The Efficacy of Intravenous Pulse Cyclophosphamide in the Treatment of Severe Lupus Nephritis in Children

KANCHANA TANGNARARATCHAKIT, M.D.*, CHALEOMSRI TAPANEYA-OLARN, M.D.*, WIWAT TAPANEYA-OLARN, M.D.*

Abstract

Background : The intermittent intravenous cyclophosphamide in the treatment of lupus nephritis in adults is well tolerated and associated with clinical improvement and long term stability of renal function. However, there are few reports about the efficacy of intravenous pulse cyclophosphamide (IPC) of severe lupus nephritis in children.

Objective : To evaluate the clinical efficacy, renal function, renal outcome and complications of IPC therapy in children with severe lupus nephritis.

Method : Prospective study.

Patients : Children with severe lupus nephritis have been followed-up for at least 6 months. Treatment regimen: Intravenous pulse cyclophosphamide 0.5-0.75 g/m^2 given monthly for 6 months with subsequent doses given at 2-3 months interval up to 3 years and combined with low dose oral prednisolone therapy.

Results : Thirty-one children (mean age : 12.31 $\pm$ 2.03 years; female : male = 24:7) with severe lupus nephritis received IPC therapy. 24 out of 28 patients (85.7%) had diffuse proliferative glomerulonephritis. After 3 months of treatment, most patients were clinically improved as evidenced by significant improvements in 24-hour urine protein, creatinine clearance, serum creatinine, BUN, serum albumin and C_3 level. These improvements were sustained up to 18 months and were accompanied by a significant reduction in prednisolone dosage. Renal outcome at the last follow-up (range = 6-76 months) demonstrated that twelve patients (38.7%) had complete remission, 18 patients (58.0%) still had significant proteinuria and only one had serum creatinine of 1.6 mg/dl at 42 months. One child progressed to end stage renal diseases during IPC therapy. Five patients had severe infections during the treatment resulting in one death. Hemorrhagic cystitis and malignancies were not found.

Conclusion : Treatment of severe lupus nephritis in children with intravenous pulse cyclophosphamide is associated with favorable short term results. Severe infections are the major complications.

Key word : Lupus Nephritis, Children, Pulse Cyclophosphamide, Treatment

* Department of Pediatrics, Faculty of Medicine, Ramathibodi Hospital, Mahidol University, Bangkok 10400, Thailand.

Systemic lupus erythematosus (SLE) is an autoimmune disease affecting multiple organ systems. Steroid is the initial drug of choice, and improves overall prognosis. However, it is not effective in patients with the severe forms of this disease. Prolonged administration of high dose steroid predisposes these patients to infections and other complications including growth retardation, osteoporosis, avascular necrosis of bone and undesirable physical appearances[1-3]. Renal disease is a common manifestation, varies in its severity and remains a major predictor of morbidity and mortality in childhood SLE.

Childhood SLE with diffuse proliferative glomerulonephritis may improve with long-term steroid therapy but progression to chronic renal failure and end stage renal disease (ESRD) remains common[4-8]. Death may result from severe renal manifestation or complications of treatment. Combined therapy of immunosuppressive agents and oral prednisolone is more effective than steroid alone in improving total mortality and preventing the progression to ESRD[9-16]. Treatment of lupus nephritis in adults with intermittent intravenous cyclophosphamide is well tolerated and associated with clinical improvement of the SLE and stability of renal function[17-21]. However there are only a few reports about the efficacy of intermittent intravenous cyclophosphamide therapy for severe lupus nephritis in children[22-24].

This research reports the result of prospective study using intravenous pulse cyclophosphamide therapy of childhood severe lupus nephritis.

METHODS

Patient selection

The patients selected for this study were 15-years-old or younger who were treated at Ramathibodi Hospital from January 1991 to April 1998 and met the following criteria :

1. fulfilled four or more of the 1982 Revised American Rheumatism Association criteria for the diagnosis of SLE[24].

