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Research Article

PREDNISOLONE ACETATE EYE DROPS IN PREVENTING GRAFT REJECTION IN SUTURE FREE- GLUE FREE PTEYGIUM EXCISION WITH CONJUNCTIVAL AUTOGRAFT SURGERY

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ABSTRACT

An analysis on the surgical techniques for pterygium excision showed that the pterygium recurrence following surgical treatment of primary pterygium are close to 6 and 25 times higher if no conjunctival autograft placement is performed. Traditionally, during pterygium surgery the conjunctival autografts are secured in place with either absorbable or non-absorbable sutures. The most common complications of allograft without suture or glue is graft oedema, rejection and dislodgement. Recently patients own autologous blood is used as a bed to place the graft without use of suture and glue. These grafts should not develop oedema so as to minimise the risk of dislodgement and rejection. Topical corticosteroids are commonly used as a routine treatment over several weeks to reduce the inflammatory reaction after ocular surgery. This retrospective analysis was done to know the efficacy of prednisolone acetate eye drops in the post operative phase to minimize inflammation and graft rejection after suture free, glue free pterygium surgery with conjunctival allograft. A total of fifty five patients with pterygium underwent surgery were analysed retrospectively. It included thirty two (32) females and twenty three (23) males. Pterygium had a higher prevalence among females. There was no rejection or recurrences in any 54 patients but one patient was not using topical prednisolone eye drops had graft oedema and congestionTopical steroids are the most common methods of administering steroids to the eye. They are used for controlling postoperative inflammation after intraocular surgery. using patients own blood as autologous bed for placing a donor graft is sufficient enough to hold the graft. Patients need to be put on topical steroids after surgery to control inflammatory response and to minimise the risk of rejection .

KEY WORDS : pterygium ,suture –gluefree surgery, predinisolone

INTRODUCTION:

Pterygium is a fibrovascular, wing-shaped encroachment of conjunctiva on to the cornea. Ultraviolet light-induced damage to the limbal stem cell barrier, with subsequent conjunctivalization of the cornea, is the currently accepted aetiology.[1,2] Indications for surgery include visual impairment, cosmetic disfigurement, motility restriction, recurrent inflammation, interference with contact lens wear and rarely, changes suggestive of neoplasia. Surgical treatmentsfor pterygium include simple excision, thiotepa drops, β-irradiation, intra- and postoperative mitomycin-C, conjunctival autografting, amniotic membrane transplantation (AMT), and combinations of the above methods.[3-9] The most common complication described, in all methods, is recurrence of the pterygium

The prevalence rate of primary pterygium varies from 0.7 to 31% in various populations around the world. [10,11] Immunohistochemical studies suggest that the p53-mutated limbal epithelial basal stem cells lead to the development of pterygium.[12]

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An analysis on the surgical techniques for pterygium excision showed that the pterygium recurrence following surgical treatment of primary pterygium are close to six and 25 times higher if no conjunctival autograft placement is performed.[13]

Traditionally, during pterygium surgery the conjunctival autografts are secured in place with either absorbable or non-absorbable sutures. The use of fibrin glue (FG) during pterygium surgery was first described by Cohen et al in 1993.[14]

The use of conjunctival autografting following pterygium excision was first described by Kenyon et al in 1985. [15] Since then, other reports have described recurrence rates of 3.8 - 39% with this procedure. The importance of including limbal tissue in the conjunctival autograft, to reduce the recurrence rate, has been described. [16]

Surgical methods to prevent pterygium recurrence like conjunctival autograft, limbal and limbal–conjunctival transplant, conjunctival flap and conjunctival rotation autograft surgery, amniotic membrane transplant, cultivated conjunctival transplant and the use of fibrin glue. All of these techniques involve the use of sutures or fibrin glue and are therefore vulnerable to associated complications like suture granuloma, viral infections etc.[23] Use of serum bed for placement of graft is a good alternative to the above methods.

The most common complications of allograft without suture or glue is graft oedema ,rejection and dislodgement.

Topical corticosteroids are commonly used as a routine treatment over several weeks to reduce the inflammatory reaction after ocular surgery. [17] Corticosteroids are successful at reducing ocular inflammation because of their ability to inhibit nearly all chemical mediators in the inflammatory cascade.

