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A LITERATURE REVIEW: PRESCRIBING TRENDS AND ADHERENCE TO STANDARD TREATMENT GUIDELINES IN TREATMENT OF RHEUMATOID ARTHRITIS

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ABSTRACT

Rheumatoid arthritis is ranked among 40th leading cause of disability worldwide. Guidelines are designed by converting research and expert opinion into recommendations for everyday practice, but health care providers are often slow to incorporate these guidelines into their daily practices intern cause inadequate treatment of disease. The aim of this study is to summarize research findings from developed and developing countries as well as from Pakistan regarding prescribing trends and adherence to standard treatment guidelines in treatment of rheumatoid arthritis. A total of 45 studies were reviewed regarding prescribing practices for arthritis. The review concluded that there is need to identify the barriers and gaps to further enhance the effectiveness of current prescribing practices for rheumatoid arthritis in developing countries. Standard treatment guidelines must be designed and implemented for routine prescribing practices by the regulatory authorities. Shortage of rheumatologists and awareness regarding their role among community needs to be addressed especially in developing countries.

KEYWORDS: Rheumatoid Arthritis, Adherence, Standard Treatment Guidelines, Prescribing Trends, Prescriber, Pakistan

INTRODUCTION

Rheumatoid arthritis is a progressive autoimmune disease which is characterized by sinusitis and bone destructions. It is ranked among 40th leading cause of disability worldwide [1].It affects 0.1-0.3% of general population in developing countries such as South Africa, Nigeria, Indonesia, Pakistan, China, Philippines and Argentina [2-8] and 1.0% of the general population in developed countries[7, 9]. It is estimated that by 2020 RA affect 60 million people alone and activity limitation of 12 million people [10]. Chronic Rheumatoid Arthritis is more prevalent among women because as it is more related to the female sex hormones and in younger at peak age under 40. Smoking [11, 12] and obesity are also risk factors for rheumatoid arthritis [7, 9, 13]. Survival rate are lower as compared to normal population if life expectancy of 50 year white women are 34 years than life expectation with RA is only 30 years[14].

OBJECTIVES OF THE STUDY

The aim of this study is to summarize research findings from developed and developing countries as well as from Pakistan regarding prescribing trends and adherence to standard treatment guidelines in treatment of rheumatoid arthritis.

METHODS

Pub Med, Google Scholar and Science direct were used as electronic database for searching articles available

from January 2000 to June 2015. The search terms used with each database were Rheumatoid Arthritis, review, adherence, standard treatment guideline, prescriber. Full articles as well as abstracts were retrieved and added in review. A total of 45 studies were retrieved from databases related to adherence of prescribers to standard treatment guideline of Rheumatoid arthritis. The studies were categorized on the basis of their country of publishing into developed countries, developing countries and Pakistan. Thirty three studies from developed countries, 4 from developing countries and 8 studies of Pakistan were included in this review (Table 1). Quantitative cross sectional surveys as well as qualitative studies were also included.

Table 1: Details of Country and Number of Included Papers

Regions	Number of Studies	Countries
Developed countries	33	USA, Germany, Canada, Ireland, UK, France, Sweden, Netherlands, Finland
Developing countries	4	Brazil, Mexico, Iran, Philadelphia
Pakistan	8	-
Total		45

RESULTS AND DISCUSSIONS

Overview of Prescribing Trends for Treatment of Rheumatoid Arthritis in Developed and Developing Countries

Disease Modifying Anti-Rheumatic Drugs (DMRADs)

Rheumatoid arthritis had been controlled in most cases with bed rest, aspirin and with alternative non steroidal anti-inflammatory drugs at later stages before 1980s. But during mid-1980s, it was recognized from clinical cohorts that most patients experienced severe functional declines, work disability radiographic progression and mortality from short-term drug efficacy. These reports led to calls for early and aggressive strategies (disease modifying anti-rheumatic drugs) to prevent further joint damage and functional disability. Present management of rheumatoid arthritis is not curative, but may lessen the progression of joint damage, and give symptomatic aid. Therapy consists of NSAIDs, disease-modifying antirheumatic drugs (DMARDs), and corticosteroids. Patients are also advice to make lifestyle changes such as increase exercise, weight reduction and wearing supportive splints. Patients are well controlled with methotrexate alone or in combination with traditional DMARDs such as sulfasalazine and/or hydroxychloroquine, without biological agents [13, 15].Aggressive initial treatment of RA with a combination of DMARDs improves 5-year outcome in terms of lost productivity in patients with RA of recent onset [16]. Most of patients are not given a DMARD during the 12 months of treatment. Rheumatologist mostly prescribe DMARD and it has been reported that older patients and those not visiting a rheumatologist were less likely been prescribed a DMARD [17].However, recently the most prescribed combination of DMARDs was methotrexate or sulphasalazine, alone or in combination, leflunomide, intramuscular gold [18].