2. had evidence of severe renal disease diagnosed by the finding of nephrotic syndrome unresponsive to steroid therapy or unacceptable steroid-induced complications and/or kidney biopsy showing diffuse proliferative glomerulonephritis.

3. had minimum of six month follow-up.

Drug administration

All patients were hospitalized and intravenous pulse cyclophosphamide (IPC) was administered at a dose of 0.5-0.75 g/m^2. Patients received intravenous hydration 24 hours before and during IPC administration. The cyclophosphamide was administered at the time of study entry and then monthly for 6 months with subsequent pulses at 2-3 months interval depend upon disease activity until 3 years. If the child's total leukocyte count was less than 4,000/μl at the cyclophosphamide scheduled, cyclophosphamide was withheld for 1-2 weeks until total leukocyte count was more than 4,000/μl and the dose of cyclophosphamide was adjusted. One patient was initially treated with intravenous methylprednisolone 1 g in three daily doses. All patients were on oral prednisolone in conjunction with the cytotoxic drug therapy. Antihypertensives, diuretics, antibiotics and symptomatic medications were given when necessary. The dose of prednisolone was reduced gradually to a maintenance level in all patients, adjusted to control lupus nephritis and other systemic manifestations of SLE.

Data collection and analysis

Twenty-four hour urine protein, creatinine clearance (CrCl), serum creatinine, blood urea nitrogen (BUN), serum albumin, the third component complement (C_3), total leukocyte count, and prednisolone dosage were recorded before starting intravenous pulse cyclophosphamide, 1 month, 3 months, 6 months, 12 months and 18 months after IPC therapy. All data were expressed as the mean $\pm$ 1 standard error of mean (SE). The data are evaluated into 2 phases. The first is the data from the initiation of IPC therapy to 6 months after treatment. The later is the data from 6 months to 18 months after therapy. During the first 6 months, the data of 24 hour urine protein, CrCl, and C_3 level were complete in 19 out of 31 patients and the data of serum creatinine, serum albumin and leukocyte count were complete in 28 out of 31 patients and prednisolone dosage data were complete in all. Friedman test and Donn's method were used for data analysis in these groups. The data of C_3 level were analysed between 6 months and 12 months in 9 patients by the Wilcoxon signed rank test. A p value of less than 0.05 was considered significant.

RESULTS

Patient population

Thirty-one patients (24 females, 7 males) with a mean age of 12.31 ± 2.03 years were included in the study. The mean duration of follow-up was 24.8 ± 16.7 months. Renal biopsies (Table 1), obtained in 28 patients, showed that 24 patients had diffuse proliferative glomerulonephritis. One child had focal proliferative glomerulonephritis with nephrotic syndrome and a CrCl of 46 ml/min/1.73 m^2. Three patients had membranous glomerulonephritis with nephrotic syndrome and CrCl of 47, 86 and 95 ml/min/1.73 m^2. Kidney biopsy in one child who had nephrotic syndrome with severe renal insufficiency, CrCl of 29 ml/min/1.73 m^2, was unsuccessful. Kidney biopsy in two patients with nephrotic syndrome (one with psychosis and the other with marked ascites) was not performed.

Twenty-one children received IPC because of active lupus nephritis and CrCl of < 80 ml/min/1.73 m^2. Two patients with membranous glomerulonephritis received IPC due to unresponse to steroid therapy. Twenty-nine patients (93.5%) had nephrotic syndrome before starting IPC therapy.

Table 1. Renal histology in 28 patients with severe lupus nephritis.

Histology (WHO)	Class	N	%
Focal proliferative glomerulonephritis	III b	1	3.6
Diffuse proliferative glomerulonephritis	IV a	19	67.8
	IV b	5	17.9
Membranous glomerulonephritis	V	3	10.7
Total		28	100

Table 2. Laboratory values and prednisolone dosage at initiation, at 1, 3, 12 and 18 months of intravenous pulse cyclophosphamide therapy.

