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ROLE OF INTRAOPERATIVE DOXORUBICIN IN PREVENTING THE RECURRENCE OF A PRIMARY PTERYGIUM – FIRST CLINICAL TRIAL

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Abstract

Purpose: The purpose of this study was to find the role of intraoperative doxorubicin in preventing the recurrence of a primary pterygium.

Materials and methods: Forty four patients including 8 males and 36 females in the age range of 22 to 55 years having primary pterygium of progressive type were enrolled. After making a complete ocular examination including visual acuity record, slit lamp biomicroscopy and tear film examination, the pterygia were examined for laterality, amount of its encroachment on cornea and its width at 5mm from the limbus. These patients were treated with pterygium excision followed by intraoperative application of doxorubicin (0.02%) for three minutes. The patients were regularly followed till one year postoperatively. At these visits, the patients were examined for visual acuity, wound condition, adverse events and recurrence of pterygium.

Results: The mean age of patients was 41.4± 12.9years. All these patients had pterygium on the medial side of cornea. The encroachment of pterygium on cornea was 0-6 (2.3±1.4)mm. The width of pterygium tissue at 5 mm from limbus was 5-15 (8.9±2.5)mm.

The side effects experienced by our patients from the use of doxorubicin were conjunctival hyperemia, corneal epithelial defect, subconjunctival hemorrhage, episcleritis, increased pain, foreign body sensation, lacrimation, irritation, diminution of vision and photophobia. These adverse events were mild and did not persist for more than 2 to 3 days following excision. Recurrence was seen in 12 patients (27.27%). The recurrence of pterygium was not influenced by age and/or sex of patients, laterality of eye involved, amount of encroachment of pterygium on cornea, width of pterygium, and preoperative complaints except photophobia and discharge.

Conclusions: The use of intraoperative doxorubicin in low concentrations during pterygium excision is effective in preventing the recurrence of a primary pterygium without causing severe side effects.

Key words: Pterygium, Pterygium and doxorubicin, Primary pterygium, Doxorubicin and ocular uses.

INTRODUCTION

Out of the various modalities used in treatment of Pterygium, antimetabolite agents are more target specific as these agents inhibit RNA, DNA and fibroblast synthesis[1] and prevent the proliferation of vascularised granulation tissue. Antifibroblastic agents which have been used previously for pterygium treatment include mitomycin C (MMC)[2] and daunorubicin.[3] Doxorubicin is an antimitotic and antimetabolite drug[4] which affects satellite cell division, maximally, during the period of active regeneration.[5] The known ocular uses of doxorubicin include treatment of blepharospasm and hemifacial spasms.[5] As it inhibits repopulation of fibroblasts, workers have advocated its use following trabeculectomy (Saika et al, 1997).[6] We used doxorubicin in form of a single intraoperative application during surgical excision of primary pterygium for the first time.

MATERIALS AND METHODS

A high degree of ethical standards were maintained and guidelines of the Helsinki Declaration were followed while carrying out this project.

Forty four patients including 8 males and 36 females in the age range of 22 to 55 years having primary pterygium of progressive type were enrolled in this study. These patients presented to us with complaints like itching, photophobia, foreign body sensation, redness, discharge and diminution of vision. Each patient underwent a complete ocular examination including visual acuity record, slit lamp biomicroscopy and tear film examination. The patients with keratitis sicca, Sjogren's syndrome, neurotrophic keratitis, acne rosacea, severe mebomian gland dysfunction or blepharitis were excluded from the study.

These patients were treated with the intraoperative use of doxorubicin during pterygium excision.

SURGICAL TECHNIQUE

0.2 mg/ml of doxorubicin was prepared by dissolving 2 mg of doxorubicin in 10 ml of distilled water. The antimitotic agent was freshly prepared each time before surgery.

The pterygia were excised using bare sclera technique.[7] As a modification of the original technique, while giving these two radial incisions, we included about 2 mm of healthy conjunctiva both on upper and lower side of pterygium. Also, the 3 mm redundant tissue at apex of free conjunctival triangle was excised along its whole length in order to remove apical abnormal conjunctival flap which was hosting the pterygium.

