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TOPICAL CYCLOSPORINE A – ROLE IN RECURRENT ANTERIOR UVEITIS

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INTRODUCTION

For many years, uveitis was considered a single disease entity; therefore, the approach to treatment varied very little. As knowledge of the disease process grew and the sophistication of immunologic and microbiologic testing increased the fact that uveitis entails a multitude of diseases became clear. Although some diseases are local ocular immune phenomena, many of them are systemic diseases with ocular manifestations. Anterior uveitis is often perceived to be the presenceof "cell and flare" in the anterior chamber, which has led to a large variability in pastreports of uveitis in the literature. Studies show that anterior uveitis is the most prevalent form of uveitis, and about half of these cases are idiopathic.[2-5] This study will evaluate the safety and effectiveness of topical cyclosporin 0.1% to treat anterior uveitis, a sight-threatening eye inflammation caused by an immune system abnormality. Previous studies in humans have shown that, taken by mouth, the drug cyclosporin is effective in treating chronic uveitis.

Uveitis may require long-term treatment with potent immune-suppressing drugs, such as cyclosporin, cyclophosphamide, methotrexate, azathioprine or steroids. Taken systemically (by mouth or injection), however, these drugs can do serious damage to the kidneys, liver or lungs, and can raise blood pressure and lower blood cell counts. Because of this, some patients cannot or will not use these medicines.

This small study evaluated the safety, and to some extent effectiveness, of cyclosporin delivered topically into the eye, to try to prevent harmful side effects. In animal studies, sustained-release cyclosporin implants did not cause the severe side effects seen with systemic use of the drug. Some animals developed opacity of the lens and slowed retinal

responses, both of which reversed when the drug was stopped. Earlier animal studies of cyclosporin injected directly into the eye reduced inflammation that had been produced experimentally.[6-9]

Patients with anterior uveitis who have active inflammation and poor vision are eligible to participate in this study.

Aims and Objectives

- To evaluate the safety, and to some extent effectiveness, of cyclosporin delivered topically into the eye.
- To see for further recurrences and period of remission.

MATERIALS AND METHODS

Study design: A study of topical Cyclosporine A 0.1% for recurrent anterior Uveitis.

Prospective randomized noncomparative Study.

Duration of study: Two Years.

Inclusion criteria

- Patients with more than one episodes of anterior uveitis of any etiologies.
- Patients who were non-respondent to topical as well as systemic steroids.
- As a steroid sparing therapy in patients with intolerable side effects from systemic steroids.
- Patients of recurrent uveitis who were steroid responders received topical cyclosporine A 0.1% twice a day for the period of six months. Before receiving drug all patients underwent detailed ocular examination including visual acuity, fundus examination, intraocular pressure, slitlamp examination. Slit lamp scoring of inflammation in anterior segment was done at each visit. Complete resolution of the inflammation was seen on slit-lamp examination. Patients were also looked for cataract development, increase in preexisting cataract, rise in intraocular pressure, signs of corneal toxicity. According to SUN working group[1] consensus inflammation was graded based on the presence of cells or flare in the anterior chamber. Patient was followed up in every week for one month and every 15th days for next month and then monthly for next eight months. (Total follow up period was 12 months).

RESULTS

Twenty two patients of recurrent anterior uveitis received 0.1% topical cyclosporine for six months period.

Out of 22 patients 5 were HLA-B27 positive, 14 were having idiopathic post viral syndrome, 1 was post traumatic and 2 were montoux positive patients.

- Out of 22 patients no recurrences found in 17 patients, 3 patients had recurrence after 4 months, and 2 patients had montoux positive uveitis in whom after receiving AKT there was complete remission of the inflammation.

- No side effects of the drug such as cataract formation or increase in cataract if existed previously and rise in intraocular pressure,corneal toxicity ,etc. were found.

Type of uveitis	Number of Patients (n= 22)
HLA-B27 associated	5
Idiopathic postviral syndrome	14
Post-traumatic	1
Mx positive	2

DISCUSSION

Acute anterior uveitis is a recurrent immune-mediated inflammatory condition involving the iris and ciliary region in man and occurs in about 4/1000 individuals. Although it may be self-limiting, it may also be chronic and lead to irreversible eye damage including cataract and glaucoma. Photophobia, and pain, with hyperemia of the vessels, hypopyon, iridiocyclitis is typical and the condition is relatively responsive to steroids. However, in some instances, the disorder is unresponsive to treatment and may lead to blindness with glaucoma, cataract and retinopathy. HLA B27 appears to be involved. Humans are usually treated with steroids, however, there are also undesirable side effects, and the condition remains an area of unmet need. In veterinary medicine, horses suffer from an analogous anterior recurrent uveitis which often leads to blindness as well and was known in the past as “Moon Blindness”

CsA is a neutral, hydrophobic, cyclic undecapeptide metabolite of the fungus *Tolypocladium inflatum*. Its major clinical effect is the perturbation of expression of interleukin-2 (IL-2) by helper T cells, preventing the proliferation of T cells.CsA was discovered in the early 1970s as an antifungal agent. Cases who were refractory to steroids were well managed by systemic cyclosporine in cases of JIA and uveitis associated with spondyloarthropathies. But side effects of Cyclosporine were: hirsutism, gum hyperplasia, hepatotoxicity, hypertension,

hyperlipidaemia were found in previous studies. Previous study showed that the cyclosporine is a hydrophobic and does not penetrate the cornea well and does not obtain a therapeutic concentration within eye. But study by Hosokawa Katsuji[2] showed complete resolution of inflammation in uveitis. But the drawback of their study was the sample size was too small. We included 22 cases of anterior uveitis and arrived at conclusion that topical cyclosporine is effective in treating the cases of recurrent anterior uveitis without any systemic and local side effects.

CONCLUSION

Complete remission of the disease activity was found in idiopathic post-viral syndrome.

It was also effective in anterior uveitis due to autoimmune diseases like HLA-B27.

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