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From the Clinic

Oral galactose in children with focal and segmental glomerulosclerosis: a novel adjunct therapy

About 85–90% of children with idiopathic nephrotic syndrome responds to steroid therapy while the remaining 10–15% fails to respond and is defined as steroid-resistant nephrotic syndrome (SRNS). The histopathological lesions in SRNS are minimal changes, focal and segmental sclerosis (FSGS) and mesangial proliferation. The response to cyclosporine alone or in combination with prednisolone therapy is variable.

Proteinuria in FSGS in some patients is associated with a permeability factor (PF). Galactose has been shown to bind with PF [1] and prevents its interaction with podocyte glycocalyx, and oral administration of galactose may lead to reduction of proteinuria [2]. In view of this, we report an observational case study where two separate courses of oral galactose were given to three children with steroid-resistant idiopathic nephrotic syndrome with FSGS in order to reduce proteinuria and increase serum albumin levels.

The patient characteristics are presented in Table 1. They had generalized oedema, urinary protein/creatinine ratio of >200 mg/mmol (>2 mg/mg), hypalbuminaemia serum albumin <25 g/L (<2.5 g/dL) and hypercholesterolaemia-serum cholesterol >5.18 mmol/L (>200 mg/dL). The children did not achieve remission with prednisolone (2 mg/kg/day) therapy administered for 4 weeks. Kidney biopsy tissues, examined in light and immunofluorescent microscopy, demonstrated focal and segmental glomerulosclerosis. The patients were tested for C_3, C_4, ANA, anti-ds DNA, HIV, Hepatitis B surface antigen and tuberculin test. Chest radiographs were normal. NPHS2 gene analysis showed R229Q polymorphism in Case 1. The protocol of the study was approved by the Institute Ethics Committee.

The children were treated with cyclosporine (4–5 mg/kg/day in two divided doses), prednisolone (1.5 mg/kg, single dose alternate days with gradual taper to a minimum of 0.5 mg/kg) and ramipril (0.2 mg/kg/day, single dose). Furosemide (1–2 mg/kg/day) was given to reduce oedema. The patients received cyclosporine, prednisolone and ramipril for 11–14 months duration and had stable serum creatinine levels. Doses of cyclosporine and ramipril remained unchanged. Patients did not achieve remission as urine protein/creatinine ratios of >200 mg/mmol (>2 mg/mg) persisted. Thereafter, oral D-galactose (Manufactured by Hi Media Laboratories Pvt. Ltd., Mumbai, India) was added at a dose of 0.2 g/kg/dose, twice daily. The patients were followed regularly at a 30-day interval during the first course of galactose trial given for 90 days. After an interval of 90 days in Case 1, 60 days in Case 2 and 105 days in Case 3, a second course of galactose treatment at the same doses was reinstituted for 30 days.

The changes in urinary protein/creatinine ratios and serum albumin levels are shown in Figure 1. In all three patients, urinary protein/creatinine ratios decreased (by 37.9, 50.6 and 77.5%), and serum albumin levels increased (by 56, 72 and 23.3%) at 90 days from their pre-galactose values. After discontinuation of galactose, urine protein/creatinine and serum albumin values showed deterioration at 120 days. After the second course of galactose, there was again a reduction of urinary protein/creatinine ratios by 46.5% in Case 1, 37.5% in Case 2 and 25.7% in Case 3 and an increase in serum albumin levels in comparison to their values 30 days before. However, parameters became again abnormal after discontinuation of galactose. No adverse events were noted following galactose therapy.

The galactose had a beneficial effect in all three patients. The galactose helps in reduction of proteinuria as it directly binds with PF and prevents interaction of PF to galactose residues of podocyte glycocalyx. Subsequently, the galactose–PF complex is cleared from plasma by hepatocytes or macrophages [2]. De Smet *et al.* [3] in one adult and Kopac *et al.* [4] demonstrated the effect of galactose in reduction of proteinuria and its benefit persisted for about 3 months in one case. In our cases, the effect lasted as long as galactose was given; indicating that a continuous treatment is necessary to maintain its positive effect on proteinuria.

Our patients had no remission with cyclosporine and prednisolone therapy given for a sufficient period. Galactose had lead to reduction of proteinuria and increase in serum albumin during the treatment period. Recently, Sgambat *et al.* [5] observed no significant difference

Table 1. Patient characteristics

Parameters	Case 1	Case 2	Case 3
1. Age (years)	8	13	12
2. Gender	Male	Female	Female
3. Body mass index (kg/m^2)	15.0	17.4	16.7
4. Blood pressure (mmHg)	106/72	110/77	120/80
5. Haematuria	Present (microscopic)	Absent	Absent
6. Blood urea (mmol/L)	9.9 (28 mg/dL)	7.1 (20 mg/dL)	11.1 (31 mg/dL)
7. Serum creatinine (μmol/L)	72.5 (0.82 mg/dL)	69.8 (0.79 mg/dL)	85.7 (0.97 mg/dL)
8. GFR (ml/min/1.73 m^2)	84.5	92.1	86.3
9. Histopathology	FSGS	FSGS	FSGS
10. NPHS2 gene analysis	Heterozygous-polymorphism (R229Q)	Absent	Absent
11. Prior treatment	Prednisolone (11 m) + cyclosporine (7 m)	Prednisolone (11 m) + cyclosporine (11 m)	Prednisolone (14 m) + cyclosporine (14 m)

Underline indicates values in SI Unit. FSGS, focal and segmental glomerulosclerosis.

