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Corneal Keratoplasty: When Immunosuppression is Necessary

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Editorial

Although the cornea is classically described as possessing immunological privilege, the protection this affords is only relative and rejection is still the commonest cause of penetrating corneal graft failure. In the majority of grafts topical corticosteroids provide sufficient immunosuppression, but in high-risk grafts other therapeutic agents may be required. So for uncomplicated first grafts performed in avascular "low-risk" beds with only local immune suppression, success rate is as high as 90%. This success in low-risk corneal transplantation, however, is overshadowed by the results of corneal grafts placed in "high risk" beds with rejection rates approaching 70%, even with maximal local and systemic immune suppression. In vascularized corneas and possibly corneas that have previously rejected a graft, the "immunological privilege" breaks down and the cornea becomes as susceptible as any other vascularized tissue in the body to rejection.

The term "high-risk" is frequently applied to grafts known to have an increased likelihood of graft-rejection, but there is not a universally accepted definition of a high-risk cornea. The usual risk factors that predispose to graft rejection, include recipient vascularization (two or more quadrants), previous graft failure, and the etiology of the original corneal disease [1,2]. Prognosis of normal risk keratoplasty is excellent, even without systemic immunosuppression. These results can be attributed to the immune privilege of the cornea and the anterior chamber, the so called anterior chamber associated immune deviation (ACAID), firstly studied in the late 1800s by Van Dooremaal, and then by Medawar in the mid-1900s to fit in with emerging concepts of transplantation immunology [3,4].

Since the introduction of systemic immunosuppression with Cyclosporine A in the postoperative treatment of high-risk keratoplasties, graft prognosis in such situations has improved considerably, but this therapeutic regimen comes with a high range of side effects and cost intensive follow up. Mycophenolate mofetil (MMF) has shown its efficacy and safety after kidney transplantation (in combination with CsA and corticosteroids), and after heart and liver transplantation. In 1997 was administered for the first time as postoperative treatment after penetrating high-risk keratoplasty [5]. MMF is a prodrug of mycophenolic acid (MPA), an inhibitor of inosine monophosphate dehydrogenase (IMPDH). This is the rate-limiting enzyme in de novo synthesis of guanosine nucletides. T and B-lymphocites are more dependent on this pathway than other cell types are. MPA suppresses DNA synthesis and proliferation of T lymphocites. So, MMF inhibits the proliferation of human T and B lymphocites, the proliferation of these cells is selectively inhibited[5]. The substance is administered at a fixed dose of 2x1 g per day with few side effects, mainly gastrointestinal disturbances caused by the enterohepatic circulation.

Micophenolate Mofetil (MMF) is an alternative to other immunosuppressive agents like Cyclosporine A (CsA). Using MMF reduces the odds of graft rejection in 77,72%, mainly after high-risk keratoplasty. MMF is safe with fewer side effects, and effective in preventing graft

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rejection, the wide therapeutic range and the omission of drug monitoring makes this compound especially interesting for ophthalmic patients [6]. Along with these considerations on treatment, it is very important to take into account blood and histocompatibility in high-risk penetrating keratoplasty. Some investigations even advice to include gender matches [7].

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