Anti-Tumor Necrosis Factor (TNF)

From the last few years, the treatment options for patients with RA have changed noticeably. Anti-tumor necrosis factor (TNF) has become a good treatment options for patients with RA. Anti-TNF inhibitors are now not only limited to moderate to severe arthritis patient. Patient with low response to methotrexate are replaced by anti-TNF inhibitor. This switching from one TNF inhibitors to another depends upon adverse effects and low response to therapy [19]. Early prescribing of anti-tumor necrosis factor (TNF) inhibitors have been reported to improve functional condition and slows radiographic development among patients with rheumatoid arthritis [20].

Biological Agents

Even though the efficiency of synthetic DMARDs (sulfasalazine. Methotrexate and leflunomide) is evident from many studies as they improve symptoms and slow down bone damage but many patients on these drugs, complain of having inflammation and progressive joint damage. In management of arthritis, Biologic agents are good addition in term of effectiveness. Where synthetic DMARDs failed to response, biological agents reduce signs of tenderness of bone in RA patients. They are more beneficial in early treatment with methotrexate but all biologic agents have a potential for higher risk of infections, administration side reaction for I/V, S/C infusion and injection. Patients should be screened for tuberculosis and should given vaccination against infection who use biological agents [21, 22].

Glucocorticoids

Most of patients with RA do not take disease-modifying anti-rheumatic drugs (DMARDs) due to old age and high cost [23]. Glucocorticoids have been used as anti-inflammatory in various inflammatory diseases since 1948. The best use of glucocorticoids remains notorious as most of the prescribers irrationally prescribe corticosteroids [24].Increase in weight, osteoporosis and neuropsychiatric side effects occur with long-term use of glucocorticoids [25-27].

Intra-articular steroid injection is one of the most general clinical actions performed by rheumatologists. Most of physician advised patients to rest after injection for one to two days. Such practices is not supported by the literature, which results into reduce days for work, mobility aids costs, and increase patient problems [28].

Non-Pharmacological Treatments

Medications can be used to alleviate symptoms of disease and help in slowing down the progression of disease but due to side effects of medicines, patients usually prefer the alternative therapies including nutritional modification. Non-pharmacological treatments are an important addition with drug treatment. Fish oil is good supplement in reducing symptoms like morning stiffness with long-standing rheumatoid arthritis. Specialized diets made for RA patients include antioxidants, seed oils vitamins (B &D), foliates, minerals and trace elements [29].

Use of rest splints or assistive devices, bathing and spa therapy, exercise and physiotherapy are also considered valuable non-pharmacological treatments. Literature supports effectiveness of aerobic capability and muscle strengthening physical exercise programs in rheumatoid arthritis (RA) patients. Exercise and cardio-respiratory aerobic training in stable RA seems to be safe and effective in management of RA patients [30].

Overview of Adherence of Prescribing Practices with Standard Treatment Guidelines for Rheumatoid Arthritis in Developed and Developing Countries

The KAP (Knowledge, attitude and practices) survey is one of the best way to gather information regarding prescribing behaviour and practices of prescribers [31]. Studies from Canada reported that very few patients visit rheumatologists and DMARDs is the most commonly prescribed drug by them. On the other hand, misoprostol was introduced in the practices as effective treatment of NSAID induced peptic ulcer disease. Although, the prescribers tend to follow most, but not all recommendation of the treatment guidelines for the clinical assessment of patients with rheumatoid arthritis. The major reason for noncompliance to some recommendations was lack of clarity in guidelines [32-34]. On the other hand, standard treatment strategies to reduce ulcer complications in susceptible populations (older patient or age more than 75year, peptic ulcer or bleeding from GI tract in past or taken anticoagulants and corticosteroids) were not been

