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AUTOLOGOUS STEM CELLS TRANSPLANTATION IN PATIENTS WITH ACTIVE LUPUS NEPHRITIS

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Background

Nowadays despite the advances in immunosuppressive and monoclonal antibody therapy there are still many patients with active systemic lupus erythematosus (SLE).

Renal involvement in SLE may lead to a fatal income in treatment-refractory patients. One of the modern therapeutic approaches to this problem is transplantation of stem cells, which appears beneficial in treatment of patients with SLE refractory to conventional treatment options.

Objectives

To determine the efficacy of autologous haematopoietic stem cell transplantation (HSCT) in patients with refractory lupus nephritis.

Methods

This is a preliminary data of prospective study, which included 14 female patients with active lupus nephritis aged 20 to 36 years underwent HSCT.

Exclusion criteria: decompensation of any chronic disease, oncopathology, alcohol or drug abuse, pregnancy or lactation,

Duration since lupus erythematosus diagnosed was 7.51±2.18 years (M±SD). Before cell therapy patients received Mycophenolate mofetil 1000 mg/day and glucocorticosteroids at a dose of 30 mg/day in terms of prednisolone.

Patients were treated with HSCT according to the scheme - 0-3-6 months. The operation was conducted in two stages: 1) mieloeksfuziya with following biotechnological separation of hematopoietic stem cells fraction; 2) intravenous cells infusion at 50 ml/hr. Bone marrow was taken from the posterior crest of iliac bone by multiple punctures.

Mononuclear fraction of stem cells was isolated and cultured with following intravenous cells infusion. The amount of viable cell was not less than 96%. Results were evaluated by changes in the Systemic lupus erythematosus disease activity index (SLEDAI) and serological features (anti-nuclear antibodies (ANA) and anti-double-stranded DNA (anti-dsDNA). Also we assessed a renal function by glomerular filtration rate (GFR), 24 h proteinuria, serum creatinine and albumin. **Results were statistically elaborated by using IBM SPSS 17.0.** This clinical trial was allowed by Ethics Committee. All of our patients gave an informed consent for HSCT.

Results

The mean follow-up period was 5.26±1.69 months.

A total of 9 patients have been followed for more than 6 month and 5 patients – not more than 3 months.

All patients undergone HSCT demonstrated clinically improved in the SLEDAI score and 24h proteinuria. Before HSCT they had 15.41±4.56 by SLEDAI and proteinuria equal 1.77±0.61g and after 3 month before second procedure its were 13.40±4.09 and 0.61±0.35 respectively (Tab.1). In 9 patients at 6-month follow-up, SLEDAI scores decreased from 15.33±5.41 to 11.09±3.8 and 24h proteinuria decreased from 2.12±0.59 to 0.54±0.32g ($p<0.04$, Tab.2). HSCT leaded to a significant increase in GRP from 82.91±31.67 to 107.9±25.31 after 3 months and 133.50±44.13 after 6 months ($p<0,03$).

Moreover non-renal-related manifestations such as levels of Anti-dsDNA, ANA, fibrinogen, γ-globulin also decreased. E.g. after a period 6 months γ-globulin decreased from 13.92±3.82% to 10.57±3.28% and fibrinogen level - from 4.16±0.93 to 3.55±0.86 g/l ($p<0.05$). Lower reduction in these parameters was also observed in patients receiving a single HSCT (after 3 month).

During 6 month we didn't observed any complications of stem cell transplantation.

