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RESEARCH ARTICLE

A COMPARATIVE EVALUATION OF EFFICACY OF METHOTREXATE VERSUS METHOTREXATE AND SULPHASALAZINE COMBINATION THERAPY IN EARLY RHEUMATOID ARTHRITIS

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Key words:

MTX(Methotrexate), SSZ(Sulphasalazine), RA(Rheumatoid Arthritis), PPF(Poor prognostic fator), DAS(Disease Activity Score), CDAI(Clinical Disease Activity Index), SDAI(Simplified Disease Activity Index), HAQ(Health Assessment Questionnaire), ACR(American College of Rheumatology), DA(Disease Activity),

ABSTRACT

Background: The study was conducted to assess the efficacy of MTX and MTX+SSZ combination in early RA with low & moderate disease activity, in absence of PPF, in terms of Disease Activity Score, to review the validity of ACR 2012 recommendation, in eastern Indian population region.
Methods: Patients with early RA with low & moderate disease activity without PPF in eastern Indian population region were allocated into mono and dual DMARD groups. Efficacy evaluated by DAS 28, CDAI, SDAI, HAQ score between two groups at 12 wks and 24 wks.
Results: The study showed no statistically significant difference of Disease Activity scores in between two groups evaluated at 12 weeks and 24 weeks. But there was significant difference in Disease activity scores in 12 weeks and 24 weeks in comparison to 0 week value in both the groups.
Conclusions: In patients with early RA with low to moderate disease activity without PPF, dual therapy is equally effective as compared to mono therapy.

INTRODUCTION

ACR 2012 recommended DMARDS monotherapy in early RA (except those with high DA and PPF), most of the clinical trials favour combination DMARDS over monotherapy in early RA[1]. Further evidences in different regional population would be worthwhile to review this issue. No study yet has been conducted in this part of the country addressing efficacy of methotrexate versus methotrexate and sulphasalazine combination therapy in early RA with low & moderate DA and in absence of PPF. This study is therefore undertaken to review the validity of ACR 2012 recommandation, in this regional population with early RA.

Aims and Objectives

To assess efficacy of MTX and MTX+SSZ combination in study population in terms of Disease Activity Scores.

MATERIALS AND METHODS

Patients with early RA with low & moderate DA without PPF were randomly allotted of mono (Group A*[n = 28]* -MTX) and dual (Group B*[n = 32]* -MTX+SSZ) DMARDS. Treatment implemented and 6 weeks dose adjustment period allowed. Efficacy evaluated in terms of disease activity scores(DAS 28, CDAI , SDAI , HAQ) between two groups at 12 wks and 24 wks. Two patients from group B were excluded because of persistent adverse drug reactions, Group B [n =32-2=30].

The prospective, comparative, interventional study was conducted over a period of approximately 1.5 years (Feb 2014-Aug 2015) in eastern Indian population region.

Patients with other morbidity including –chronic liver disease, severe anemia, active tuberculosis, HIV, IBD, pregnancy, hypersensitivity to SSZ, renal failure, diabetes, patients with child bearing age were excluded from the study.

Data was analyzed by Epi-info 7.1.2.0, (CDC-ATLANTA), and are presented in simple Proportions. Chi square test were applied as test of significance for non parametric data. P value of <0.05was considered to be significant.

RESULTS & ANALYSIS

There was no statistically significant difference of different Disease Activity scores between two groups at initial evaluation (Table1, Figure 1).

The study showed no statistically significant difference of Disease Activity scores in between two groups evaluated at 12 weeks and 24 weeks (Table 2 and Figure 2, 3).

But there was significant difference in Disease activity scores in 12 weeks and 24 weeks in comparison to 0 week value in both the groups (Table 3, 4 and Figure 4, 5, 6, 7).

