



Cyclophosphamide therapy in children with nephrotic syndrome



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Background

Cyclophosphamide (CPM), one of the corticosteroid-sparing agents, is a therapeutic option for children with frequently relapsing (FRNS) or steroid dependent nephrotic syndrome (SDNS). There is a lack of pediatric study data in Korea, although Kidney Disease Improving Global Outcomes (KDIGO) guideline recommends the use of CPM.

Purpose

To provide data on effectiveness of cyclophosphamide treatment in pediatric patients with FRNS/SDNS and identify parameters associated with sustained remission.

Material and methods

- Monocentric, retrospective study
- 72 patients diagnosed as FRNS or SDNS
- 12 weeks-single course of oral CPM from 2005 to 2015
- Exclusion criteria
 - Patients who were more than 19 years old,
 - Steroid-resistant nephrotic syndrome
 - If treatment period was less than 4 weeks
 - Follow up lost within a year after CPM treatment
- Primary outcomes
 - 2-year, 5-year cumulative sustained remission rate (Cox proportional hazard model)
 - Relapse frequency before and after CPM (Multiple regression analysis)
- Secondary outcomes
 - Safety evaluation : Adverse drug reaction (ADR) recorded on electronic medical records

Results

Table 1. Patient characteristics (n=72)

Characteristics	Mean±SD
Age (years)	
Onset nephrotic syndrome	4.54±2.72
Cyclophosphamide start	6.69±2.88
Cyclophosphamide medication	
Dose (mg/kg/day)	2.11±0.27
Durations (weeks)	11.65±0.95
Renal biopsy (n)	5
Minimal change disease (n)	4
Focal segmental glomerulosclerosis (n)	1
Follow-up after cyclophosphamide treatment (years)	4.54±2.72

Table 2. Factors associated with sustained remission rate (by Cox regression multivariate analysis)

Variables	HR	95% CI	P
Leukopenia	0.412	0.204-0.833	0.014
Age at onset nephrotic syndrome (≥3.82 vs <3.82)	1.864	0.866-4.014	0.112
Age at cyclophosphamide start (≥5.93 vs <5.93)	0.806	0.368-1.766	0.590
Interval from nephrotic syndrome onset to cyclophosphamide start (≥1.88 vs <1.88)	0.724	0.378-1.388	0.331

Figure 1. Sustained remission rate after cyclophosphamide treatment with (Thick line, n=21) or without (Thin line, n=51) leukopenia after cyclophosphamide treatment (by Kaplan-Meier analysis)

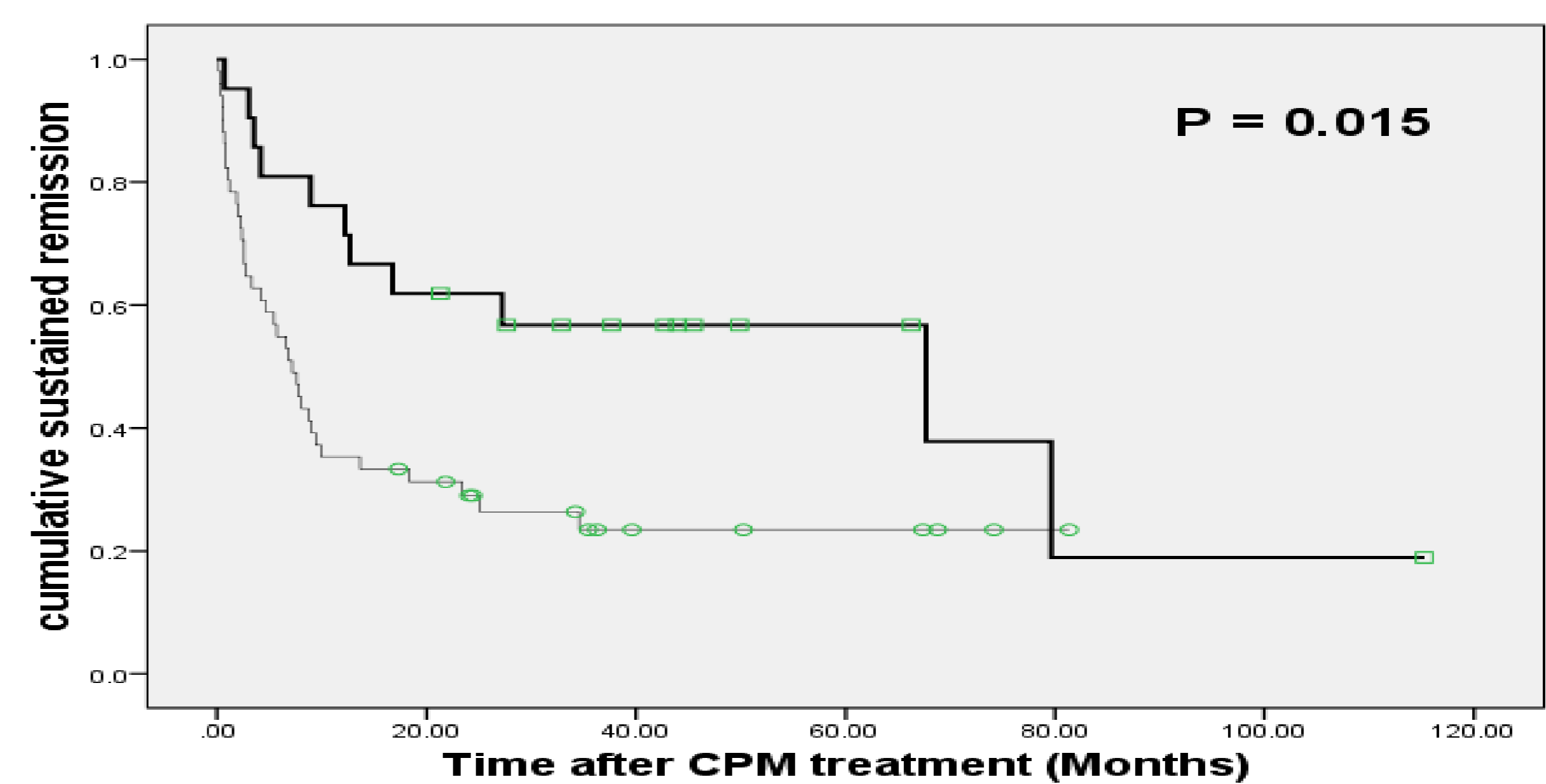


Table 3. Parameters associated with relapse frequency after cyclophosphamide treatment (by multiple regression analysis)

Variables	B	S.E	β	P
Age at onset nephrotic syndrome	-0.126	0.073	-0.223	0.092
Interval from nephrotic syndrome onset to CPM start	-0.545	0.186	-0.379	0.005

R² = 0.181, F=5.416, p=0.005

Conclusion

- Cyclophosphamide is quite effective and safe alternative treatment for children with FRNS/SDNS.
- Parameter associated with sustained remission is the event of leukopenia.
- The interval from the nephrotic syndrome onset to cyclophosphamide start is the factor associated with relapse frequency.

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