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CHARACTERIZATION OF PRESCRIBING PATTERN IN THE MANAGEMENT OF OSTEOARTHRITIS AND RHEUMATOID ARTHRITIS IN A TERTIARY CARE HOSPITAL

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Abstract:
Objectives: Osteoarthritis (OA), a progressive disorder characterized by destruction of articular cartilage with synovial changes. Rheumatoid arthritis (RA), a systemic inflammatory and autoimmune disease characterized by synovial inflammation, autoantibody production and joint space narrowing. Drugs like non-steroidal anti-inflammatory drugs (NSAIDs), symptomatic slow acting drugs (SYSADOA) disease modifying anti-rheumatic drug (DMARDs), steroids etc are using widely in OA and RA therapy. A prescribing pattern study analyzes the trend of prescribing drugs, its rationality and provides feedback to the prescribers. We aimed to study the prescription patterns in OA and RA therapy through a prospective observational analysis. Methodology: We studied 100 outpatients for six months between June 2017 - December 2017. We reviewed prescriptions and analysed the patterns. Results: Out of 100 patients, 35% were with OA and 65% were RA. 25% are males and 75% are females. OA and RA were more prevalent in the age groups of 51-60 years (45.7%) and 41-50 years (35.4%) respectively. Out of 239 prescribed drugs, Aceclofenac (26.31%) and Naproxen (26.31%) were the first choice of drugs in OA patients and Methotrexate (25.4%) for RA. Of the patient total, 14.3% were treated in monotherapy and 85.7% received two or more drugs. Conclusion: We found combinational therapy (SYSADOA+NSAIDs & DMARDs) was more often than monotherapy in OA and RA. We also found the prescribed drugs are rational and are in essential drug list.

Key Words: *Prescription patterns, Rheumatoid arthritis, Osteoarthritis*

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INTRODUCTION:

Osteoarthritis (OA) is a progressive disorder characterized by destruction of articular cartilage and subchondral bone associated with synovial changes. It is the most common chronic joint disease of the older patients, primarily affecting the knee and hip [1]. It is most common arthritis and prevalence increases with age. Cartilage loss frequently precedes the development of pain, which explains why patients often present with advanced joint degeneration. Pain can arise from several of the diseased tissues of the joint, including bone, synovium or other periarticular structures such as entheses, bursae or tendons. The damaged articular cartilage also produces factors, including nerve growth factor that can sensitize local pain fibres. Chronic pain, resulting from local sensitization of nerve fibres and central nervous system changes, is common over time [2].

Pharmacological treatment for OA includes analgesics (Acetaminophen, Tramadol and Codeine), non-steroidal anti-inflammatory drugs (Naproxen, Aceclofenac, Diclofenac and Etodolac), SYSADOA (Symptomatic Slow Acting Drugs): Chondroitin, Diacerein and Glucosamine, intra-articular injections of Corticosteroids and Hyaluron, topical agents (Capsaicin, Methyl salicylate and topical NSAIDs) [3].

Rheumatoid arthritis (RA) is a systemic inflammatory and autoimmune disease characterized by synovial inflammation, autoantibody production and joint space narrowing. The etiology of RA is still not clear, many studies have reported that activated inflammatory T cells, B cells and macrophages invading the joint synovium is the cause of joint and cartilage damage. Besides, tissue damage can be aggravated by reactive oxygen species (ROS) in the synovial fluid which are released from inflammatory cells. RA has a significant negative impact on the ability to perform daily activities, including work and household tasks, and health related quality of life, and it increases mortality [4-11].

RA is treated with Disease modifying anti-rheumatic drugs (DMARDs) that are of two types such as Biologics and Non-Biologics. Biologics include Tumor necrosis factor alpha (TNFα) blockers (Etanercept, Infliximab, Adalimumab, Certolizumab and Golimumab), Interleukin 1 (IL-1) Blockers (Anakinra), monoclonal antibodies against B cells (Rituximab), T cell co-stimulation blockers (Abatacept) and Interleukin 6 (IL-6) blockers (Toclizumab). Non biologics include Hydroxychloroquine, Leflunomide, Methotrexate (MTX), Sulfasalazine (SSZ), Cyclophosphamide, Azathioprine, Cyclosporine, and D-penicillamine. Analgesics such as Acetaminophen, Tramadol, Diproqualone, and topical Lidocaine are used to treat RA. Glucocorticoids and Non-steroidal anti-inflammatory drug (NSAIDs) for control of pain and inflammation. NSAIDs used in the treatment of RA include Ibuprofen, Naproxen, Meloxicam, Etodolac, Sulindac, Tolementin, Choline magnesium salicylate, Diclofenac, Indomethacin, Ketoprofen and Piroxicam. Other drugs include gastroprotective agents (Omeprazole, Esomeprazole, Rabeprazole, Ranitidine, Famotidine) and Vitamin or Mineral supplements (Calcium, Vitamin-D) [12].