	Initial	1 mo	3 mos	6 mos	12 mos	18 mos
24-h urine protein (g/d)						
mean±SE	4.45±0.59	2.79±0.58	1.82±0.39*	1.41±0.35*	1.45±0.44	1.04±0.39
range	0.69-13.76	0.45-5.84	0.078-6.88	0.00-6.84	0.00-8.37	0.00-5.58
CrCl (ml/min/1.73m^2)						
mean±SE	58.0±6.1	70.2±6.7	73.4±5.7*	81.6±4.9*	79.4±7.8	90.6±7.7
range	9.0-131.0	13.5-142.0	26.3-125.0	43.5-127.4	3.7-134.0	59.0-171
Serum creatinine (mg/dl)						
mean±SE	1.25±0.17	0.88±0.07*	0.83±0.06*	0.78±0.06*	1.02±0.21	0.77±0.06
range	0.05-5.40	0.32-2.10	0.43-1.70	0.33-1.70	0.47-6.70	0.50-1.60
BUN (mg/dl)						
mean±SE	45.60±4.73	31.48±4.95*	20.37±2.46*	18.03±2.12*	22.03±4.44	14.36±1.25
range	10-172	8-98	7-56	8-54	8-130	8-26
Serum albumin (g/dl)						
mean±SE	2.26±0.10	2.86±0.12	3.41±0.14*	3.61±0.14*	3.78±0.18	3.88±0.15
range	0.99-3.39	1.67-4.13	2.01-4.63	1.93-4.67	2.16-5.31	2.36-4.58
C_3 (mg/L)						
mean±SE	370.0±43.6	576.0±72.7	752.8±84.98*	777.3± 91.5*	812.2±97.7	886.8±82.4
range	66-1034	200-1120	318-1690	189-1800	237-1580	467-1370
Leukocyte count (x10^3/µl)						
mean±SE	10.2±0.9	10.5±0.6	9.0±0.7	8.5±0.6	7.7±0.6	8.8±0.7
range	3.4-29.0	2.9-20.3	1.8-21.1	3.9-15.6	5.0-12.5	5.1-15.1
Prednisolone (mg/d)						
mean±SE	52±2	39±2*	26±2*	20±1*	17±2*	13±1*
range	20-60	20-60	10-50	7.5-30	7.5-45	5-22.5

* Significantly different from initial value, $p < 0.05$; Friedman test and Donn's method.

Therapeutic effect

During the first month after initiation of IPC, active lupus nephritis continued in some patients. However, there was a trend towards improvement in the mean of 24 hour urine protein, creatinine clearance, serum creatinine and C_3 as shown on Table 2 despite no statistical significance, and prednisolone dosage could be reduced in most cases. Most patients were clinically improved by the third month of IPC as evidenced by significant improvement in 24-hour urine protein, creatinine clearance, serum creatinine, BUN, serum albumin, and C_3 level ($p < 0.05$). These improvements were sustained up to 6 months of IPC therapy ($p < 0.05$) and were accompanied by a significant reduction in prednisolone dosage ($p < 0.05$). One patient with severe renal insufficiency received nine monthly IPC due to flare up of active lupus nephritis at the seventh month. One child had to stop IPC therapy at 12 months despite substantial improvement in renal function because of her pulmonary and hip joint tuberculosis and then she lost follow-up. One child had rapidly progressive glomerulonephritis which progressed to ESRD requiring dialysis after one year of treatment.

Twenty patients were followed until 18 months of IPC therapy. The complete data of creatinine clearance, 24 hour urine protein, serum creatinine, BUN, serum albumin were available for analysis in 8, 15, 17, 17, 15 out of 20 patients, respectively. Complete data of total leukocyte count and prednisolone dosage were available in all patients. There were no significant changes in 24-hour urine protein, creatinine clearance, serum creatinine, BUN, serum albumin and C_3 level from 6 months to 18 months of IPC treatment ($p > 0.05$) although prednisolone could be substantially decreased from 20 ± 1 to 13 ± 1 mg/day ($p < 0.05$). This suggests that the improvement of renal function could be maintained from 6 months up to 18 months of IPC therapy despite prednisolone dosage reduction. Seven children had no significant proteinuria and 9 out of 14 patients with initial renal insufficiency (CrCl < 80 ml/min/1.73 m^2) had normal renal function at 18 months of IPC treatment.

