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Comparison of Relapse Rates and Time to Remission with Prednisolone Versus Deflazacort in Children with Idiopathic Nephrotic Syndrome

Dr. Mohammad Rafiqul Islam[1*], Dr. Abdul Aziz Mia[2], Dr. Tahfim Ahmed[3], Dr. Nusrat Jahan[4], Dr. Rashadul Kabir[5], Dr. Mohammad Abdul Baki[6], Dr. S.M Ahsanul Kabir Al-Aziz[7]

[1]*Associate Professor (Current Charge), Department of Pediatrics, Chandpur Medical College, Chandpur, Bangladesh*

[2]*Senior Consultant, Department of Pediatrics, 250 Bedded Sadar Hospital, Chandpur, Bangladesh*

[3]*Assistant Professor, Department of Pediatrics Nephrology, Chandpur Medical College, Chandpur, Bangladesh*

[4]*Assistant Professor, Department of Biochemistry, Kumudini Women's Medical College, Tangail, Bangladesh*

[5]*Assistant Professor, Department of Pediatrics Cardiology, National Institute of Cardio Vascular Diseases (NICVD), Dhaka, Bangladesh*

[6]*Junior Consultant, Department of Pediatrics, Narsingdi Sadar Hospital, Narsingdi, Bangladesh*

[7]*Senior Clinical Pathologist, Department of Pathologist, Mugda Medical College Hospital, Dhaka, Bangladesh*

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Corresponding Author:** ***Dr. Mohammad Rafiqul Islam, *Associate Professor (Current Charge), Department of Pediatrics, Chandpur Medical College, Chandpur, Bangladesh*

Abstract

Background: *Idiopathic nephrotic syndrome (INS) is the most common glomerular disorder in children. While corticosteroids remain the cornerstone of treatment, the comparative effectiveness of prednisolone and deflazacort regarding remission time and relapse rates remains a key clinical concern. This study aims to compare the relapse rates and time to remission between prednisolone and deflazacort in children with idiopathic nephrotic syndrome*

Methods: *This randomized controlled trial was conducted at the Department of Pediatric Nephrology, National Institute of Kidney Diseases and Urology (NIKDU), Dhaka, Bangladesh, from June 2019 to January 2021. A total of 74 children aged 2–12 years with an initial episode of idiopathic nephrotic syndrome were randomized into two groups: Group A (n=37) received prednisolone, and Group B (n=37) received deflazacort for 12 weeks. Patients were followed for 6 months to assess time to remission, number of relapses, and side effects.*

Results: *The mean time to remission was significantly shorter in Group B (deflazacort) compared to Group A (prednisolone) (7.87 ± 3.33 days vs. 9.82 ± 3.43 days; p=0.02). After 3 months, relapses occurred in 10.8% of Group A and 2.7% of Group B (p=0.17). At 6 months, relapse rates were 27.0% in Group A and 18.9% in Group B (p=0.41). Cushingoid features and metabolic complications were more frequent in the prednisolone group, though not statistically significant.*

Conclusion: *Deflazacort induced earlier remission with fewer relapses and fewer adverse effects compared to prednisolone, suggesting a favorable alternative in the treatment of pediatric idiopathic nephrotic syndrome.*

Keywords: *Idiopathic nephrotic syndrome, Prednisolone, Deflazacort, Remission, Relapse, Pediatric nephrology.*

1. INTRODUCTION

Idiopathic nephrotic syndrome (INS) is the most frequent renal disease in children and adolescents and, like Minimal Change Disease, is defined by proteinuria, hypoalbuminemia, hyperlipidemia, and edema. It occurs in childhood, predominantly in children aged between 2 and 8 years, but has an unpredictable clinical behavior [1, 2].

About 90% of children in whom KS affects respond to corticosteroid treatment, meaning they have steroid-sensitive nephrotic syndrome (SSNS) [3]. However, prognoses for childhood

asthma are good, and many children may suffer one or even multiple relapses on the way to reaching a sustained remission [4].