Table 1 Mean values of Disease Activity scores at initial evaluation

Parameters	Mono	Dual	P value
DAS-28	4.19±0.3	4.16±0.35	0.697
SDAI	12.8±2.6	12.81±2.93	0.987
CDAI	11.64±2.28	11.53±2.54	0.859
HAQ DI	1.46±0.16	1.52±0.157	0.141

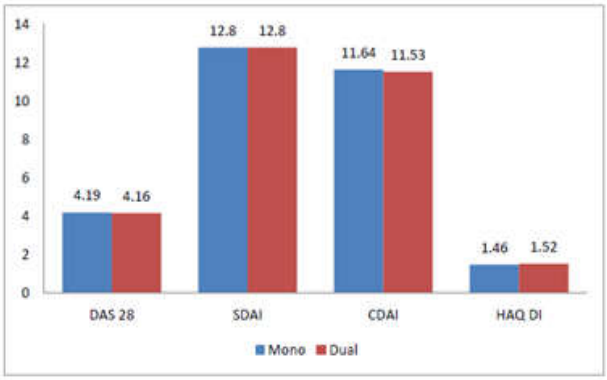


Figure 1 Bar diagram showing mean values of different disease activity scores among mono & dual groups at initial evaluation.

Table 2 showing different Disease Activity scores at 12 weeks and 24 weeks between mono and dual groups.

Parameters	At 12 weeks		P value	At 24 weeks		P value
	Mono	dual		mono	dual	
DAS-28	2.32±0.69	2.35±0.6	0.837	2.03±0.78	2.08±0.77	0.823
SDAI	3.28±1.85	3.42±1.85]	0.771	2.35±2.67	2.2±2.07	0.815
CDAI	2.82±1.78	2.93±1.78	0.812	1.82±2.43	1.67±1.86	0.786
HAQ DI	0.63±0.38	0.60±0.4	0.788	0.44±0.57	0.46±0.54	0.879

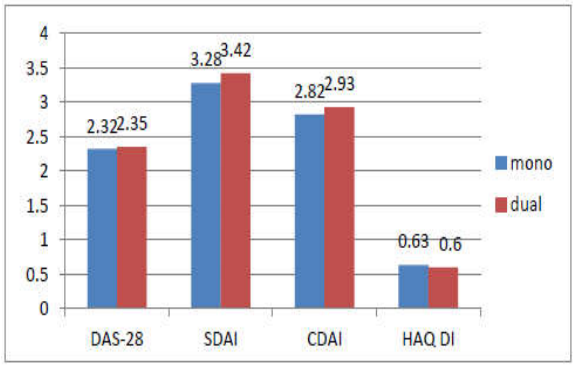


Figure 2 Bar diagram showing comparison of different Disease activity scores at 12 weeks between mono and dual groups.

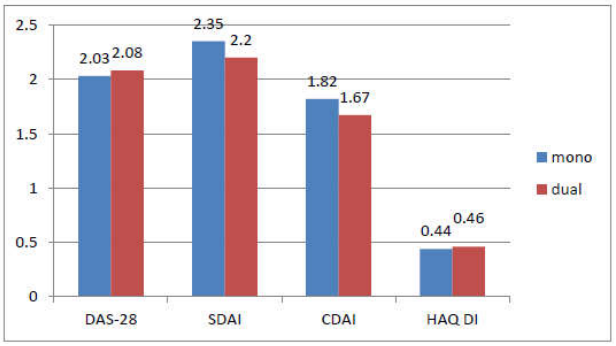


Fig-3 Bar diagram showing comparison of different Disease activity scores at 24 weeks between mono and dual groups.

Table 3 Comparison of different Disease Activity scores at 0 and 12 weeks in both groups

Parameters	Mono		P value	Dual		P value
	0 week	12week		0 week	12 week	
DAS-28	4.19±0.3	2.32±0.69	<.001	4.16±0.35	2.35±0.6	<.001
SDAI	12.8±2.6	3.28±1.85	<.001	12.81±2.93	3.42±1.851	<.001
CDAI	11.64±2.28	2.82±1.78	<.001	11.53±2.54	2.93±1.78	<.001
HAQ DI	1.46±0.16	0.63±0.38	<.001	1.52±0.157	0.60±0.4	<.001

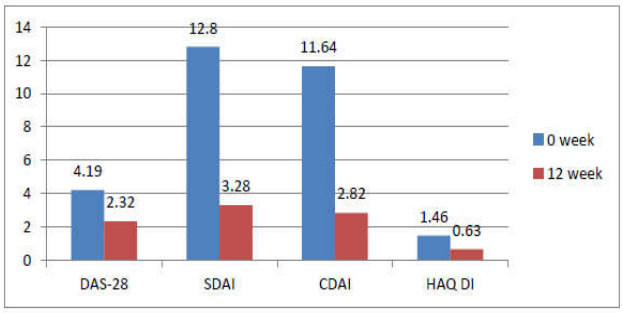


Fig-4 Bar diagram showing comparison of different Disease Activity scores at 0 and 12 weeks in mono group.