Cyclophosphamide therapy was continued every 2-3 months in this protocol until the total duration of therapy reaches 3 years but the number of children completing 3 years of treatment is too small for analysis. During receipt of 3 months interval of IPC therapy, 5 patients had active lupus nephritis and IPC was changed to 2 months interval. There were 7 children completing 3 years IPC therapy. Their serum creatinine ranged between 0.6 to 1.1 mg/dl. Renal function remained normal in 3 children and one of these had no proteinuria. All children had normal serum albumin. One child completing 3 years of treatment with normal renal function had a severe lupus nephritis 6 months later. Renal status at the last follow-up is shown in Table 3. Twelve patients (38.7%) had complete remission. Eighteen patients (58.0%) still had significant proteinuria and only one of these had serum creatinine > 1.5 mg/dl (1.6 mg/dl at 42 months). One child progressed to ESRD.

Table 3. Renal status at the last follow-up in 31 patients.

	Patients (n)	%
Complete remission	12	38.7
Significant proteinuria	18	58.0
Serum creatinine > 1.5 mg/dl	1	3.2
Chronic renal failure or ESRD	1*	3.2

* Death occurred after patient progressed to ESRD

Table 4. Complications and causes of death in patients treated with intravenous pulse cyclophosphamide.

Side effects	Patients* (n)
Nausea/vomiting	11
Alopecia	2
Leukopenia (< 4000/μl)	4
Infection	
Urinary tract infection	3
Bronchitis/pneumonia	6
Pyoderma/cellulitis	7
Peritonitis	1
Oral moniliasis	2
Sinusitis	1
Salmonella septicemia	1
Pulmonary and hip joint tuberculosis	1
Hemorrhagic pancreatitis	1
Causes of death	
ESRD with sepsis	1
Sepsis	1

* Some patients had more than one side effect.

Toxic effects

The complications of IPC therapy and causes of death are shown in Table 4. Nausea and vomiting occurred during the first 24 hours after cyclophosphamide administration. Mild alopecia occurred during first 6 months and all improved after 6 months of IPC therapy. Transient leukopenia (< 4,000/μl) occuring in the first 6 months was found in 4 patients and only one had severe infection. Infections were common. Five children had severe infections including peritonitis, salmonella septicemia, tuberculosis and sepsis. There were 2 deaths during follow-up. The cause of death was sepsis in one patient and the nephritis progressed to ESRD in another child at one year of IPC therapy requiring dialysis for 18 months before death. Hemorrhagic pancreatitis occurred in one case during the first 3 months. Hemorrhagic cystitis and malignancies were not seen in any patients during follow-up.

DISCUSSION

Although the prognosis of childhood lupus nephritis had improved substantially in this decade, severe renal involvement continues to be a major cause of morbidity and mortality[4-8]. The intermittent use of intravenous cyclophosphamide in the treatment of lupus nephritis in adults is well tolerated and associated with favorable long term outcome of renal function[15,17-20]. Moreover some studies found that IPC therapy would have greater efficacy and fewer toxic effects than oral administration[13,17,25,26].

Our prospective study has demonstrated that IPC therapy had resulted in significant improvements of symptoms, renal function, proteinuria and complement level after 3 months of treatment and stabilization of renal function continued over 18 months of treatment and a significant reduction in prednisolone dosage. Renal outcome at the last follow-up showed complete and partial remission in most children. Only 2 children had poor renal outcome.

