosages and once in contact with the ocular environment, in response to changes in environmental conditions, as pH or ion concentration, they undergo a phase transition and form a viscoelastic gel promotes their retention in the ocular surface and in controlling the release of drugs [17].

From our experience we can only achieve this by fostering multidisciplinary research collaboration based ophthalmic anti-infective therapy and vehicle design to improve arrival to optimize antifungal therapeutics fungal keratitis.

References

1. Fernández-Ferreiro A, González-Barcia M, Dominguez Alba J, Otero Espinar FJ (2014) Use of fortified eye drops on eye infections. Eur. J. Clin. Pharm 16.
2. Rautaraya B, Sharma S, Kar S, Das S, Sahu SK (2011) Diagnosis and treatment outcome of mycotic keratitis at a tertiary eye care center in eastern India. BMC Ophthalmol 11: 39.
3. Fernández-Ferreiro A, González Barcia M (2014) Eye Pharmacotherapy, In: Handbook resident freshmen hospital pharmacy.
4. Miller D (2013) Pharmacological treatment for infectious corneal ulcers. Expert Opin Pharmacother 14: 543-560.
5. Prajna NV, Krishnan T, Mascarenhas J, Rajaraman R, Prajna L, et al. (2013) The mycotic ulcer treatment trial: a randomized trial comparing natamycin vs voriconazole. JAMA Ophthalmol 131: 422-429.
6. Pammolli F, Magazzini L, Riccaboni M (2011) The productivity crisis in pharmaceutical R&D. Nat Rev Drug Discov 10: 428-438.
7. Fernández-Ferreiro A, Santiago-Varela M, Gil-Martinez M, González-Barcia M et al. (2015) DI-023 Effect of different antifugal eye drops on human corneal cells in vitro. Eur J Hosp Pharm 22: A84-A84.
8. González-Barcia M (2011) Ophthalmology Pharmaceutical Compounding, in: Asp. Practical Farm. In a Serv. Farm., Master Line Prodigy, Galpagar.
9. Fernández-Ferreiro A (2015) Dissertation: Management, safety and optimization of ophthalmic topical formulations in Hospital Pharmacy Services, University of Santiago de Compostela.
10. Guideline on the Evaluation of Medicinal Products Indicated for treatment of bacterial infections (2011) Rev. 2 Committee for Medicinal Products for Human Use (CHMP).
11. Keay LJ, Gower EW, Iovieno A, Oechsler RA, Alfonso EC, et al. (2011) Clinical and microbiological characteristics of fungal keratitis in the United States, 2001-2007: a multicenter study. Ophthalmology 118: 920-926.
12. Fernández-Ferreiro A, Santiago-Varela M, Gil-Martinez M, García-Caballero T, Pardo M et al. (2015) Ocular safety comparison of non-steroidal anti-inflammatory eye drops used in pseudophakic cystoid macular edema prevention. Int J Pharm 495: 680-691.
13. Fernández-Ferreiro A, Santiago-Varela M, Gil-Martinez M, González-Barcia M, Pineiro-Ces A, et al. (2014) Effect of different fortified antibiotic eye drops on human and bovine corneal cells "in vitro" Invest. Ophthalmol. Vis Sci 55: 4891-4891.
14. Fernandez-Ferreiro A; Santiago-Varela M; Pardo M; González-Barcia M; Pineiro-Ces A; Blanco-Mendez J; Lamas MJ; Otero- Espinar FJ (2014) [Analysis of ocular toxicity of fluconazole and voriconazole eyedrops using HET-CAM]. Farm Hosp 38: 300-304.
15. Fernández-Ferreiro A, Fernández Bargiela N, Santiago Varela M, Gil-Martínez M, Pardo M, Piñeiro Ces A, Blanco Méndez J, González-Barcia M, et al. (2014) Cyclodextrin-polysaccharide-based, in situ-gelled system for ocular antifungal delivery. Beilstein J Org Chem 10: 2903-2911.
16. Fernández-Ferreiro A, Llovo-Taboada J, González-Barcia M, Lamas MJ, Otero Espinar FJ, Blanco Mendez J (2014) Eyedrops econazol 10 mg / ml as a therapeutic alternative in the treatment of fungal keratitis.
17. Fernández-Ferreiro A, González-Barcia M, Gil-Martínez M, Vieites-Prado A, Lema I, Argibay B, Blanco Méndez J, Lamas MJ, Otero-Espinar FJ (2015) In vitro and in vivo eye safety and eye surface permanence determination by direct and Magnetic Resonance Imaging of ion-sensitive hydrogels based on gellan gum and kappa-carrageenan, Eur J Pharm Biopharm.