AIM OF THE STUDY

The purpose of this study is to analyze prescription patterns in the management of osteoarthritis and rheumatoid arthritis with a view to provide a deeper knowledge of drug use with current medications in our country. These studies analyze the trend of prescribing drugs; help to identify the problems associated with and provides feedback to the prescribers. Also helps to achieve more appropriate use of these drugs and better patient management with improved quality of life.

ETHICS APPROVAL

The study was conducted after obtaining ethics approval from the Institutional Ethics Committee of Sri Venkateshwara Institute of Medical Sciences (SVIMS) IEC No: 629

METHOD

Study design

We conducted a prospective observational study to analyze prescribing patterns in the management of rheumatoid arthritis and osteoarthritis over a period of six months in rheumatology department in Sri Venkateshwara Institute of Medical Sciences (SVIMS).

Inclusion Criteria

All the patients with a diagnosis of RA and OA of age group ≥18 years of both genders (male and female).

Exclusion Criteria

- Patients who are not willing to participate.
- Pregnant women and lactating women.
- Patients of age < 18 years**.**
- Patients diagnosed with other connective tissue diseases.

RESULTS:

Out of 100 outpatients who visited orthopedic department, 65% were diagnosed with RA and 35% with RA. Table 1 shows the demographic characteristics of patients. OA and RA were predominantly found in females (77.1% & 73.8%) than males (22.9%, 26.2%). Most commonly presenting age group of OA and RA were 51-60

and 41-50 years respectively. 100% of patients were brought to the hospital with joint pain as a symptom in both the diseases. Old age was the second risk factor for OA and RA (57.1% & 30.8% respectively) before gender. The co-morbid condition for OA and RA was hypertension of 20.1% and 23.1% respectively followed by diabetes mellitus, hypothyroidism and bronchial asthma. NSAIDS (85.7%) and DMARDS (100%) were the most common class of drugs prescribed in OA and RA respectively (Table 2). Naproxen (26.3%), Aceclofenac (26.3%) and methotrexate (26.3%) were the most commonly prescribed drugs in OA and RA (Table 3). The preferred route of administration was found as oral (100%). We found 50% of acetic acid derivatives as NSAIDs in OA and 16.9% of propionic acid derivatives for RA management. 54.2% of glucosamine in SYSADOA were prescribed for OA and 83.1% of glucocorticoids were for RA. Of the patient total, 14.3% were treated in monotherapy and 85.7% received two or more drugs. In monotherapy of RA, methotrexate (21.5%) was prescribed majorly. Two drug therapies in OA showed 34.2% of SYSADOA+NSAIDs combination, where as in RA, 52.3% of DMARD+DMARD combinations were prescribed. Other drugs such as antiulcer drugs, calcium and iron supplements were found in the prescriptions (Table 4).

Table 1: Prevalence and disease pattern in patients

Disease pattern of patients			
Disease pattern	**Prevalence (%)**	**Males (%)**	**Females (%)**
Osteoarthritis	35 %	22.9 %	77.1 %
Rheumatoid arthritis	65 %	26.2 %	73.8 %

Table 2: Age distribution, signs & symptoms, risk factors, co-morbiditis, types of drugs prescribed in patients

