

A Study Evaluating Adherence and Compliance of Anti-rheumatic Drugs in Women Suffering from Rheumatoid Arthritis

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ABSTRACT

Background: Treatment of Rheumatoid arthritis (RA) has always remained challenging, complex and associated with high level of non adherence, noncompliance in clinical practice.

Aim: To evaluate the satisfaction/adherence/compliance rates of most commonly prescribed anti-rheumatic drugs among Indian women.

Materials and Methods: A cross-sectional descriptive observational study was undertaken to evaluate the adherence/compliance rates of most commonly prescribed anti-rheumatic drugs among women in a tertiary care teaching hospital in North India. Hundred women on anti rheumatic treatment for rheumatoid arthritis diagnosed by American College of Rheumatology (ACR) criteria were evaluated at one point analysis for adherence/compliance/satisfaction.

Results: Dissatisfaction rate with the anti rheumatic treatment was significantly high $p < 0.0001$ among 68% of the women. Non compliance/ non adherence rate was also recorded very high among 52% and interrupted compliance rate was noticed among 6% of the women suffering from RA. Switch over rate to other treatment or doctors was also significantly ($p < 0.0001$) very high among 66% of the women. Switch over to alternative treatment, treatment under quacks and intermittent self medication was recorded by 12%, 4% & 16% respectively. Among the self medication 12% of the women took corticosteroids and 4% preferred taking intermittent NSAIDs.

Conclusion: Treatment compliance is not very good with anti-rheumatic drugs among women patients of RA due to multi-factorial reasons.

Keywords: Compliance, DMRDs, Women health

INTRODUCTION

Barriers to medication adherence to the treatment of chronic illnesses requiring long-term use of pharmacotherapy are complex and varied [1]. The problem of medication adherence gets augmented with multiple morbidity, co-morbidity and poly-pharmacy [2]. The timely and appropriate intervention however done to look at the factors and reasons responsible for non adherence may help largely to enhance adherence and compliance of even chronic illnesses [3].

Rheumatoid arthritis (RA) is an autoimmune systemic disease with chronic inflammation of the synovial joints, progressive destruction of cartilage and bone with an increased prevalence in women and advancement of age (4th - 5th decade) [4,5].

High level of non adherence, noncompliance, adverse drug reactions, requirement of frequent follow up are monitoring are some of the factors evident in clinical practice make treatment of RA challenging and complex and responsible for patient dissatisfaction leading to frequent switch over to other doctors particularly due to inherent wax and waning nature of the disease [5].

The studies are available to address this problem but are from the western cohorts [6-12]. However, reports on adherence among patients with RA particularly women [4] who are more affected by the menace of this disease are lacking from India.

Hence, the current study was under taken to evaluate the adherence/compliance rates of most commonly prescribed anti-rheumatic drugs among Indian women in a tertiary care teaching hospital in India.

MATERIALS AND METHODS

A cross-sectional descriptive observational one year study was undertaken after institutional Ethics committee clearance to evaluate the adherence/compliance rates of most commonly prescribed anti-rheumatic drugs among women in a tertiary care teaching hospital in North India. Hundred women on anti rheumatic treatment for RA diagnosed by American College of Rheumatology (ACR) criteria [4]

were evaluated for one point analysis in a standardized 30 minute face to face conversation with regard to their disease detail and importance of treatment and need to follow up using predesigned/preliminary pretested questionnaire to come to conclusion for various reasons and factors for non adherence to the treatment in such patients. For each medicine, the patients were asked about adherence, consumption and perceived (side) effects. After the interview, the patients received self-report questionnaires to assess adherence/compliance as per the information available from records of the respective patients.

Patients with only stable co-morbid conditions, ambulatory, non-hospitalized, non-critically ill, in any stage of disease, any duration of disease on any anti rheumatic treatment were included in the current study. Treatment adherence rate, non compliance rate and switching over to other treatment/doctors were also recorded.

STATISTICAL ANALYSIS

Analysis was carried out with the help of computer software SPSS Version 15 for windows. The data was expressed in n (%). Chi-sq test was applied for some of the parameters to prove their statistical significance. P-value < 0.05 was considered significant.

