COMPARISON BETWEEN INTRAVENOUS CYCLOPHOSPHAMIDE (IVC) AND MYCOPHENOLATE MOFETIL (MMF) AS INDUCTION AGENT IN LUPUS NEPHRITIS

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Objectives:

Lupus nephritis (LN) is a serious complication in systemic lupus erythematous (SLE) , and proliferative lupus nephritis usually predicts poorer outcome. In Malaysia, LN accounts as high as 74% amongst the SLE patients(1). Intravenous cyclophosphamide (IVC) is an established treatment for proliferative LN (2). However, many recent publications have demonstrated mycophenolate mofetil (MMF) has comparable treatment outcome with IVC (3),(4). In our centre, patients with proliferative LN will either receive IVC or MMF. We decided to compare outcome of these cohort patients who presented to Hospital Serdang from 2006-2012 and clinical predictors of renal outcome .

Methods:

All SLE patients with biopsy proven proliferative LN (Class III, IV, V or mixed groups) were reviewed. A total of 58 patients who were either given IVC or MMF for the first 6 month were included in this study. Baseline characteristics and renal outcome at 6 month and 12 month were prospectively collected. Renal outcome was categorized into (5) :
Complete Remission (CR) : Return of serum creatinine (SCr) to previous baseline plus decline in 24hr urine protein (or UPCI equivalent) to < 0.5 g/day
Partial Remission (PR) : Stabilization (±25%) or improvement in SCr but not to normal plus decrease in 24hr urine protein >50% and < 3.0g/day.
Not in remission (NR) : No improvement in SCr plus no decrease in 24 hr urine protein.
Composite end point included : NR or death or developed end stage renal disease (ESRD)

Statistical analysis were done via SPSS version 19.0. Categorical data was analyzed using chi square test, continuous data was analyzed using paired t-test (parametrical distributed) and Mann Whitney U (non-parametrical distributed).

Results:

There were 58 patients included in this study, of which 46 patients received IVC monthly at dose 0.5g/m_2, and 12 patients received MMF with maximum dose 2 g per day for 6 months. Doses were adjusted according to side effects or transaminitis.

Table 1 : Comparison between baseline parameters for IVC and MMF

Baseline Parameters	IVC group (n=46)	MMF group (n=12)	P value
Age (years)	23.0 (12.0)	20.5 (8.0)	0.27
Gender (Male : Female)	7 (15.2%):39(84.8%)	1(8.3%):11(91.7%)	0.47
Albumin at presentation (g/dL)	24.0 (11.0)	26.5 (7.0)	0.19
Creatinine at presentation+ (umol/L)	85.0 (106.0)*	70.0 (39.0)*	0.15
eGFR (ml/min/1.73m2)	74.2 (70.9)	93.3 (64.4)	0.11
24 hr urine protein or equivalent (g/day)	3.3 (3.9)	3.5 (4.9)	0.80
Hb (g/dL)	10.3 (2.8)	10.5 (2.8)	0.60
Blood pressure (mmHg) Systolic Diastolic	 138 (37) 89 (24)	 121 (28) 79 (26)	 0.07 0.09

+ Nonparametric test *Values stated in median (Interquartile range)