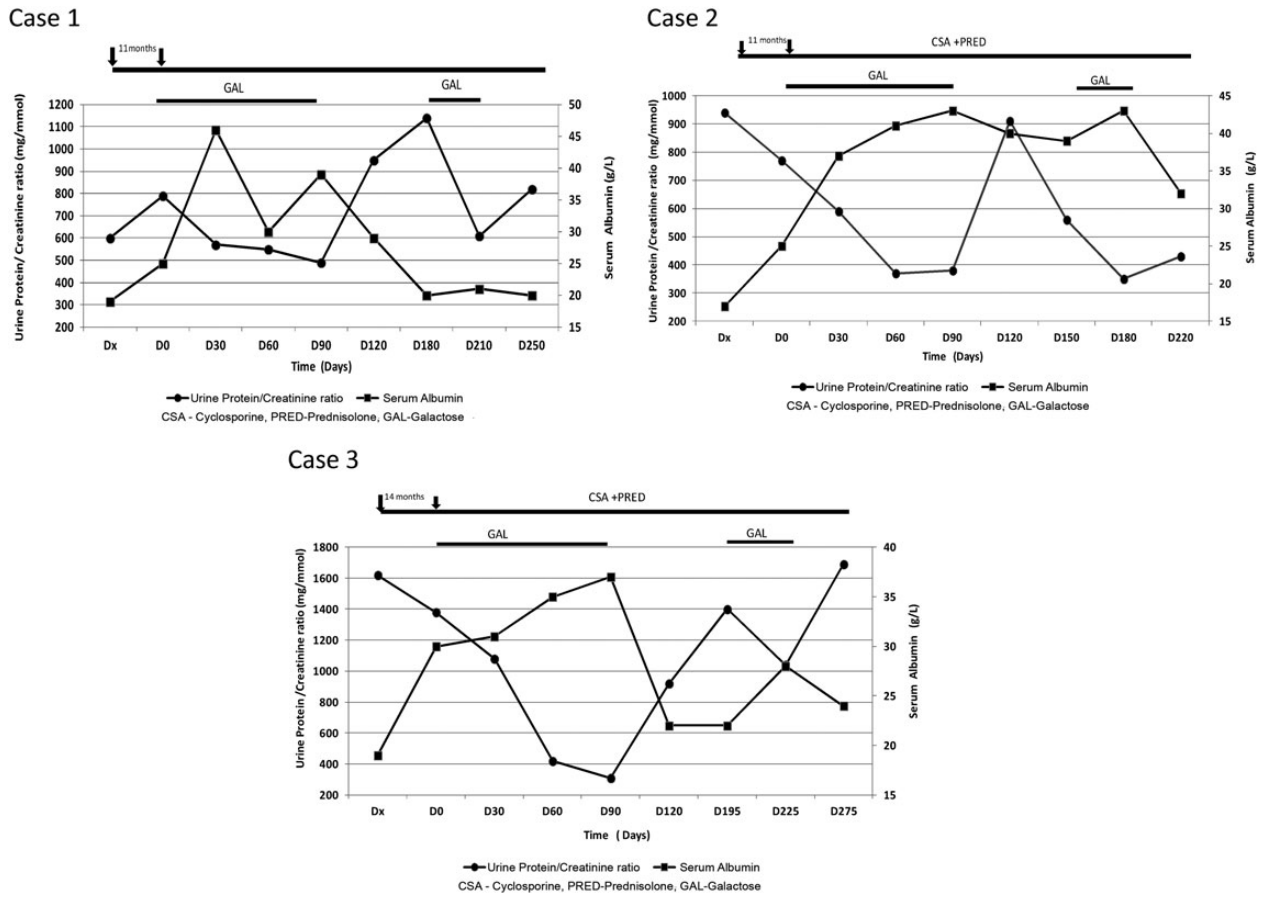

Fig. 1 Urine protein/creatinine ratios and serum albumin levels during the two periods of galactose therapy and the interval period. It showed gradual reduction in urine protein/creatinine ratios and rise in serum albumin values during, deterioration after discontinuation and improvement after reinstitution of galactose treatment.

between pre- and post-treatment mean urine protein/creatinine ratios after 16 weeks of galactose administration, and the authors concluded that it failed to improve proteinuria. In our study, though no patient achieved complete remission (urine protein/creatinine ratio <0.2), there was a significant reduction in proteinuria above that which can be accounted for by day-to-day variation [6]. Besides, no patient had a change in cyclosporine dose or other intercurrent infection to account for the changes in proteinuria. Patients with SRNS and persistent proteinuria carry a high risk of developing renal insufficiency. Oral galactose may partially protect the tubular epithelium from the toxic effects of heavy proteinuria. In conclusion, galactose treatment has shown reduction in proteinuria in unresponsive FSGS patients. However, more studies are needed to confirm the value of galactose as an adjunct therapy.

Conflict of interest statement. None declared.

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