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ORIGINAL RESEARCH

Assessment of Efficacy of High versus Low–Medium Prednisone Doses for the Treatment of Systemic Lupus Erythematosus Patients

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ABSTRACT

Background: To compare efficacy of high versus low–medium prednisone doses for the treatment of systemic lupus erythematosus patients.

Materials and Methods: Seventy- four adults patients diagnosed with systemic lupus erythematosus of either gender was divided equally (37) into 2 groups. Group I received prednisone doses ≤30 mg/day and group II received prednisone doses >30 mg/day. Activity was measured using the SLEDAI-2K score. Damage accrual was calculated using the SLICC damage index (SDI)**.**

Results: Group I comprised of 20 male and 17 female and group B had 18 male and 19 female (Table I). Age at diagnosis was 36.7 years in group I and 34.6 years in group II, Anti-Ro was seen in 34% and 38%, Anti-La in 24% and 18%, Anti-SM in 18% and 20%, Anti-RNP in 9% and 14%, Anti-DNA in 65% and 50% and Antiphospholipid antibodies in 24% and 32%. SLEDAI at baseline was 9.84 and 9.81 and SDI at baselined was 0.14 and 0.14 in group I and II respectively. The difference was significant (P< 0.05). Main organ systems affected were skin in 4 and 3, CNS in 2 and 1, vasculitis in 1 and 2, articular in 17 and 22, serosal in 5 and 6, kidney in 3 and 4 and haematological in 2 and 4 in group I and II respectively. The difference was significant (P< 0.05). The mean maximum prednisone 1st year was 14.2 and 64.1, average prednisone 1st year was 5 and 24, average prednisone years 1–2 was 3.6 and 18.5, average prednisone years 1–3 was 3.2 and 15.8, average prednisone years 1–4 was 2.7 and 15.1, pulse methyl-prednisolone during the 1st year was 12 and 3, hydroxychloroquine during the 1st year was seen in 37 and 9 and immunosuppressive drugs during the 1st year was seen in 9 and 8 in group I and II respectively. The difference was significant (P< 0.05).

Conclusion: Prednisone doses ≤30 mg/day were similarly effective and safer than higher doses for treating Systemic lupus erythematosus.

Keywords: Systemic lupus erythematosus, Prednisone, haematological.

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INTRODUCTION

Systemic lupus erythematosus (SLE) is a chronic, prototypic autoimmune disorder which may affect almost any organ or system.[1] The high heterogeneity of SLE has been long

recognized. With the advance in early detection and proper management, mortality of SLE has intensely fall from 63.2% in the 1950s to 95% in the 2020s.[2]

Irreversible organ damage accrues during the course of systemic lupus erythematosus (SLE). It is well evident that damage is a predictor of further damage and mortality in patients with SLE.[3] Thus, prevention of damage, either attributable to lupus activity or to lupus treatments, should be one of the main therapeutic objectives. The association of oral glucocorticoid therapy with damage has been well established. During the past few years extensive research on the genetic bases of SLE has emerged.[4] Genetic variation was first shown to be important in SLE in the 1970s with associations in the human leukocyte antigen region. Almost four decades later, and with the help of increasingly powerful genetic approaches, more than 25 genes are now known to contribute to the mechanisms that predispose individuals to lupus.[5]

Buttgereit et al[6] have proposed a specific terminology for prednisone doses according to the level of activation of the genomic and non-genomic ways: low doses (up to 7.5 mg/day), medium doses (up to 30 mg/day), high doses (N30 mg/day), very high doses (N100 mg/day) and pulses (≥250 mg/day). Research studies have shown a great increase of toxicity, including irreversible damage, with the use of high doses along with a good safety profile of low doses and short-term pulse therapy. Considering this, we conducted present research to compare efficacy of high versus low–medium prednisone doses for the treatment of systemic lupus erythematosus patients.

MATERIALS & METHODS

Seventy- four adults patients diagnosed with systemic lupus erythematosus of either gender was recruited in this prospective, observational study. After considering the utility of the study and obtaining approval from ethical review committee of the institute, we obtained written consent from all patients. All patients met American College of Rheumatology (ACR) classification criteria.

