Research Article

Cyclosporine A cationic emulsion in patients after conjunctival tumors surgery

Abstract

Purpose: The aim of this study is to present subjective patients symptoms present after surgical excision of various epibulbar lesions and their reduction after local use of cyclosporine a cationic solution eye drops.

Methods: A group of patients after the surgery of the epibulbar tumors in the January-March 2017 period. After surgery cyclosporine A (CsA) treatment was administered once a day. We evaluate results 12months of treatment.

Results: A group of 8 patients, an average age of 43years. Indications of treatment: recurrent epibulbar carcinoma-2 patients (25%), dysplastic melanocytic nevus-4 patients (50%), malignant melanoma of the conjunctiva-1 patient (12.5%), epibulbar MALT lymphoma-1 patient (12.5%). We evaluate the course of healing for the first 12 months after surgery. The calculation results confirmed that treatment by CsA after surgery of the melanocytic lesions group is considered to be statistically significant (P value equals 0.0351) and the treatment by CsA after surgery of the non-melanocytic lesions group is considered to be not statistically significant (P value equals 0.1027).

Conclusion: The function of tear film in patients with epibulbar tumors is limited. CsA specifically affects only the function of T lymphocytes, diminishing the production of cytotoxic T lymphocytes. Application of CsA is another option for treating dry eye syndrome and post-surgery complications of epibulbar tumors, which, in the post-surgery course, is especially important in the treatment of the inflammatory component of the post-surgery response.

Keywords: epibulbar, tumor, dry eye syndrome, cyclosporine A, conjunctival lesion

Introduction

Tumors of the conjunctiva and cornea comprise a large and varied spectrum of lesions, congenital and acquired lesions. Ocular surface tumors include a variety of lesions originating from squamous epithelium, melanocytic tumors and lymphocytic resident cells of the conjunctival stroma. One of the first symptoms in these patients can be dry eye syndrome.

Dry eye is a multi-factorial disease of the ocular surface characterized by a loss of homeostasis of the tear film, and accompanied by ocular symptoms, in which tear film instability and hyperosmolarity, ocular surface inflammation and damage, and neurosensory abnormalities play etiological roles. This is an actualized definition of the dry eye disease according to the TFOS DEWS II Definition and Classification Subcommittee published in 2017. Common symptoms of dry eye disease (DED) include dryness, irritation and foreign body sensation, light sensitivity, increased tearing or itching. The pathogenesis of the disease is not clear. Reduced lacrimal tear secretion and volume causes tear hyperosmolarity leading to hyperosmolarity of the ocular surface epithelial cells. This stimulates a cascade of inflammatory events which play an important role. Mediators such as cytokines, chemokines, and matrix metalloproteinases promote the activation of immature antigen-presenting cells (APCs). This leads to expansion of autoreactive CD4+ helper T cells followed by self-perpetuating cycle of inflammation. Prevalence of the DED is between 5 and 35% according to many published studies depending on diagnostic criteria. Increased prevalence is present in women and older population. The severe form of the disease is characterized by persistent and recurrent symptoms that are poorly correlating with the objective clinical findings.

Tumors of the ocular surface have a wide clinical spectrum and include several forms of epithelial, stromal, caruncular and secondary tumors. Complete excision is the treatment of choice in majority of these tumors with specific approach applied in some of them. For instance, in case of ocular surface squamous neoplasia complete but gentle surgical excision using a “no-touch” technique is the treatment of choice. Resulting superficial defects can be overlaid with an amniotic membrane. On the other hand treatment of conjunctival melanoma is based on certain established principles. These extend from complete excision of the lesion in the episcleral plaque with 4mm clinically clear margins and post-surgery adjuvant plaque brachytherapy to the eyelid sparing exenteration, proton beam radiotherapy and systemic chemotherapy. Part of the ocular surface lesions needs only a periodical observation. In general, benign tumors and choristomas are excised only if there is a cosmetic or functional concern. Malignant tumors generally need complete excision with clear margins and excision edge cryotherapy. One of the ways to avoid itching, dry eye symptoms and irritation after surgery of epibulbar tumors is cyclosporin A therapy.

Methods

A group of patients after the surgery of the epibulbar tumor was observed in the January-March 2017 period. After surgery cyclosporine A (CsA) treatment was administered once a day. We evaluate results 12months of treatment.

Results

A group of 8 patients, an average age of 43year (23 to 65years). Indications of treatment were: recurrent epibulbar carcinoma-2 patients (25%), dysplastic melanocytic nevus-4 patients (50%), and malignant melanoma of the conjunctiva-1 patient (12.5%), epibulbar MALT lymphoma-1 patient (12.5%).