We have used Prednisolone in combination with Moxifloxacin hydrochloride in post operative period following conjunctival autograft without suture or glue in tapering dose over four weeks. We did a retrospective analysis of surgeries done with use of topical prednisolone acetate eye drops to know the ability of autologous serum to act as adhesive to the graft and to assess to efficacy of prednisolone to prevent graft oedema and rejection in these patients where there were no sutures or glue used to fix the graft.

MATERIALS AND METHODS:

This is a retrospective study and analysis of surgeries done between December 2011 and December 2013 at ESIC Medical college and PGIMSR, Bangalore. A total of 55 patients with grade 2 or 3 pterygium underwent excision with conjunctival limbal autograft. Subconjunctival injection of lignocaine with adrenaline was injected in the head of pterygium and 0.5ml infiltration in the supero temporal fornix of the conjunctiva . pterygium was excised and sent for histo pathological examination. A conjunctival flap of size more than 0.5 mm than the defect was taken from the supero temporal region and placed over a serum bed formed by bleeding vessels of the excised pterygium. Gentle pressure is given over the placed graft and pad bandaged after subconjunctival gentamycin and dexamethasone injection. The pad was removed on first post operative day and

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graft observed for oedema, rejection , dislodgement .patient was started on topical prednisolone acetate 1% eye drops in combination with Moxifloxacin hydrochloride eye drops 8 times a day over next 5 days , and tapered over next four weeks. Patient was followed regularly till about three months after the surgery.

RESULTS:

A total of fifty five patients with pterygium underwent surgery. It included thirty two(32) females and twenty three(23) males .Pterygium had a higher prevalence among females (58.1%) than males(41.8%).The age group of females ranged from 30 to75 years with an average of 46 years and from 28 to 68 years in males at an average of 40 years .Patients with grade 2 and grade 3 pterygium underwent excision with conjunctival limbal autograft without suture or glue, a cut paste of the superior limbal autograft was performed on these patients. Patients were followed up on post operative day 1, day 7 and day 40. There was no rejection or recurrences in any 54 patients but one patient was not using topical prednisolone eye drops had graft oedema and congestion. He was managed with steroids after 7 days of surgery.

DISCUSSION:

Pterygium is a worldwide condition commonly seen in the Cameron belt located between 37° north and south of the equator. Pterygium is a triangular fibrovascular subepithelial ingrowth of degenerative bulbar conjunctival tissue encroaching onto the cornea. The exact cause of pterygium is not well understood.

However, long-term exposure to sunlight, especially ultraviolet rays and chronic eye irritation from dry, dusty conditions seem to play an important role. [18, 19]

Conjunctival flap as a surgical procedure was first described by Scholer in 1887. Gundersen[20] in 1958 described a new technique and a number of surgical indications for conjunctival flaps, especially for recalcitrant corneal ulceration and poor epithelialization.

Current surgical methods to prevent pterygium recurrence include conjunctival autograft, limbal and limbal–conjunctival transplant, conjunctival flap and conjunctival rotation autograft surgery, amniotic membrane transplant, cultivated conjunctival transplant, lamellar keratoplasty, and the use of fibrin glue. [23] All of these techniques involve the use of sutures or fibrin glue and are therefore vulnerable to associated complications.

The presence of sutures may lead to prolonged wound healing and fibrosis. [21, 22] Subsequent complications such as pyogenic granuloma formation are easily treated; others such as symblepharon formation, forniceal contracture, ocular motility restriction, diplopia, scleral necrosis, and infection are much more difficult to manage and may be sight threatening. [24, 25]

Although generally considered safe, fibrin glues are currently manufactured from human plasma and therefore carry the theoretical risk of transmissible disease.23

A conjunctival autograft technique has recurrence rates reported to be as low as 2 percent and as high as 40 percent in several prospective studies. The procedure involves obtaining an autograft, usually from the superotemporal bulbar conjunctiva, and suturing the graft over the exposed scleral bed after excision of the pterygium. Complications are infrequent, and for optimal results Stark and coworkers3 stress the importance of careful dissection of Tenon's tissue from the conjunctival graft and recipient bed, minimal manipulation of

tissue and accurate orientation of the graft. A large incision for pterygium excision and a large graft and has reported a very low recurrence rate with this technique. [26]