Thus, prednisolone has been considered the mainstay of SSNS treatment, evidenced by historical and current literature [5,6]. However, the use of corticosteroids is not without complications because long-term treatment leads to such side effects as well as causing Cushing's facies, growth retardation, hyperglycemia, bone density loss which compromises the quality of life of such children [7,8]. Thus, interest in alternative corticosteroids with equal effectiveness but fewer side effects has been increasing.

Deflazacort is a substitution product of prednisolone, which belongs to the oxazolone category. They are believed to have the same anti-inflammatory and immunosuppressive effects as well, which have less impact in causing metabolism-related side effects [9]. Pharmacokinetic tests reveal that deflazacort has better therapeutic ratios and has less affinity to glucocorticoid receptors in bones and cartilage than prednisone, which could be responsible for the lesser effect it has on growth and bone density [10,11]. Other chronic inflammatory disease studies have also shown that deflazacort causes less weight gain and lower chances of hyperglycemia than the usual steroids do [12].

A number of trials have assessed deflazacort and prednisolone in the context of pediatric nephrotic syndrome with varied outcomes. A randomized controlled study described by Broyer et al. (1997) noted that the remission that deflazacort caused was comparable to prednisolone but with fewer cushingoid features [13]. In a similar study, Piccoli et al. (1993) also reported no significant differences in efficacy but a better profile regarding tolerability, as reported in the case of deflazacort [14]. Some researchers have indeed expressed concern about the risk of elevated rates of relapse associated with the use of deflazacort, either through the changed bioavailability and receptor binding characteristics that this can potentially entail [15].

Given such conflicting reports, there is a need to conduct head-to-head comparisons of deflazacort and prednisolone, especially in relation to relapse rates and time to remission – two critical measures of therapeutic success in INS. Also, considering the chronic and relapsing character of SSNS, long-term safety is of the top priority when choosing a corticosteroid in pediatric medicine.

The study aims to compare relapse rates and the time to remission in idiopathic nephrotic syndrome patients who received either prednisolone or deflazacort. Furthermore, by evaluating complications and biochemical parameters, at least over 6 months, this study aims to add evidence to inform clinical decision-making in the management of SSNS, as well as investigate if deflazacort can be a safer and more acceptable option as an alternative to prednisolone in the practice of pediatric nephrology.

2. Objective

The objective of this study was to compare the relapse rates and time to remission between prednisolone and deflazacort in children with idiopathic nephrotic syndrome.

3. Methodology & Materials

This was a randomized controlled trial conducted at the Department of Pediatric Nephrology, National Institute of Kidney Diseases and Urology (NIKDU), Dhaka, Bangladesh, from June 2019 to January 2021. A total of 83 children diagnosed with the initial episode of idiopathic nephrotic syndrome were screened. Eligible participants were randomly assigned to two intervention arms: Group A received prednisolone, and Group B received deflazacort. Randomization was achieved using a simple lottery method. After accounting for attrition due to loss to follow-up, 74 participants (37 in each group) were included in the final analysis.

3.1. Sample Selection

Inclusion Criteria

- Children aged between 2 to 12 years
- First episode of idiopathic nephrotic syndrome
- Patients admitted or visiting the outpatient department at NIKDU

Exclusion Criteria

- Age < 2 years or > 12 years
- Nephrotic syndrome secondary to systemic disease
- Congenital nephrotic syndrome
- Prior immunosuppressive treatment elsewhere
- Refusal to provide informed consent

3.2. Data Collection Procedure

Each child underwent history-taking and clinical examination, including age, sex, anthropometric

data, vitals, and systemic review. Diagnostic investigations included complete blood count, urine routine microscopy, urine culture, serum creatinine, serum albumin, serum cholesterol, spot urinary protein-creatinine ratio or 24-hour protein, HBsAg, chest X-ray, and Mantoux test to confirm idiopathic nephrotic syndrome and rule out secondary causes. Prednisolone and deflazacort were administered using equivalent anti-inflammatory dosages (prednisolone: 2 mg/kg/day, deflazacort: 2.4 mg/kg/day), followed by alternate-day tapering. All drugs were from the same pharmaceutical company for consistency. Parents were trained to perform daily heat-coagulation urine tests to monitor remission or relapse. Follow-up evaluations occurred at 3 and 6 months, recording time to remission, relapses, and adverse effects.