Figure 1 :Renal Outcome LN Patients after 6 month follow up

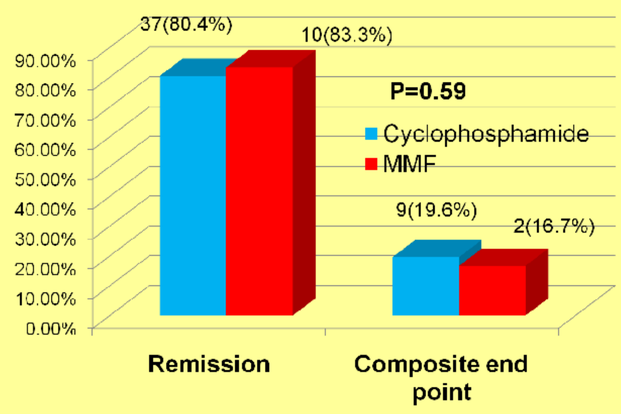

Figure 2 :Renal Outcome LN Patients after 12 month follow up

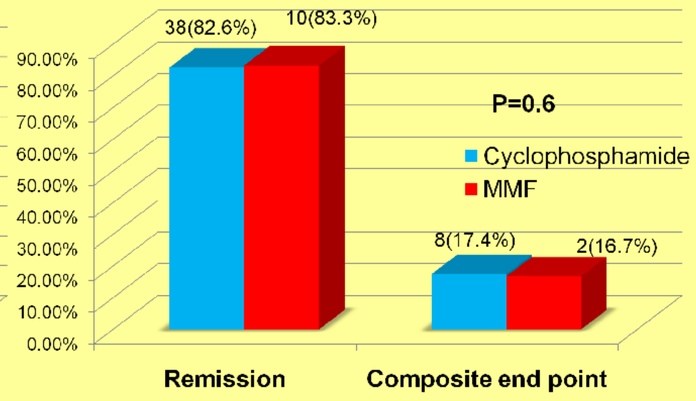

Table 2 : Clinical Predictors of Renal Outcome at 12 month follow up

Clinical Predictors	CR	PR	NR	P value
Age	21.5 (11.0)	23.5 (10.0)	26.5 (8.0)	0.25
eGFR (ml/min/1.72m2)	76.7 (74.3)	78.5 (67.1)	114.8 (168.2)	0.45
Creatinine at presentation (umol/L)	74.0 (87.0)	100.6 (123.0)	64.5 (91.0)	0.42
24-hour Proteinuria at presentation or equivalent (g/ day)	2.49 (2.9)	5.3 (3.4)	4.1 (6.9)	0.005
Albumin (g/dL)	25.0 (12.0)	26.0 (8.0)	18.0(12.0)	0.06

Table 3: Serial changes in parameters at 6 month and 12 month comparing IVC and MMF

	(IVC GROUP)			(MMF GROUP)		
	Baseline	At 6 month follow up	At 12 month follow up	Baseline	At 6 month follow up	At 12 month follow up
Creatinine	85.0 (106.0)	87.6 (47.0)	69.0 (42.0)	70.0(39.0)	63.5 (11.0)	62.5 (11.0)
eGFR	74.2 (70.9)	100.6 (53.2)	98.1 (44.9)	93.3 (64.4)	116.1 (48.9)	120.3 (55.6)
Albumin	24.0 (12.0)	38.0 (8.0)	36.0 (5.0)	26.5 (10.0)	39.0 (14.0)	37.5 (13.0)
Hb	10.3 (3.2)	12.0 (2.3)	11.7 (2.2)	11.1 (3.4)	12.2 (3.0)	12.2 (2.8)

+ No difference observed in baseline parameters between patients receiving IVC and MMF
+ No difference in renal outcome and composite endpoint at 6 month and 12 month follow up.

Conclusions:

1. There is no difference between IVC and MMF in achieving renal remission at 6 month and 12 month follow up amongst proliferative LN groups. IVC is still the preferred regime in our centre due to cost factor however, MMF provides alternative treatment regime in these group of patients.
2. Degree of proteinuria at presentation showed to be significant predictor of renal remission and 24-hour urine protein or equivalent less than 3g/ day predicts positive response to complete remission from our study.
3. The limitations in our study include small number of cohort in MMF group as compare to IVC group, and we would like to look into potential side effects between these two treatment regimes in our follow up cohort patient.

References:

1. Boumpas DT, austin HA et al. Controlled trial of pulse methylprednisolone versus two regimes of pulse cyclophosphamide in severe lupus nephritis. Lancet 1992; 340:741-745
2.F Wang, CL Wang, CT Tan and M.Manivasgar. Systemic Lupus Erythematous in Malaysia: a study of 539 patients and comparison of prevalence and disease expression in different racial and gender groups. Lupus,1997 :6,248-53.
3. Appel GB, Contreras G et al. Mycophenolate Mofetil versus Cyclophosphamide for induction Treatment of Lupus Nephritis. J Am Soc Nephrol 2009; 20:1103-1112
4.Ong LM,Hooi LS et al. Randomized controlled trial of pulse intravenous cyclophosphamide versus mycophenolate mofetil in induction therapy of proliferative lupus nephritis. Nephrology 2005;10:504-510
5. Kidney Disease: Improving Global outcomes (KDIGO) Glomerulonephritis Workgroup. KDIGO Clinical Practice Guideline for Glomerulonephritis. Kidney Inter, Suppl. 2012;2 :139-274

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