Inflammation of the graft may slough and cause rejection or dislodgement of the graft. It has been shown that simultaneous blockade of CD28- and CD40-mediated costimulatory signals significantly prolong allograft survival. [27-29] Although these results led to an expectation of the establishment of specific immuno-tolerant therapy for organ transplantation, it became evident that these treatments rarely resulted in indefinite allograft survival. [30-32]

Inflammation involves the production of various inflammatory cytokines, chemokines and the increased expression of costimulatory molecules on endothelial cells. [33]

Prednisolone acetate is the synthetic form with its prodrug as prednisone. It is 4 times more potent than cortisol and also has mineralocorticoid activity. The half –life is 12 hours and is less toxic as compared to dexamethasone sodium with half -life of 36-72 hours. [34]. It is chemically designated as 11β 17, 21-trihydroxypregna-1,4-diene-3,20-dione 21-acetate. [35]

Prednisolone suppress the inflammatory response to mechanical, chemical, or immunologic agents. Corticosteroids inhibit edema, fibrin deposition, capillary dilation, leukocyte migration, capillary proliferation, fibroblast proliferation, deposition of collagen, and scar formation associated with inflammation. [36-38]

Topical steroids are the most common methods of administering steroids to the eye. They are used for controlling postoperative inflammation after intraocular surgery. Steroids act by inhibiting production of factors (prostaglandins, leukotrienes etc.), which are critical in generating the inflammatory response by multiple type of cells. [39, 40]

They downregulate inflammation by inhibiting deoxyribonucleic acid (DNA) transcription in the cell nucleus and interrupt the inflammatory cascade by increasing histaminase production in cell walls. Arachidonic acid is the main precursor to inflammatory mediators, such as prostaglandins and leukotrienes. [41] Prednisolone acetate 1% has been used for inflammation control in cataract surgery, an important factor in the healing process. [42, 43] This corticosteroid achieves its highest aqueous level (669.9 ng/ml) within 120 min and maintains a significant level over 24 h; thus, a twice-daily application of prednisolone acetate 1% may be suitable for uncomplicated postoperative cataract cases. [44]

The three essential requirements for the initiation of the allograft response are: non-self transplantation antigens, antigen-presenting cells, and host immunocytes. All are present in rejecting corneal allografts. During the indirect pathway of presentation, which is the most important in corneal allograft rejection, host antigen-presenting cells process alloantigen, and present it to the host immunocyte. Antigen processing is likely to occur in the cornea. [45]

CONCLUSION:

In patients undergoing pterygium surgery , using patients own blood as autologous bed for placing a donor graft is sufficient enough to hold the graft. Patients need to be put on topical steroids after surgery to control inflammatory response and to minimise the risk of rejection . Prednisolone acetate eye1% drops are effective in maintaining graft insitu by reducing inflammatory response at the recipient bed.

REFERENCES:

[1]. Dushku N, Reid TW. Immunohistochemical evidence that human pterygia originate from an invasion of vimentin-expressing altered limbal epithelial basal cells. Curr Eye Res 1994;13:473-81. [PUBMED]
[2]. Kwok LS, Coronea MT. A model for pterygium formation. Cornea 1994;13;219-24.

[3]. Sebban A, Hirst LW, Kynaston B, Bain C. Pterygium recurrence rate at the Princess Alexandra Hospital. Aust NZ J Ophthabnol 1991;19:203-6.

[4]. Mackenzie FD, Hirst LW, Kynaston B, Bain C. Recurrence rate and complications after beta-irradiation for pterygia. Ophthalmology 1991;98:1776-81. [PUBMED]
[5]. Joelson GA, Muller P. Incidence of pterygium recurrence in patients treated with thiotepa. Am J Ophthalmol 1976;81:891-92.

