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Original Article

Pharmacology Section

Study to Assess the Prescription Pattern and Quality of Life in Osteoarthritis Patients at a Tertiary Care Hospital

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ABSTRACT

Introduction: Osteoarthritis (OA) often called wear and tear arthritis is a chronic progressive musculoskeletal joint disease with multifactorial aetiology, affecting millions of people around the world. It is one of the leading causes of morbidity, having major impact on Quality of Life (QoL) of the patient with substantial economic and social burden. OA can have a negative impact on health related QoL and psychological well-being of the individual.

Aim: To evaluate the prescribing trends of drugs in the management of OA in a tertiary care teaching hospital and to assess the effect of pharmacotherapy on QoL of OA patients in terms of subjective and functional status using Western Ontario and McMaster Universities Arthritis index scale (WOMAC)-modified Centre for Rheumatic Disease (CRD) Pune version OA patients.

Materials and Methods: Prospective observational study conducted among the OA patients in Orthopaedic Department over the period of one year between November 2014-December 2015. Adult patients of either gender diagnosed with OA for minimum period of three months were enrolled for the study. Out of 285 eligible patients, drug therapy of 256 patients' data were analysed and they were given treatment by the treating orthopaedician. All the patients were asked to personally complete the WOMAC index scale during their first visit. They were followed-up for one month of pharmacotherapy in order to assess change in the WOMAC index scale. Data were analysed using Statistical Package for the Social Sciences (SPSS) software 16.0 version. The p-value <0.05 was considered statistically significant.

Results: Among 256 patients who completed the study, the most frequently prescribed drug class was NSAIDs (82.1%). Acelofenac with Paracetamol combination (117) and Diclofenac monotherapy (44) were most commonly prescribed. Statistically significant reduction in the WOMAC (pain, stiffness and physical function) score was observed in the follow-up visit when compared to first visit (p<0.0001) after one month of pharmacotherapy in patients taking Diclofenac and Aceclofenac with Paracetamol combination.

Conclusion: This study highlighted the significant improvement in QoL and significant reduction in WOMAC scores with Aceclofenac-Paracetamol combination and Diclofenac monotherapy in OA patients.

Keywords: Analgesics, Combination therapy, Follow-up, Monotherapy

INTRODUCTION

The OA is a chronic progressive musculoskeletal degenerative joint disease causing substantial morbidity among elderly people in both developing and developed countries [1]. Worldwide estimate showed that the elderly population suffer from symptomatic OA with limitation of movement and unable to perform their daily activities [2]. In India, nearly 60 million people will be affected by arthritis by 2025 and it is found to be the fourth leading cause of disability and death in the world [3,4]. Among pharmacological therapy, Nonsteroidal Anti-Inflammatory Drugs (NSAIDs) pretend to play a necessary role in the treatment of OA. The analgesic effects of the different NSAIDs are more or less identical but Coxibs were associated with a lower risk for upper Gastrointestinal (GI) side effects [5]. Newer treatment strategies like drugs that target chondrogenesis and angiogenic factors are also used [6]. The QoL of OA determined by clinical condition and physical functioning decreases due to the disease advancement [7]. Studies had been conducted to evaluate and improve the QoL of the OA patients with NSAIDs therapy across the world [8-10]. However, there is sparseness of data focusing on QoL impact in OA in South India [11]. Hence, the present study was planned to evaluate the prescribing trends of drugs and to assess its effect on QoL using Western Ontario and McMaster Universities Arthritis index scale (WOMAC)- modified Centre for Rheumatic Disease (CRD) Pune version among the South Indian population.

MATERIALS AND METHODS

Prospective observational study was conducted in the Department of Orthopaedics in collaboration with Department of Pharmacology in a tertiary care teaching hospital over a period of one year (November 2014-December 2015). The study was initiated after obtaining permission from the Institutional Ethics Committee (Code No: 87/2014). Sample size was calculated using the formula $4pq/l^2$ considering 16% improvement in QoL by pharmacotherapy in OA patients [12]. With 10% non-response rates and 95% confidence interval, the sample size was calculated as 256. Confidentiality was maintained throughout the study. Total of 285 eligible patients diagnosed with OA, attending Orthopaedic (outpatient and inpatient) Department at a tertiary care hospital were screened for the study. The details about the study were explained to each patient in their vernacular language. Written informed consent was obtained from all of them. The OA patients were screened and who had met the eligibility criteria were enrolled in the study.

Inclusion criteria

- Patients with OA of either gender
- Age between 20 to 70 years
- Those who were fulfilling the clinical or radiological American College of Rheumatology Diagnostic Guidelines for Osteoarthritis Knee (ACR) suffering from joint pain for at least three month duration with Minimum WOMAC Index score of 40 at the time of screening [13].

