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CORRELATION BETWEEN TREATMENT OF RHEUMATOID ARTHRITIS USING NON BIOLOGICAL DMARDS AND DISEASE ACTIVITY USING RAPID-3 SCALE

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ABSTRACT
Rheumatoid Arthritis (RA) is a chronic inflammatory autoimmune disorder which results in destruction of joints with increased morbidity and mortality. Due to requirement of prolonged therapy it is need of hour to evaluate the correlation between RAPID-3 (Routine Assessment of Patient Index Data 3) and disease activity among patients treated for RA using non-biological disease modifying anti rheumatoid drugs. Hence this randomized cross sectional study was planned to done among patients attending Orthopaedic OPD, found suitable after applying inclusion and exclusion criteria. Patients were divided into 5 groups on the basis of drugs prescribed to them. Group A was prescribed with Methotrexate, Hydrxychloroquine, Deflazacort and Piroxicam. Group B was prescribed with Methotrexate, Salfasalazine, Deflazacort and Piroxicam. Group C was prescribed with Methotrexate, Hydroxychloroquine and Piroxicam. Group D was prescribed with Methotrexate Salfasalazine and Aceclofenac and Group E was prescribed with Methotrexate, Hydroxychloroquine and Aceclofenac. RAPID-3 score of patients at day 0 and after 60 days of treatment were noted and evaluation was done for correlation and efficacy of treatment. In our study this was observed that (n=08) patients of Group A had shown the most efficacy towards treatment of RA which was reflected by significant decrease in mean RAPID-3 score of these patients after 60 days of treatment. Our study indicates that RAPID-3 scoring system can used as a reliable tool for quick assessment of disease activity and efficacy of treatment in a busy clinical environment.

KEYWORDS: Rheumatoid Arthritis, RAPID-3, Disease Modifying Anti-Rheumatoid Drugs.

INTRODUCTION
Rheumatoid Arthritis is a slow progressive autoimmune disease, with widespread systemic effects, with main effect on muscular-skeletal system which results in progressive destruction and deformity of joints. Patients of RA have destruction of joints which cause severe disability, decreased quality of life, early onset of co-morbidities increased morbidity and early mortality.[1]

BACKGROUND
RA is a chronic disease and needs long term treatment. Patients of RA are treated either with Non Biological conventional Disease Modifying Anti-Rheumatoid Drugs (DMARDs) or Biological DMARDs usually along with Non Steroidal Anti-Inflammatory drugs (NSAIDs). Other drugs like Folic Acid (FA), Proton Pump Inhibitors (PPI) etc are also combined some times to either increase efficacy or compliance with treatment or to reduce adverse effects of the treatment. When conventional non biological DMARDs are used, major drugs used are Methotrexate (MTX), Sulfasalazine (SSZ), and Hydroxychloroquine (HCQ). Steriods are also used for their excellent inflammation suppression property; some major candidates used in this group are Prednisolone (PDS), Deflazacort (DZC) and Methylprednisolone (MPS). Among NSAIDSs Piroxicam (P), Aceclofenac (ACF) and Diclofenac (D), are commonly used. Rabeprazole and Pantoprazole are most commonly used PPIs.

As far as treatment duration is concerned, treatment is long term with use of multiple drugs simultaneously. This prolonged exposure to drugs demands regular estimation of disease activity so that modifications in drug regime can be done accordingly. First measurement tool to be used in RA was developed as early as in 1950.[2] Since then many tools and scoring patterns have been developed and used to monitor the efficacy of RA treatment among treated group. Out of these 63 currently available disease activity assessment tools, American College of Rheumatology filtered and ultimately recommended use of 6 of theme i.e. CDAI (Clinical

Disease Activity Index), DAS28 (Disease Activity Score -28), PAS (Patient Activity Scale), PAS II (Patient Activity Scale-II), RAPID-3 (Routine Assessment of Patient Index Data 3) and SDAI (Simplified Disease Activity Index).

Patient-driven composite tools which were found to be appropriate to be used in clinical practice are PAS,[3] PAS-II[3] and RAPID-3.[4] Out of them RAPID-3 scoring system is found to have acceptable reliability (test-retest, reliability for composite has not been evaluated), good validity and responsiveness acceptable for individual component.[5] RAPID-3 is a pooled index of the 3 patient-reported American College of Rheumatology rheumatoid arthritis (RA) Core Data Set measures: function, pain, and patient global estimate of status. Each of the 3 individual measures is scored 0 to 10, for a total of 30. Disease severity may be classified on the basis of RAPID3 scores: >12 = high; 6.1–12 = moderate; 3.1–6 = low; ≤3 = remission. RAPID-3 is relatively easy to use in clinical practice as they don't require formal joint counts. RAPID-3 has been tested in other Rheumatic conditions too and its use is not only limited to RA and therefore can be applied more broadly in clinical practice.