[6]. Singh G, Wilson MR, Foster CS. Long term follow up study of mitomycin eye drops as adjunctive treatment of pterygia and its comparison with conjunctival autograft transplantation. Cornea 1990;9:331-34. [PUBMED]
[7]. Frucht-Pery J, Ilsar M, Hemo I. Single dose of mitomycin C for prevention of recurrent pterygium: Preliminary report. Cornea 1994;13:411-13. [PUBMED]
[8]. Kenyon KR, Wagoner MD, Hettinger ME. Conjunctival autograft transplantation for advanced and recurrent pterygium. Ophthalmology 1985;92:1461-70. [PUBMED]
[9]. Prabhasawat P, Barton K, Burkett J, Tseng SCG. Comparison of conjunctival autografts, amniotic membrane grafts and primary closure for pterygium excision. Ophthalmology 1997;104:974-85

[10]. Detels R, Dhir SP Pterygium: a geographical survey. Arch Ophthalmol 1967;78:485.

[11]. Sivasubramaniam P Pterygium in Ceylon. Br J Ophthalmol 1971;55:55.

[12]. Chowers I, Pe′er J, Zamir E, et al Proliferate activity and p53 expression in primary and recurrent pterygium. Ophthalmology 2001;108:985–8.

[13]. Sanchez-Thorin JC, Rocha G, Yelin JB Meta-analysis on the recurrence rates after bare sclera resection with and without mitomycin C use and conjunctival autograft placement in surgery for primary pterygium. Br J Ophthalmol 1998;82:661–5.

[14]. Cohen RA, McDonald MB Fixation of conjunctival autografts with an organic tissue adhesive [letter]. Arch Ophthalmol 1993;111:1167–8.

[15] Kenyon KR, Wagoner MD, Hettinger ME. Conjunctival autograft transplantation for advanced and recurrent pterygium. Ophthalmology 1985;92:1461-70.

[16]. Rao SK, Lekha T, Mukesh BN, Sitalakshmi G, Padmanabhan P. Conjunctival-limbal autografts for primary and recurrent pterygia: Technique and results. Indian J Ophthalmol 1998;46:203-9.

[17]. Laurell CG, Zetterstrom C. Effects of dexamethasone, diclofenac, or placebo on the inflammatory response after cataract surgery. Br J Ophthalmol. 2002;86(12):1380–4. [PMC free article] [PubMed]

[18] Austin P, Jakobiec FA, Iwamoto T. Elastodysplasia and elastodystrophy as the pathologic bases of ocular pterygia and pinguecula. Ophthalmology 1983;90:96-109.

[19] Saw SM, Tan D. Pterygium: Prevalence, demography and risk factors. Ophthalmic Epidemiol 1999;6:219-28.

[20]. Gunderson T. Conjunctival flaps in the treatment of corneal disease with reference to a new technique of application. Arch Ophthalmol 60:888, 1958.

[21] Koranyi G, Seregard S, Kopp ED. Cut and paste: a no suture, small incision approach to pterygium surgery. Br J Ophthalmol 2004; 88: 911–914.

[22] Allan BD, Short P, Crawford GJ, Barrett GD, Constable IJ.Pterygium excision with conjunctival autografting: an effective and safe technique. Br J Ophthalmol 1993; 77: 698–701.

[23] Ang LP, Chua JL, Tan DT. Current concepts and techniques in pterygium treatment. Curr Opin Ophthalmol 2007; 18: 308–313.

[24] Solomon A, Pires RT, Tseng SC. Amniotic membrane transplantation after extensive removal of primary and recurrent pterygia. Ophthalmology 2001; 108: 449–460.

[25] Vrabec MP, Weisenthal RW, Elsing SH. Subconjunctival fibrosis after conjunctival autograft. Cornea 1993; 12: 181–183.

[26] Hirst, L. W. Ophthalmology 2008;115(10):1663–1672.

[27] .Turka LA, Linsley PS, Lin H et al. T-cell activation by the CD28 ligand B7 is required for cardiac allograft rejection in vivo. Proc Natl Acad Sci USA 1992; 89: 11102 – 11105.

[28] Pearson TC, Alexander DZ, Winn KJ, Linsley PS, Lowry RP, Larsen CP. Transplantation tolerance induced by CTLA4-Ig. Transplantation 1994; 57: 1701 – 1706.