The blunt end of the indigenously prepared bamboo swab stick was sharpened by peeling it with 11 number surgical blade. The fashioned end was dipped in antimitotic solution and applied on bare sclera as well as undersurface of sutured conjunctival flap while keeping about 2mm away from cornea. It was assumed that drug must have reached limbal stem cells through a contiguous spread. The total application time was 3 minutes. Following this, about10 c.c. of normal saline was used to flush the bare sclera and subconjunctival space to remove the antimitotic agent.

The first follow-up was done next day of surgery and the second follow up was done at one week. At these visits, the eyes were examined for visual acuity, wound condition and other adverse events. The patients were re-examined at 2 weeks, 1 month, 6 months and one year postoperatively.

STATISTICAL METHOD

Students't' test was used to compare mean values in recurrence/no-recurrence.

RESULTS

Forty four patients underwent surgical excision of pterygium with doxorubicin. The mean age of patients was 41.4± 12.9years. All these patients had pterygium on the medial side of cornea. The encroachment of pterygium on cornea was 0-6 (2.3±1.4) mm in these patients. The width of pterygium tissue at 5 mm from limbus was 5-15 (8.9±2.5) mm. The side effects experienced by our patients from the use of doxorubicin were conjunctival hyperemia, corneal epithelial defect, subconjunctival hemorrhage, episcleritis, increased pain, foreign body sensation, lacri-

mation, irritation, diminution of vision, and photophobia. These adverse events were only mild and did not persist for more than 2 to 3 days following surgery. Doxorubicin was noticed to cause increased capillary fragility and resultant increased oozing of blood. This caused the appearance of subconjunctival hemorrhage postoperatively in some patients.

Recurrence was seen in 12 patients (27.27%). The recurrence of pterygium was not influenced by age of patients, laterality of eye involved, amount of encroachment of pterygium on cornea, width of pterygium or preoperative complaints except that photophobia and discharge had a statistically significant relation with the recurrence of pterygium.

DISCUSSION

When excised along with antimitotic agents, the primary pterygium recurs with a frequency varying from 2.7% to 44%.[8-19]

We modified the original surgical excision of pterygium described by O'Brien[20] and along with pterygium excision, also removed the diseased conjunctival tissue which was hosting it. We also made it a point to cleave the adjacent healthy conjunctival tissue so as to decrease its scaffold action which could permit migration of abnormal cells from limbus onto the undersurface of conjunctiva and in the opposite direction spreading over the cornea.

Doxorubicin is considered to be more potent than MMC in reducing cellular viability, mitotic activity, and production of peptides in human tenon's capsule fibroblasts.[6] Due to its influence on the wound healing response,[6] local administration of doxorubicin after pterygium surgery should decrease the recurrence of pterygium.

We have used swab stick application of this drug over bare sclera in order to control the amount and limit the extent of drug delivery. The swab stick application has been used not been used earlier in pterygium surgery and mostly sponge application has been in practice.

We had a recurrence rate of 27.27% in our patients and this is comparable to that seen with other antimitotic agents. Other workers have found that recurrence was more common in young patients.[10,13] We, however, did not notice any relation between recurrence of pterygium and parameters like age and/or sex of patients, laterality of eye involved, amount of encroachment of pterygium on cornea, width of pterygium, preoperative complaints and postoperative adverse events. The mean time for recurrence of pterygium in our patients was about 2.5 months which is somewhat less than the usual time period i.e. about six months found previously.[10,13,21] We feel that the rate and time of recurrence of a pterygium might have some relation with the population or racial group enrolled.

From our experience of intraoperative Doxorubicin application during pterygium surgery, we found that this agent has a potential of preventing recurrence of a primary pterygium. As an additional precaution, we advocate the use of modified technique for surgical excision of pterygium, as described here by us.

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