EFFICACY AND SAFETY OF DEFLAZACORT IN THE TREATMENT OF PAEDIATRIC NEPHROTIC SYNDROME

Paediatrics

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ABSTRACT

Nephrotic syndrome, an acute renal disorder mostly affects children but may occur in adults also. It is characterized by generalized swelling, proteinuria, excess albuminuria, low serum albumin and hyperlipidemia. It can be classified as primary, secondary and miscellaneous type. Corticosteroid is the main drug to treat NS but their side effects are bigger challenges. We elucidate the efficacy and safety of Deflazacort in paediatric NS.

KEYWORDS

Deflazacort, Nephrotic syndrome, Prednisolone

INTRODUCTION

Nephrotic syndrome (NS), an acute renal disorder mostly affects children but may occur in adults also. It is characterized by generalized swelling, proteinuria, excess albuminuria, low serum albumin and hyperlipidemia. (Bagga et al., 2008) Nephrotic syndrome can be classified as primary, secondary and miscellaneous forms. Patients with primary NS shows minimal change disease, membranous nephropathy and focal segmental glomerulosclerosis. Secondary NS includes human immunodeficiency virus, hepatitis B and C, malaria, syphilis and toxoplasmosis. Miscellaneous type includes systemic lupus erythematosus (SLE), diabetes mellitus and immuoglobulin A nephropathy. (Kumar et al., 2017) Corticosteroids are main drug to treat NS to achieve more clinical advantage with lesser side effects. The adverse effect of corticosteroids may be associated with growth and adrenal retardation in children. Therefore, an alternate is needed with less adverse effect. Deflazacort, an oxazoline derivative is suggested to reduce osteoporosis, growth suppression and weight gain. (Singhal et al., 2015). In present study we explored the efficacy and safety of Deflazacort in paediatric NS.

MATERIALS AND METHODS

We conducted a cross sectional study on 40 patients with NS below the age of 19 years to observe the efficacy and safety of Deflazacort in S.N Children Hospital, Department of Paediatrics, M.L.N Medical College, Allahabad. All newly diagnosed patients of NS and patient with frequent relapse were included in the study. Patients with oedema at presentation, proteinuria, hypoalbuminemia and those previously diagnosed as a case of NS attending hospital as follow up were considered for the study. Previous history of disease, medications and Family history was also recorded. We performed clinical, radiological examination along with biochemical, microbiological and pathological investigations to confirm the diagnosis. The investigations included urine, total serum protein, serum albumin, and serum cholesterol, serum urea, globulins and creatinin analysis. Drug sensitivity test was also performed. A written consent was obtained from the parents/guardian.

TREATMENT

Deflazacort was administrated in all patients according to ISKDC protocol in bioequivalent doses of prednisolone. For first episode of NS, Deflazacort was given daily as 2.4mg/kg/day in divided dose for 6 weeks followed by 1.8mg/kg/day on alternate day for 6 weeks. Outcome was measured in term of changes in the biochemical parameter, time taken in remission, time for which patients remained in remission and number of relapse in one year follow up. Remission was defined as: Nil BSUP for 3 days. Relapse was defined as 3+ to 4+ : protein in urine for more than 3-4 days. Frequent relapse was defined as more than 4 relapse in a year. All the patients were followed up at the interval of 15- 30 days. A thorough clinical re-examination was done on each subsequent visit.

RESULTS

Table 1: Relationship of ESR (in mm) with duration of treatment

Time of Determination	0-10	11-30	31-60	>60	No. of cases
At Admission	4 (7.5%)	6 (15%)	12 (30%)	18 (47.5%)	40
After one month	5 (12.5%)	9 (22.5%)	20 (50%)	6 (15%)	40
After two months	13 (32.5%)	27 (67.5%)	0	0	40

Table 2: Relationship of Haemoglobin (gm%) with duration of treatment

Time of duration	Haemoglobin (in gm%)			No. of cases
	10	10-12	>12	
At Admission	15 (37.5%)	17 (42.5%)	8 (20%)	40
After one month	4 (10%)	24 (60%)	12 (30%)	40
After two months	7 (17.5%)	17 (42.5%)	16 (40%)	40

Microscopic findings of urine

Hematuria was present in 12 cases while significant hematuria was observed in 4 cases. In 5 cases cast hematuria and pus cells was present in urine. In 2 cases, hematuria persisted even after prednisolone therapy.

Proteinuria

Twelve cases (30%) had proteinuria less than 5gm/litre and 14 cases (35%) had proteinuria between 5-10 gm/litre and 14 cases (35%) had proteinuria above 10 gm/litre.

