ORIGINAL RESEARCH PAPER

Rheumatology

COMPARATIVE EFFICACY AND TOLERABILITY OF INFLIXIMAB VERSUS SULFASALAZINE ADD ON METHOTREXATE IN EARLY RHEUMATOID ARTHRITIS WITH POOR PROGNOSTIC FACTORS

KEY WORDS: Rheumatoid Arthritis, Methotrexate, Sulfasalazine, Infliximab

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ABSTRACT

Introduction- Rheumatoid arthritis (RA) is a chronic multisystem disorder, characterised by persistent inflammatory synovitis usually involving peripheral joints in a symmetric fashion. **Aims & Objectives**-To compare the efficacy and tolerability of sulfasalazine + methotrexate (arm A) versus infliximab + methotrexate (arm B) in patients with early rheumatoid arthritis with poor prognostic factors. **Materials & method**-54 adult patients with early RA with poor prognostic factors, attending BSMC&H, IPD and OPD ,excluding patients with established RA, contraindications to the drugs and patients with other comorbidities are taken into consideration for this randomised single blind clinical trial. **Observations**-The result showed that both the treatment regimens were similar to each other in term of DAS28 and CDAI scores except HAQ score which was better with arm B. **Conclusion**-Our study have shown noninferiority of infliximab to sulfasalazine add on methotrexate in treatment of early RA , and both regimens are well tolerated.

INTRODUCTION

In the Indian literature, Charak Samhita (Approx.300-200 BC) describes pain, joint swelling and loss of function.[1] Camroe(1940) coined the term Rheumatoloist while the word Rheumatology appease first time in the text book by Hollander (1949).[2] A B Garrod(1858) coined the term Rheumatoid Arthritis(RA).

RA is perhaps the most common inflammatory polyarthritis in adult populations.[3] It is basically a chronic multisystem immunologically mediated disease in association with HLA, some genetic & environmental factors.

Although cartilage destruction, bony erosion, joint deformity are hallmark of the disease, the course of RA is quite variable. RA affects 0.5-1% of adult population worldwide. RA occurs more commonly in females than males with a 2-3;1 ratio.[4] The incidence of RA increases between 25 and 55 years of age, after whichit plateaus until the age of 75 then decreases.[5] Destructive potential of the disease exerts considerable physical and economical burden to the effected populations as well as society in turns substantial morbidity, disability, accelerated mortality, loss of working days and consumption of heath care resources.[6]

Optimum care of patients with RA requires an integrated approach that includes non-pharmacological therapies & pharmacological agents such as non-biologic & biological Disease Modifying Antirheumatic Drugs (DMARDs), NSAIDs, analgesics & corticosteroids. Early RA is defined as disease duration <6 months.[7] This period is known as "window-of-opportunity."[8] According to ACR 2012 treatment guideline patient with early RA (with moderate or high disease activity) With poor prognostic factors, should be treated with combination DMARD therapy which includes non-biologic or biologic DMARDs.[9]

MATERIALS &METHODS

It is a single bind randomised clinical trial. 54 patients attending OPD and IPD of BSMC & H were taken into consideration and divided into two arms containing equal no of patients i. e arm A(sulfasalazine + methotrexate), & arm B (infliximab + methotrexate).

All patients are adult with early RA with poor prognostic factors. Patient with established RA, contraindication to infliximab, sulfasalazine, methotrexate and with other comorbidities that can impair disease activity like cardiac failure, chronic liver disease, chronic kidney disease, diabetes mellitus, hypertension etc are excluded. Disease activity is monitored through DAS 28, CDAI and HAQ. Tolerability is monitored by emergence of effects of drugs.

RESULTS &ANALYSIS

The table shows that the individuals belonging to the Arm B have significantly low level of serum SGOT & SGPT at the beginning of the study. After treatment with respective regimen the subjects of each Arm became alike in respects of all the parameters except the platelet count which seemed to be significantly low among the patients belonged to Arm B.

Table 1:distribution Of Study Subjects According To Various Laboratory Parameters At Diffrent Levels Of Evalution.