Our study is aimed to find correlation between treatment of RA and disease activity by using patient driven tool i.e. RAPID-3 scoring system. As per our search no study had till now used RAPID-3 scale as a single tool to asses disease.

MATERIALS AND METHODS

Diagnosed patients of Rheumatoid Arthritis attending the Orthopaedic OPD at Teerthanker Mahaveer Medical College, Moradabad, over a period of six months were selected after applying inclusion and exclusion criteria. Informed consent was taken from every participant of this study. Record of each patient is maintained individually which include personal history, medical history, family history, drug history and allergic history. Details of drug prescribed are then noted, patients are maintained on same medication with minimal changes in dosing schedule if necessary for entire duration of study i.e. 60 days.

Inclusion Criteria: Known cases of RA not on regular medication for 8 weeks or more or newly diagnosed patients of either gender aged 18 years to 70 years attending Orthopaedic OPD were included in the study after taking written informed consent.

Exclusion Criteria: Patients aged less than 18 years and more than 70 years, pregnant females and lactating mothers, patient suffering from terminal diseases, patients with serious infections like pulmonary Tb, HIV etc and patients with serious hepatic or kidney dysfunctions or refused to give informed consent were excluded from study.

Evaluation of efficacy was done with the help of RAPID-3 scoringRAPID-3 Score of each patient was obtained at 0 and 60 days of treatment and compared to know the efficacy of treatment.

Study was approved by Institutional Ethical Committee. Statical analysis was done using Microsoft excel and SPSS ver. 20. Paired "t" test was applied to get P value. P value <0.001 at 95 confidence interval is statically significant. Correlation coefficient "r" was derived using mean and standard deviation.

RESULTS

Total 72 patients were selected for evaluation after applying inclusion and exclusion criteria, during follow-up 12 patients left the study in between and final data is of 60 patients.

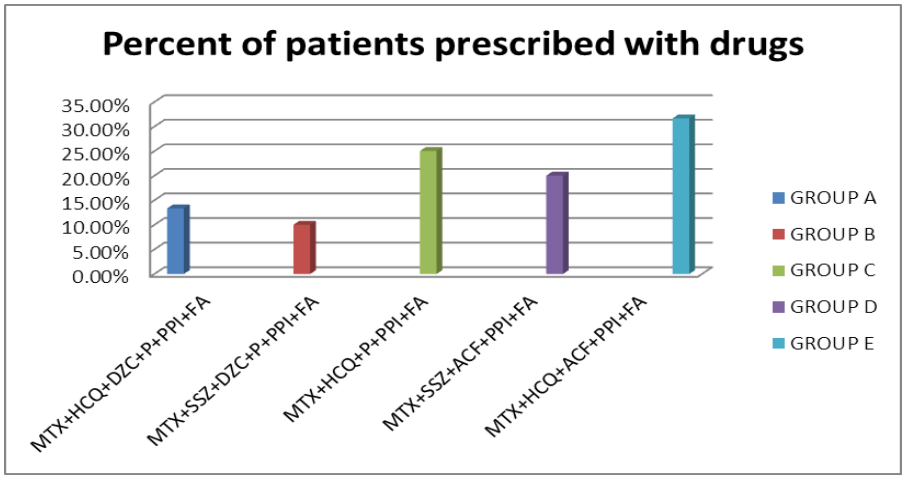
Demographic Distribution

After evaluation of results we came to know that RA is much evident in females n=49 (81.66%) as compared to males n=11 (18.33%). Age wise distribution is RA is shown in table below.

Table. 1: Demographic distribution of patients.

S. No	Age Group (Years)	SEX	No. of Pt.	New Case	Old Case	Rural	Urban	Co-Morbidity Present	Average Duration of symptoms
1	18 to 30	Male	00	-	-	-	-	-	-
		Females	01	01	-	-	01	-	2 months
2	31 to 40	Male	05	02	03	02	03	-	2 months
		Female	21	21	-	06	15	-	1.8 months
3	41 to 50	Male	04	03	01	02	02	-	1.5 months
		Female	16	07	09	08	08	04	1.6 months
4	51 to 60	Male	01	-	01	-	01	-	2 months
		Female	08	05	03	04	04	02	1.5 months
5	61 to 70	Male	01	-	01	-	01	-	1 month
		Female	03	01	02	-	03	01	1.3 months

All patients are divided into 5 groups as per drugs used in treatment. Drugs used in percent of patients in each treatment group are shown below.



Graph. 1: Percent of patients prescribed with drugs of each group.

