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Original Article

Deflazacort and Prednisolone in the Treatment of Initial Episode of Idiopathic Nephrotic Syndrome in Children

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Abstract

Background: *Prednisolone is the 1st choice of drug in Idiopathic Nephrotic Syndrome (INS). Deflazacort (DFZ) is a new step in this regard. Aim of this study was to compare the efficacy of prednisolone and DFZ in children with INS.*

Materials and methods: *76 children of 2-16 years with INS were enrolled in a Randomized Controlled Trial (RCT). Patients were randomized to either group-A (DFZ) or group-B (Prednisolone) and 38 children were allocated in each groups. After giving treatment with both drugs, these patients were followed up at 3 months interval for 2 times to compare the clinical effects. Due to lost follow up finally 65 patients were analyzed. Data was documented on pre-structured data sheet and analyzed by SPSS version 22.0. Chi square test for categorical data and unpaired t-test for continuous data were done. A probability (p) value < 0.05 was considered statistically significant.*

Results: *Mean time to get remission was 5.32±1.28 days in DFZ group and 8.00±2.55 days in prednisolone group. It was statistical significant (p= <0.001). Mean duration of remission was 171.29±19.27 days and 146.66±54.61 days in Group A and Group B respectively and was statistically significant (p= 0.020). Total number of relapse by treatment with DFZ is less in comparison of prednisolone.*

Conclusion: *DFZ was more effective as shorter time was required to induce remission and achieved remission was maintained for longer durationin INS. Number of relapse by using DFZ was less than prednisolone. Number with no relapse were more in DFZ than prednisolone on follow up time.*

Key words: Children; Deflazacort; Nephrotic syndrome; Prednisolone.

INTRODUCTION

Nephrotic Syndrome (NS) is a common clinical state in children. INS is the most common cause among its different varieties.[1] In each year, approximately 2–16 per 100,000 children are affected by this disease.[2] It is characterized by generalizededema, massive proteinuria and hypoalbuminemia. South Asian children are thought to have the highest incidence of NS.[3] In INS, more than 95% patients respond to steroid therapy and no need to do renal biopsy.[4] After 1978, prednisolone forms the 1st line of treatment for idiopathic nephrotic syndrome.[5] Long term prognosis of steroid responsiveness in INS is good. According to Kidney Disease Improving Global Outcome (KDIGO) guide line (June 2012) administration of prednisolone for three months reduces the risk of relapse in children with initial episode of steroid sensitive idiopathic nephrotic syndrome with an increase in benefit seen with up to 6 months of treatment. So, prednisolone is used for prolonged period and repeatedly for relapses and relapse rate in INS is about 70%.[6]

In this view, high dose of prednisolone is frequently used with longer duration alone or in combination with other immunosuppressive medication that induces many side effects especially in children. In this regard, a search for an alternative steroid with fewer side effects is underway. DFZ, a oxazoline derivative of prednisolone is equally effective with fewer side effects as compared with prednisolone.[7] According to various studies, it is more effective in taking shorter time to achieve remission and in maintaining longer duration after relapse with less side effects.[8] DFZ is equipotent to prednisolone in term of efficacy in inducing remission.[9] Dose is equivalent to prednisolone and noted to be superior to prednisolone in maintaining remission in the patients with relapsing and steroid dependent nephrotic syndrome.[10] In this point of view, the study was conducted to compare the effectiveness of DFZ and prednisolone in children with initial episode of INS in Bangladesh.

MATERIALS AND METHODS

A Randomized Controlled Trial (RCT) was done in the Department of Pediatric Nephrology, Bangabandhu Sheikh Mujib Medical University (BSMMU) Dhaka from September 2016 to August 2017. Total 76 patients with initial episode of INS age 2-16 years, were included in this study. Age < 2 years and > 16 years, NS due to any secondary causes, NS with atypical presentation like persistent hypertension, hematuria, Azotemia etc, previous H/O of taking any immunosuppressive agents for initial episodewere excluded. Patients were divided into GroupA (DFZ group)and Group B (Prednisolone group).Treatment allocation was made according to simple randomized method of doing lottery by drawing a paper from the container and accordingly each group contained 38 patients.History was taken and physical examination was done. Routine investigation, such as complete blood count, urine routine microscopic examination and urine culture, Spot urinary protein Creatinine ratio in case of OPD patient and 24hours total urinary protein in case of admitted patients, Serum cholesterol, serum albumin, Serum Creatinine, serum HBsAg, serum C3, Mantoux test (MT test) X-ray chest were done to confirm INS and to exclude infection before starting of treatment. Patient characteristics (Age, sex, height and weight) age of onset, associated complaints, Immunization history, physical examination like appearance , temperature, pulse, respiratory rate, blood pressure, other systemic examination were done and recorded on data collection sheet.