[29] Larsen CP, Alexander DZ, Hollenbaugh D et al. CD40-gp39 interactions play a critical role during allograft rejection. Suppression of allograft rejection by blockade of the CD40-gp39 pathway. Transplantation 1996; 61: 4 – 9.

[30] Larsen CP, Elwood ET, Alexander DZ et al. Long-term acceptance of skin and cardiac allografts after blocking CD40 and CD28 pathways. Nature 1996; 381: 434 – 438.

[31] Khoury S, Sayegh MH, Turka LA. Blocking costimulatory signals to induce transplantation tolerance and prevent autoimmune disease. Int Rev Immunol 1999; 18: 185 – 199.

[32] Shimizu K, Schonbeck U, Mach F, Libby P, Mitchell RN. Host CD40 ligand deficiency induces long-term allograft survival and donor-specific tolerance in mouse cardiac transplantation but does not prevent graft arteriosclerosis. J Immunol 2000; 165: 3506 – 3518.

[33] Bingaman AW, Ha J, Waitze SY et al. Vigorous allograft rejection in the absence of danger. J Immunol 2000; 164: 3065 – 3071.

[34] Somen Misra MS, Sulbha Gaydhankar MS, Rajen Mehta MS ,Comparative evaluation of the anti-inflammatory effect of topical 0.1% dexamethasone sodium and topical 1% prednisolone acetate eye drops after small incision cataract surgery in Indian eyes . Delhi Journal of Ophthalmology Vol. 22, No.4, April - June, 2012

[35] Syed Naeem Razzaq, Islam Ullah Khan, Irfana Mariam and Syed Saleem Razzaq , Stability indicating HPLC method for the simultaneous determination of moxifloxacin and prednisolone in pharmaceutical formulations, Chemistry Central Journal 2012, 6:94

[36] Allergan, Inc. Poly-Pred (prednisolone acetate, neomycin sulfate, polymyxin B sulfate ophthalmic suspension) prescribing information. Irvine, CA; 2004 Dec.

[37] AHFS drug information 2008. McEvoy GK, ed. EENT corticosteroids general statement. Bethesda, MD: American Society of Health Systems Pharmacists; 2008: 2867-9.

[38] Allergan, Inc. Pred-Forte (prednisolone acetate ophthalmic suspension) prescribing information. Irvine, CA; 2004 Mar.

[39]. Watson D, Noble MJ, Dutton GN, Midgley JM, Healey TM. Penetration of topically applied dexamethasone alcohol into human aqueous humor. Arch Ophthalmol 1988; 106:686-7.

[40]. McGhee CNJ, Noble MJ, Watson DG, Dutton GN, Fern Al, Healey TM, et al. Penetration of topically applied prednisolone sodium phosphate into human aqueous humour. Eye 1989; 3:463-7.

[41]. Ilyas H, Slonim CB, Braswell GR, Favetta JR, Schulman M. Long-term safety of loteprednol etabonate 0.2% in the treatment of seasonal and perennial allergic conjunctivitis. Eye Contact Lens. 2004;30(1):10–3. [PubMed]

[42]. Reddy R, Kim SJ. Critical appraisal of ophthalmic ketorolac in treatment of pain and inflammation following cataract surgery. Clin Ophthalmol. 2011;5:751–8. [PMC free article] [PubMed]

[43]. Campos M, Muccioli C, Malta JB, Gerade RA, LA Salame A, Belfort R. Efficacy and tolerability of a combined gatifloxacin plus prednisolone formulation for topical prophylaxis after LASIK. Clin Ophthalmol. 2011;5:209–14. [PMC free article] [PubMed]

[44]. Awan M A, Agarwal PK, Watson D G, McGhee CNJ, Dutton G N. Penetration of topical and subconjunctival corticosteroids into human aqueous humour and its therapeutic significance. Br J Ophthalmol. 2009;93(6):708–13. [PubMed]

[45] Kuffova L, Netukova M, Duncan L, Porter A, Stockinger B, Forrester JV. Cross presentation of antigen on MHC Class II via the draining lymph node after corneal transplantation in mice. J Immunol 2008; 180: 1353–1361.