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Research Article

A Study Of Treatment Of Steroid Resistance And Steroid Dependent Nephrotic Syndrome By Mycophenolate Mofetil & Deflazacort In Pediatric Age Group –A Study From Tribal Population In Developing State (India).

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Abstract

A total no of patients included in study are 28.The mean age of the patient is 11 ± 2.86 years. Out of 65 % patients are Male while 35 % patients are female. All patients are having Hypoalbuminea. The mean 24 hour urine protein is 3.1 ± 1.2 grams. 46 % patients are Hypothyroid out of them 62 % was male & 38 % was female.72 % patients shows electrolyte imbalance.97 % patients shows abnormal usg findings in which, ascites, increased echotexture pleural effusion seen in 43.5%, 28%, 28.5 % respectively.

Average weight of the Nephrotic Syndrome patient is 28 ± 13.69 kg. Average weight reduction in week duration is 6.78± 0.78 kg .Dose of Deflazacort used is 1 mg/kg body weight. Dose of Mycophenolate mofetil used is 12mg/kg body weight.

No patients shows complication related to mycophenolate mofetil..96.4% patients shows improvement in 6 month follow up & only 1 patient had relapse because of irregular medication.

Keywords: Mycophenolate Mofetil, Deflazacort, Steroid Dependent Nephrotic Syndrome.

INTRODUCTION

Idiopathic nephrotic syndrome affects 1–3 per 100,000 children <16 years of age [1]. Whereas most children will be responsive to corticosteroid therapy, approximately 20 % will be classified as steroid resistant [McKinney PA et al], i.e., failure to achieve complete remission after initial therapy with corticosteroids. Children with steroid-resistant nephrotic syndrome (SRNS) may have minimal-change disease (MCD), mesangial proliferative glomerulonephritis (MesPGN), or focal segmental glomerulosclerosis (FSGS), although other histopathologic diagnoses also occur. Mycophenolate mofetil, as a new immunosuppressive drug, is a specific inhibitor of inosine monophosphate dehydrogenase, which is involved in de novo purine synthesis. MMF is a suppressor of both T and B cell proliferation. The drug can produce selective inhibition of the lymphocyte functions, deoxyguanosine nucleotide depletion and also has effects on non-immune cells preventing fibrosis and vascular smooth muscle cell proliferation (. Badid C et al). MMF can improve the disease in glomerular diseases with nephrotic syndrome including membranous nephropathy. It can reduce the proteinuria with a consequent improvement or stabilization of the renal function. We administered MMF in patients with membranous nephropathy and severe nephrotic syndrome. The entire group of patients responded to the treatment, and proteinuria decreased significantly after 6 months, be it still within the nephrotic range. Non-nephrotic proteinuria was achieved after 12 months of follow-up under treatment. (Passerini P et al, Zhao M et al). Deflazacort (DFZ) had been described as equally effective and with fewer side effects as compared with other steroids. The limited evidence suggested that DFZ appeared to be equally effective in inducing remission or decreasing proteinuria in patients with nephrotic syndrome. It caused

significantly less decrease in bone mineral content (BMC) in spine as compared with prednisolone.

Deflazacort (DFZ) is an oxazoline derivative of PDN with anti-inflammatory and immunosuppressive activity.[Ferraris JR et al] The potency ratio of DFZ *vs* PDN is estimated to be 1.28 (6 mg of DFZ : 5 mg PDN). The use of DFZ in Duchenne Muscular Dystrophy, Juvenile Idiopathic arthritis (previously, juvenile chronic or rheumatoid arthritis),chronic inflammatory diseases in adults,renal transplantation, various hematological disorders (non-Hodgkin's lymphoma, idiopathic thrombocytopenic purpura, etc.), drug-resistant epilepsies in children, (Schärer K et al) and type 1 autoimmune hepatitis is found to be as efficacious as other steroids with less worrying adverse-effect profile. (Ferraris JR et al)

Method:

The study was conducted in the Department of Medicine, Pt. J.N.M. Medical College and Dr. B.R.A.M.Hospital, Raipur. 28 patient of pediatric age group of Nephrotic Syndrome were included for the purpose of study admitted in Nephrology Unit, Pt.J.N.M.Medical College Raipur from was studied. All patients were subjected to routine investigations like complete blood counts,urea,creatinine, serum bilirubin ,liver enzymes, electrolytes (sodium ,potassium,chloride calcium),urine routine microscopy,24 hour urinary protein.Thyroid Function Test, chest xray and ultrasonography of abdomen.

Results

A total no of patients included in study are 28.The mean age of the patient is 11 ± 2.86 years. Out of 65 % patients are Male while 35 % patients are female. All patients are having Hypoalbuminea. The mean 24 hour urine protein is 3.1 ± 1.2 grams. 46 % patients are Hypothyroid out of them 62 % was male & 38 % was female.72 % patients shows electrolyte imbalance.97 % patients shows abnormal usg findings in which, ascites, increased echotexture pleural effusion seen in 43.5%, 28%, 28.5 % respectively.

Average weight of the Nephrotic Syndrome patient is 28 ± 13.69 kg. Average weight reduction in week duration is 6.78± 0.78 kgDose of Deflazacort used is 1 mg/kg body weight. Dose of Mycophenolate mofetil used is 12mg/kg body weight.

