

Immunosuppression Medication as an Approach to Treat Chronic Idiopathic Urticaria in Children

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Doshi DR, Weinberger MM: Experience with cyclosporine in children with chronic idiopathic urticaria. *Pediatr Dermatol* 2009, 26:409–413.

Rating

- Of importance.

Introduction

That chronic idiopathic urticaria (CIU) has been found to be resistant to antihistamine treatment in many cases has prompted the use of corticosteroids to treat this disorder. Corticosteroids act on antigen-presenting cells and T lymphocytes by inhibiting cytokine production and blocking chemokine production. However, the failure of corticosteroids and their adverse side effects have led investigators to pursue new steroid-sparing treatments.

Cyclosporine is a steroid-sparing agent that inhibits calcineurin that thereby disrupts T-cell signaling and prevents T-lymphocyte activation. Since the introduction of cyclosporine in the late-1970s, it has been used mainly for immunosuppression in organ transplantation. In more

recent years, cyclosporine's use broadened to include treatment of autoimmune diseases in adults and children (eg, juvenile arthritis and lupus). A randomized, double-blind, placebo-controlled study using cyclosporine in adults with CIU yielded promising results. This prompted the present study, which evaluated cyclosporine use in children with antihistamine-resistant CIU.

Aims

The study was designed to report and assess the treatment response of cyclosporine in children with CIU.

Methods

A total of 54 pediatric patients with CIU and no other underlying systemic diseases were identified at the tertiary care center at the University of Iowa College of Medicine between 2000 and 2005. CIU was diagnosed on the basis of the presence of daily hives that recurred for more than 6 weeks without another known cause. Seven of the 54 patients (9–16 years old) failed conventional treatment with antihistamines and prednisone. These seven patients received cyclosporine (3 mg/kg per day twice daily) while attempts were made to taper corticosteroids. Baseline blood urea nitrogen (BUN) and creatinine levels were measured. Cyclosporine serum concentration, BUN and creatinine levels, and blood pressure were routinely monitored. Cyclosporine peak levels were kept no higher than 200 ng/mL to minimize side effects. After patients remained hive-free for 1 month, cyclosporine was tapered every 2 to 4 weeks to a low-dose maintenance for hive prevention and then discontinued completely. The remaining 54 pediatric patients with CIU were treated with antihistamines (hydroxyzine) and low-dose or high-dose corticosteroids.

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Results

All seven patients who failed this traditional treatment and thus were started on cyclosporine achieved remission. Four of the seven had relapses that required further cyclosporine treatment. The relapses were successfully treated with subsequent doses of cyclosporine. None of the patients developed side effects, and all patients had stable BUN, creatinine, and blood pressure. Cyclosporine levels did not exceed 200 ng/mL in any of the patients.

Discussion

The authors concluded that low-dose cyclosporine is safe and efficacious in children and adolescents with CIU resistant to conventional treatment.

Comments

Every practicing allergist knows that one of the most frustrating problems we deal with is the management of patients with CIU. Standard initial therapy consisting of antihistamines is more often than not ineffectual or only partially effective. In most instances, when standard doses are not sufficient, higher doses are given, and quite often, even in these cases, treatment fails. Thus, the ongoing search for alternative therapies that would be effective and relatively safe continues. Multiple agents have been evaluated in this regard. They include leukotriene modifiers, dapsone, sulfasalazine, hydroxychloroquine, colchicine, mycophenolate, androgens, estrogens, methotrexate, intravenous immunoglobulin, phototherapy, anticoagulants, cyclophosphamide, calcium

channel blockers, chrysotherapy, plasmapheresis, calcineurin inhibitors, and various others [1, 2].

Because of the nature of these agents, most such trials have been carried out in adults. Despite attempts to control chronic urticaria with these agents, most patients who are nonresponsive to antihistamines remain difficult to control, and in many instances, the side effects from the alternative agents prevent their common usage. Thus, in many cases, we use corticosteroids in the lowest doses possible, using intermittent bursts, and occasionally low-dose daily management.

Of course, none of these options have been totally acceptable; therefore, any reasonable alternative is extremely welcome. This is why the report by Doshi and Weinberger is extremely encouraging. Their use of the calcineurin inhibitor cyclosporine in these children 9 to 16 years of age was generally associated with good relief and a good side effect profile. Thus, these agents may well offer us a useful alternative in the management of difficult cases of CIU, and it is possible that tacrolimus, a similar agent that is perhaps associated with even a better side effect profile, will be an even more acceptable agent.

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