Attributes	group	N	Mean	Std. Deviation	Unpaired , P at df 52*
Hb gm% 0wk	A	27	10.35	0.741	0.219, 0.828
	B	27	10.30	0.753	
TLC 0wk	A	27	6711.11	1241.071	0.972, 0.335
	B	27	6362.96	1386.237	
PLAT 0wk	A	27	2.38	0.606	0.048, 0.962
	B	27	2.37	0.526	
SGOT 0wk	A	27	35.37	5.001	3.666, 0.001
	B	27	30.74	4.248	
SGPT 0wk	A	27	34.22	5.033	3.060, 0.003
	B	27	30.11	4.838	
HB gm% 12wk	A	27	10.49	0.662	1.249, 0.217
	B	27	10.72	0.645	
TLC 12wk	A	27	6614.81	1392.205	0.913,0.366
	B	27	6251.85	1527.031	
PLAT 12wk	A	27	2.44	0.544	0.800, 0.427
	B	27	2.33	0.474	
SGOT 12wk	A	27	33.74	6.419	0.037,0.971
	B	27	33.85	14.411	
SGPT 12wk	A	27	38.07	15.645	1.936, 0.058
	B	27	30.59	12.586	
HB gm% 24wk	A	27	10.51	2.209	1.204, 0.234
	B	27	11.04	0.520	

TLC 24wk	A	27	6250.00	1710.544	0.452, 0.653
	B	27	6060.00	1354.866	
Platelet 24wk	A	27	2.42	0.665	2.685, 0.010
	B	27	1.94	0.663	
SGOT 24wk	A	27	35.48	9.039	0.620, 0.538
	B	27	33.78	11.057	

Table-10: Distribution of participants according to their ESR level at 0, 12 and 24 weeks of study

Arms	0 weeks		12 weeks		24 weeks	
	mean±sd		mean±sd		mean±sd	Unpaired t at df 51,p
A(n_1=27)	45.48		25.41		15.92*	2.479,0.017
B(n_2=27)	49.59		26.22		14.07	

*Arm-A contains 26 participants

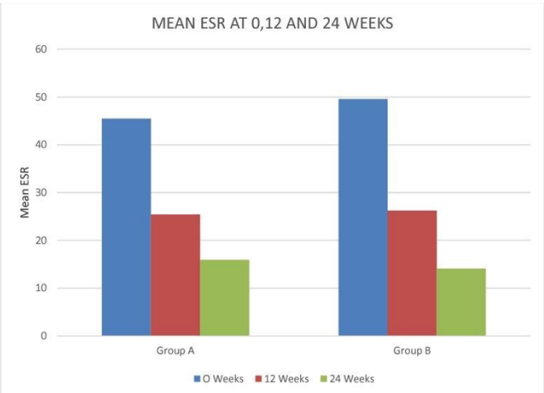


FIG 10: Bar diagram showing mean ESR at 0,12 & 24 weeks

Table-12: Distribution of participants according to their DAS 28 score at 0, 12 and 24 weeks of study

DAS28 level	Weeks of evaluation								
	0			12			24		
	A(n_1=27)	B(n_2=27)	χ^2, p	A(n_1=27)	B(n_2=27)	χ^2, p	A(n_1=26)	B(n_2=27)	χ^2, p
	No. (%)	No. (%)		No. (%)	No. (%)		No. (%)	No. (%)	
>5.1	13 (48.15)	16(59.26)	0.67,0.412	01(3.7)	-	1.02*, 0.312	-	-	---
>3.2-≤5.1	14(51.85)	11(40.74%)		24(88.89)	23(85.19)		3(11.54)	2(7.41)	1.06*, 0.588
>2.6-<5.1	-	-	--	2(7.41)	4(14.81)		14(53.85)	12(44.44)	
≤2.6	-	-	--	-	-	--	9(34.61)	13(48.15)	
Total	27(100)	27(100)	----	27(100)	27(100)	---	26(100)	27(100)	--

*Row with small value was clubbed with next row with comparatively higher value & df forχ^2 test was 1in all cases.

According to the DAS28 criteria most of the patients of both the Arms were suffering from severe to moderate disease status at the beginning of the study. No significant between arms difference in this regard. At 12 week's evaluation it was found to be mainly of moderate to mild variety and the arms were comparable regarding this. In the final evaluation done at 24 weeks it was found that most of the patients were revealed to sustain mild or remission status of the disease. However, the groups were comparable in this matter.[Table-12]

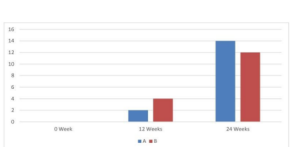


Fig 14: Bar diagram showing Low DA at 12 & 24 weeks as per DAS28 Score

Analysis shows:

2(7.41%) and 4(14.81%) patients in Arm A and Arm B respectively, achieved Low DA at 12 weeks

14(53.8%) and 12(44.44%)patients in Arm A and Arm B respectively, achieved low DA at 24 weeks

Fig 15: Bar diagram showing Remission at 12 & 24 weeks as per DAS28 Score

Remission was achieved in 9(34.61%) vs 13(48.15%) patients in Arm A and Arm B respectively.