Patients underwent surgery under local anesthesia. Lesion was excised with clear margins and excision edge cryotherapy. Part of the ocular surface lesions needs only a periodical observation. In general, benign tumors and choristomas are excised only if there is a cosmetic or functional concern. Malignant tumors generally need complete excision with clear margins and excision edge cryotherapy. One of the ways to avoid itching, dry eye symptoms and irritation after surgery of epibulbar tumors is cyclosporin A therapy.
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removal with a 2mm clinically tumor-free conjunctival part peripheral to the tumor and a thin scleral flap beneath the tumor. During the surgery Mitomycin C was applied topically. The corneal epithelium 2mm anterior to the tumor was not treated with absolutely alcohol and we did not use cry therapy as well. After surgery antibiotics and steroids were used for 10days and patients continued therapy with CsA solution once per day use. We evaluated the course of healing for the first 12months after surgery – patients’ dry eye, pain, itching and foreign body feeling after surgery (Table 1). We divided patients into 2 subgroups – patients with melanocytic epibulbar lesions and non-melanocytic epibulbar lesions (Table1), (Figure 1), (Figure 2).

Table 1 Symptoms in group of patients before and after surgery

| Treatments/symptoms | Before surgery | After surgery |
|---------------------|----------------|--------------|
|                     | Melanocytic lesion | Non-melanocytic lesion | Melanocytic lesion | Non-melanocytic lesion |
| Dry Eye             | 5               | 62.5         | 3               | 37.5         | 1              | 12.5           | 1              | 12.5           |
| Pain                | 1               | 12.5         | 1               | 12.5         | 0              | 0              | 1              | 12.5           |
| Itching             | 4               | 50           | 3               | 37.5         | 0              | 0              | 0              | 0              |
| Foreign Body Feeling| 2               | 25           | 1               | 12.5         | 0              | 0              | 0              | 0              |

Figure 1 Non-melanocytic epibulbar lesion (carcinoma) before surgery (A), first week after surgery (B) and 3months after surgery and treatment with CsA cationic solution (C).

Figure 2 Melanocytic epibulbar lesion (dysplastic neovascular melanocytic nevus) before surgery (A), seven weeks after surgery (B) and six months after surgery and treatment with CsA cationic solution.

We calculated paired t-test with the significance level 0.05 for melanocytic lesions group and non-melanocytic lesions group. The calculation results confirmed that treatment by CsA after surgery of the melanocytic lesions group is considered to be statistically significant (P value equals 0.0351) and the treatment by CsA after surgery of the non-melanocytic lesions group is considered to be not statistically significant (P value equals 0.1027).

Discussion

Clinical manifestation of the epibulbar tumors is variable. Benign lesions may be stable and asymptomatic and sometimes even undergo spontaneous resolution. 3 Other can cause redness, discomfort, local swelling, erythema. 1 Ocular surface squamous neoplasia can present even with a course resembling chronic conjunctivitis. 11 The most common presentation of conjunctival melanoma is a raised, irregular, unilateral pigmented area, brownish-black in color and most often without other associated symptoms. Less common is the foreign body sensation and pain in the affected eye. 11,12

Subjective symptoms following surgical treatment of the epibulbar tumors are also various, including patients’ complaints resembling symptoms of DED. Many published studies also reported origin or escalation of the DED symptoms after other kinds of eye surgery. 13–15 Long term artificial tears supplementation is often needed, which typically provides only short-term relief from DED symptoms. 16 Cyclosporine A has received increased attention in recent years as a therapeutic agent providing inhibition of the inflammatory responses associated with DED. 17,18 Long term treatment is required to achieve the resolution of symptoms such as reduction of inflammatory markers and tear osmolarity, antiapoptotic effects and recovery of reduced conjunctival goblet cell density. 19 Cationic emulsion formulation containing 0.1% (1mg/ml) CsA (CsA CE) has been developed and registered in 2015. 3 It is a cationic emulsion with a long-lasting presence of the CsA in the tear film. 18 In our study we did not confirm in non-melanocytic lesions group to be statistically significant benefit of use after surgical removal of the lesion, but in melanocytic lesions group it was considered to be statistically significant.

The function of tear film in patients with epibulbar tumors is limited. Cyclosporine A is a cyclic polypeptide and belongs to the group of immunosuppressants-calcineurin inhibitors (CNI). CsA specifically affects only the function of T lymphocytes, diminishing the production of cytotoxic T lymphocytes and also antifungal effect was confirmed. 19 Application of CsA is another option for treating dry eye syndrome and post-surgery complications of epibulbar tumors, which, in the post-surgery course, is especially important in the treatment of the inflammatory component of the post-surgery response.