Figure 1. Laboratory and clinical parameters before and after HSCT

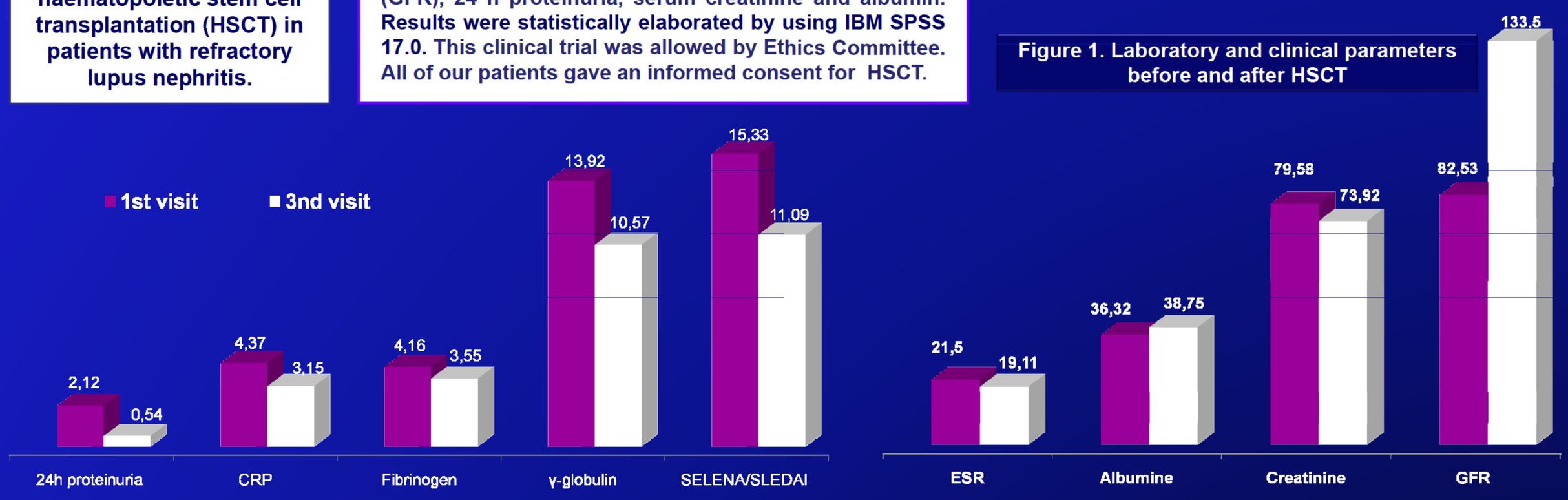

Table 1. Results of comparison of clinical and laboratory indicators before and after single stem cell transplantation

Parameters [Mean±SD]	1st visit (before HSCT)	2nd visit (3 months after 1st HSCT)	P
Hb, g/L	108.11±20.54	114.5±18.91	0.147
RBC, ×10⁹/mL	4.24±0.78	4.41±0.71	0.421
ESR, mm/h	21.5±4.10	20.0±5.14	0.347
24h proteinuria	1.77±0.61	0.61±0.35	0.159
Albumine, g/L	36.32±5.65	35.99±11.10	0.304
Creatinine, μmol/L	79.58±26.56	76.64±39.44	0.082
CRP, mg/dl	4.37±0.76	4.62±3.35	0.297
γ-globulin, %	13.92±3.82	11.69±3.49	0.144
Fibrinogen, g/L	4.02±0.93	3.91±0.88	0.546
GFR	82.91±31.67	107.9±25.31	0.050
SELENA/SLEDAI	15.41±4.56	13.40±4.09	0.048

Table 2. Results of comparison of clinical and laboratory indicators before and after twice stem cell transplantation

Parameters [Mean±SD]	1st visit (before HSCT)	3rd visit (6 months after 2nd HSCT)	P
Hb, g/L	108.11±20.54	116.15±11.24	0.266
RBC, ×10⁹/mL	4.24±0.78	4.56±0.82	0.180
ESR, mm/h	21.5±4.10	19.11±7.61	0.267
24h proteinuria	2.12±0.59	0.54±0.32	0.039
Albumine, g/L	36.32±5.65	38.75±4.22	0.207
Creatinine, μmol/L	79.58±26.56	73.92±33.49	0.031
CRP, mg/dl	4.37±0.76	3.15±2.41	0.092
γ-globulin, %	13.92±3.82	10.57±3.28	0.050
Fibrinogen, g/L	4.16±0.93	3.55±0.86	0.046
GFR	82.53±27.15	133.50±44.13	0.031
SELENA/SLEDAI	15.33±5.41	11.09±3.80	0.044

Conclusion

HSCT in patients with refractory lupus nephritis resulted in decrease of disease activity, improvement in serological markers and stabilization of renal function. These findings indicated autologous stem cell therapy seems like a promising direction in the treatment of lupus nephritis. Further studies with a large number of patients and control group arm may help to achieve better results.

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