Table-13: Distribution of participants according to their HAQ, CDAI and DAS 28 scores at 0, 12 and 24 weeks of study

Week	Parameters/Criteria of evaluation								
	DAS28			CDAI			HAQ		
	Arm-A [n_1=27] (mean±sd)	Arm-B [n_2=27] (mean±sd)	Independent t, p	Arm-A[n_1=27] (mean±sd)	Arm-B[n_2=27] (mean±sd)	Independent t, p	Arm-A [n_1=26] (mean±sd)	Arm-B [n_2=27] (mean±sd)	Independent t, p
0	5.36	5.51	0.838, 0.406	22.11	22.22	0.083, 0.934	1.42	1.48	0.872, 0.387
12	3.95	3.85	1.354, 0.181	10.96	9.74	1.021, 0.312	0.97	0.96	0.693, 0.492
24	2.68	2.48	1.521,0.135	3.88	3.11	1.339, 0.196	0.63	0.55	2.197, 0.033

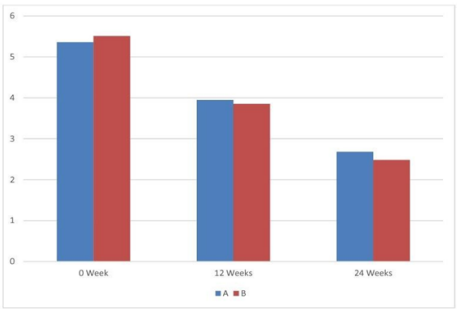
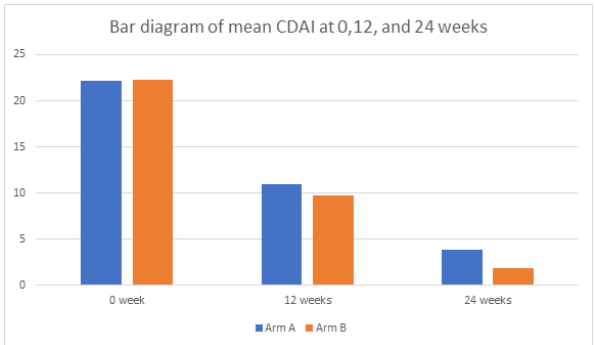
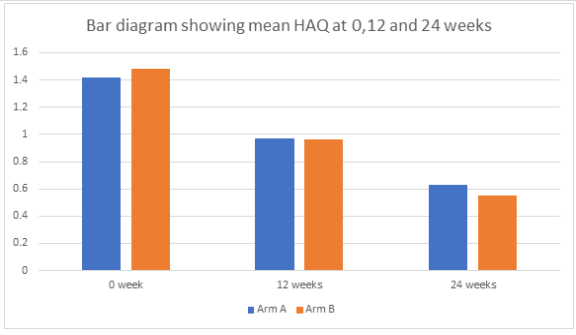


Fig 16: Bar diagram of mean DAS28 at 0,12 and 24 weeks





DISCUSSION

In this study , majority of patient are in age group 26-45 yrs, female to male ratio 3.96:1.There was no statistical difference in gender ratio between the two arms. At the time of enrollment there was no significant difference in disease activity (DAS 28, CDAI, HAQ) among arm A & arm B . Analysis revealed that over the time the group the groups were found to similar in respect of all the three measuring disease markers except HAQ score which was found to be significantly lower in arm B at 24 weeks. There was no flare or relapse , neither any Adverse Drug Reaction requiring drug withdrawal in any of the arms during the period of study in both the treatment arms.

CONCLUSION

Our study have shown non-inferiority of infliximab to sulfasalazine add on methotrexate in treatment of early RA with poor prognostic factors (with moderate to severe disease activity) in this regional population catered by BSMC&H. Bother the treatment regimens are similar in respect of all

disease activity markers except HAQ which was found to be better with infliximab plus methotrexate at 24 weeks . All drugs are well tolerated.

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