Table 3: Relationship of Spot protein: Creatinine ratio with duration of treatment

Time of Admission	Spot protein: Creatinin ratio			No. of cases
	>4	>3	>2	
Admission	6 (15%)	30 (75%)	4 (10%)	40
After one month	0	21 (52.5%)	19 (47.5%)	40
After two months	0	4 (10%)	36 (90%)	40

Table 4: Relationship of total serum proteins (gm%) with duration of treatment

Time of determination	3-4.5 gm%	4.6- 5.5gm%	5.6- 6.5gm%	>6.5gm %	No. of cases
At Admission	26 (65%)	11 (27.5%)	3 (7.5%)	0	40
After one month	5 (12.5%)	11 (27.5%)	23 (57.5%)	1 (2.5%)	40
After two months	2 (5%)	9 (22.5%)	21 (52.5%)	8 (20%)	40

Table 5: Relation of serum albumin with duration of treatment

Time of determination	Upto 1 gm%	1.1- 2gm%	2.1- 3.2gm%	>3.2gm%	No. of cases
At admission	2 (5%)	20 (50%)	16 (40%)	2 (5%)	40
After one month	0	5 (12.5%)	24 (60%)	11 (27.5%)	40
After two months	0	4 (10%)	11 (32.5%)	23 (57.5%)	40

Relationship of oedema with serum albumin

Majority of patients with serum albumin between 1-2 gm% had severe oedema whereas patients with serum albumin between 2.1-3.2 gm% had mild to moderate oedema ($p < 0.01$).

Table 6: Relationship of serum cholesterol (in mg/dl) with duration of treatment

Time of Admission	Serum Cholesterol (in mg/dl)				No. of cases
	Upto 225	225-350	350-500	>500	
Admission	5 (12.5%)	20 (50%)	11 (27.5%)	4 (10%)	40
After one month	2 (31.5%)	21 (55.2%)	4 (10.5%)	1 (2.6%)	38
After two months	16 (53.3%)	14 (46.6%)	-	-	30

Relationship between serum cholesterol and serum albumin

Out of 24 patients with serum albumin between 1-2 gm% had serum cholesterol level above 225 mg%. Among them 12 cases were found with serum cholesterol level above 350 mg%. Normal serum cholesterol (in six cases), serum cholesterol ranged from 225-350 mg% (in six cases) and serum cholesterol ranged from 350-500 mg% (in three cases) were recorded in patients with serum albumin level between 2-3.2 gm%.

Response to Deflazacort

Patients were grouped in to four types according to response of Deflazacort therapy:

- Responder :completely recovered after treatment
- Infrequent relapse: <3 relapse in one year follow up
- Frequent relapse: >4 relapse in one year follow up
- Non-responder

Table 7: Clinical classification according to Deflazacort response

Type of response	No. of cases	%age	Male	Female
Responder	18	45	10	8
Infrequent relapse	11	27.5	6	5
Frequent relapse	6	15	4	2
Non- responder	5	12.5	4	1
Total	40		26	14

Out of 40 patients, 18 cases were responder, 11 cases were infrequent relapse, five cases were frequent relapse and five were non-responder. Urine was found without protein within 10 days of onset of Deflazacort therapy. Cushingoid facies were observed in 12 cases, marked hirsutism in two cases, hypertension in one cases and GIT disturbance in six cases.

DISCUSSION

Present study showed all cases with oedema, the cardinal sign of NS. Six cases were found with hypertension whereas oligouria and pallor was noticed in 18 cases. Proteinuria was found in 36 cases. Ascites was demonstrable in 62.5% cases with severe oedema. Our findings tally with the study of Ghosal SP, Chaudhuri (1958) who reported incidence of ascites with oedema in 66% of cases. Pus cells were observed in 42.55% cases, among which urine culture (growth of E.coli, Klebsiella and Streptococci) was positive. This showed that urinary tract infection can be a preceding factor of NS. ESR was raised in 90% cases at the time of admission which showed a decline with treatment and reached normal. (Table: 1) Our study was supported Ghosal and Chaudhuri (1958) finding where raised ESR attained normal value after treatment. In present study total serum level ranged from 3-6.5gm%. (Table: 4) After two months treatment serum protein was estimated more than 5.5 gm% in 72.5% cases. We observed out of 27 patients with severe oedema, 22 has serum albumin less than 2 gm%, while in 7 cases serum albumin was above 2.1gm%. (Table: 5). We found higher blood urea level (80-100 mg%) in three cases which reached below 40 mg% after treatment.

A study conducted by Arneil (1971) found 38% patients completely recovered after first attack. In a study performed by Gulati et al (1995), infrequent relapse constituted 34.6%, frequent relapse 25%, steroid dependent 28% and steroid nonresponder 12.5%. Another study showed that Deflazacort was much efficient than Prednisolone in controlling relapse in steroid-dependent idiopathic NS, weight gain, cushingoid features and reduction of bone mineral density. (Broyer et al., 1997). In present study, 18 out of 40 patients completely recovered after first attack, 11 cases were infrequent relapse, 6 cases were frequent relapse and 5 cases were non-responder to therapy.

CONCLUSION

Our study concluded that Deflazacort was as efficient as Prednisolone in inducing remission in NS. Changes in biochemical parameter are also alike but long term adverse effects of Deflazacort need further evaluation.

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