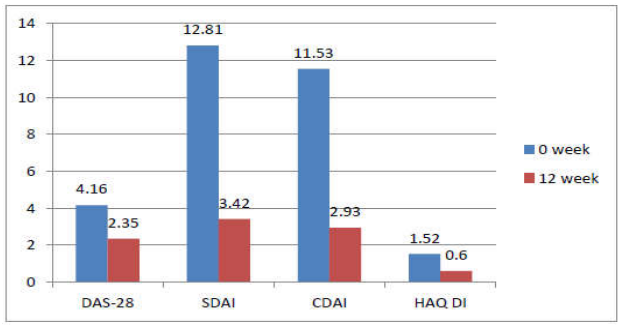


Fig -5 Bar diagram showing comparison of different Disease Activity scores at 0 and 12 weeks in dual group.

Table 4 Comparison of different Disease activity scores at 0 and 24 weeks in both groups

Parameters	Mono		P value	Dual		P value
	0 week	24week		0 week	24week	
DAS-28	4.19±0.3	2.03±0.78	<.001	4.16±0.35	2.08±0.77	<.001
SDAI	12.8±2.6	2.35±2.67	<.001	12.81±2.93	2.2±2.07	<.001
CDAI	11.64±2.28	1.82±2.43	<.001	11.53±2.54	1.67±1.86	<.001
HAQ DI	1.46±0.16	0.44±0.57	<.001	1.52±0.157	0.46±0.54	<.001

Fig-6 Bar diagram showing comparison of different Disease activity scores at 0 and 24 weeks in mono group.

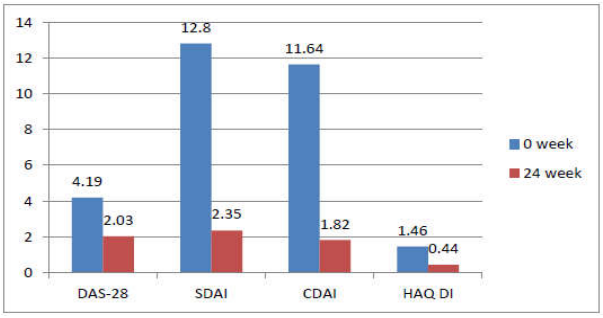
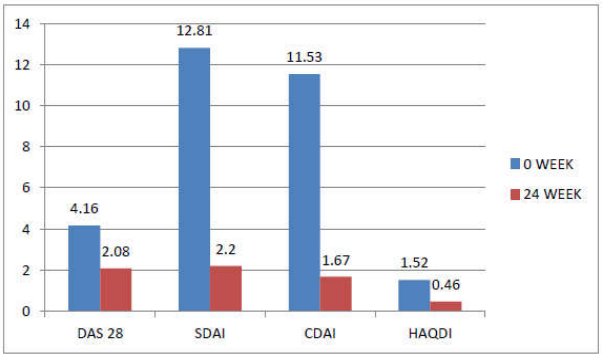


Fig-7 Bar diagram showing comparison of different Disease activity scores at 0 and 24 weeks in dual group.



DISCUSSION

In these study patients with ERA the initial mean values of the all disease activity indices were within the low to moderate disease activity range.

Mean value of DAS 28 score in mono group was 4.19±0.3 and that of dual group was 4.16±0.35. Mean value of SDAI in mono group was 12.8±2.6 and that of dual group was 12.81±2.93. Mean value of CDAI score in mono group was 11.64±2.28 and that of dual group was 11.53±2.54. At the time of enrolment there was also no significant difference in disease activity (DAS-28, SDAI, CDAI, HAQDI) among mono and dual groups of patients.