Conclusion

The function of tear film in patients with epibulbar tumors is limited. CsA specifically affects only the function of T lymphocytes, diminishing the production of cytotoxic T lymphocytes. Application of CsA is another option for treating dry eye syndrome and post-surgery complications of epibulbar tumors, which, in the post-surgery course, is especially important in the treatment of the inflammatory component of the post-surgery response.

Acknowledgments

None.

Conflict of interest

None of the authors has conflict of interest with this submission. All authors have read and approved of the manuscript being submitted.

Financial/proprietary interest

None of the authors has financial interest related to this study to disclose.

Citation: Furdova A, Kapitanova K, Sekac J, et al. Cyclosporine A cationic emulsion in patients after conjunctival tumors surgery. Adv Ophthalmol Vis Syst. 2018;8(6):291–293. DOI: 10.15406/avs0.2018.08.00323
Declaration of Helsinki

The manuscript does not report the results of an experimental investigation on human subjects.

Informed consent

This article does not include results of experimental investigations on human subjects.

References

1. Craig JP, Nichols KK, Akpek EK, et al. TFOS DEWS II definition and classification report. Ocul Surf. 2017;15(3):276–283.
2. Stevenson W, Chauhan SK, Dana R. Dry eye disease: an immune-mediated ocular surface disorder. Arch Ophthalmol. 2012;130:90–100.
3. Kaštelan S, Tomić M, Salopek-Rabatić J, et al. Diagnostic procedures and management of dry eye. BioMed Res Int. 2013;2013:309723.
4. Baudouin C, Messmer EM, Aragona P, et al. Revisiting the vicious circle of dry eye disease: a focus on the path physiology of meibomian gland dysfunction. Br J Ophthalmol. 2016;100(3):300–306.
5. Leonard A. Management of Vernal Keratoconjunctivitis. Ophthalmol Ther. 2013;2(2):73–88.
6. Krčová I, Stanislavová M, Peško K, et al. [amniotic membrane applications - our experience]. Česk Slov Oftalmol. 2016;72(6):204–208.
7. Honavar SG, Manjandavida FP. Tumors of the ocular surface: A review. Indian J Ophthalmol. 2015;63:187–203.
8. Shields JA, Shields CL, De Potter P. Surgical management of circumscribed conjunctival melanomas. Ophthal Plast Reconstr Surg. 1998;14(3):208–215.
9. Shields CL, Shields JA. Tumors of the conjunctiva and cornea. Surv Ophthalmol. 2004;49(1):3–24.
10. Akpek EK, Polcharoen W, Chan R, et al. Ocular surface neoplasia masquerading as chronic blepharoconjunctivitis. Cornea. 1999;18(3):282–288.
11. Salcedo-Hernández RA, Luna-Ortiz K, Lino-Silva LS, et al. Conjunctival melanoma: survival analysis in twenty-two Mexican patients. Acta Ophthalmol. 2014;92(3):155–158.
12. Halas JM, Svetloșakova Z, Babal P. Therapy of melanocytic conjunctival tumors. Bratisl Lek Listy. 2013;114(8):446–450.
13. Cetinkaya S, Mestan E, Acir NO, et al. The course of dry eye after phacoemulsification surgery. BMC Ophthalmol. 2015;15:68.
14. Yu Y, Hua H, Wu M, et al. Evaluation of dry eye after femtosecond laser-assisted cataract surgery. J Cataract Refract Surg. 2015;41(12):2614–2623.
15. Denoyer A, Landman E, Trinh L, et al. Dry eye disease after refractive surgery: comparative outcomes of small incision lenticule extraction versus LASIK. Ophthalmology. 2015;122(4):669–676.
16. Gayton JL. Etiology, prevalence, and treatment of dry eye disease. Clin Ophthalmol. 2009;3:405–412.
17. Pisella P-J, Labetoulle M, Doan S, et al. Topical ocular 0.1% cyclosporine A cationic emulsion in dry eye disease patients with severe keratitis: experience through the French early-access program. Clin Ophthalmol. 2018;12:289–299.
18. Daull P, Lallemand F, Philips B, et al. Distribution of cyclosporine A in ocular tissues after topical administration of cyclosporine A cationic emulsions to pigmented rabbits. Cornea. 2013;32(3):345–354.
19. Pandit RT. Antifungal effects of cyclosporine A. Cornea. 2003;22(1):92.