RESULTS

Dissatisfaction rate with the anti rheumatic treatment was significantly high $p < 0.0001$ among 68% of the women. Non compliance/non adherence rate was also recorded very high among 52% and interrupted compliance rate was noticed among 6% of the women suffering from RA. Switch over rate to other treatment or doctors was also significantly ($p < 0.0001$) very high among 66% of the women. Twenty eight percent, 12%, 8%, 4%, 6% & 8% of the RA patients recorded switch over to 2,3,4,5,6&7 treatments/doctors respectively from the first start of their diagnosis and treatment for RA. Switch over to Alternative Treatment, treatment under quacks and intermittent self medication was recorded by 12%, 4% & 16% respectively. Among the self medication 12%

of the women took corticosteroids and 4 % preferred taking intermittent NSAIDs [Table/Fig-1].

While evaluating factors for non satisfaction with anti rheumatic treatment many factors as indicated in [Table/Fig-2] were statistically significant $p < 0.0001$ responsible for the non satisfaction about the treatment.

DISCUSSION

Poor adherence to prescribed treatments is apparently widespread in clinical practice particularly for RA treatment but the causes of discontinuation and low compliance are very complex, poorly defined and minimally researched in Indian setup. Non-adherence in patients with rheumatoid arthritis (RA) using disease modifying antirheumatic drugs (DMARD) may result in unnecessarily high levels of disease activity and function loss [9].

In the current study, dissatisfaction & Non compliance/ non adherence rate with the anti rheumatic treatment was significantly high $p < 0.0001$ among 68% & 52 % among the women suffering from RA. Switch over rate to other treatment or doctors was also significantly ($p < 0.0001$) very high among 66% of the women. The current study, while evaluating factors for non satisfaction with anti rheumatic treatment illiteracy, low income, rural population, poly pharmacy, lack of any corticosteroids in the prescription, concomitant treatment for co-morbid condition, ignorance about the disease and course of disease, lack of motivation, no prevention of functional loss and no clinical remission of disease were statistically significant $p < 0.0001$ responsible for the non adherence to the treatment. The results of the various previous studies [6-12] are highly variable which is also evident from the current study.

van den Bemt BJ et al., reported, 32%-40% of the patients not adhering to their DMARD prescription [6]. In their study, non-adherence noticed with DMRDs was not associated with demographic, clinical characteristics, satisfaction about information and medication concerns. However, the disease duration, side-effects and beliefs about the necessity of the medicine were weakly associated with adherence of DMRDs in their study [6].

Study Variables	Numerical Variables	p-value
Mean Age (y)	48.08	
Raised ESR Vs Normal ESR	96(96%) Vs 4 (4%)	Chi-square =169.280; DF=1; $p < 0.0001$
RF + ve Vs Sero-negative RF -ve	80(80%) Vs 20(20%)	Chi-square=72.000; DF=1; $p < 0.0001$
Satisfaction rate with Treatment Vs Dissatisfaction Rate with treatment	32 (32%) Vs 68 (68%)	Chi-square=25.920; DF=1; $p < 0.0001$
Compliance/ Adherence rate Vs Non Compliance/ Adherence Rate Vs Interrupted Compliance/Adherence	42 (42%) Vs 52 (52%) Vs 6 (6%)	Chi-square=5.; DF=1; $p = 0.0237$
Switch Over Rate to Other Treatment or Doctors Vs No Change of Treatment	66 (66%) Vs 34 (34%)	Chi-square=20.480; DF=1 $p < 0.0001$
Number of Switch Over's to different treatment/ Doctors	2 3 4 5 6 7	28 (28%) 12 (12%) 8 (8%) 4 (4%) 6 (6%) 8 (8%)
Switch over to Alternative Treatment Vs No Switch Over	12 (12%) Vs 88 (88%)	Chi-square= 115.520 DF=1; $p < 0.0001$
Switch Over to Quacks Treatment Vs No Switch Over	4 (4%) Vs 96 (96%)	Chi-square=169.280 DF=1; $p < 0.0001$
Switch over to Intermittent Self Medication Vs No Switch over - To Corticosteroid -To NASIDs	16 (16%) Vs 84 (84%) 12 (12%) 4 (4%)	Chi-square= 92.480 DF=1; $p < 0.0001$

[Table/Fig-1]: Showing satisfaction and compliance/adherence rate of anti-rheumatic treatment among women RA Patients (n=100)