There was no significant difference between both the groups, at 12 and 24 weeks, regarding disease activity indices.

There was significant difference of disease activity (p value <0.01) in patients of mono and dual groups at 12 weeks and 24 weeks compared to disease activity at 0 week.

The study showed significant a benefit with MTX with early RA establishing a window opportunity in the treatment of RA, as shown by PROMPT trail [2].

It was found that dual therapy did not provide any significant additional benefit, as compared to monotherapy using either agent, also corroborated by Haagsma *et al*.[3] This study has got similar result to that of Schipper LG *et al* [4] –demonstrating that in rheumatoid arthritis (RA) patients who failed to sulphasalazine (SSZ), the clinical efficacy of methotrexate (MTX) monotherapy was similar to that of the dual therapy.

On the contrary this study did not support the findings of Dougados *et al* [5] which demonstrated that combination therapy produced a statistically greater improvement in 1-year disease activity score compared with either monotherapy in early RA. Similarly MASCOT trial[6], COBRA trial[7] and FIN-RACO trail[8] showed better response in group where combination DMARDS started earlier.

Variability of efficacy of therapy with mono and dual DMARDs in different studies may be due to different inclusion criteria, absence of specification of prognostic factors and disease activity related categorization as well as number of patients enrolled.

This study included relatively small number of patients of a specific subgroup. Efficacy of DMARDS on disease activity indices may not be appreciable in this small study population. Larger studies are needed to establish the validity the study result.

CONCLUSION

Mono therapy (MTX) and Dual therapy (MTX+SSZ) were equally effective in similar group of in patients with early RA with low to moderate disease activity without poor prognostic factors at 12 and 24 weeks.

References

1. Singh JA, Furst DE, Bharat A, *et al*. 2012 Update of the 2008 American College of Rheumatology (ACR) Recommendations for the use of Disease-Modifying Anti-Rheumatic Drugs and Biologics in the treatment of Rheumatoid Arthritis (RA). *Arthritis care & research*. 2012; 64 (5): 625-639. doi:10.1002/acr. 21641.
2. Contreras-Yáñez I, Pascual-Ramos V. Window of opportunity to achieve major outcomes in early rheumatoid arthritis patients: how persistence with therapy matters. *Arthritis Research & Therapy*. 2015; 17(1):177. doi:10.1186/s13075-015-0697-z.
3. Haagsma CJ, van Riel PL, de Jong AJ, *et al* (1997) Combination of sulphasalazine and methotrexate versus the single components in early rheumatoid arthritis: a randomised, controlled, double-blind, 52 week clinical trial. Br J Rheumatol. 1997 Oct;36(10):1082-8
4. 4. LG Schipper, J Fransen, P Barrera *et al* Methotrexate in combination with sulfasalazine is more effective in rheumatoid arthritis patients who failed sulfasalazine than in patients naïve to both drugs. Rheumatology (Oxford). 2009 Jul; 48(7):828-33. doi: 10.1093/rheumatology/kep090. Epub 2009 May 20
5. Dougados M, Combe B, Cantagrel A, *et al*. Combination therapy in early rheumatoid arthritis: a randomised, controlled, double blind 52 week clinical trial of sulphasalazine and methotrexate compared with the single components. *Annals of the Rheumatic Diseases*. 1999;58(4):220-225.
6. Capell HA, Madhok R, Porter DR *et al* (2006) Combination therapy with sulphasalazine and methotrexate is more effective than either drug alone in rheumatoid arthritis (RA) patients with a suboptimal response to sulphasalazine: results from the double blind placebo controlled MASCOT study. Ann Rheum Dis. 2007 Feb; 66(2):235-41. Epub 2006 Aug 22
7. Landewé RB, Boers M, Verhoeven AC *et al*. COBRA combination therapy in patients with early rheumatoid arthritis: long-term structural benefits

of a brief intervention. Arthritis Rheum. 2002 Feb;46(2):347-56

8. Mottonen-T, Hannonen-P, Nissila M. *et al*. Comparison of combination therapy with single-drug therapy in early rheumatoid arthritis: a randomised trial. FIN-RACo trial group. Lancet. 1999 May 8; 353 (9164):1568-73.