Research Article

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An observational study of treatment outcome in cutaneous systemic sclerosis

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Objective: An observational method was used for estimation of the effectiveness of different current treatment regimens on skin thickening of PSS. Method: 34 patients of scleroderma were treated with cyclophosphamide-MMF (15); cyclophosphamide-AZA (4); MMF (3), cyclophosphamide (3); Azathioprine (1.8) were only on sildenafil. The primary outcome measure was Modified Rodnan Skin Score (MRSS). Result: The study included 34 patients. 15 patients were on cyclophosphamide followed by MMF. MRSS improved from mean 20.33 to 16.07. 4 patients treated with cyclophosphamide followed by AZA, MRSS improved from mean 23 to 16. 3 patients on MMF alone, MRSS improved from mean of 10.33 to 8. 3 were only on cyclophosphamide MRSS improved from 17 to 15 (mean). One patient was on Azathioprine, MRSS improved from 6 to 4. 8 patients were only on Sildenafil for Raynaud's phenomenon and MRSS worsened from mean 12 to 13.38. Conclusion: Improvement observed in all regimens of immunosuppressant and skin thickening worsened in those without on any immunosuppressant.

Keywords: systemic scleroderma ▪ modified rodnan ▪ skin score

Introduction

SSC is a rare disease. It is subdivided into limited cutaneous scleroderma and diffuse cutaneous scleroderma depending upon the extent of skin involvement. Diffuse variety not only involves extremities and face but also Trunk which is spared in limited cutaneous scleroderma. SSC has worldwide distribution and occurs in every ethnic group. The community based survey of SSC yielded a prevalence of 286 cases/million population [1]. To assess the extent of skin involvement by MRSS the maximum value of 51 when all 17 areas of body are maximally revealing the skin thickness. For each site skin thickness is graded from 0 to 3 as per severity [2-4]. In addition to cutaneous thickening of SSC, the disease also involves lungs, GIT, kidneys and heart.

Method

34 patients who attended the Rheumatology unit of Medicine from September 2012 to September 2015 and had in addition to diffuse scleroderma ILD with those FVC <70% were given one of the following four regimens:

- IV cyclophosphamide monthly for 6 months followed by MMF 18 months (15 patients).
- IV cyclophosphamide monthly for 6 months followed by Azathioprine 18 months (4 patients).
- MMF for 2 years (3 patients).
- IV cyclophosphamide monthly for 12 months (3 patients).

8 patients were only on sildenafil for Raynaud's phenomenon as their FVC >70% predicted.

Results

The mean MRSS improved from 17.12 to 14.6 in all 34 patients. Out of 34 patients 15 who were on regime 1 mean MRSS improved from 20.33 to 16.07. In regime 2 mean MRSS improved from 23 to 16. In regime 3 mean MRSS improved from 10.33 to 8. In regime 4 mean MRSS improved from 17.33 to 15. MRSS worsened from 12 to 13.38 in the group of patients who were not on immunosupressants.

In one patient, only on Azathioprine; MRSS improved from 6 to 4 **(TABLES 1-8)**.

Discussion

In our study mean MRSS fell from 17.12 to 14.28 which was statistically significant (P<0.05). Consistent with the study of ESOS [5]; ASTIS [6] and SLS-I [7] and SLS-II [8] which suggests benefit in MRSS from immunosuppressant. In our study at 24 months a mean change of

Table 1. Mean MRSS.

No. of Pts (N)	Pre-treatment MRSS (Mean)	Post treatment MRSS (Mean)	Sig.
34	17.12	14.26	0.000

Table 2. Different regime statistics.

Regime	Pre-treatment MRSS	Post-treatment MRSS	Sig.
Cyclo+MMF N=15	20.33	16.07	0.000
Cyclo+AZA N=4	23	16	0.004
MMF N=3	10.33	8	0.121
Cyclo N=3	17.33	15.00	0.073
No treatment N=8	12	13.38	0.000

Table 3. Paired samples statistics.

		Mean	N	Std. Deviation	Std. Error Mean
Pair 1	Initial RSS	17.12	34	8.950	1.535
	post_tt	14.26	34	8.262	14.17

Table 4. Paired samples correlations.

	N	Correlation	Sig.
Pair Initial RSS & post tt	34	0.913	0.000

Table 5. Paired samples test.

