

Prednisolone-induced Steroid Dependent Nephrotic Syndrome: A Case Report

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ABSTRACT

Nephrotic syndrome is a kidney condition that affects the kidney's glomeruli and causes protein to be excreted in the urine. In paediatric population, the drug of choice for nephrotic syndrome is prednisolone which resolves the signs and symptoms. Prednisolone is a corticosteroid that acts on the immune system to reduce inflammation, swelling, and redness. The International Study of Kidney Disease in Children (ISKDC) proposed a standard initial treatment for children with nephrotic syndrome, consisting of prednisolone therapy for 8 weeks. This case report presents a 4-year-old female patient was presented to the hospital with the complaints of decreased urine output, increased albumin levels (6.8g/dl) and increased protein concentration(15.5mg/m²/day). Tab. Prednisolone (2mg/kg/day) was administered to the patient. After tapering the dose of Prednisolone, the patient again showed proteinuria (400mg/m²/day). Upon restarting the Tab.Prednisolone the urine protein concentration came back to normal levels. Therefore, it is summarized that despite being the first-line drug prednisolone can also cause steroid dependence in patients with nephrotic syndrome. An alternative therapy should be implied along with dose tapering. This implies a wide role for clinical pharmacists in the therapeutic evaluation among paediatric patients.

Keywords: Prednisolone, Nephrotic Syndrome, Steroid Dependent Nephrotic Syndrome, Proteinuria, Tapering of the dose.

INTRODUCTION

Nephrotic syndrome is a kidney condition that affects the kidney's glomeruli and causes protein to be excreted in the urine. A triad of symptoms, including elevated proteinuria (>1 g/m²/day), hypoalbuminemia (urine albumin levels < 2.5g/dl) and edema are used to make the diagnosis. In the paediatric population, the drug of choice for nephrotic syndrome is prednisolone which resolves the signs and symptoms. The response of a patient to prednisolone is a significant prognostic indicator. Approximately 85% of the population with idiopathic nephrotic syndrome respond to prednisolone treatment (complete remission of proteinuria and normal serum albumin).¹ Prednisolone suppresses the immune system, reducing swelling, redness, and inflammation. It stimulates lymphoid

cells to apoptosis, boosting the expression of anti-inflammatory protein molecules and hindering cytokine-mediated inflammatory pathways.² The International study of Kidney Disease in Children (ISKDC) proposed a standard initial treatment for children with nephrotic syndrome, consisting of prednisolone therapy for 8 weeks. In the paediatric population, prednisolone resolves the symptoms and reduces inflammation but in majority of cases, prednisolone can lead to steroid dependent nephrotic syndrome.³ Prednisolone when given to NS patient it causes an increase in glomerular permeability of protein leading to proteinuria. It obstructs proximal tubular water transport, electrolytes, amino acids and there will be a relatively increase of urinary albumin excretion. During the course of prednisolone treatment regimen, the different subcategories of the

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Table 1: Subcategories of Nephrotic Syndrome based on KDIGO.

Remission	Urine albumin nil or trace (or proteinuria <4mg/m ² /h) for 3 consecutive early morning specimens.
Relapse	Urine albumin 3+ or 4+ (or proteinuria >40 mg/m ² /h) for 3 consecutive early morning specimens, after having been in remission previously.
Frequent relapses	Two or more relapses in the initial 6-months period or more than 3 relapses in any 12 months.
Steroid dependent NS	Two consecutive relapses when on alternate day steroid therapy or within 14 days of its discontinuation.
Steroid resistance NS	Absence of remission despite therapy with daily Prednisolone at a dose of 2 mg/kg/d for 4 weeks.

nephrotic syndrome are identified by Kidney Disease: Improving Global Outcomes (KDIGO) based on the urine protein level (Table 1).⁴

In children, the most prevalent type of NS is steroids-dependent nephrotic syndrome (SDNS) and more than half cases experience relapse after 8 weeks of prednisolone therapy.⁵ It is estimated that 90%–95% of patients with proteinuria receive remission with prednisolone. However, 60%–90% of the initial responder's experience relapses. In around 20%–60% of patients, the disease progresses to frequent relapses, often accompanied by steroid dependence. Prednisolone is typically given at a dose of 1.5 mg/kg on alternate days for 4 weeks after being given at a daily dose of 2 mg/kg for 4 weeks to treat the initial episode. More than 90% of patients experience an immediate remission when using this regimen.⁶

CASE DESCRIPTION

A female patient, aged 4 years with weight of 15 kg came to S.S.I.M.S & RC, Davangere, Karnataka, with complaints of decreased urine output and abdominal distension since Day 1. On physical examination her BP was found to be 120/80 mmHg, heart rate was found to be 90 beats per min, and Spo2 was 99% at room air and patient was found to have facial edema and bilateral pitting edema. The child was admitted for Nephrotic syndrome in the past year (urine protein levels were 480 mg/m² /day) and was discharged with Tab. Prednisolone at 2mg/kg/hr on previous admission.

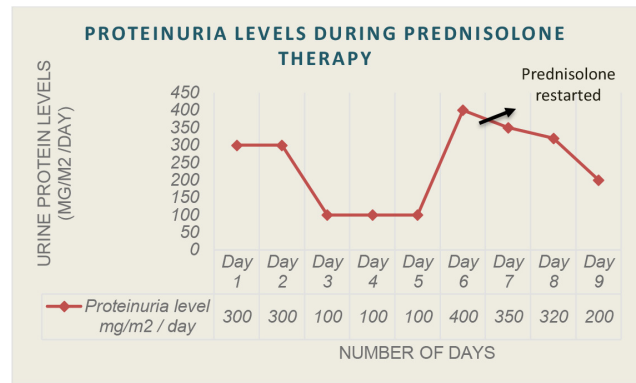


Figure 1: Urine protein levels during the course of prednisolone regimen.

