

Comparison of efficacy of single dose versus split dose prednisolone therapy in achieving remission in patients with nephrotic syndrome in children

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ABSTRACT

Background: Nephrotic syndrome is a medical problem clinically characterized by proteinuria, generalized body edema and hypercholesterolemia. We did this study to compare the effectiveness of single dose versus split dose prednisolone in achieving remission in patients with nephrotic syndrome in children.

Patients and methods: This open-ended randomized control trial was done in pediatric unit of tertiary care hospital from January to December 2019. We included one hundred Patients of nephrotic syndrome in the study who met the inclusion criteria. We divided total Patients into 2 groups (group A & B) 50 patients in each group. Group A was given single dose prednisolone, while group B was given split dose prednisolone therapy. Both groups were compared with respect of achievement of remission.

Results: Out of 50 patients of group A who were given single dose prednisolone 37 (74%) were male, while in group B who were given split dose prednisolone 22 (44%) were male (p-value=0.137). Mean age of patients of study group A and B was 4.5 ±1.67 years and 4.9 ±1.49 years respectively (p-value=0.1876). Mean serum creatinine level in study group A and B was 0.744±0.189 and 0.736±0.167 (p-value=0.823). Similarly mean serum albumin level in study group A and B was 2.34±0.358 and 2.39±0.33 (p-value=0.473). When both groups were compared with regard to response to treatment, in group A mean remission duration was 16.48 ±3.69. In group B mean remission duration was 19.42 ±3.11 days (p-value<0.05).

Conclusion: From our study we concluded that single dose prednisolone is more effective in achieving remission in steroid sensitive nephrotic syndrome as compared to split dose prednisolone.

Keywords

Nephrotic syndrome, Prednisolone, Remission, Single dose, Split dose

INTRODUCTION

Edema, hypoalbuminemia, hypercholesterolemia and heavy (nephrotic-range) proteinuria are the characteristics of Nephrotic syndrome.¹ We can define Nephrotic-range proteinuria, as proteinuria > 40mg/m²/hour, or a urine protein: creatinine ratio >2². In every 100,000 global cases of children around 2-7 are related to nephrotic syndrome. Certain population groups like the south Asians and Africans have shown higher frequency of nephrotic syndrome indicating its relation with genetic and environmental factors.³

Primary or idiopathic, congenital and secondary nephrotic syndrome are the classifications of Nephrotic syndrome. Above 90% of cases seen in children, the most common one is Idiopathic nephrotic syndrome.² Certain infections, medications, malignancies and

vaccines are associated with the etiology of nephrotic syndrome.⁴ Bacterial infections and thrombo-embolism are considered to be the most life threatening out of all the complications caused by Idiopathic Nephrotic syndrome.

Primary nephrotic syndrome is a chronic condition which has several remissions and relapses and is responsive to steroids. Steroid therapy can be refractory to focal segmental glomerulosclerosis which leads to chronic kidney disease. Fortunately, primary nephrotic syndrome is sensitive to corticosteroids and long-term prognosis is good. After diagnosis, < 5% children (of age 10) lead to chronic kidney disease.⁵

Corticosteroids are given in the form of oral prednisolone for the management of patients. Patients of nephrotic syndrome in the pediatric age group are managed by different protocols. According to American Academy of Pediatrics, daily oral prednisolone is administered in a dose of 2mg/kg/day or 60mg/m²/day in divided doses daily for 6 weeks without tapering the dose.⁶ In another regimen, the initial dose of 60mg/m²/day recommended by kidney disease

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improving global outcome (KDIGO), for 4 to 6 weeks. After this initial period, the dose is reduced to 40 mg/m² / day (1.5 mg/kg) on alternate day for 2 months to 5 months, with tapering of the dose⁷. Comparison between 12 weeks of therapy and 8 weeks of corticosteroids treatment was done by a study. Fewer relapses were faced by patients who were given long durations of therapy.⁸ In one study, the prednisolone is given in a dose of 60 mg/m² /daily for 28 days, followed by 40 mg/m² /every other day for 28 days.⁹ Most children having primary nephrotic syndrome experience relapsing course of the disease, but ultimate long-term prognosis is good¹⁰. There is also controversy over steroids given as single dose daily versus given in split daily doses. In our study we used oral prednisolone in a dose of 2mg/kg/day as single morning dose for 4 to 6 week followed by 1.5mg/kg every other day for next 2 to 5 months. This study was conducted to compare the effectiveness of single dose versus split dose prednisolone in achieving remission in patients with nephrotic syndrome in children.