Age distribution in patients		
Age distribution (years)	**In OA patients (%)**	**In RA patients (%)**
21-30	0 %	9.2 %
31-40	14.3 %	24.6 %
41-50	28.6 %	35.4 %
51-60	45.7 %	20 %
61-70	11.4 %	10.8 %
Details of signs and symptoms in patients		
Pain	100%	100 %
Swelling	37.1%	40 %
Early morning stiffness	22.8%	40 %
Fever	5.7%	10.7 %
Difficulty to move	2.8%	3.1 %
Low back ache	20%	4.6 %
Parasthesias	11.4%	4.6 %
Generalized weakness	0%	7.7 %
Numbness	0%	1.5 %
Risk factors in patients		
Old age	57.1%	30.8%
Family history	51.4%	17%
Gender (females)	77.1%	73.8%
Trauma	11.4%	0 %
Post menopausal	14.28%	0 %
Others	2.85%	6.15%
Details of co-morbidities in patients		
Hypertension	20 %	23.1%
Diabetes mellitus	11.4 %	18.4%
Hypothyroidism	5.7 %	9.2%
Bronchial asthma	2.8%	3.1%
Types of categories of drugs prescribed in patients		
NSAIDs	85.7%	24.61%
SYSADOA	62.8%	3.07%
DMARDs (Hydroxychloroquine)	2.8%	0%
DMARDs	0%	100%
Steroids	0%	86.1%

Table 3: Drugs prescribed in OA and RA patients

OA	RA
Naproxen (26.3%)	Methotrexate (25.4 %)
Aceclofenac (26.3%)	Prednisolone (24.8 %)
Diclofenac (21.1%)	Hydroxychloroquine (23.8 %)
Acetaminophen (15.8%)	Leflunomide (10 %)
Hydroxychloroquine (2.6%)	Naproxen (5.5 %)
Celecoxib (2.6%)	Aceclofenac (5 %)
Tramadol (2.6%)	Sulphasalazine (3 %)
Etodolac (2.6%)	Methyl prednisolone (2 %)
	Azathioprine (0.5 %)

Table 4: Prescribing pattern of drugs in OA and RA patients

OA	RA
Route of administration in patients	
Oral (100%)	Oral (100%)
Injections (0%)	Injections (23.1%)
Topical (7.1%)	Topical (0%)
Approach to treatment	
Monotherapy (14.3 %)	Monotherapy (11.1 %)
Combination therapy (85.7 %)	Combination therapy (98.6 %)
Drugs used in monotherapy	
Acetaminophen (2.8%)	Methotrexate (21.5%)
Aceclofenac (2.4%)	Hydroxychloroquine (4.6%)
Tramadol (2.8%)	Leflunomide (3.1%)
Drugs in combination therapy	
NSAID + NSAID (20%) **(**Etodolac + Thiocolchicine) + Aceclofenac Diclofenac + Aceclofenac	**DMARDS + STEROIDS (27.6%)** Methotrexate + Prednisolone Hydroxychloroquine + Prednisolone Leflunomide + Prednisolone
DMARDS + NSAIDs (2.85%) Hydroxychloroquine + Aceclofenac	**DMARDs + DMARDs (52.3%)** Methotrexate + Hydroxychloroquine Leflunomide + Hydroxychloroquine Sulphasalazine + Hydroxychloroquine Methotrexate + Leflunomide Azathioprine + Hydroxychloroquine
SYSADOA + NSAIDs (34.2%) Glucosamine + Naproxen Glucosamine + Diclofenac Cholecalciferol + Naproxen Glucosamine + Aceclofenac Glucosamine + Celecoxib	**DMARDs + NSAIDs (15.4%)** Methotrexate + Aceclofenac Hydroxychloroquine + Naproxen Hydroxychloroquine + Aceclofenac Methotrexate + Naproxen Leflunomide + Aceclofenac
SYSADOA + SYSADOA (2.85%) Glucosamine + Cholecalciferol	
Other drugs prescribed as a supplementation	
Anti-ulcer drugs Esomeprazole (71.42%)	Esomeprazole (78.04%)
Pantoprazole (0%)	Pantoprazole (14.65%)
Ranitidine (7.14%)	Ranitidine (7.31%)
Omeprazole (7.14%)	Omeprazole (0%)
Pantocid DSR (14.3%)	Pantocid DSR (03%)
Calcium supplements Calcium carbonate + vitamin D3 (84.84%)	Calcium carbonate + vitamin D3 (93.44%)
Calcium + calcitriol (12.12%)	Calcium + calcitriol (4.93%)
Calcitriol + calcium + zinc (3.03%)	Calcitriol + calcium + zinc (1.63%)
Iron supplements Folic acid (0%)	Folic acid (90.74%)
Ferrous fumarate + folic acid (100%)	Ferrous fumarate + folic acid (9.26%%)

DISCUSSION:

A total of 100 patients were enrolled in the study out of which 35% were presented with OA and 65% with RA. We found both OA and RA were high in females (77.1% and 73.1%) respectively, suggesting that it is predominantly a disease of women [13-15].