Demographic data such as name, age, gender etc. was entered in case history proforma. A careful oral and systemic examination was carried out. Patients were divided equally (37) into 2 groups. Group I received prednisone doses ≤30 mg/day and group II received prednisone doses >30 mg/day. Activity was measured using the SLEDAI-2K score at baseline and after one year of follow-up. The difference between both scores was the efficacy outcome variable. Damage accrual was calculated using the SLICC damage index (SDI). The results were compiled and subjected for statistical analysis using Mann Whitney U test. P value less than 0.05 was set significant.

RESULTS

Table I Patients distribution

Groups	Group I	Group II
Drug	Prednisone ≤30 mg/day	Prednisone >30 mg/day
M:F	20:17	18:19

Group I comprised of 20 male and 17 female and group B had 18 male and 19 female (Table I).

Table II Baseline clinical characteristics

Parameters	Group I	Group II	P value
Age at diagnosis (years)	36.7	34.6	0.81
Anti-Ro	34%	38%	0.94

Anti-La	24%	18%	0.71
Anti-SM	18%	20%	0.95
Anti-RNP	9%	14%	0.05
Anti-DNA	65%	50%	0.04
Antiphospholipid antibodies	24%	32%	0.05
SLEDAI-0	9.84	9.81	0.96
SDI-0	0.14	0.14	1

Age at diagnosis was 36.7 years in group I and 34.6 years in group II, Anti-Ro was seen in 34% and 38%, Anti-La in 24% and 18%, Anti-SM in 18% and 20%, Anti-RNP in 9% and 14%, Anti-DNA in 65% and 50% and Antiphospholipid antibodies in 24% and 32%. SLEDAI at baseline was 9.84 and 9.81 and SDI at baselined was 0.14 and 0.14 in group I and II respectively. The difference was significant (P< 0.05) (Table II).

Table III Main organ systems affected

Parameters	Group I	Group II	P value
Skin	4	3	0.94
CNS	2	1	0.12
Vasculitis	1	2	0.12
Articular	17	22	0.51
Serosal	5	6	0.95
Kidney	3	4	0.04
Haematological	2	4	0.05

Main organ systems affected were skin in 4 and 3, CNS in 2 and 1, vasculitis in 1 and 2, articular in 17 and 22, serosal in 5 and 6, kidney in 3 and 4 and haematological in 2 and 4 in group I and II respectively. The difference was significant (P< 0.05) (Table III).

Table IV Comparison of drug therapy in both groups

Parameters	Group I	Group II	P value
Maximum prednisone 1st year	14.2	64.1	0.01
Average prednisone 1st year	5	24	0.02
Average prednisone years 1–2	3.6	18.5	0.02
Average prednisone years 1–3	3.2	15.8	0.03
Average prednisone years 1–4	2.7	15.1	0.01
Pulse methyl-prednisolone during the 1st year	12	3	0.04
Hydroxychloroquine during the 1st year	37	9	0.03
Immunosuppressive drugs during the 1st year	9	8	1

The mean maximum prednisone 1st year was 14.2 and 64.1, average prednisone 1st year was 5 and 24, average prednisone years 1–2 was 3.6 and 18.5, average prednisone years 1–3 was 3.2 and 15.8, average prednisone years 1–4 was 2.7 and 15.1, pulse methyl-prednisolone during the 1st year was 12 and 3, hydroxychloroquine during the 1st year was seen in 37 and 9 and immunosuppressive drugs during the 1st year was seen in 9 and 8 in group I and II respectively. The difference was significant (P< 0.05) (Table IV).

