Low Dose VS High Dose Cyclophosphamide As Induction Therapy For Renal Remission In Lupus Nephritis Patients

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Background

- Lupus Nephritis(LN) is the renal manifestation of Systemic Lupus Erythematosus (SLE) which is the main contributor of
  - mortality and
  - morbidity

  of SLE patient

- The aims of treating LN are to
  - induce and
  - maintain remission

thereby reducing the risk of progression to renal failure.

- Immunosuppressive drugs combined with prednisolone are more efficacious than prednisolone alone for treating LN.

Background

- The most popular therapeutic regimen consists of long term pulses intra-venous (IV) Cyclophosphamide (CYC) in combination with corticosteroid.

- However, some investigators have drawn attention to the limitation of IV CYC for
  - toxicity during long-term use
  - possibility of relapse

- Despite skepticism, CYC remains the most effective therapy for initial treatment for aggressive LN (ISN/RPS Class III and IV) [International Society of Nephrology/ Renal Pathology Society].

Background

- The American College of Rheumatology (ACR-2012) recommended two regimens of CYC
  - high dose (500 mg/M^2 body surface area) monthly for 6 months
  - low dose (500 mg fixed) biweekly for 6 doses

- Low dose was trialed in European white people by Euro Lupus Nephritis Trial (ELNT).
- In our country there is no study to show the efficacy of low dose CYC.
- So this study was conducted to observe whether low dose is as effective as high dose CYC in our people.

Aims and objectives:

- To compare the efficacy of two regimens of CYC as induction therapy for renal remission in Lupus Nephritis.

Study design

- Prospective interventional comparative study

MATERIALS & METHODS

- This study was done in the Department of Medicine and Nephrology Unit in Sylhet M.A.G. Osmani Medical College from January, 2013 to 31st December, 2014.

- Total 15 biopsy proven ISN/RPS Class III and IV LN patients were randomly selected in two groups.
  - Group I received low dose CYC (seven patients) and
  - Group II received high dose CYC (eight patients) and monitored for 6 months.

- All patients had received daily pulses of 750 mg of methylprednisolone for 3 days.

- After the last dose of methylprednisolone every patient had received one liter of normal saline over four hours

MATERIALS & METHODS

- CYC was then reconstituted and diluted in 150ml of normal saline and infused over one hour.
- All the patients were instructed to drink at least one liter of fluid every 6 to 8 hourly and void as frequently as possible for 24 hours.
- Oral glucocorticoids therapy at an initial dose of 0.5 mg/kg/day of prednisolone for 4 weeks was given at the day of IV CYC therapy.
- After 4 weeks glucocorticoids doses was taper by 2.5 mg of prednisolone every 2 weeks.

MATERIALS & METHODS

- Azathioprine at a dosage of 2 mg/kg/day started/recommended after 2 weeks of last CYC injection and was continued/recommended in both group as a remission maintenance therapy.

Result

- Among 15 patients 14 patients were female and one patient was male. Female and male ratio was 14:1.

- Mean age was 23.85 (±8.22) years in Group I and 24.25(±7.34) years in Group II.

RESULT

Group	Responder	Non responder
Group I(N-7)	5 (71.428%)	2(28.57%)
Group II (N-8)	7 (87.5%)	1 (12.50%)

Complete renal remission was five patients in low dose group (71.43%), six patients in high dose group (75%).

Partial renal remission observed only in one patient in Group II(12.50%) but none was in Group I.

Non responder was two in Group I (28.57%) and one(12.5%) was in Group II.

Result

- **Adverse events during study period**

Adverse events	Group I	Group II
Death	1	1
Infection Flulike illness Urinary tract infection Respiratory tract infection	 2 2	 3 3 1
Leucopenia		1
Pancytopenia		2
Hospitalization due to side effects		2

Two patients of Group II developed severe pancytopenia, but none in Group I.

Conclusion

- Low dose was not inferior to high dose of CYC for renal remission in Lupus Nephritis patients.
- There was no significant difference between two groups (P-value was 0.5692) for inducing renal remission.
- Severe pancytopenia developed in two patients in high dose group.