AMERICAN UVEITIS SOCIETY

Cyclosporine

A Patient Education Monograph prepared for the American Uveitis Society **January 2003**
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Introduction

Cyclosporine A (CsA) belongs to the general group of medications called "immunosuppressants or immunomodulators" which alter the immune response and are therefore useful in the management of immune-based inflammatory diseases, such as non-infectious uveitis. CsA is marketed under brand names which include Sandimmune®, Gengraf, and Neoral®.

Chemistry

CsA is a neutral, hydrophobic, cyclic polypeptide (11 amino acids) which is classified as an immunosuppressive antibiotic (others being rapamycin, tacrolimus and dapsone). It is a powdery crystalline compound which is highly lipophilic, meaning that the drug dissolves in liquid fats and organic solvents but not in water. For this reason it has to be dissolved in oil (usually castor or olive oil) for clinical use.

How it works

The precise mechanism of the immunosuppressive activity of CsA is not completely understood. Uveitis of non-infectious cause is considered to be an autoimmune disease, mainly mediated by T-helper cells (a certain type of white blood cell). It is known that CsA stops the production of some of the molecules required to activate T-cells. CsA is therefore a potent immunosuppressant.

History of usage

Non-eye disease

CsA was initially isolated as an antifungal agent in 1970. But it was soon noted to have an important immunosuppressive activity against T lymphocytes. Based on this action, CsA was used to prevent transplant rejection of solid organs such as the kidney, heart, liver, pancreas, lung, and bone marrow. Success in this area of medicine prompted its use in the treatment of autoimmune diseases.

Eye disease
CsA was initially utilized in the treatment of uveitis in 1983. Its first use was in cases resistant to corticosteroid treatment or in patients in whom corticosteroids caused intolerable side effects.

How it is given
CsA can be taken as a pill, solution, through the vein, or as an eye drop. A new oral formulation of soft gelatin capsules (Neoral®) has better absorption into the blood stream and therefore is usually preferred. Administration of CsA with food increases its blood levels, although this effect seems to be less important with the Neoral® formulation. CsA eye drops have recently been approved by the United States Food and Drug Administration (FDA) for use in dry eye disease. Experience with CsA eye drops has shown little benefit in their use for uveitis, however.

Monitoring
The most worrisome side effects of CsA include high blood pressure and a decrease in kidney function. Both side effects are typically reversible by reducing the dosage or discontinuing the drug. It is therefore important that blood pressure and blood chemistry (especially kidney function) are routinely monitored. A decrease in the white blood cell count does not usually occur. More common side effects include nausea and vomiting, tingling in the arms and legs, increased sensitivity to temperature changes, hand tremor, hirsutism (excess growth of hair on the face, chest, and back) and gingival hyperplasia (enlargment of the gums, which can be minimized by good oral hygiene). These side effects are typically reversible. All patients on immunosuppressive therapy are at increased risk for infections, especially atypical or "opportunistic" infections. The extent of this risk is generally slight, but increases if other immunosuppressive medications are being taken in conjunction with cyclosporine. Malignancies possibly secondary to cyclosporine therapy have been described but are extremely rare.

Conclusions
CsA is useful for sight-threatening intraocular inflammation. Routine monitoring of blood pressure and blood chemistry are mandatory.

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