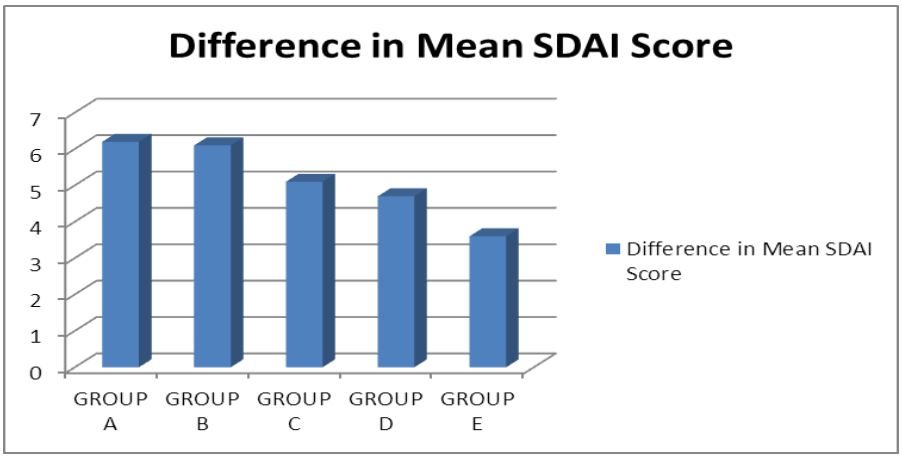
RAPID-3 score were obtained at starting of treatment i.e. at 0 and again after 60 days of treatment. Mean RAPID-3 score, with standard deviation P value and correlation coefficient "r" are then derived from these scores.

Table. 2: Group wise mean standard deviation and P value.

S. No	GROUP	Mean ± SD RAPID-3 score at 0 days	Mean ± SD RAPID-3 score at 60 days	P value*	Correlation Coefficient "r"
1	GROUP A	21.75 ± 2.43	15.5 ± 1.78	0.0001	0.364
2	GROUP B	22 ± 2.82	15.83 ± 2.40	0.0022	0.117
3	GROUP C	21.07 ± 2.49	15.93 ± 2.86	0.0001	0.62
4	GROUP D	20.92 ± 3.06	16.17± 3.63	0.0022	0.842
5	GROUP E	18.57 ± 2.50	14.9 ± 3.21	0.0003	0.609

* P value <0.001 is statically significant with 95% confidence interval.

When we look at the difference in mean RAPID-3 scores between 0 and 60 days we found results as shown here.



Graph. 2: Difference in mean score of RAPID-3 from 0 to 60 days in different groups.

When we look at the efficacy of drugs in reducing disease activity as seen with decrease in mean RAPID-3 score from day 0 to day 60, we found that GROUP A and GROUP B have similar efficacy with mean RAPID-3 score difference of 6.2 and 6.1 when compared to GROUP E it was almost twice as effective as GROUP E with difference in mean RAPID-3 score of 3.6 only. In our study GROUP C and GROUP D shows almost similar efficacy with difference in mean RAPID-3 score of 5.1 and 4.7 respectively.

DISCUSSION

As per our study using RAPID-3 scoring system it is evident that Group A with MTX+HCQ+DZC was most efficacious followed by Group B having MTX+SSZ+DZC, these results are in correlation with work done by O Dell and co workers in 1996[6] in which superior efficacy was found when MTX was combines with SSZ or HCQ as compared to MTX alone. Haagsma and Colliyes[7] reported moderate trends in favour of SSZ+MTZ versus SSZ or MTX alone. COBRA trail[8]

found that patient treated with combination of MTX with SSZ and prednisolone had higher clinical and radiological improvement as compare to patients treated with SSZ alone.

Other treatment groups with MTX+HCQ+P and MTX+SSZ+ACF had similar efficacy but had lower than GROUP A & B, similar results are found by Dougados and colleagues[9] with significant of DAS score was achieved when combined therapy was given as compared to monotherapy. GROUP E was least efficacious group with MTX+HCQ+ACF.

There was no study which uses RAPID-3 scoring system alone and independently for assessment of efficacy of treatment in RA. Some studies compared RAPID-3 score with DAS-28 scoring systems to estimate disease activity in RA. These studies Pincus et al.[10] Castrejon and Pincus[11] Singh et al.[12] Bossert et al.[13] and Kim et al.[14] found moderate to strong positive correlation between RAPID-3 and DAS-28 when used for estimation of disease activity in RA. One study done by Boone et al.[15] 2015 found that there was poor agreement between RAPID3 and DAS28-ESR when used in common clinical practice, secondly they found that there was only moderate correlation between these two scores at best. One more recent study done by Jesús Giovanny Ballesteros Muñoz, Rodrigo B. Giraldo, et al[16] 2016 says that RAPID-3 had a high correlation with tools which are regularly used in clinical practice for assessing disease activity.

CONCLUSION

From our study we would like to emphasise that in a busy clinical setting RAPID-3 screening system can also be used as a fairly reliable and acceptable tool for assessing disease activity and treatment efficacy. RAPID-3 system in combination with other scoring systems can improve patient outcome with less time consumption of busy clinical practitioner. However more studies with large sample size and cross comparison of all scoring systems with RAPID-3 are needed to prove its usability in clinical setups.

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