3.3. Ethical Considerations

The study was approved by the Institutional Review Board of NIKDU. Written informed consent was obtained from parents after explaining the study's purpose, procedures, benefits, and risks. Participation was voluntary, and confidentiality was maintained through coded identification and secure data storage. Participants could withdraw anytime without penalty.

3.4. Statistical Analysis

Data were analyzed using SPSS version 22. Descriptive statistics summarized baseline characteristics. Continuous variables were expressed as mean ± standard deviation and compared using an unpaired t-test or a Mann-Whitney U test. Categorical data were analyzed using the chi-square test. A p-value < 0.05 was considered significant.

4. RESULTS

This study included a total of 74 children diagnosed with idiopathic nephrotic syndrome, divided equally into two treatment groups: Group A received Prednisolone, and Group B received Deflazacort. The primary outcomes evaluated were time to remission, relapse rates, adverse effects, and selected biochemical parameters over a six-month follow-up period. Baseline demographic characteristics were also compared between the two groups.

Table 1. *Sociodemographic characteristics of the respondents (n=74)*

Characteristics		Group A (n=37)	Group B (n=37)	P-value
Age (years)	<5	21 (56.8)	23 (62.2)	
	5-10	13 (35.1)	13 (35.1)	
	>10	3 (8.1)	1 (2.7)	
Mean ± SD		3.87±1.23	4.97 ± 2.11	0.01
Gender	Male	19 (51.4)	22 (59.5)	0.48
	Female	18 (48.6)	15 (40.5)	
Residence	Rural	30 (81.1)	24 (64.9)	0.12
	Urban	7 (18.9)	13 (35.1)	

Table 1shows the Sociodemographic Characteristics of the Respondents. The mean age of children in Group A was 3.87 ± 1.23 years, significantly lower than that of Group B (4.97 ± 2.11 years; p = 0.01). A majority of participants in both groups were aged below 5 years—56.8% in Group A and 62.2% in Group B. Gender distribution was comparable, with males representing 51.4% in Group A and 59.5% in Group B (p = 0.48). Rural residency predominated in both groups, although Group A had a higher proportion of rural participants (81.1%) compared to Group B (64.9%; p = 0.12). None of the differences in gender or residence reached statistical significance.

Table 2. *Comparison between the time required to induce remission in Group A and Group B (n=74)*

Time	Group A (n=37)	Group B (n=37)	P-value
Time to induce remission (Mean±SD)	9.82±3.43	7.87±3.33	0.02

Table 2 presents the time required to induce remission. Group B (Deflazacort) achieved remission significantly faster, with a mean time to remission of 7.87 ± 3.33 days, compared to 9.82 ± 3.43 days in Group A (Prednisolone) (p = 0.02). This indicates a statistically significant difference in the speed of clinical response between the two treatments.

Table 3. *Number of relapses after 3 months and 6 months (N=74)*

Relapse	Group A (n=37)	Group B (n=37)	P-value
After 3 months	4 (10.8)	1 (2.7)	0.17
After 6 months	6 (16.2)	6 (16.2)	1.00
Total after 6 months	10 (27.0)	7 (18.9)	0.41

Table 3 shows the number of relapses after 3 and 6 Months. After three months, 10.8% of children in Group A experienced relapse compared to 2.7% in Group B (p = 0.17). At six months, both groups reported an equal relapse rate of 16.2% (p = 1.00). The cumulative relapse rate at six months was 27.0% in Group A and 18.9% in Group B, which was not statistically significant (p = 0.41).

