Abstracts

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Acanthamoeba Keratitis: Diagnosis and Treatment Update 2009

Dart JKG, Saw VPJ, Kilvington S
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Most ophthalmologists will know that acanthamoeha keratitis (AK) is a recently recognized infectious disease entity that is difficult to treat. There are good recent reviews of this subject. This perspective focuses on the diagnosis and treatment of this complex corneal infectious disease. In particular, we consider the management of diagnostic dilemmas, evidence for choice of initial therapy, and treatment of the challenging clinical problems of persistent ulceration, severe inflammation, and persistent infection, and provide guidelines for surgery.

The purpose of this study was to describe the current management of acanthamoeba keratltis (AK).

Early diagnosis and appropriate therapy are key to a good prognosis. A provisional diagnosis of AK can be made using the clinical features and confocal microscopy, although a definitive diagnosis requires culture, histology, or identification of Acanthamoeba deoxyribonucleic acid by polymerase chain reaction. Routine use of tissue diagnosis is recommended, particularly for patients unresponsive to treatment for AK. Topical biguanides are the only effective therapy for the resistant encysted form of the, organism in vitro, if not always in vivo. None of the other drugs that have been used meet the requirements of consistent cysticidal activity and may have no therapeutic role. The use of topical steroids is controversial, but probably beneficial, for the management of severe corneal inflammatory complications that have not responded to topical biguanides alone. The scleritis associated with AK is rarely associated with extracorneal invasion and usually responds to systemic anti-inflammatory treatment combined with topical biguanides. Therapeutic keratoplasty retains a role for therapy of some severe complications of AK but not for initial treatment. With modern management, 90% of patients can expect to retain visual acuity of 6/12 or better and fewer than 2% become blind, although treatment may take 6 months or more.

Authors concluded with the remarks that better understanding of the pathogenesis of the extra corneal complications, the availability of polymerase chain reaction for tissue diagnosis, and effective licensed topical anti-amoebics would substantially benefit patients with AK.

Azathioprine for Ocular Inflammatory Diseases

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Immunosuppressive drugs have been used widely to control severe cases of ocular inflammation, Azathioprine a purine nuleoside analog that acts as an antimetabolite by interfering with deoxyribonucleic acid and ribonucleic acid synthesis is one of the immunosuppressive drugs recommended for this purpose. Azathioprine is approved by the United States Food and Drug Administration for the treatment of rheumatoid arthritis and also has been used widely for organ transplantation and various dermatologic, gastro intestinal and rheumatologic diseases, including psoriatic arthritis and systemic lupus erythematosus. For ophthalmic disease azathioprine has been used for treatment of corneal graft rejection and noninfectious ocular inflammatory conditions, such as chronic active iridocycliris, retinal vasculitis, Behcet disease, and sympathetic ophthalmia. It also has been used in combination with other immunosuppressive agents for serpiginous retinochoroidiris. Randomized clinical trials data are limited to use of azathioprine for Behcet disease and a small trial evaluating its use for anterior uveitis.

The Systemic Immunosuppressive Therapy for Eye Diseases (SITE) Cohort Study! Includes

information regarding the outcomes of a large number of ocular inflammation patients managed at tertiary ocular inflammation centers in the United States using a variety of agents, including azathioprine. In this report, we evaluate the incidence of successful control of inflammation, of corticosteroid-sparing benefits, and of treatment related complications leading to discontinuation of therapy in patients from the cohort treated with azathioprine as a sole (noncorticoste-roid) immunosuppressive agent who were followed up from the initiation of azathioprine therapy.

The purpose of this study was to evaluate treatment outcomes of azathioprine for noninfectious ocular inflammatory diseases.

Medical records of 145 patients starting azathioprine as a sole noncorticosteroid immunosuppressant at 4 tertiarv uveitis services were reviewed. Main outcome measures included control of ocular inflammation, sustained control after tapering prednisone to ≤ 10 mg/day, and discontinuation of treatment because of side effects.

