Preparation, Characterization, and In Vivo Evaluation of Triamcinolone Acetonide Microspheres After Intravitreal Administration

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Abstract

Purpose: The aim of this study was to evaluate the intraocular pressure (IOP) increasing effect and bioavailability of triamcinolone acetonide (TA) microspheres, as a novel drug delivery system, after intravitreal administration.

Methods: Microspheres loaded by TA were prepared by the solvent evaporation method. After encapsulation, the final microspherical formulation was tested in an animal model. The left eyes of rabbits received microspherical TA and the right eyes were injected with conventional TA suspension. The drug concentration in the vitreous samples at days 7, 14, 28, and 56 after the injection was determined by high-performance liquid chromatography. The IOP was also checked at the same days with the Schiotz tonometer.

Results: There was no statistically significant (P > 0.05) difference between mean concentration of TA in the vitreous of right and left eyes at the different sampling times except day 56. Mean IOP of eyes that received microspherical TA was increased less than that of the eyes injected with TA suspension, and the difference was statistically significant (P < 0.05) for each measurement day. TA was detectable in both eyes after 8 weeks. Both TA microsphere and suspension showed the sustained release profile.

Conclusion: The results of this study showed less IOP increasing effect of triamcinolone microspheres in comparison with suspension form.

Introduction

In recent years, the use of intravitreal triamcinolone acetonide (IVTA) has emerged as a valuable treatment of variable diseases, including cystoid macular edema (pseudophakic, after venous occlusion, diabetic, and uveitic),1–8 adjunctive therapy for age-related macular degeneration,9 and posterior uveitis.10,11

The most commonly reported complication of intravitreal administration of TA is elevation of intraocular pressure (IOP). Bakri and Beer showed that, after a single IVTA injection, 48.8% of the eyes demonstrated an increase in IOP of 5 mm Hg or more, and 27.9% of patients experienced an increase in IOP of 10 mm Hg or more.12 In another study, Smithen et al. showed that IOP elevation after IVTA administration was common with rates ranging from 20% to 60%.13

Despite the high incidence, up to 50%, there is no consensus about the cause of IOP rise.14 Im et al. found that two-thirds of eyes with clinically significant IOP elevation after IVTA administration developed gonioscopy changes, characterized by particulate matter in the inferior angle, which was not present at the baseline examination. Presence of this particulate matter might be related to poor solubility and precipitation of suspension particles in trabecular meshwork.15

Microspheres are defined as colloidal systems made of solid polymers and falling in the size range of 1–1,000 μm.16,17 They comprise a polymeric matrix with drug molecules distributed inside the matrix.18 There are extensive microsphere preparations for delivery of a variety of drugs.19 The controlled drug delivery systems such as microspheres have numerous advantages compared to conventional dosage forms, including improved homogeneity and solubility, improved efficacy, and reduced toxicity.20

In the present study, microspheres containing TA were prepared and characterized. The vitreous drug concentration–time profile and IOP were determined in an animal model after intravitreal injection of TA suspension and TA microspheres.

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