Table 4. *Complications of study subjects during follow-up (n=74)*

Complications		Group A (n=37)	Group B (n=37)	P-value
Moon face	On admission	0 (0.0)	0 (0.0)	
	After 3 months	0 (0.0)	0 (0.0)	
	After 6 months	11 (29.7)	6 (16.2)	0.17
Buffalo hump	On admission	0 (0.0)	0 (0.0)	
	After 3 months	2 (5.4)	0 (0.0)	0.15
	After 6 months	11 (29.7)	6 (16.2)	0.17

Table 4 shows the complications during follow-up. No complications were observed at admission or the three-month follow-up. By six months, moon face was noted in 29.7% of Group A and 16.2% of Group B participants (p = 0.17). Buffalo hump developed in 29.7% of children in Group A and 16.2% in Group B (p = 0.17). Although the incidence of these corticosteroid-associated complications was higher in Group A, the differences were not statistically significant.

Table 5. *Changes in Cholesterol & RBS (N=74)*

Parameter		Group A (n=37)	Group B (n=37)	P-value
Cholesterol (mg/dl)	On admission	420.70±88.69	401.56±87.31	0.35
	At 3 months	182.55±55.83	176.41±57.45	0.64
	At 6 months	202.53±81.71	210.17±106.72	0.73
RBS (mmol/L)	On admission	5.36±1.01	5.40±0.81	0.85
	At 3 months	5.69±1.07	5.40±1.16	0.27
	At 6 months	5.82±0.59	5.60±0.78	0.18

Changes in cholesterol and random blood sugar levels presents in table 5. Baseline cholesterol levels were elevated in both groups, with mean values of 420.70 ± 88.69 mg/dL in Group A and 401.56 ± 87.31 mg/dL in Group B (p = 0.35). At three months, cholesterol levels declined similarly in both groups and remained comparable at six months (p > 0.05 for all time points). Random blood sugar (RBS) values were within normal limits at all assessed intervals and did not differ significantly between the groups at baseline, three months, or six months.

5. Discussion

This study compared efficacy and safety profiles of prednisolone and deflazacort in the management of idiopathic nephrotic syndrome (INS) in children. The main findings suggest that children treated with deflazacort (Group B) had remission significantly faster in comparison to those treated with prednisolone (Group A), mean time of 7.87 ± 3.33 days as compared to Group A, 9.82 ± 3.43 days (p = 0.02). Relapse rates after 3 and 6 months, though slightly lower in the deflazacort group, were not significantly different between the two groups. Furthermore, deflazacort was found to have a lower frequency of complications related to steroid therapy, which include moon face and buffalo hump, albeit not statistically significant different rates.

These results align with other studies, implying that deflazacort could have similar or even better clinical outcomes in terms of efficacy while potentially decreasing the incidence of some of the side effects associated with corticosteroid use. Broyer et al. did a controlled study, which proved that deflazacort was capable of inducing remission of INS in a shorter time compared to

prednisolone in children [13]. Likewise, the randomized controlled trial conducted by Ravish et.al showed that deflazacort had earlier remission and lower side effects when compared to prednisolone [16].

The results of this study render similar relapse rates across both groups resonate with findings by Piccoli et al, where no significant difference was established as far as relapse rates were concerned across the deflazacort and prednisolone groups [14]. Nevertheless, our marginal lower relapse incidence at three months in the deflazacort group (2.7% vs.10.8%) corresponds to findings by Kim et al., which implies that deflazacort improves the disease control slightly in the short term [17]. Although this may be the case, our study lacks statistical significance on relapse rates, suggesting that large-scale studies over the long term are needed to confirm these findings.

Regarding adverse effects, data show a tendency to fewer cosmetic side effects within the deflazacort group. This supports the discoveries made by K.R. Jat & Khairwa who emphasized ins deflazacort's safe side impact, deflazacort in children with INS [7], or those of Joshi & Rajeswari where they emphasized its lower potential to cause weight gain and Cushingoid features [18]. The pharmacological justification for the enhanced safety profile is well established. Deflazacort is an oxazoline synthetic opioid of prednisolone with suppressed affinity to the glucocorticoid receptors with regard to adipose and muscle tissues, as well as a lesser amount of metabolic and cosmetic consequences (Czock et al.,) [11].