DISCUSSION

The fundamental goals of treatment of patients with SLE are to improve long-term patient outcomes. Management should aim at remission of disease symptoms and signs, prevention of damage accrual and minimization of drug side-effects, as well as improvement of quality of life.[7] Complete remission (absence of clinical activity with no use of GC and IS drugs) is infrequent. To this end, newly defined low disease activity states (based on a SLEDAI score ≤ 3 on antimalarials, or alternatively SLEDAI ≤ 4, PGA ≤ 1 with GC ≤ 7.5 mg of prednisone and well-tolerated IS agents) have shown comparable rates with remission, regarding halting of damage accrual.[8,9] Accordingly, treatment in SLE should aim at remission or, if this state cannot be achieved, at low disease activity in all organ systems. Prevention of disease flares is an additional milestone of SLE treatment. Although a universally accepted definition is lacking, most experts agree that a flare is a measurable increase in disease activity usually leading to change of treatment.[10] We conducted present research to compare efficacy of high versus low–medium prednisone doses for the treatment of systemic lupus erythematosus patients.

Group I comprised of 20 male and 17 female and group B had 18 male and 19 female. Arruzza et al[11] compared the efficacy and safety of high vs. low–moderate oral doses of prednisone to treat patients with highly active lupus at diagnosis. Patients from the Lupus-Cruces cohort with an SLEDAI score ≥6 at diagnosis and treated with regimes containing low–medium prednisone doses (≤30 mg/day) were identified (group M). Glucocorticoid related damage was considered in the presence of cataracts, osteonecrosis, osteoporotic fractures and/or diabetes mellitus. 30 patients were included in each group. Patients in group H received 5-fold higher doses of prednisone, less hydroxychloroquine and less methyl-prednisolone pulses. SLEDAI improvement was similar in both groups. Patients in group H were more likely to accrue new damage. No patients in group M suffered glucocorticoid-related damage, vs. 5 patients in group H ($p = 0.02$). The average daily prednisone dose during the first year predicted accrual of new damage and accrual of glucocorticoid-related damage. Likewise, average doses of prednisone N7.5 mg/day were an independent predictor of new damage.

Our results showed that age at diagnosis was 36.7 years in group I and 34.6 years in group II, Anti-Ro was seen in 34% and 38%, Anti-La in 24% and 18%, Anti-SM in 18% and 20%, Anti-RNP in 9% and 14%, Anti-DNA in 65% and 50% and Antiphospholipid antibodies in 24% and 32%. SLEDAI at baseline was 9.84 and 9.81 and SDI at baselined was 0.14 and 0.14 in group I and II respectively. Our results showed that main organ systems affected were skin in 4 and 3, CNS in 2 and 1, vasculitis in 1 and 2, articular in 17 and 22, serosal in 5 and 6, kidney in 3 and 4 and haematological in 2 and 4 in group I and II respectively. Kong et al[12] found that all patients had active disease at the time of pulse MEP. There were +ve newly diagnosed SLE patients. In the other 15 individuals a significant increase in the SLEDAI score had occurred in the month prior to the pulse MEP. The mean MEP dose given was 9.24 + 2.22 mg/ kg/day. The average oral prednisolone dose immediately post-MEP was 57.5 + 17.8 mg (1.1 + 0.3 mg/ kg) and this was reduced to 14.7 + 3.8 mg (0.3 + 0.1 mg/kg) daily at six months ($P < 0.0001$). Monthly pulse intravenous cyclophosphamide at a dose of 0.5 g/m 2 was given to 15 patients (75%) for six months. Azathioprine was prescribed in two individuals and mycofenolate mofetil in one.

We observed that the mean maximum prednisone 1st year was 14.2 and 64.1, average prednisone 1st year was 5 and 24, average prednisone years 1–2 was 3.6 and 18.5, average prednisone years 1–3 was 3.2 and 15.8, average prednisone years 1–4 was 2.7 and 15.1, pulse methyl-prednisolone during the 1st year was 12 and 3, hydroxychloroquine during the 1st

year was seen in 37 and 9 and immunosuppressive drugs during the 1st year was seen in 9 and 8 in group I and II respectively. Badsha et al[13] found that pulse MEP is beneficial for several serious manifestations of SLE, such as neuro-psychiatric lupus, pulmonary hemorrhage, severe blood dyscrasias, cardiomyopathy, and vasculitis. However, significant side effects may occur, mostly infections, which are worse in patients with hypoalbuminemia.

CONCLUSION

Prednisone doses ≤30 mg/day were similarly effective and safer than higher doses for treating Systemic lupus erythematosus.

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