On performing the cystoscopy at age 1 she was diagnosed with right-sided hydroureteronephritis. The patient was having increased albumin (6.8 g/dl) and increased total protein (15.5mg/m² /day) concentration as well as increased ALP (186U/L). Urine protein levels were 3+ (300 mg/m² /day). Weight of the child dropped from 12.5 kg to 11.5 kg. From the complaints, she was started again with Tab. Prednisolone (2 mg/kg/day). On the 2nd day, Inj. Human Albumin (2g/kg) was infused for over 8 hrs. Post transfusion, Inj. Furosemide (10 mg) was administered. After tapering the dose of prednisolone (1.5 mg/kg/day) the patient showed proteinuria (400 mg/m² /day) on the 6th day and again prednisolone was continued as per the doctor's instruction. On 9th day, partial remission of proteinuria was observed (Figure 1). This directly indicates that the patient is steroid dependent.

CAUSALITY EVALUATION

To evaluate the relationship between the drug and adverse reaction, causality assessment was done using World Health Organisation-Uppsala Monitoring Centre (WHO-UMC) scale. According to WHO-UMC scale the ADR was classified as probable ADR. The probable ADR includes event of laboratory test abnormality, which is explained by increased urine protein concentration and decreased albumin levels during the tapering of the prednisolone. Prednisone was re-administered and urine protein concentration was decreased to 200 mg/m² /day i.e., partial remission, which highlights the concept of de-challenge and re-challenge.⁷

DISCUSSION

Prednisolone is a corticosteroid that is prescribed to patients with nephrotic syndrome. Longer courses of prednisolone do not reduce the risk of relapse in

paediatric patients during the early episodes of nephrotic syndrome, but induces remission in nephrotic syndrome.⁸ As there is an increase in prednisolone usage among patients with nephrotic syndrome, proper patient counselling and monitoring is required to avoid adverse drug reactions (ADR). Prednisolone is administered in a dose of 2mg/kg/day until urine protein is a trace or nil and subsequently tapered to 1.5 mg/kg/day. But steroid dependence or relapses that happen frequently needed to be managed.

Prednisolone is gradually tapered to prevent remission, where it is given on alternative days (0.5-0.7mg/kg) for 9-18 months. In general, prednisolone decreases the protein concentration in urine but in some patients, continuous administration of prednisolone itself can lead to corticosteroid induced nephrotic syndrome. In patients with nephrotic syndrome, prednisolone can increase glomerular permeability of proteins. Prednisolone-induced proteinuria was reported earlier in the year 2019 by Gia I. Oh *et al.* stated that prednisolone can acutely increase proteinuria among NS patients. The fact that renal hemodynamic and protein reabsorption are unaffected suggests that this effect is brought on by changes in glomerular permselectivity. It remains to be seen how changes in glomerular permselectivity are performed.

As per Cochrane renal group, the use of certain drugs like levamisole on alternative days at a dose of 2-2.5 mg/kg for 12-24 months, cyclophosphamide of 2-2.5 mg/kg/day for 12 weeks or calcineurin inhibitors like cyclosporin of 4-5 mg/kg/day for 12-24 months and mycophenolate Mofetil (MMF) of 800-1200mg/m² along with the tapering dose of prednisolone are suggested for SDNS. Non-pharmacologically, appropriate patient counselling to have balanced diet with enough protein (1.5-2 g/kg) and calories are advised.⁹

CONCLUSION

Prednisolone-dependent nephrotic syndrome is common among the paediatric population. The steroid dependence is a challenging issue in the management of idiopathic nephrotic syndrome, leading to increased morbidity, complications and cost of treatment. This case highlights the consequence of prednisolone administration in NS, that can be fatal if not monitored on time. Early and accurate detection of potential ADRs can help to improve treatment strategy with careful monitoring. An alternative therapy should be implied along with dose tapering. This also entails a broad role for clinical pharmacist in

therapeutic evaluation of paediatric patients.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

ABBREVIATIONS

NS: Nephrotic Syndrome; **SDNS:** Steroid-Dependent Nephrotic Syndrome; **ADR:** Adverse Drug Reaction; **KDIGO:** Kidney Disease: Improving Global Outcomes; **ISKDC:** International Study of Kidney Disease in Children

SUMMARY

Nephrotic syndrome is a kidney condition that affects the kidney's glomeruli and causes protein to be excreted in the urine. In paediatric population, the drug of choice for nephrotic syndrome is prednisolone which resolves the signs and symptoms. Prednisolone is a corticosteroid that acts on the immune system to reduce inflammation, swelling, and redness. In this case report, it was observed that the patient showed partial remission after the administration of prednisolone. When the dose was tapered the patient again showed increase in urine protein concentration. The urine protein level was brought back to normal range after the re-administration of prednisolone, indicating that the patient has developed steroid dependence. As there is an increase in prednisolone usage among patients with nephrotic syndrome, proper patient counselling and monitoring is required to avoid adverse drug reactions (ADR). An alternative therapy should be implied along with dose tapering.

Consent for Publication

Written informed consent was obtained from the patient's father for publication of this case report. A copy of the written consent is available for review by the Editor of this journal.

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