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Patterns of Drug Prescription among Rheumatoid Arthritis Patients in King Hussien Medical City (KHMC)

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Abstract **Original Research Article**

Aim: This study was carried out in order to report the prescribing pattern of drugs used in the treatment of Rheumatoid Arthritis (RA) among Jordanian patients who receive their medical care at Royal Rehabilitation Center in Royal Medical Services (RRC/RMS) Amman/Jordan during the period from October 2013 to March 2014, in addition, we evaluated if the pattern of prescriptions of disease-modifying anti-rheumatic drugs (DMARDs) used is rational and was it in accordance with international guidelines for management of RA. ***Methodology:*** A retrospective cross sectional study was conducted in the out-patient pharmacy of the RRC/RMS. RRC is a tertiary care hospital which receives RA referrals from other clinics and hospitals; it covers 15 rheumatology subspecialty clinics weekly and is directed through specialist and consultant physicians. Inclusion criteria include all the prescriptions with the diagnosis of RA that were dispensed from the pharmacy during the period of October 1st 2013 till March 31st, 2014, or any prescription that contain at least one DMARD for patients whom ages are ≥18 years. These prescriptions were studied and analyzed for the number of drugs in the prescription, name of the drug, dose, and frequency. The demographic profile of the patients regarding age and sex was also obtained from the prescription. Statistical analysis was performed using the statistical package for social science SPSS version 17. The study had been ethically approved from the ethical committee in the Directorate of Royal Medical Services. ***Results:*** There were a total of 800 prescriptions for DMARDs during the study period, 557 were female patients and 243 were for male (F: M ratio =2.3:1) with ages ranging from 18-82 year (mean 49.2 ± 5.8 year). The distribution of age was such that the highest percentages (46.3%) of patient were between the age group of 40-60 followed by 38.5% above 60 years. The overall average number of drugs per prescription was 6.41 ranging from 1-8 drugs. All the patients included in the study were prescribed DMARDs either alone or in combination, the percentage of prescriptions with DMARDs monotherapy and combination therapy was 28% and 72%, respectively. Almost most of combination therapies (77%) were prescribed two DMARDs while only 23% were given 3 DMARDs. It was found that methotrexate was prescribed for 96% of the prescriptions (25% as monotherapy, 30% with salazopyrine, 25% with hydroxychloroquine and 16% with both salazopyrine and hydroxychloroquine). ***Conclusion:*** Our study represents the current pattern of drug prescribing among RA patients in a tertiary care hospital. It is obvious that the leading drug for treatment of RA is methotrexate either alone or in combination, also it was found that treatment with combination therapy were more common than monotherapy in most RA patients and those practices is in accordance with the current recommendations and guidelines. Management of RA is continuously changing and new drugs are being added, our study constitutes a baseline data, extra studies could give more insights about the prescribing practice of the clinician.

Key words: Rheumatoid Arthritis; DMARDs; combination therapy.

INTRODUCTION

Rheumatoid arthritis (RA) is a chronic systemic inflammatory disease of unknown cause, chiefly affecting synovial membranes of multiple joints. RA has a high prevalence and approximately affects 1-2%of the general population worldwide [1]. The disease has a wide clinical and extra-articular manifestations

and it is an established risk factor for many complications that affect the quality of life [2, 3].

Many treatment protocols and algorithms have been used for the management of RA. Protocols are mainly based on a group of drugs known as disease-modifying anti-rheumatic drugs (DMARDs). They had improved control of disease activity, slowed down joint erosions and improved the quality of life as well as reduced associated cardiovascular-morbidity; such as ischemic heart disease [4, 5, and 6]. Immediate and aggressive DMARDs therapy is recommended now by most current treatment approaches and algorithms. DMARDs also represent the standard of care for RA in the recent clinical practice. Currently, more than 90% of RA patients are treated with DMARDs in the major rheumatologic societies, and in rheumatic disease specialty practices [7-9],

An effective method to study and evaluate the prescribing pattern of the physicians and drug dispensing attitude of pharmacists is through conducting a survey based on prescriptions review. Studying the prescribing pattern is a component of medical audit which is necessary to determine areas that require improvements and corrections in order to provide rational and cost effective medical care.

This study was carried out in order to report the prescribing pattern of drugs used in the treatment of RA among Jordanian patients who receive their medical care at RRC/ RMS during the period from October 2013 to March 2014, in addition, we evaluated if the pattern of prescriptions of DMARDs used is rational and was it in accordance with international guidelines for management of RA.