Previous studies in children treated with this regimen and followed for 6 to 12 months showed favorable results in the clinical activity, serologic activity and renal function after 6 months of therapy[21,22]. Our study supports the short term efficacy of this regimen and the results are not different from those in adults[18,25]. The short term studies in children showed safety of IPC therapy. Only transient nausea and/or vomiting occurred after cyclophosphamide administration. Five children had life-threatening infections during treatment resulting in one death. Hemorrhagic cystitis and malignancies were not seen. Serious complications of IPC therapy seen in our study were also reported in adults[27-30]. Other major side effects associated with long term use of oral cyclophosphamide are hemorrhagic cystitis, bladder fibrosis and malignancies. Intravenous hydration before, during and after the intravenous cyclophosphamide had been used to prevent these complications in some studies[18,21,25]. There had been no reports of bladder complications or malignancies in patients receiving 3 months interval of IPC with follow-up more than 60 to 220 months[27].

A major goal of therapy in severe lupus nephritis is not only short term improvement and stabilization of renal function but also prevention of chronic renal failure. Progression to ESRD was found in 15-20 per cent of patients with severe lupus nephritis treated by IPC in adults[20,28,29]. In children, no long term study of IPC therapy was reported. Although our study is prospective and the data are not complete for analysis after 18 months of treatment, this study has more patients and demonstrates the good renal outcome of this regimen in longer period compared with previous reports[7,21]. Only one case progressed to ESRD during the mean follow-up of 24.8 months (range 6-76 months) in this study. Because of short term follow-up, the percentage of progression to ESRD is very low.

SUMMARY

Treatment of severe lupus nephritis in children with intravenous pulse cyclophosphamide is associated with favorable short term results. Severe infections are the major complications. Further studies are needed to evaluate long term efficacy of this regimen in children.