Among 145 patients (255 eyes) treated with arathioprine, 63% had uveitis, 23% had mucous membrane pemphigoid, 11% had scleritis, and 3% had other inflammatory diseases. By Kaplan-Meier analysis, 62% (95% confidence interval [CI], 50% to 74%) of patients with active disease initially gained complete inactivity of inflammation sustained over at least 28 days within 1 year of therapy, and 47% (95% CI, 37% to 58%) tapered systemic corticosteroids to ≤ 10 mg daily while maintaining control of inflammation within 1 year of therapy. Treatment success was most common for intermediate uveitis (90% with sustained inactivity within 1 year; 95% CI, 64% to 99%). Over the median follow-up of 230 days (interquartile range, 62 to 679 days), azathioprme was discontinued at a rate of 0.45 per person years (/PY): 0.16/PY because of side effects, 0.10/PY because of ineffectiveness, 0.09/PY because of disease remission, and 0.10/PY because of unspecified causes.

Authors concluded with the remarks that azathioprine was moderately effective as a single corticosteroid-sparing immunosuppressive agent in terms of control of inflammation and corticosteroid-sparing benefits, but required several months to achieve treatment goals; it seems especially useful for patients with intermediate uveitis. Treatment-limiting side effects occurred in approximately one-fourth of patients within 1 year, but typically were reversible.

The Effect of Biomicroscope Illumination System on Grading Anterior Chamber Inflammation

Wong IG, Nugent AK, Varcas-Marttn F
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Inflammatory cells in the aqueous easier to detect with certain biomicroscopes than others of identical make and model. Detecting inflammatory cells in the aqueous is critical in deciding whether to continue or discontinue a patient's treatment. A small number of cells in the aqueous beam can be difficult to see, and if presumed absent, treatment may be discontinued prematurely.

The ability to see cells in the aqueous depends on the characteristics of the cells, the biomicroscope optics, the illumination system, and the observer's skills- Characteristics of the cells include the type and size of cells. The smallest inflammatory cell, the lymphocyte, measures approximately 5 µm in diameter and the largest, the macrophage, measures from 15 to 30 µm in diameter. The inflammatory cell's cytoplasmic granules and inclusions such as pigment affect its ability to absorb, reflect, refract, and scatter light. The contrast between the cell and aqueous fluid, particularly when the 'aqueous is turbid, affects the visibility of cells.

Inflammatory cells are detected more easily when the slit-beam is brighter. However, seeing cells in the aqueous may be more related to the contrast ratio between the reflected light and the background, which would remain fairly constant even with reduced light. The ratio is assumed to be constant because the amount of light hitting the cells and the background are dependent on the same light source. Thus, both would increase and decrease proportionately as the slit-beam light is adjusted up or down.

The purpose of this study was to determine how the biomicroscope illumination system affects the grading of anterior chamber (AC) inflammation. Does a brighter light allow for more inflammatory cells to be counted? Does the width of the light beam affect the cell count? Is there variation in illumination among biomicroscopes and does this variation influence the counting of inflammatory cells? If the illumination settings are critical for grading cells, clinical practice and clinical trials should require uniform standards to have comparable and reproducible grading data.

An artificial AC was designed to replicate optically a human AC and was filled with 5-µm polystyrene beads suspended in ethanol. A high-definition video eyepiece camera recorded the moving beads. Using image processing software, the main outcomes measures determined were the average number of beads in a 1 X 1-mm field at varying widths of the slit-beam.

The volume of light and number of beads observed increased significantly as the slit-beam widened. Additionally, 3 separate biomicroscopes of identical make and model were found to produce different levels of luminance at the same aperture dial settings, influencing the number of beads observed, with the brighter biomicroscope yielding higher bead counts.

Authors concluded with the remarks that ability to count beads and perhaps the ability to count inflammatory cells in an inflamed eye depend on a number of factors, including the level of illumination and width of the slit-beam. This study demonstrated that the brighter the illumination and the wider the beam, the more beads were observed. This illustrates the importance of standardizing biomicroscope, particularly where consecutive observations are used to make clinical decisions and in cases of multi-center clinical trials where clinical data are evaluated across different facilities.

Rapid detection of Acanthamoeba cysts in frozen sections of corneal scrapings with Fungiflora Y

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Acanthamoeba keratitis (AK) is an intractable, sight-threatening infection of the cornea and is frequently seen in contact lens wearers. The incidence of AK has increased with increasing numbers of contact lens wearers. The problems with AK include the difficulty in making a correct diagnosis at an early stage, and the lack of specific drugs to treat AK. The early clinical signs of AK are subepithelial infiltrates, pseudo-dendritic keratitis and radial neurokeratitis and these lesions often lead to AK being misdiagnosed as herpetic keratitis and or fungal keratitis, resulting in delays in initiating proper treatment. In addition, the ability to grow and identify acantoamoeba in culture is between 30% and 60%, and it requires a relatively long time to obtain the results from cultures.

