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Nephrotic syndrome in children: challenges and solutions

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Abbreviations: NS: Nephrotic Syndrome, UTRI: Upper respiratory Tract Infection, MMF: Mycophenolate Mofetil, SD: Steroid Dependent, FR: Frequent Relapse.

Introduction

Nephrotic syndrome (NS) is found to be commonest glomerulopathy in pediatric age group. The reported incidence is 2 to 7 per 100,000 children and a prevalence of about 16 per 100,000 children amongst [1].

Of Pediatric age group 80-90% are found to be Steroid – sensitive, however around 80% of them do relapse after initial response. Half of them adopt steroid dependent (SD) course which is defined as relapse while on tapering doses of steroids or within 14 days of cessation of treatment. Frequent relapses (FR) are 2 or more relapses in six months and 4 or more relapses in one year. Relapses are associated with increases morbidity and mortality related to increased chance of infections, thrombosis and acute kidney injury [2,3]. Relapses are treated with high doses of steroids for induction of remission which lead to increased steroid toxicity and side effects.

Most frequent trigger blamed for relapses are upper respiratory tract infections (URTIs). URTIs lead to lymphocyte up-regulation and cytokine release which in turn lead to occurrence of relapse. Interleukin 2, 4, and 13 are commonly thought to be implicated in this regard. Immunosuppressant medications like prednisolone and cyclosporine induce remission by their effect on cytokine release [4].

Although most common infections leading to relapse are URTIs which are responsible for 50-70% relapses in developing countries but lower respiratory tract infections and gastrointestinal infections can also contribute to relapses. Developing countries experience this increase susceptibility of infection due to poor living condition, overcrowding and prevalence of malnutrition.

Although availability of newer agents like mycophenolate mofetil (MMF), calcineurin inhibitors has been found to decrease the number of relapses in FRNS/SDNS and result in decrease dose requirement of steroids in but cost and side effects of these alternate agents is a serious concern Various studies has documented reduction in number of relapses when patients with NS on low dose alternate daysteroidwere switched to daily dose of steroids for 5-7 days, which in turn lead to smaller cumulative steroid dose and less frequency of side effects. Patients maintaining remission on low dose (0.6mg/Kg) on alternate day when switched to same dose on daily dose basis at onset of URTI led significant reduction of relapses. Comparison of groups treated with daily dose steroids during URTI *vs* without daily doses, when followed for 2 years, were found to have same risk of serious infections, risk of hospitalization and steroid side effects.

Patients who were off steroids for >3 months, when treated with daily dose of steroids for 5 days during URTIs were also found to have less number of relapses.

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However so far studies have documented this beneficial effect in children on doses of 0.5-0.75mg/Kg steroids on AD, few questions are still unanswered which are,

1. Whether this intervention is equally effective when patients are maintaining remission on doses lower than this?
2. Usefulness of this protocol when patients are on added immunosuppressant other than steroids and levamisole?
3. Still it has not been validated for infections other than URTI

Various therapeutic regimens being used for control of nephrotic state in SD and FRNS are either use of prolonged course of steroids or addition of other immunosuppressant like levamisole, cyclosporine, mycophenolate mofetil, cyclosporine, tacrolimus or rituximab. These therapies have been used with variable response rate ranging from 30-65% response rate. However their cost and potential side effects like increases susceptibility to opportunistic infection and risk of future malignancy which is a serious concern that cannot be denied [5]. We can safely recommend that treating URTIs with small dose of steroid can significantly reduce relapse rate in nephrotic syndrome.

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