METHODOLOGY

A retrospective cross sectional study was conducted in the out-patient pharmacy of the RRC/RMS. RRC is a tertiary care hospital which receives RA referrals from other clinics and hospitals; it covers 15 rheumatology subspecialty clinics weekly and is directed through specialist and consultant physicians.

Inclusion criteria include all the prescriptions with the diagnosis of RA that were dispensed from the pharmacy during the period of October 1st 2013 till March 31st, 2014, or any prescription that contain at least one DMARD for patients whom ages are ≥18 years. These prescriptions were studied and analyzed for the number of drugs in the prescription, name of the drug, dose, and frequency. The demographic profile of the patients regarding age and sex was also obtained from the prescription.

Statistical analysis was performed using the statistical package for social science SPSS version 17. The study had been ethically approved from the ethical committee in the Directorate of Royal Medical Services.

RESULTS

There were a total of 800 prescriptions for DMARDs during the study period, 557 were female patients and 243 were for male (F: M ratio =2.3:1) with ages ranging from 18-82 year (mean 49.2 ± 5.8 year). The distribution of age was such that the highest percentages (46.3%) of patient were between the age group of 40-60 followed by 38.5% above 60 years. The demographics of the study group are presented in table (1). The overall average number of drugs per prescription was 6.41 ranging from 1-8 drugs.

Table-1: Demographic Characteristics of the study group (N=800)

Patient Characteristics		**Males N = 243**	**Females N=557**	**Total patients N=800**
Age group (years)	18-40	21	101	122
	40-60	141	229	370
	≥60	81	227	308
Mean age (years)		50. 7	49. 8	50.25
Average number of drugs per prescription		6.41	7.32	6.87

Figure (1) reveals the prescribing pattern for the RA patients in the study. The majority of them (92%) were prescribed non-steroidal anti-inflammatory drugs (NSAIDs) on regular frequency or when required. About one-fourth (26%) of all RA patients were prescribed prednisolone tablet usually in a daily dose of 5-12.5mg.

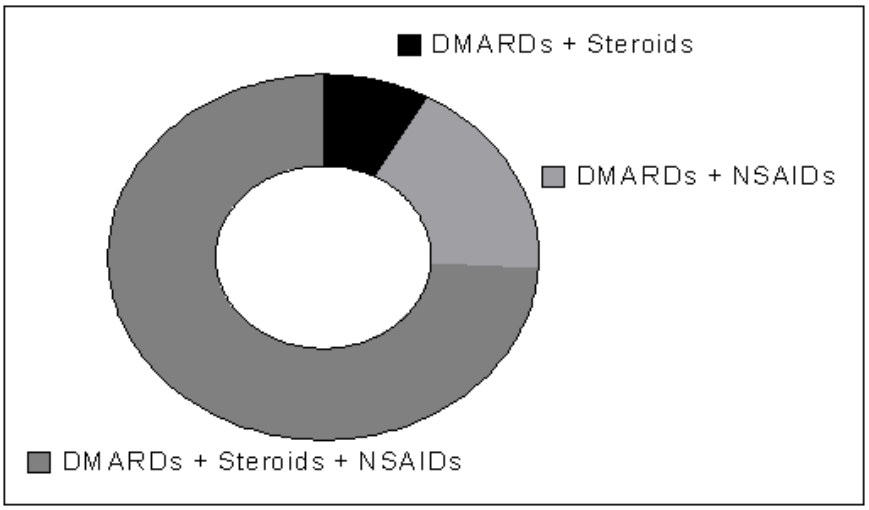

Fig-1: Prescribing pattern of medications. NSAIDs: Non-steroidal anti-inflammatory drugs

All the patients included in the study were prescribed DMARDs either alone or in combination, the percentage of prescriptions with DMARDs monotherapy and combination therapy was 28% and 72%, respectively. Almost most of combination therapies (77%) were prescribed two DMARDs while only 23% were given 3 DMARDs. The prescribing patterns for DMARDs therapy for the treatment of RA patients in this study is presented in Figure (2).