The highly affected age group was 51-60 years (45.7%) in OA and 41-50 years (35.4%) in RA, in accordance with Anjali C et al13. The study showed that the predominant symptom of OA and RA was joint pain (50%, 47.10%) respectively [16].

In our study, female gender (75%) followed by old age (57.1%) has the high disease burden which contributes as the major risk factor in both OA and RA. Hypertension (30.43%, 34.9%) followed by diabetes mellitus (17.39%, 27.90%) were the most common comorbidities in both OA and RA [17].

In our study, majorly observed route of administration in the management of OA was oral (85.4%) followed by topical (14.6%) which was similar to the study of Anjali et al [13] and Mohamed et al [14] whereas in case of RA, majority of patients were prescribed of oral medications (81.3%) followed by injectables (18.7%) which were similar to the study conducted by Anjali et al [13]. This implies that oral route is the most convenient route of administration for the patients, preferable one for physicians and is efficacious as well.

The results revealed that DMARDs (46.8%) were the first choice of drugs prescribed in RA patients whereas NSAIDs in OA patients. As RA being a disease with autoimmune mechanism, DMARDs are considered the first choice and as proven in trials till date, NSAIDs are considered efficacious for disease control in OA. The study showed that Naproxen (26.31) and Aceclofenac (26.31 %) were majorly prescribed for OA as Naproxen causes lesser side effects like GI disturbances and cardiac risks than other NSAIDS, whereas Aceclofenac was beneficial over other analgesics for function improvement and to minimize gastrointestinal adverse events [18, 19]. We found methotrexate (25.4%) was the predominantly prescribed drug in RA. As methotrexate not only reduces pain and swelling, it can actually slowdown the joint damage and disease progression over time RA [20, 21].

In our study, we found the preferred therapy was combinational therapy (85.7%) than monotherapy (14.3%) [14]. Based on the recommendations by EULAR, combination therapy is considered superior to monotherapy in RA and the same pattern was found in our study too. In combinational therapy also, two drug therapies was mostly prescribed than three and four drug therapy in both OA and RA. The drug prescription patterns in two drug combinational therapy was found as SYSADOA + NSAIDs (34.2%) followed by NSAIDs + NSAIDs (20%) in OA where as DMARD + DMARD (52.3%) followed by DMARD + Steroid (27.6%) in RA.

In two drug therapy, the most widely prescribed SYSADOA +NSAID combinations were found as glucosamine+ naproxen, glucosamine + diclofenac, Cholecalciferol + naproxen, glucosamine + Aceclofenac, glucosamine + Celecoxib in OA whereas in RA, we found DMARD + DMARD combinations were Methotrexate + hydroxyl chloroquine, Leflunomide + hydroxychloroquine, sulphasalazine + hydroxychloroquine, methotrexate + leflunomide and azathioprine + hydroxyl chloroquine [21].

In the study, we found prescriptions with other supplements also such as antiulcer drugs, calcium supplements and vitamin D3. Esomeprazole was being the most prescribed antiulcer drug. This indicates that patients were on medications which had the potential tendency to cause GI disturbance. Routinely calcium supplements of calcium carbonate + vitamin D3 (84.84%, 93.44%) was prescribed in both OA and RA. Iron supplements such as Ferrous fumarate+folic acid (100%) was prescribed in OA, whereas folic acid (90.74%) in RA.

CONCLUSION:

From our results, it was concluded that majority of drugs in the prescriptions were from rational drug list. OA and RA were found more in females. In both the conditions of OA and RA, combinational therapy was preferred more than monotherapy. Either DMARD+DMARD or DMARD+Steroids were majorly prescribed for RA. For OA therapy, SYSADOA+NSAIDs or NSAIDs+NSAIDs were prescribed. Supplements such as antiulcer drugs, calcium and iron were routinely prescribed. We also found the prescribed drugs are rational and are in essential drug list.

CONFLICTS OF INTEREST

The authors declare that there is no conflict of interest.

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