followed by prescribers in USA. Use of NSAID with suggested anti-ulcer therapy or use of a selective cyclooxygenase 2–inhibiting drug (coxib) was recommended to reduce the risk of ulcer but was not followed in practice [35]. Another study from USA reported that only half of the rheumatologists were familiar with the treatment guidelines for RA. Methotrexate was used as initial therapy by most of the them. They did not prefer biologics because of the risk of infection. Respondents highlighted the importance of patient education and reported provision of verbal counselling in 98% of the cases and written counselling in 42% of the cases of RA [36]. It is duty of rheumatologist to perform screening tests before starting biological in treatment. But unfortunately rheumatologists have little knowledge regarding screening programs. Only 69% of the prescribers in USA were performing screening earlier to the start of the therapy with biologic disease-modifying anti-rheumatic drugs. Prophylaxis treatment is rarely provided to patients against HBV reactivation while getting immunosuppressant. Education of rheumatologists regarding risks of HBV reactivation and its prevention techniques for patients must be emphasized [37].

Data of ten years from the National Database of the German Collaborative Arthritis Centres showed that the trends in treatment and outcome of disease of rheumatoid arthritis have been changed during the last decade. Methotrexate was reported most commonly prescribed medication followed by ant malarial in Germany. DMARDs were given by rheumatologist who resulted in slow disease progression and decrease treatment cost while non-rheumatologist did not prefer DMARDs. German rheumatologists were following recent guidelines but non-pharmacological care like occupational therapy and patient education was not much emphasized [38, 39].

On the other hand, the practice of Irish rheumatologists did not comply with the guidelines with regard to vaccination. Majority of the rheumatologists did not recommend vaccination. They believed that the rheumatology clinic is not the appropriate place for vaccination and the vaccination setup should be outside the rheumatology clinic [40].

The temporal trends in DMARD prescriptions indicate that rheumatologists in Mexico adopted an aggressive approach towards early treatment of RA during 1997 to 2001. The use of quality and surveillance arthritis registers helped to identify and define areas of unwarranted variation, which may be even more important when considering the increasing use of effective but expensive biological drugs [41]. Recently patients were reported well controlled with methotrexate alone or in combination with traditional DMARDs such as sulfasalazine and/or hydroxychloroquine, without biological agents according to national scheme of treatment in Mexico. These schemes used by Mexican rheumatologists were in line with current international recommendation[15].

Results from a study conducted in Brazil revealed that guidelines for management of RA were followed by the majority but not all Brazilian rheumatologists in their daily practice [42].

Overview of Management of Rheumatoid Arthritis in Pakistan

The prevalence of musculoskeletal disease in Pakistan has been reported comparatively lower than in other developed countries [43]. The prevalence of RA is 0.142%, and 0.55% in northern area of Pakistan [3].The relationship of specific HLA-DR alleles and the common epitope with rheumatoid arthritis (RA) is now well recognized which depends on races. The shared epitope proposition was also supported by the distribution of HLA-DR alleles in Pakistanis with RA. In harmony with some other studies, the shared epitope was not an indicator for more severe disease [44]. DMARDs has been the most commonly used drugs for treatment of RA in Pakistan, however, their slower therapeutic effect has been reported. Although, MTX is generally used as second-line drug in management of RA but most of the patients in Pakistan

show good to excellent response to the drug with no exhibited side effects. Studies conducted in Pakistan has reported Methotrexate currently as the most effective, well tolerated and cost effective treatment in Pakistan [45, 46].

RA is most commonly treated by general practitioners and consultants (all non-rheumatologists) in Pakistan. They usually prescribe mostly steroids in their prescriptions which depict side effects among patients [47]. Beside this mood disorders have reported in most of the patients with chronic rheumatologic disorders in Pakistan. Systematic assessment of all patients for mood disorders and psychosomatic distress in rheumatology clinics needs to be emphasized [48]. Standard treatment guidelines for RA are not available at healthcare facilities and most of the prescribers are unaware regarding them. Very few studies in Pakistan have been conducted on RA and most of them are on assessment of prevalence and therapeutic efficacy of drugs. There is scanty of evidence based data on KAP and adherence of prescribers to RA guidelines in Pakistan.

CONCLUSIONS

The review concluded that there is need to identify the barriers and gaps to further enhance the effectiveness of current prescribing practices for rheumatoid arthritis in developing countries. Standard treatment guidelines must be designed and implemented for routine prescribing practices by the regulatory authorities. Shortage of rheumatologists and awareness regarding their role among community needs to be addressed especially in developing countries. All stakeholders must work together to devise an action plan to promote inexpensive therapeutically effective pharmacological and non-pharmacological intervention strategies to enhance quality of life in patients with rheumatoid arthritis.

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