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REFERENCES

1. Wallace DJ, Podell T, Weiner DPG, Klineraberg JL, Forougesh S, Dubois EL. Systemic lupus erythematosus-survival pattern: experience with 60 patients. JAMA 1981; 245:934-8.
2. Nived O, Sturfelt G, Wollheim F. Systemic lupus erythematosus and infections: a controlled and prospective study including an epidemiological group. Q J Med 1985; 218:271-87.
3. Steinberg AD, Gourley MF, Klinman DM, Tsoko GC, Scott DE, Krieg AM. Systemic lupus erythematosus. Ann Intern Med 1991; 115:548-59.
4. Tapaneya-Olarn W. Renal involvement in SLE. In: Lolekha S, Direkwatanachai C, Tuchinda M, eds. Clinical immunology and allergy. Bangkok: Chaichareon Publisher, 1991:80-2.
5. Caeiro F, Michielson FMC, Bernstein BH, King KK, Hanson V. Systemic lupus erythematosus in childhood. Ann Rheum Dis 1981; 40:325-31.
6. Abeles M, Urman JD, Weinstein A, Lowenstein M, Rothfield NF. Systemic lupus erythematosus in younger patient: survival studies. J Rheumatol 1980; 7:512-22.
7. Yan LY, Chen WP, Lin CY. Lupus nephritis in children-a review of 167 patients. Pediatrics 1994; 94:335-40.
8. Baqi N, Moazami S, Singh A, et al. Lupus nephritis in children: a longtitudinal study of prognostic factors and therapy. J Am Soc Nephrol 1996; 6: 924-9.
9. Sztejnbok M, Stewart A, Diamond H, Kaplan D. Azathioprine in the treatment of systemic lupus erythematosus: a controlled trial. Arthritis Rheum 1971; 14:639-45.
10. Donadio JV Jr, Holley KE, Ferguson RH, Ilstrup DM. Progressive lupus glomerulonephritis: treatment with prednisolone and combined prednisolone and cyclophosphamide. Mayo Clin Proc 1976; 51:484-94.
11. Cade R, Spooner G, Schlein E, et al. Comparison of azathioprine, prednisolone and heparin alone or combined in treating lupus nephritis. Nephron 1973; 10:37-56.
12. Steinberg AD, Decker JL. A double-blind controlled trial comparing cyclophosphamide, azathioprine and placebo in the treatment of lupus glomerulonephritis. Arthritis Rheum 1974; 17: 923-37.
13. Dinant HJ, Decker JL, Klippel JH, Balow JE, Plotz PH, Steinberg AD. Alternative modes of cyclophosphamide and azathioprine therapy in lupus nephritis. Ann Intern Med 1982; 96:728-36.
14. Felson DT, Anderson J. Evidence of the superiority of immunosuppressive drugs and prednisolone over prednisolone alone in lupus nephritis: results of pooled analysis. N Engl J Med 1984; 311: 1528-33.
15. Bamsal VK, Beto J. Treatment of lupus nephritis: a meta-analysis of clinical trials. Am J Kidney Dis 1997; 29:193-9.
16. Balow JE, Austin HA, Muenz LR, et al. Effect of treatment on the evolution of renal abnormalities in lupus nephritis. N Engl J Med 1984; 311:491-5.
17. Austin HA, Klippel JH, Balow JE, et al. Therapy of lupus nephritis controlled trial of prednisolone and cytotoxic drugs. N Engl J Med 1986; 314: 614-9.
18. McCune WJ, Golbus J, Zeldes W, Bohlke P, Dunne R, Fox DA. Clinical and immunological effects of monthly administration of intravenous cyclophosphamide in severe systemic lupus erythematosus. N Engl J Med 1988; 318:1423-31.
19. Sanguansakkosol Y. Pulse intravenous cyclophosphamide therapy in SLE. In: Indraprasit S, Tapaneya-Olarn W, Tapaneya-Olarn C, eds. Tropical renal diseases and management of common renal diseases in Thailand. Bangkok: Pimsuoy Printing, 1991:81-90.
20. Martinelli R, Perira LSC, Santos ESC, Rocha H. Clinical effects of intermittent intravenous cyclophosphamide in severe systemic lupus erythematosus. Nephron 1996; 74:313-7.
21. Lehman TJA, Sherry DD, Wagner-Weiner L, et al. Intermittent intravenous cyclophosphamide therapy for lupus nephritis. J Pediatr 1989; 114: 1055-60.
22. Yan DC, Chou CC, Tsai MJ, Chaing BL, Tsau YK, Hsieh KH. Intravenous cyclophosphamide pulse therapy on children with severe active lupus nephritis. Acta Paediatr Surg 1995; 36:203-9.
23. Saberi MS, Jones BA. Remission of infantile systemic lupus erythematosus with intravenous cyclophosphamide. Pediatr Nephrol 1998; 12:136-8.
24. Tan EM, Cohen AS, Fries JF, et al. The 1982 revised criteria for the classification of systemic lupus erythematosus. Arthritis Rheum 1982; 25: 1276-7.
25. Balow JE, Austin HA, Tsokos GC, Antonovych TT, Steinberg AD, Klippel JH. Lupus nephritis. Ann Intern Med 1987; 106:79-94.
26. Sessoms SL, Kavarsky J. Monthly intravenous cyclophosphamide in the treatment of severe systemic lupus erythematosus. Clin Exp Rheumatol 1984; 2:249-51.
27. Steinberg AD, Steinberg SC. Long term preservation of renal function in patients with lupus nephritis receiving treatment included cyclophosphamide versus those treated with prednisolone alone. Arthritis Rheum 1991; 34:945-59.
28. Valeri A, Radhakrishnan J, Ester D, et al. Intravenous pulse cyclophosphamide treatment of severe

lupus nephritis: a prospective five-year study. Clin Nephrol 1994; 42:71-8.
29. Belmont HM, Storch M, Buyon J, Abramson S. New York University Hospital for joint disease experience with intravenous cyclophosphamide treatment efficacy in steroid unresponsive lupus nephritis. Lupus 1995; 4:104-8.
30. Gourly MF, Austin HA, Scott D, et al. Methylprednisolone and cyclophosphamide, alone or combination, in patients with lupus nephritis: a randomized, controlled trial. Ann Intern Med 1996; 125:549-57.