PATIENTS AND METHODS

The study was done in pediatric unit-II tertiary care Hospital Bahawalpur, after taking approval from the ethical committee of medical education department of Quaid-e-Azam medical college Bahawalpur. The study design was randomized open ended clinical control trial. The study duration was one year from 01-01-2019 to 31-12-2019. The Patients who were recruited in the study were in the age group of 1 year to 10 years after taking informed consent from parents. All children aged 1-10 years presenting with a first episode of nephrotic syndrome defined as proteinuria >40 mg/m²/h or urine protein/creatinine ratio >2 mg/mg and hypo albuminemia <2.5 g/dL, were included for the study. The children having age less than 12 months or more than 10 years, children either with congenital or secondary or steroid resistant or steroid dependent nephrotic syndrome, children with relapse of nephrotic syndrome, children with nephrotic syndrome having macroscopic hematuria, persistent hypertension, renal failure or hypo- complementemia or having complications were excluded from the study. Verbal

consent was taken from the parents/ guardians before including in the study. Baseline serum creatinine and serum albumin was recorded. Hundred patients of nephrotic syndrome were included and divided into two groups by parallel group design. Allocation concealment method was used between two groups for treatment purpose. Group A patients were given single dose oral prednisolone 2mg/kg/day, while group B patients were given split dose (three times a day) oral prednisolone 2mg/kg/day⁷. Daily dipstick urinalysis was done for presence of protein urea. Serum creatinine was also done regularly to assess renal functions. Both groups were followed and compared till the achievement of remission (defined as urine protein: creatinine ratio <0.2 or <1+protein on urine dipstick for 3 consecutive days). Data was recorded on a specially designed proforma. Data was analyzed by using SPSS version 23. For the comparison of qualitative data, Chi-square test applied while t-test was applied to compare quantitative data like age and duration of remission, serum albumin and serum creatinine and to calculate the p-value. A p-value of <0.05 was taken as significant.

RESULTS

Out of 50 patients of group A who were given single dose prednisolone 37(74%) were male, while in group B who were given split dose prednisolone 22(44%) were male. Mean age of patients of study group A and B was 4.5 ±1.67 years and 4.9 ±1.49 years respectively. Mean serum creatinine level in study group A and B was 0.744±0.189 and 0.736±0.167 (p value 0.823). Similarly mean serum Albumin level in study group A and B was 2.34±0.358 and 2.39±0.33. When both groups were compared with regard to response to treatment, in group A mean remission duration was 16.48 ±3.69 (days). In group B mean remission duration was 19.42 ±3.11 (days). The p-value was <0.05.

DISCUSSION

Both the single dose prednisolone and split dose prednisolone have been used for the management of patients with steroid sensitive nephrotic syndrome. Both have advantages and disadvantages. It is thought that single dose prednisolone is more compliant than

Table 1. Comparison of characteristics and outcome of two groups

Characteristics	Group A (n=50)	Group B (n=50)	p-value
Age(years) Mean ±S.D	4.56±1.67	4.98±1.49	0.1876
Male (%)	37 (74%)	22 (44%)	0.137
Serum Creatinine (Mean±SD)	0.744±0.189	0.736±0.167	0.823
Serum Albumin (Mean±SD)	2.34±0.358	2.39±0.33	0.473
Remission in days, Mean±S.D	16.48±3.69	19.42±3.11	0.0001

split dose and there are less chances of adrenocortical suppression. In one study conducted by Bimal and Arvind showed that single dose prednisolone is more effective in treating relapse of nephrotic syndrome as compared to split dose nephrotic syndrome¹¹. The results of this study are favoring results of our study. A study conducted by Esezober C et al also used single daily dose prednisolone therapy in managing nephrotic syndrome with good results¹². A retrospective study conducted by Deschênes G and colleagues also found single daily dose steroids more beneficial than split dose prednisolone¹³. In one study conducted by Moorani et al in Karachi also used single dose oral prednisolone along with levamisole in frequent relapsing patients with good results¹⁴. Similar observations were made by Fallahzadeh M and colleagues by using single daily dose prednisolone in achieving remission in steroid sensitive nephrotic syndrome.¹⁵

In one study Warshaw and Hymes found similar remission time in patients received prednisolone either single or divided doses¹⁶. Two randomized controlled trials showed that, there was no significant difference in the meantime of achievement of remission, whether given corticosteroids as single dose or in divided doses¹⁷. These results are not favoring our study.

CONCLUSION

From our study we concluded that single dose prednisolone is more effective in achieving remission in steroid sensitive nephrotic syndrome as compared to split dose prednisolone. Further multicenter comparative studies with large sample size are needed for confirmation of results.

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