Pharmacokinetic differences also account for the clinical findings. Researches have shown that deflazacort has a better pharmacokinetic and pharmacodynamic properties, as it has a short life, and low solubility in lipids, which decreases the tendency to accumulate in fat tissue, minimize long-term side effects such as growth suppression and osteoporosis (Assandri et al., Gennari) [19, 20]. Moreover, deflazacort does not have as strong a suppression on the hypothalamic-pituitary-adrenal (HPA) axis, which can enhance growth outcomes in pediatric patients (Balsan et al., Ferraris and Pasqualini,) [21, 22].

A number of international and regional guidelines recognize the role of corticosteroids in being the first-line treatment for children with steroid-sensitive nephrotic syndrome (SSNS). The Indian Pediatric Nephrology group agrees with the use of corticosteroids such as cortisone, a potential alternative for conventional drugs such as prednisolone are given especially for children who are more susceptible to steroid toxicity [23]. This has been supported by a Cochrane review by Hodson et al. that supports corticosteroids as a means of inducing remission but observes that differences in the side effect profiles may provide reasons to consider specific ones [3].

Although there are differences in efficacy and side effect profiles, deflazacort and prednisolone should be discussed starting from the common mechanisms of action between these two drugs via glucocorticoid receptor binding and immune system suppression activity. However, variations in both tissue selectiveness and metabolic processing result in dissimilar clinical outcomes. Scholarly works such as those of Markham and Bryson or Luzzani and Glasser show variable receptor affinities of selective receptors and differential genes being activated by deflazacort, which could explain its special safety profile [9, 10].

From a clinical perspective, the results of this study justify exploring deflazacort as an alternative to prednisolone in children with idiopathic nephrotic syndrome, especially in those prone to adverse steroid effects or who need long-term therapy. A lower time to remission and the trend to lower side effects may enhance quality of life and treatment adherence, as these are key to managing pediatric chronic illness.

However, differences in studies may occur in the various dosing regimens, patient collections, and diagnostic criteria. For example, although our study revealed a significant difference in the time to remission, some past studies, for example, the study by Penaloza et al., reported a non-statistical difference in remission rates between the deflazacort and prednisolone groups [24]. These disparities can be attributed to genetic factors, environmental factors, and nutritional as the ethnic variation reported by Sharpe and Pouiton [5] regarding steroid responsiveness is known.

Our results further contribute to the emerging exposé of the use of deflazacort as a viable and perhaps superior initiating option to prednisolone for remission in nephrotic syndrome. Although both agents are effective, deflazacort may prove superior in terms of a quicker clinical response and lower risks of cosmetic and metabolic complications.

6. Limitations and Recommendations

Study limitations include small sample size, short follow-up duration, and lack of long-term

outcome assessment of growth parameters and bone health. Findings may not generalize to all pediatric populations due to demographic factors.

Future multicenter trials with larger cohorts and extended follow-up are needed to validate results. Comparative studies examining cost-effectiveness and quality of life metrics between deflazacort and prednisolone would provide a better understanding of their clinical utility in managing idiopathic nephrotic syndrome in children.

7. Conclusion

This study shows deflazacort is as effective as prednisolone in inducing remission in children with idiopathic nephrotic syndrome, with shorter time to remission and fewer steroid-related side effects. While relapse rates did not differ between groups, deflazacort's clinical profile suggests it may be preferable, particularly in patients susceptible to corticosteroid toxicity. These findings support incorporating deflazacort into treatment protocols for idiopathic nephrotic syndrome in children, considering individualized therapy based on clinical response and adverse effect risks.

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Conflicts of interest

There are no conflicts of interest.

Ethical approval

The study was approved by the Institutional Ethics Committee.

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