Factors for Non Adherence	Numerical Variables	p-value
Active Vs Sedentary Life style	22 (37.93%) Vs 36 (62.06%)	Chi-square= 6.7; DF=1; $p = 0.0093$
Literate Vs Illiterate	12 (20.68%) Vs 46 (79.31%)	Chi-square=39.86 DF=1; $p < 0.0001$
Low Income Vs High Income	48 (82.75%) Vs 10 (17.24%)	Chi-square= 49.793 DF=1; $p < 0.0001$
Rural Vs Urban Population	40 (68.96%) Vs 18 (31.03%)	Chi-square=16.690 DF=1; $p < 0.0001$
Poly-pharmacy Vs Less no. of Medication	50 (86.20%) Vs 8 (13.79%)	Chi-square=60.828 DF=1; $p < 0.0001$
Corticosteroid in Prescriptions Vs No Corticosteroid in Prescription	17 (29.3%) Vs 41(70.68%)	Chi-square=19.862 D p value is less than 0.0001
DMRDs alone Vs Combination	28 (48.27%) Vs 30 (51.72%)	Chi-square= 0.138 DF=1; $p = 0.7103$
Type of DMRDs Methotrexate Vs Sulphasalazine Vs Hydroxychloroquine Vs Leflunomide	4 (6.89%) Vs 26 (44.82%) Vs 18 (31.03%) Vs 10 (17.24%)	
Concomitant Treatment for co morbid condition vs No concomitant treatment for Co Morbid	41 (70.68%) Vs 17 (29.31%)	Chi-square= 19.862 DF=1; $p < 0.0001$
Ignorance about disease Vs Knowledge about the disease	48 (82.75%) vs 10 (17.24%)	Chi-square= 49.793 DF=1; $p < 0.0001$
Ignorance about course of disease Vs Knowledge about the course of disease	48 (82.75%) vs 10 (17.24%)	Chi-square=49.793 DF=1 $p < 0.0001$
Lack of motivation Vs Motivation	42(72.41%) Vs 16(27.58%)	Chi-square= 23.310 DF=1; $p < 0.0001$
Physician's failure to stress the need Vs attempt to stress the need	26 (44.82%) Vs 32 (55.17%)	Chi-square= 1.241 DF=1 $p = 0.2652$
No clinical Remission of Disease vs Clinical Remission of Disease	45 (77.58%) Vs 13 (22.41%)	Chi-square= 35.310 DF=1; $p < 0.0001$
No prevention of Functional Loss Vs prevention	51 (87.93%) vs 7 (12.06%)	Chi-square= 66.759 DF=1; $p < 0.0001$
No Perceived Symptoms Decrease Vs Decrease	34 (58.62%) Vs 24 (41.37%)	Chi-square= 3.448 DF=1; $p = 0.0633$
Cost of treatment affected Vs Not Affected	12 (20.68%) vs 46 (79.31%)	Chi-square= 39.862 DF=1; $p < 0.0001$
Fear of ADR resulted Vs Not resulted	12 (20.68%) vs 46 (79.31%)	Chi-square= 39.862 DF=1; $p < 0.0001$
Adverse Drug Reaction resulted Vs not resulted	10 (17.24%) Vs 48 (82.75%)	Chi-square =49.793; $p < 0.0001$
Intolerance resulted Vs Not Resulted	4 (6.89%) Vs 54 (93.10%)	Chi-square = 86.207 DF=1; $p < 0.0001$
Forgetfulness resulted Vs Not Resulted	8 (13.79%) vs 50 (86.20%)	Chi-square = 60.828 DF=1; $p < 0.0001$

[Table/Fig-2]: Factors for non adherence/compliance prevalent among Women suffering from Rheumatoid arthritis (n=58)

In a systematic review by Blum MA et al., adherence to biologic treatments in patients with RA at 12 months ranged from 32.0% to 90.9% [8]. Higher continuation rates were reported with the addition of methotrexate or other disease-modifying anti-rheumatic drugs. However, no biologics were used for the treatment of RA in the current study cohort.

The results of the current study were contrary to the study of Salt E & Frazier SK et al., as medication adherence to DMARDs ranged from 30% to 107% [9]. Self-efficacy, patient-healthcare provider relationships, social support, patient beliefs about medications and age were some of the factors affecting medication adherence. This variance from the current study could be attributed to different tools and methods used to analyse the adherence rate.

Study findings of Quinlan P et al., indicated that in the patients of RA, health literacy is not associated with medication adherence [10].

The average medication knowledge score was 0.73. Adherence to medication regimen was 0.84. Race, neighborhood income and confidence with contacting provider about medications were predictors of adherence in their study. However, in the current study low income, rural population, ignorance about the disease and course of disease were significantly ($p < 0.0001$) found responsible for the non satisfaction/non adherence about the treatment.