None of the patients showed complication related to mycophenolate mofetil..96.4% patients shows improvement in 6 month follow up & only 1 patient had relapse because of irregular medication

Discussion

Nephrotic syndrome is an important chronic disease in children, characterized by minimal change disease in the majority. Research on pathogenesis has emphasized the importance of T lymphocyte dysregulation and vascular permeability factors that might alter podocyte function and permselectivity. While mutations in genes that encode important podocyte proteins have also been identified, a hypothesis unifying available evidence on pathogenesis is yet to be proposed.

Patients with nephrotic syndrome are at risk for life threatening infections and thromboembolic episodes. Long-term effects of persistent hyperlipidaemia and prolonged steroid therapy are increasingly recognized. Remission of proteinuria following corticosteroid therapy has greater prognostic value, in relation to long-term outcome, than the precise renal histology. Prospective studies show that prolonged duration of therapy for the initial episode results in sustained remission and reduced frequency of relapses.

The management of steroid-resistant nephrotic syndrome is difficult; most patients failing to achieve remission show progressive renal damage. (Arvind Bagga et al). Mycophenolate mofetil is one of the immunosuppressant drugs which have been used to prevent rejection in organ transplantation. Generally it is used as part of a three-compound regimen of immunosuppressants, including a calcineurin inhibitor (cyclosporine or tacrolimus) and prednisolone. As an immunosuppressant that has drastically decreased the incidence of acute rejection in solid transplant recipients, mycophenolate is increasingly utilized as a steroid-sparing treatment in immune-mediated disorders including immunoglobulin A nephropathy, small vessel vasculitis as well as psoriasis. Mycophenolate mofetil administration usually generates less frequent and gentle side-effects. It should be re-considered even in patients with initially low GFR, although the final decision as regards its administration in that group of patients should be evaluated after 3 months to 6 months of treatment. Otherwise, expected benefits could be less than progressive

side-effects. (Walsh M et al) Common adverse drug reactions associated with mycophenolate therapy include diarrhoea, nausea, vomiting, infections, leukopenia, and/or anaemia. Mycophenolate mofetil is also believed to be commonly associated with fatigue, headache, and/or cough [Brister K]. Intravenous administration of MMF is sometimes associated with thrombophlebitis and thrombosis. Infrequent adverse effects (0.1-1% of patients) include oesophagitis, gastritis, gastrointestinal tract haemorrhage, and/or invasive cytomegalovirus (CMV) infection [Brum S et al]

Corticosteroids (specifically prednisolone [PDN]) form first line of treatment for nephrotic syndrome in children and it is used for prolonged period and sometimes repeatedly for relapses Although there is lack of clinical guidelines for management of nephrotic syndrome in adults, it is managed by controlling edema, using angiotensin-converting enzyme inhibitors with controversial role of steroids The response rates to corticosteroids in adult minimal change disease is variable (remission in 37% to 50% within four weeks, 51% to 76% within eight weeks, and 76% to 97% within 16 weeks with failure in 10% and relapse in about two third patients) as compared with similar disease in children. Cyclophosphamide, cyclosporine, chlorambucil, and other immunosuppressive have been used for patients with either steroid-resistant or frequently relapsing nephrotic syndrome. Immunosuppressive therapy for nephrotic syndrome is not without adverse effects which such as infection, malignancy, peptic ulceration, diabetes mellitus, infertility, kidney failure, bone marrow suppression, hypertrichosis, and alopecia. (Joshi N et al)

Important side effects of steroids in adults include fall in bone mineral content (BMC), Cushingoid appearance, and increased blood pressure. In children particularly, corticosteroids have known adverse effects such as obesity, impaired growth, hypertension, impaired glucose tolerance, osteoporosis, Cushingoid symptoms, and adrenal suppression and these are more prevalent in those children who relapse frequently requiring multiple courses of corticosteroids.

Deflazacort (DFZ) is an oxazoline derivative of Prednisolone with anti-inflammatory and immunosuppressive activity. The potency ratio of DFZ *vs* PDN is estimated to be 1.28 (6 mg of DFZ : 5 mg PDN)..The use of DFZ in Duchenne Muscular Dystrophy,Juvenile Idiopathic arthritis (previously, juvenile chronic or rheumatoid arthritis), chronic inflammatory diseases in adults, renal transplantation, various hematological disorders (non-Hodgkin's lymphoma, idiopathic thrombocytopenic purpura, etc.), drug-resistant epilepsies in children, and type 1 autoimmune hepatitis is found to be as efficacious as other steroids with less worrying adverse-effect,profile.(Avioli.LV,etal)

Although therapeutic effects are inseparable from adverse metabolic effects of steroids, the goal of corticosteroid therapy should be to achieve maximum clinical benefit with minimum side effects. DFZ appeared to have almost similar efficacy with fewer side effects for various immune-mediated diseases as compared with PDN or other steroids. In management of nephrotic syndrome, steroids are used for long duration resulting in many adverse effects. Thus, it will be prudent to find a drug with similar efficacy but fewer side effects for patients with nephrotic syndrome. (Campbell C et al)

Conclusion:

Male shows greater improvement than female.Maximum weight reduction was from 69 kg to 59 kg at the time of discharge Hypoalbuminemia and hypothyroidism was common in female than male. 96.4% patients shows improvement with Deflazacort & Mycophenolate mofetil. Deflazacort & Mycophenolate mofetil shows better results in treatment of nephritic syndrome.

Bibilography

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