การรักษาไตอักเสบลูปัสชนิดรุนแรงในเด็ก ด้วยยาซัยโคลฟอสฟาไมค์ ขนาดสูงทางหลอดเลือดดำ

กาญจนา ตั้งนรารัชชกิจ, พ.บ.,*
เฉลิมศรี ตปนียโอฬาร, พ.บ., วิวัฒน์ ตปนียโอฬาร, พ.บ.**

ภูมิหลัง : การรักษาไตอักเสบลูปัสชนิดรุนแรงในผู้ใหญ่ด้วยยา cyclophosphamide ขนาดสูงทางหลอดเลือดดำได้ผลดีและทำให้ไตทำงานดีขึ้นในระยะยาว การศึกษาในผู้ป่วยเด็กยังมีน้อย

จุดประสงค์ : ประเมินผลการรักษาไตอักเสบลูปัสชนิดรุนแรงด้วยยา cyclophosphamide ขนาดสูงทางหลอดเลือดดำในผู้ป่วยเด็ก โดยดูผลทางคลินิก ผลต่อไตและการทำงานของไต ภาวะแทรกซ้อนจากการรักษา

วิธีการ : การศึกษาแบบ prospective study

ผู้ป่วย : ผู้ป่วยเด็กที่เป็นไตอักเสบชนิดรุนแรงและได้ติดตามผลการรักษาอย่างน้อย 6 เดือน การรักษาใช้ยา cyclophosphamide ขนาด 0.5-0.75 กรัมต่อตารางเมตร ทางหลอดเลือดดำทุกเดือนรวม 6 ครั้ง และทุก 2-3 เดือน จนครบ 3 ปี ร่วมกับการกินยา low dose prednisolone

ผลการรักษา : ผู้ป่วย 31 ราย (อายุ 12.31 $\pm$ 2.03 ปี เพศหญิง : ชาย เป็น 24:7) ที่มีไตอักเสบ ลูปัสชนิดรุนแรงได้รับการรักษาข้างต้น ผู้ป่วย 24 ใน 28 ราย (ร้อยละ 85.7) มีผลการตรวจเนื้อไตเป็น diffuse proliferative glomerulonephritis หลังการ รักษา 3 เดือน ผู้ป่วยมีอาการดีขึ้น โดยโปรตีนในปัสสาวะ creatinine clearance ระดับของ creatinine, urea nitrogen, albumin และ C_3 ในเลือดดีขึ้น และผลนี้อยู่นานถึง 18 เดือน โดยที่สามารถลดขนาดยา prednisolone ลงมาได้ตามลำดับเมื่อประเมินผู้ป่วยครั้งสุดท้าย (6-76 เดือน) พบว่าร้อยละ 38.7 มีการทำงานของไตปกติ ร้อยละ 58 ยังตรวจพบโปรตีนในปัสสาวะและผู้ป่วย 1 ราย มีระดับของ creatinine ในเลือดเป็น 1.6 มก./ดล. ขณะรักษา ผู้ป่วย 1 รายมีอาการเลวลงจนเป็นไตวายระยะสุดท้าย และ 5 รายเสียชีวิตจากการติดเชื้อรุนแรงไม่พบภาวะแทรกซ้อนของยา cyclophosphamide เช่น hemorrhagic cystitis และมะเร็ง

สรุป : การรักษาไตอักเสบลูปัสชนิดรุนแรงในเด็กด้วยยา cyclophosphamide ขนาดสูงทางหลอดเลือดดำได้ผลดี แต่มีภาวะแทรกซ้อนที่สำคัญคือการติดเชื้อที่รุนแรง

คำสำคัญ : Lupus Nephritis, Children, Pulse Cyclophosphamide, Treatment

* ภาควิชากุมารเวชศาสตร์, คณะแพทยศาสตร์โรงพยาบาลรามาธิบดี, มหาวิทยาลัยมหิดล, กรุงเทพ ฯ 10400