Acanthamoeba cysts can be detected in corneal scraping, impression cytology or biopsies by a variety of staining methods including special stains such as Calcofluor White and Acridme Orange, and also by immunohistochemisfcry. Routine stains such as Haematoxylin and Eosin (H&E), Giemsa, Cram, Periodic Acid Schiff (FAS), and Lactophenol Cotton Blue can also provide a positive identification. However, some of the special stains are time-consuming and more complicated, and the routine stains require skilled and experienced examiners to identify the Acanthamoeba cysts or trophozoites.

Fungiflora Y (FFY) was originally developed to detect fungi, and it has a specific affinity for chitin and cellulose, which are components of the cell wall of fungi. However, it has been shown that FFY also stains Acanthamoeba cysts because cysts also contain cellulose.

The purpose of this study was to evaluate the usefulness of serial frozen sections of corneal scrapings stained with Fungiflora Y (FFY) to diagnose Acanthamoeba keratltis (AK).

Eight patients with suspected AK were studied. Serial frozen sections were made from part of the corneal epithelial scrapings and stained with FFY. The remaining corneal epithelial scrapings were submitted for laboratory culture.

The FFY stained frozen sections were completed within an hour, and Acanthamoeba cysts were detected under a fluorescence microscope in all eight patients. The same sections were examined with a light microscope, and Acanthamoeba cysts were confirmed to be present from their morphological characteristics. Five of the eight patients had positive laboratory cultures for Acanthamoeba.

Authors concluded with the remarks that FFY staining of frozen sections of corneal scrapings is a rapid and reliable technique which can be used to make an early diagnosis of AK.

One-year outcomes of a bilateral randomised prospective clinical trial comparing PRK with mitomycin C and LASIK

Wallau AD, Campos M
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Excimer laser photorefractive keratectomy (PRK) with adjunctive mitomycin C (MMC; MMC-PRK) has recently been used as an alternative to laser in situ keratomileusis (LASIK) for surgical correction of refractive errors. Although surface ablation usually has a slower visual recovery and more early postoperative discomfort, it avoids LASIK flaps complications and possibly results in less corneal biomechanical instability.

Mitomycin C is an alkylating agent that inhibits DNA and RNA replication and protein synthesis. It regulates ribroblast proliferation and differentiation. and subsequently blocks myofibroblast formation, which is responsible for corneal haze after PRK in high myopic corrections. Recent studies have shown that low-dose MMC (0.002%) has a similar efficacy to standard MMC concentration (0.02%) in preventing postoperative haze following surface ablation for moderate myopia corrections, and also minimise potential side effects.

The purpose of this study was to compare 1-year follow-up results of photorefractive keratectomy (PRK) with mitomycin C (MMC) and laser in situ keratomileusis (LASIK) for custom correction of myopia.

Eighty-eight eyes of 44 patients with moderate myopia were randomised to PRK with 0.002% MMC for 1 min in one eye and LASIK in the fellow eye. The 1-year follow-up was evaluated.

There were no differences between LASIK and MMC-PRK eyes preoperatively. Forty-two patients completed the 1-year follow-up. MMC-PRK eyes achieved better uncorrected visual acuity ($p = 0.03$) and better best-spectacle-corrected visual acuity ($p<0.001$) 1 year after surgery. SE did not differ in the two groups during follow-up ($p = 0.12$). Clinically significant haze was not found in surface ablation eyes. LASIK eyes showed a greater higher-order aberration ($p = 0.01$) and lower contrast sensitivity ($p<0.05$) than MMC-PRK eyes postoperatively. Excellent vision was reported in 64% of LASIK and 74% of MMC-PRK eyes 1 year after surgery. The corneal resistance factor and corneal hysteresis (ORA, Reichert) were higher in LASIK than in MMC-PRK eyes ($p<0.01$) at the last follow-up.

Authors concluded with the remarks that wavefront-guided PRK with 0.002% MMC was more effective than wavefront-guided LASIK for correction of moderate myopia. Further research is necessary to determine the optimal concentration, exposure time and long-term corneal side effect of MMC.