Similar results were reported by Joplin S et al., like the current study that poor medication adherence is a complex issue [12]. Low educational levels and limited health literacy are contributory factors. Higher drug cost exhibited reduced/poor adherence by de Klerk et al to the prescribed medication in patients of RA unlike our study [13].

RA is progressive disease and as such there is no cure as none of the conventional treatment is completely effective in RA. NSAIDs and steroids because of low efficacy and both short term and long term adverse effects. Combination of conventional DMARDs is a reasonable, cost effective and most important component of treatment of RA. It however also requires frequent monitoring and is not free from ADRs whereas, prohibitive costs, serious risks of infection and malignancy are barriers to more widespread use of biologic agents in developing countries [14].

The patients taking sulfasalazine when compared to patients taking methotrexate alone had a lower medication possession ratio/ Adherence rate in the study of Grijalva et al., [15]. The finding are however contrary to the finding of our study where in methotrexate containing prescription had the better adherence rate, probably it had to be taken weekly unlike other drugs which need to be taken daily.

Similarly the prescription containing corticosteroid had been reported to have higher compliance and satisfaction rate like our study as reported by Treharne et al., probably because wellbeing provided by corticosteroids [16].

The results of current study recorded similar results as reported by Berry et al., that perceived benefits in decrease symptoms and prevention of functional loss are significantly ($p < 0.001$) reasons for compliance/adherence/satisfaction for the anti rheumatic treatment [17]. Although, no attempt was made to correlate the results with disease activity score- 28 in the current study.

In the study, of Markusse IM et al., from Netherlands reported that RA treatment protocol adherence decreased over time from 100% to 60% with dissatisfaction & the level of disease suppression was the main risk factors for non-adherence like our study [18].

Gadallah MA et al., in their study reported that higher adherence was associated with more positive beliefs on medication, greater satisfaction with health care and less disease activity [19]. The barriers reported were fear of side effects, nonavailability of drugs and cost of medications. However, in current study these were not the major barriers for adherence. Further, in their study younger patients were more adherent. Such correlation with the age was also not studied in the current study.

Bliddal H et al., recorded that treatment at hospital or in private practice did not influence the adherence to MTX [20]. However, the main determinants of nonadherence reported were female gender, younger age and time from diagnosis to initiation of MTX. In our study also least non adherence was reported with methotrexate in comparison to other DMARDs among women suffering from RA. The possible reasons for it may be that the drug has to be taken on weekly basis. However, like the study of Bliddal H et al., no attempt was made to study specific reasons for its better compliance in the current study [20].

Since women after 40, suffer more with rheumatic diseases as reported by our own previous study and are significantly associated with disability index [21]. Further RA is more common after 40 in women. Hence the current study was undertaken. However, we

failed to cite any similar study specifically done in women suffering with RA, thus it is beyond the scope of current study to compare the findings with men suffering with rheumatoid arthritis.

While comparing the result in postmenopausal women with other rheumatological disorders like postmenopausal osteoporosis, the results of our own previous study by Tandon VR et al., suggested poor treatment compliance and adherence with alendronate, weekly risedronate and monthly ibandronate regimens of bisphosphonates [22]. Similarly de Achaval S et al., recorded poor treatment adherence to disease-modifying antirheumatic drugs in patients with rheumatoid arthritis and systemic lupus erythematosus [11].

de Klerk E et al., reported that patients have poor compliance and adherence with rheumatic disorders like rheumatoid arthritis, polymyalgia rheumatic and gout [23].

Similar to the results of the current study Laba TE et al., documented that adherence to arthritis treatment in patients osteoarthritis which is fourth leading cause of disability globally is low [24]. Thus most of the rheumatic disorders which demand long term treatment have poor compliance and adherence rate to the respective treatment. Thereby, indicating that patient education should be the integral part of management to enhance the adherence of the patients for successful outcome in rheumatic disorder including rheumatoid arthritis.

LIMITATION

The current study had some of the limitation as it was one point analysis and was dependant on the old records to evaluate compliance. No attempt was made to co relate the dissatisfaction rate with disease activity and quality of life scores.

CONCLUSION

Treatment compliance is not very good with anti-rheumatic drugs among women patients of RA due to multi-factorial reasons. There is a need to create awareness and education regarding the course of the disease and necessity of continuous treatment with proper follow up and monitoring with the stress on proper compliance / adherence to the prescribed therapy to avoid the morbidity and mortality in the patients of RA.

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