In initial episode, Group A were treated with DFZ, 2.4mg/kg/day (2-3 divided dose) for 6 weeks then 1.8mg/kg/day in alternate day for next 6 weeks and Group B were treated with prednisolone, 2mg/kg/day (2-3 divided dose) for 6 weeks then 1.5mg/kg/day in alternate day for next 6 weeks.Bed side urine albumin by heat coagulation test or dipstick test by albu strip was done daily till it was albumin free for three consecutive days and patient was advised to do this heat coagulation test daily even after getting remission or after discharging from hospital for recognize the relapse on follow up period. In case of OPD patients or after discharge from hospital (Indoor patient) each patient was advised for follow up visit in hospital according to follow up schedule.After giving treatment, these patients were followed up at 3 months interval for 2 times (Total 6 months) to compare the clinical effects.To prevent defaulters, ensuring proper drug compliance and to know the appearance of relapse each patient was monitored by over telephone and parents were advised to take empty blister or bottle of drugs during follow up visit for checking drug compliance. The parents were counselled about effects of drug discontinuation and reappearance of albumin by heat coagulation test (White precipitation in urine). Relapse was detected from history, clinical examination and by doing bed side heat coagulation test of urine for three consecutive days and was confirmed by dipstick test (Albu strip). Parents wereadvised to contact immediately in hospital without follow up schedule if relapse occur. In relapse case, the dose of deflazacort for group A was 2.4 mg/kg/day (Two or three divided doses) till urine was albumin free/traces for 3 consecutive days. Then 1.8 mg/kg/alternate day (Single dose) for 4weeks or gradually tapered by 5 mg in every 2 weeks. The dose of prednisolone was 2.0 mg/kg/day (Single dose daily) till urine was albumin free/traces for 3 consecutive days than 1.5 mg/kg/day on every alternate day (Single dose) for 4 weeks or gradual tapered of 5 mg by every 2 weeks in relapse cases. A patient once enrolled in one group was treated with the same drug used earlier.

During follow up, clinically vital signs and systemic examination was done and data about number of relapses after initial episode, days to achieve remission on treatment by either DFZ or Prednisolone and duration of remission (Time from urinary remission to development of 1ts relapse) by either DFZ or Prednisolone after initial episode was collected in preformed structured data sheet. Patient number of without relapse were also collected. Among 76,eleven patients were excluded, seven from group A (Lost follow up, n=5, treatment discontinued, n =2) and four from group B (Lost follow up, n=3, treatment discontinued, n =1) at follow up period. Finally 65 (A=31and B=34) patients were analyzed at the end of study.

Collected data was analyzed by software SPSS, version 22.For all statistical test, p value < 0.05 was considered as statistically significant. Continuous variable was presentedas mean±SD. Continuous variable was compared through unpaired t-test and categorical variable by chi-square test were done as applicable. The study protocol was approved by the Institutional Review Board of BSMMU, Dhaka.

RESULTS

There was no significant difference in number of patient, mean age, number of male and female in two groups (Table I). Regarding base line characteristics, no significant deference was found (Table II). Rural patients were more affected (54.8% and 67.6% respectively) by Idiopathic nephrotic syndrome than

urban patients. (Fig:1) Mean time to get remission after starting treatment was 5.32±1.28 days by DFZ and was 8.00± 2.55 days by prednisolone (Table III). This deference was statistically significant (p<0.01). Duration of remission after initial episode was also long in A (DFZ) than B (Prednisolone). It was 171.29±19.27 days in Group A and 146.55 ± 54.61days in group B. This deference was also statistically significant (p=0.02). Within follow up period, total number of relapses in group A was less than group B, but this deference was not statistically significant(p= 0.49) (Table IV). Only 1 relapse occurred 8 patients in group A and 11 patients in group B.

2 relapses occurred 3 patients in group A and 2 patients in group B. but 3 relapses occurred more in of group B (3) than group A (1). Number of the patients without any relapse was more in group A (61.3%) than group B(52.9%) on follow up time (Fig 2).

Table I Demographic characteristics of two groups (n= 65)

Characteristic	Group		p value
	Group A n (%)	Group B n (%)	
Patients (n)	31	34	
Age (Year)			
[Mean ± SD]	5.34 ± 2.94	5.43 ± 3.66	
Gender (n %)			0.91
Male [n (%)]	21 (67.71)	23 (67.65)	
Female [n (%)]	10 (32.37)	11 (32.44)	

Table II Characteristics of the patients at the beginning of study (n=65)

Base line characteristics	Group		p-Value
	Group A Mean ± SD	Group B Mean ± SD	
Weight (kg)	19.13 ± 8.74	19.85±10.61	0.77
Height (cm)	105.44±19.66	107.88± 21.60	0.64
Blood Pressure (mm of Hg)			
Systolic	95.65±8.83	93.82± 10.74	0.46
Diastolic	61.13±8.54	61.32± 9.15	0.93
Serum total cholesterol(mg/dl)	438.39±106.70	455.65±134.89	0.37
Serum albumin (gm/L)	18.25±7.43	18.56± 9.12	0.74
Urinary Protein Creatinine ratio (> 2 significant)	3.87±1.42	4.59±1.58	0.45