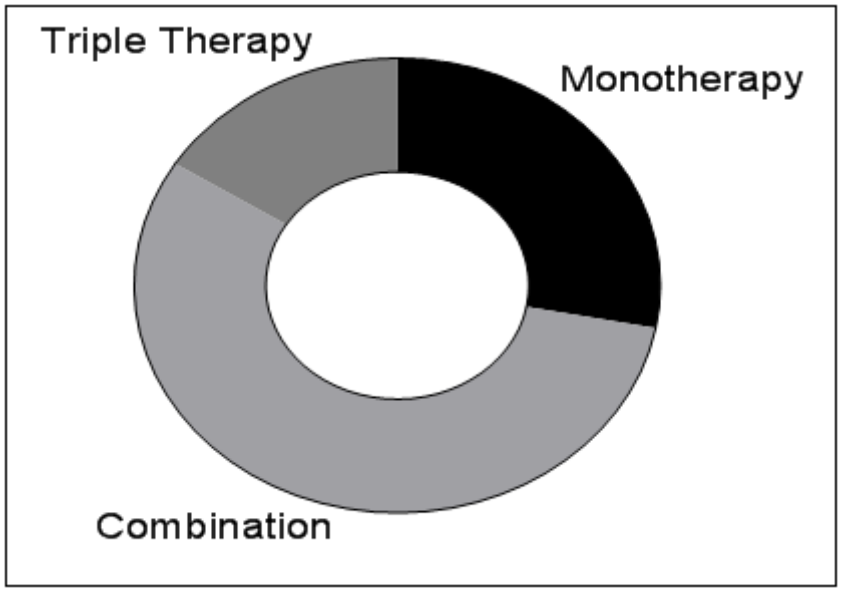

Fig-2: The prescribing pattern for DMARDs therapy

Figure (3) is a breakdown for various DMARDs prescription patterns among RA patients. It was found that methotrexate was prescribed in 25% of the total patients as monotherapy while salazopyrine and hydroxychloroquine were given to 3% and 2% of the total patients respectively.

Concerning patients who were on two DMARDs, our study revealed that 375 (56%) of the total patients were on two drugs. Methotrexate was the leading drug in combination therapy (55%) of the total patients. The most frequently used combination were methotrexate and salazopyrine (30%) of the total patients, followed by methotrexate and hydroxychloroquine (25%). Patients who were on three DMARDs therapy constitute (16%) from total patients, all of them were on methotrexate, hydroxychloroquine and salazopyrine. Although the biologic DMARDs are available in the drug formulary of the RMS but there wasn't any prescription for them during the six months of the study period.

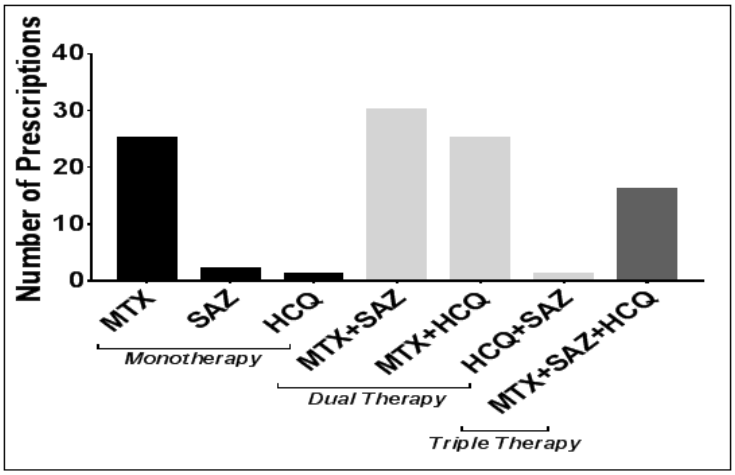

Fig-3: Breakdowen for various DMARDs prescription pattern. MTX: methotrexate, SAZ: salazopyrine, HCQ: hydroxychloroquine

Analyzing the prescribing patterns among our RA patients reveals that additional drug therapy was also co-prescribed along with DMARDs as shown in Figure (4).

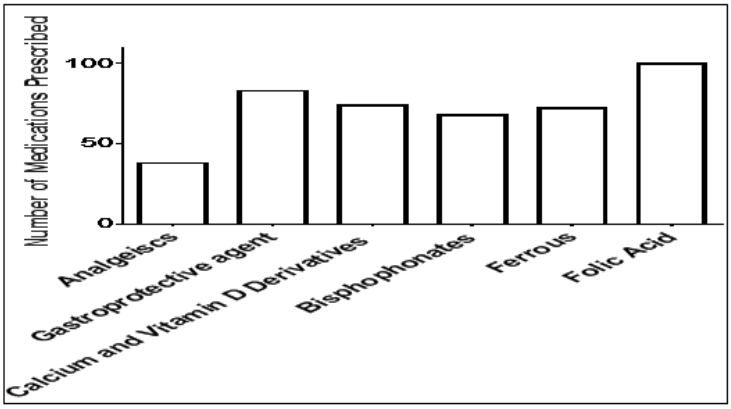

Fig-4: Additional medications prescribed for RA patients

About one third of the patients (37%) were prescribed concomitantly an analgesic (the widely used analgesic agent was paracetamol). A significant proportion (83%) of the patients was treated with a gastroprotective agent either a proton pump inhibitor such as omeprazole or H2 –blocker such as famotidine. Calcium salts and vitamin D derivatives' were also co-prescribed to a large number of patients (81%), bisphosphonates and iron supplementation were also given to 66% and 76% of the patients respectively. All of the methotrexate patients received a folic acid supplementation usually in a dose of 5mg twice weekly maintenance therapy.