Paired differences						t	df	Sig. (2-tailed)
	Mean	Std. Deviation	Std. Error mean	95% Confidence interval of the difference				
				Lower	upper			
Pair1 Initial RSS-post_tt	2.853	3.653	0.626	1.578	4.127	4.554	33	0.000

Table 6. Paired samples test[a].

Treatment Received	Paired Differences					t	df	Sig. (2-tailed)
	Mean	Std. Deviation	Std. error Mean	95% confidence interval of the difference				
				Lower	Upper			
Cyclo_mmf pair1 initialRSS-post_tt	4.267	3.353	0.913	2.309	6.224	4.675	14	0.000
Cyclo_azuro n pair1 initialRSS-post_tt	7.000	1.155	0.577	5.163	8.837	12.124	3	0.001
mmf pair1 initialRSS-post_tt	2.333	0.577	0.333	0.899	3.768	7.000	2	0.020
Sildanafil pair1 initialRSS-post_tt	-1.375	1.061	0.375	-2.262	-0.488	-3.667	7	0.008
Cyclo pair1 initialRSS-post_tt	2.333	2.082	1.202	-2.838	7.504	1.941	2	0.192

[a]No statistics are computed for one or more split lines.

Table 7. Paired sample statistics[a].						
Treatment Received			**Mean**	**N**	**Std. Deviation**	**Std. Error Mean**
cyclo	Pair1	initialRSS	20.33	15	9.933	2.565
		post_tt	16.07	15	9.595	2.477
cyclo azuron	Pair1	initialRSS	23.00	4	9.309	4.655
		post_tt	16.00	4	10.066	5.033
mmf	Pair1	initialRSS	10.33	3	1.528	0.882
		post_tt	8.00	3	2.000	1.155
sildanafil	Pair1	initialRSS	12.00	8	5.099	1.803
		post_tt	13.38	8	6.116	2.162
cyclo	Pair1	initialRSS	17.33	3	5.033	2.906
		post_tt	15.00	3	7.000	4.041
azuron il	Pair1	initialRSS-sildenaf post_tt	6.00 4.00	1[a] 1[a]	-	-

[a]The correlation and t cannot be computed because the sum of case weight is less than or equal to 1.

Table 8. Paired samples correlation[a].					
Treatment Received			**N**	**Correlation**	**Sig.**
Cyclo mmf	Pair1	initialRSS post_tt	15	0.935	0.000
Cyclo azuron	Pair1	initialRSS post_tt	4	0.996	0.004
MMF	Pair1	initialRSS post_tt	3	0.982	0.121
Sildanafil	Pair1	initialRSS post_tt	8	0.999	0.000
Cyclo	Pair1	initialRSS post_tt	3	0.993	0.073

[a]No statistics are computed for one or more split files.

-2.86 from baseline mean of 17.12 as compared to mean change of -6.7 from median baseline MRSS 21 in ESOS study. In the study conducted by Herrick et al., MRSS decreased from 24 at baseline to 15.5 at 3 years [9].

In our study MMF group MRSS improved from 10.33 to 8. In a prospective observational study of MMF treatment in SSC of recent onset MRSS improved from 24.56 to 14.53 at 18 months of treatment [10].

In ESOS trial there were -4.1 fall in MMF group. In Cyclophosphamide group MRSS improved from 17.33 to 15.00 (-2.3) as compared to -3.3 in ESOS study. In no immunosuppressant limb MRSS worsened from 12.00 to 13.38. However in ESOS there was improvement and a fall of -2.2 in MRSS. In our study 15 patients who were on monthly doses of cyclophosphamide for 6 months followed by 18 months MMF mean MRSS improved from 20.33 to 16.07. In 4 patients who were on monthly IV cyclophosphamide 6 doses followed by Azathioprine 18 months mean MRSS improved from 23 to 16. One patient among 34 patients was on Azathioprine for 24 months whose MRSS improved from 6-4. In our study those patients on immunosuppressant improved in MRSS scoring and the group not on any immunosuppressant worsened (12-13.38). Thus, confirming the importance of immunosuppressant for managing skin thickening in scleroderma.

Conclusion

Improvement observed in all regimens of immunosuppressant and worsened in those without immunosuppressant. So thought for patients with diffuse scleroderma of significant magnitude without any indication for immunosupressants for other system involvement like ILD with FVC more than 70% deserves a consensus among the Rheumatologists.

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