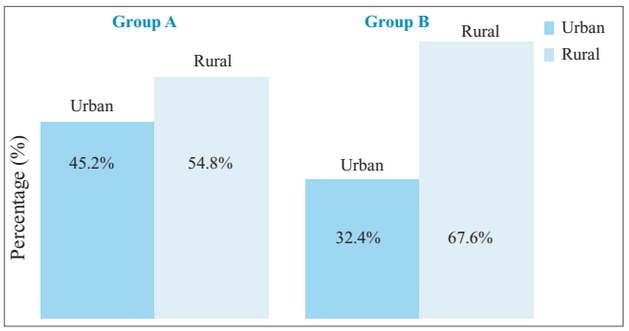

Figure 1 Bar chart showing the patients according to residence

Table III Comparison between time required to induce remission and duration of remission after starting of treatment in Group A and Group B (n=65)

	Group		
	Group A Mean± SD (n=31)	Group B Mean± SD (n=34)	p value
Time to get remission (Days) (Mean)	5.32 ± 1.28	8.00 ± 2.55	<0.001
Duration of remission (Days) (Mean)	171.29 ± 19.27	146.55 ± 54.61	0.020

Table IV number of relapses in both groups after initial treatment (n=65)

Number of relapses	Group		p value
	Group A (n=31) [n(%)]	Group B (n=34) [n(%)]	
1	8 (25.80)	11 (29.43)	
2	3 (9.67)	2 (5.90)	
3	1 (3.22)	3 (11.84)	
Total	12 (38.70)	16 (47.05)	0.4

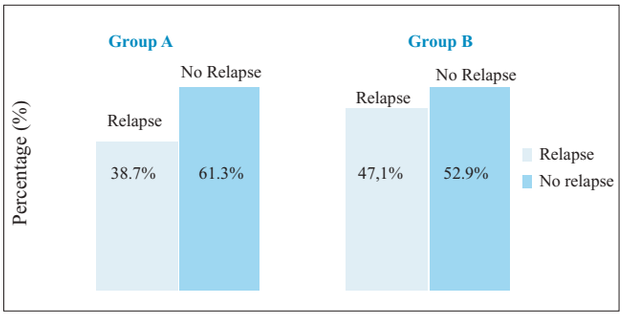

Figure 2 Comparison between numbers of relapses of the patients in two groups

DISCUSSION

The present study is a RCT in children with initial episode of idiopathic nephrotic syndrome to see the effectiveness of deflazacort in comparison of Prednisolone. In the study of Ravish et al time taken to get remission was shorter in DFZ (10.25±2.4) than prednisolone group (12.55±1.44 days) and this difference was significant (p value =0 .012).[8] Broyer et al. showed, equipotent dose of deflazacort relative to prednisolone inhibits T cell function for long period. So, mean time for attaining remission was shorter in DFZ group than prednisolone in their study. INS is a disease due to T cell dysfunction. Effects of DFZ in case of T cell depletion, reduction of lymphocytic function and on the ratio of helper T cell and cytotoxic T cell persists for up to 72 hours. But in case of prednisolone this change returns to base line within 24 hours.[10,11] So, DFZ is more effective in inducing early remission with the patients of idiopathic nephrotic syndrome.[11] In the study of Ravish et al. time taken to get remission was

shorter in DFZ (10.25±2.4) than prednisolone group (12.55±1.44 days) and this difference was significant (p value =0 .012).[8] In this study, time to achieve remission was shorter in deflzacort group (5.32 ± 1.28 days) as compared to prednisolone group (8.00 ± 2.55 days) and this deference was statistically significant (p= <0.001). Duration of remission after initial episode was also higher in group A (171.29 ± 19.27 days) than group B (146.55±54.61days) and this deference was also statistically significant (p= 0.020). Number of the patient without relapses on follow up time were 61.3% in group A and 52.9 % in group B in this study. Caterina et al, showed, number of patients of without relapses were more in prednisolone group than DFZ group and the difference was statistically significant in their study (p value <0.001).[12] So DFZ causes less relapse than prednisolone. Deflazacort is equally and some times more effective in comparison of prednisolone. These characteristics made it more acceptable as a new option of therapy in the treatment of steroid sensitive idiopathic nephrotic syndrome.

CONCLUSION

DFZ required shorter time to induce remission and achieved remission was maintained for longer duration in case of initial episode of INS. Number of relapse in treatment with DFZ was less than prednisolone during follow up period.

DISCLOSURE

All the authors declared no competing interest.

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