DISCUSSION

According to the Current treatment paradigms in RA, early aggressive and persistent use of DMARDs should be followed to prevent joint destruction and long-term physical disability in those patients [9].

There is widespread acceptance and many evidence based clinical guidelines recommendations about early referral to a specialist rheumatologist when a diagnosis of RA is suspected, for definitive diagnosis and early introduction of DMARDs and continued follow-up of a rheumatologist to assess response to treatment and review the treatment plan [4, 5, 8, 12-14].

All of the prescriptions that were prescribed to our patients in our study contain at least one DMARD this fellow the recommended guidelines**.** In this study, it is notable that methotrexate was the most commonly prescribed drug for RA (96%) either alone (25%) or in combination therapy (71%) followed by salazopyrine (49%) and hydroxychloroquine (45%) either alone or in combination therapy. For many decades methotrexate was the most commonly used DMARDs as a single agent or in multidrug therapy, its disease modifying quality and tolerability account for long duration of therapy [15-17]. Our result is similar to other recent studies about rheumatologist prescribing patterns and other recommendation that methotrxate has an established efficacy in rheumatoid arthritis and it is still considered as the main drug for treating RA, showing

the superiority over hydroxychloroquine and salazopyrine [18-22].

Our study revealed that combination therapy using two DMARDs or more (72%) was more common than monotherapy (28%), this result is also indicating that the prescribers are following the guidelines recommendation for treating RA which recommend that early diagnosis of RA prompted the use of DMARDs in higher doses and often in combination therapy to control the disease activity and this result is supported by other studies that showed that RA could be adequately controlled with the use of combination therapy, furthermore multiple drug therapy seems to be a rational approach in the management of RA to decrease the mortality.

The demographic characteristics of our study group is in agreement with the current epidemiological concepts regarding age and sex prevalence in RA since RA is one of many chronic inflammatory diseases that affect female gender more frequently than male with an age of onset at middle age . In our study there was a higher female predominance (69.6%) (2.3 times greater in females than in males) and the highest percentage of patients 46.3% were in the middle age group of (between the age group of 40-60 year) [23, 24].

The prescription trend in our study reveals the pattern of polypharmacy. the average number of drugs per prescription was found to be 6.41, that is above the recommendations of the WHO which has recommended that the limit of number of drugs prescribed per prescription should be two and that justification for prescribing more than two drugs would be required because of the increased risk of drug interactions that increases the likely hood of nonadherance with the medication prescribed, but in patients with RA polypharmacy is a common practice since those patients often have a greater number of co morbidities with associated disability and complex medication regimens [25-27].

The noted polypharmacy obvious in our study (63% of the prescriptions contains 5 drugs or more) may be attributed to the adherence of most clinician to the guidelines of RA management since that some patients need their disease to be more controlled by using more than one DMARDs, also other medications like NSAIDs and analgesics are co prescribed to those patients for more control of the pain associated with disease, as the control of pain is an important aim in the management of RA. Gastroprotective agents are also co prescribed with DMARDs to overcome the gastrointestinal side effects associated with the use of these drugs. A high number of patients were concomitantly prescribed folic acid along with methotrexate in order to reduce some of its side effects. Osteoporosis is well recognized among RA patients and prescribing calcium salts, vitamin D derivatives and bisphosphonates increase the number of drugs that are prescribed concomitantly and give a high incidence of polypharmacy among those patients.

CONCLUSION

Our study represents the current pattern of drug prescribing among RA patients in a tertiary care hospital. It is obvious that the leading drug for treatment of RA is methotrexate either alone or in combination, also it was found that treatment with combination therapy were more common than mono therapy in most RA patients and those practices is in accordance with the current recommendations and guidelines. Management of RA is continuously changing and new drugs are being added, our study constitutes a baseline data, extra studies could give more insights about the prescribing practice of the clinician. It is recommended that regular education for both the clinician on rational use of drugs and also for the patient for more drugs compliance in order to achieve better control of the disease with the lowest possible medication use.

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