AB0522

TACROLIMUS IN REFRACTORY LUPUS NEPHRITIS: A PROSPECTIVE MULTICENTRIC STUDY CARRIED OUT IN CLINICAL PRACTICE SETTING

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Background: The efficacy of tacrolimus (TAC) in lupus nephritis (LN) has been recently demonstrated in several randomised controlled trials in asian cohorts.¹ Nevertheless, data on real-life experience and long-term safety of TAC are still lacking.

Objectives: To assess efficacy and safety of TAC in SLE patients with refractory LN in a multi-centric prospective cohort.

Methods: Adult SLE patients with refractory LN from 4 Italian centres were prospectively followed for at least 12 months. Clinical and serological variables and previous/concomitant medications were collected at baseline, 3, 6, 12 months after starting TAC. Renal response was assessed by using EULAR/ERA-EDTA definitions.² Adverse events (AEs) included non-infectious and infectious AEs; they were defined severe (SAE) when hospitalisation and/or death and/or life-threatening manifestations occurred. Data were analysed using SPSS (v.24.0).

Results: Thirteen SLE patients (8 females, 5 males, mean age 33.7±10.2, mean disease duration 11.9±5.9) were enrolled (table 1). Concomitant medications included: prednisone (100%), mycophenolate mofetil (92.3%), hydroxychloroquine (53.8%), azathioprine (7.7%), belimumab (7.7%) and cyclosporine (7.7%). The average number of previous immunosuppressants taken by each patient was 3.15±1.90. Six-months renal response was achieved by 5/13 patients (38.5%): complete renal response (CRR) in 3 (60.0%) and partial renal response (PRR) in 2 patients (40.0%). Twelve-months renal response occurred in 4/13 patients (30.8%): CRR in 2/13 (50.0%) and PRR in 2/13 (50.0%). One patient achieved CRR at 6 and 12 months; one patient achieved PRR at 6 months and CRR at 12 months. Six patients (46.1%) discontinued TAC after an average follow up period of 10.2±7.8 months. Causes of discontinuation were: 3 non-infectious non-SAEs, 1 flare, 1 non-infectious SAE, and 1 non-response. Concerning AEs, no severe infections or deaths occurred.

Abstract AB0522 – Table 1. Demographic, clinical and serological features at baseline, 3, 6, 12 months after starting TAC (mean±SD)

	Baseline	3 months	6 months	12 months
Prednisone daily dosage (mg/day)	17.1 ±11.3	12.7±9.5	12.8±13.1	9.6±5.6
Tacrolimus daily dosage (mg/day)	4.1±1.3	3.5±1.9	4.2±1.8	4.0±0.8
Creatinine (mg/dL)	0.8±0.5	0.8±0.3	0.7±0.3	0.9±0.5
24 hour proteinuria (g/day)	3.8±2.2	1.4±1.2	1.5±1.6	2.0±1.6
SLEDAI-2k	8.8±2.4	7.2±4.5	7.5±4.3	7.4±4.4
SLICC-DI	1.3±1.4	/	1.6±1.5	1.4±1.1

SLEDAI-2k: Systemic Lupus Erythematosus Disease Activity Index 2000; SLICC-DI: Systemic Lupus International Collaborating Clinics Damage Index.

Conclusions: Our preliminary data from clinical practice setting suggest that TAC could be a therapeutic rescue strategy for refractory LN. Further studies are needed to prove TAC efficacy in the long term.

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METFORMIN COMBINED WITH CONVENTIONAL THERAPY INCREASES ABSOLUTE NUMBER OF REGULATORY T CELLS IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Systemic lupus erythematosus (SLE) is multisystem and multiorgan autoimmune diseases and the main treatment is hormone combined with immunosuppressant and biological agents. Since the conventional treatment regimens have not achieved expected effects, it is of great practical value to search for good efficacy, lower side-effects, and low-cost drugs. Recently, we have found that the absolute number of CD4⁺CD25⁺FOXP3⁺ regulatory T (CD4⁺ Treg) cells reduced in SLE. Metformin, a basic hypoglycemic drug, has been shown to increase the number of Treg cells and decrease the number of Th17 cells.^[1,2,3]

Objectives: To observe the clinical efficacy of metformin on the treatment of SLE and levels of CD4⁺Treg and Th17 cells.

Methods: Twenty-three patients with SLE were enrolled in this study. They fulfilled the ACR 1997 standard, their average age was 32.22±8.18 years, and duration was 51.41±15.52 months. These patients were administered metformin (250 mg Bid) combined with conventional therapy for 6 weeks. At week 0 and week 6, the absolute numbers of Th17 cells and Treg, the symptoms, and laboratory indicators were collected.

Results: After metformin treatment combined with conventional therapy, average absolute number of Treg cells in 23 patients increased significantly from 20.2 (20.28) (week 0) to 25.76 (25.1) (week 6) (p=0.073) while that of Th17 cells increased slightly from 5.29 (6.43) (week 0) to 5.57 (6.05) (week 6) (p=0.956), which led to reduce average ratio of Th17/Treg from 0.25 (0.31) (0 week) to 0.19 (0.23) (6 weeks) (p=0.147). The treatment attenuated the symptoms of the patients and meantime, the dose of prednisone was decreased. At week 6, metformin combined with interleukin-2, the dosage of prednisone in SLE patients were decreased from 23.70±19.41 mg/d(0 week) to 20.44±17.03 mg/d(6 weeks) (p=0.548).

Abstract AB0523 – Figure 1

Conclusions: Our findings suggest metformin can effectively up-regulate Treg cells as well as increase Th17 to a certain extent, which restores the balance of Th17/Treg cells in SLE, metformin combined with conventional therapy can reduce the dosage of glucocorticoid, but the long-term effect needs further investigation.

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