Exclusion criteria

- Other inflammatory joint diseases (rheumatoid arthritis, ankylosing spondylitis, psoriasis, gout, neuropathic, congenital or metabolic conditions affecting joints).
- Medical history of congestive cardiac failure, chronic kidney disease, active peptic ulcer and oesophageal varices.
- Pregnant and lactating women.
- Past history of any orthopaedic surgery.

The general physical examination and baseline investigations were advised to rule out any co-morbid medical condition. Patient's demographic details namely name, age, sex, occupation, address and phone/mobile number were noted. Details of patient complaints, duration of the disease, affected joint and progression of the disease were recorded. Data on drug details in terms of dose, route of administration and duration of the course were also recorded.

The WOMAC index scale was used in OA patients to assess the QoL during their first and second visit after one month (follow-up). WOMAC is widely used by healthcare professionals, a proprietary set of standardised questionnaires to assess OA patients. Patients were explained about the WOMAC index scale in their vernacular language. Literate patients were asked to personally complete the WOMAC index scale and in case of illiterate patients, the questions were asked verbally and their responses were recorded to assess baseline pain characteristics, stiffness factors and physical function parameters. The WOMAC index scale for Indian population (i.e.,) the WOMAC scale modified CRD Pune version was used [14].

(a) The intensity of pain was assessed using Likert scale (5 items): during walking, using stairs, in bed, sitting or lying and standing.

(b) The stiffness characteristics were assessed by (2 items): after first walking and later in the day.

(c) The physical function ability was assessed by (17 items): stair use, raising from sitting, standing, bending, walking, getting in/out of a car or bus, shopping, raising from bed, lying in bed, sitting, getting on/off toilet, heavy household duties, light household duties sitting cross legged, raising from cross legged position and squatting were noted. All the patients were followed-up after one month of pharmacotherapy (follow-up visit) in order to assess change in the WOMAC index scale from baseline (first visit).

Scoring and Interpretation

Two scales are available in WOMAC index namely: a) Likert scale; and b) Visual analogue scale [15].

(a) Likert Scale:

It consists of following responses for each question and individual scores for each response, None-0, mild-1, moderate-2, severe-3, extreme-4

Score range: Pain → 0-20, Stiffness → 0-8, Physical function → 0-68

(b) Visual Analogue Scale

The 100 mm Visual Analog version uses: a) No pain/stiffness/difficulty; b) Extreme pain/stiffness/difficulty. For measuring visual analog scale a ruler is used to measure the distance (in mm) from the left end marker to the patient's mark. For each item, the possible range of scores is 0-100. Scores range: Pain → 0-500, Stiffness → 0-200, Physical function → 0-1700. In the present study, WOMAC Score was analysed using only the Likert Scale.

STATISTICAL ANALYSIS

Data were entered and analysed using SPSS software version 16.0 version and expressed in descriptive statistics. WOMAC scores (pain, stiffness and physical function) were expressed as mean±standard deviation (SD). WOMAC scores at the first visit and follow-up visit were analysed using student paired t-test. The p-value <0.05 was considered as statistically significant.

RESULTS

A total of 285 OA patients were screened and among them 275 patients who satisfied the eligibility criteria were recruited for the study. Nineteen patients lost their follow-up visits even after sending more than three reminders and finally analysis were done for 256 patients data. Among the study population, females were predominant accounting for 64.8% (166) and 35.2% (90) were males. Majority of the patients 62.9% (161) belonged to the age group of 40 to 60 years. More than half of the patients had bilateral OA knee (58.6%) [Table/Fig-1]. Most frequent co-morbid conditions were hypertension seen in 19 patients (7.4%) followed by diabetes mellitus in 14 patients (5.5%), asthma in 4 patients (1.6%), Coronary Artery Disease (CAD) in 2 patients (0.8%) and hypothyroidism in 2 patients (0.8%). The study observed that about 71.5% (183) of the patients received four and more than four drugs. Only one patient received nine drugs [Table/Fig-2]. Among the various drug class prescribed, NSAIDS (Paracetamol-500 mg TID, Diclofenac-50 mg BID, Aceclofenac-100 mg BID, Ibuprofen-400 mg BID, Indomethacin-25 mg BID, Etodolac-300 mg BID, Ketorolac-60 mg) prescribed were estimated to be 35.8% (379) followed by Opioids (Tramadol-50 gm BID, Tapentedol-100 mg BID) 3.7% (33) and others (Diacerein-50 mg OD) 1.3% (14), gastro protective agents 23.1% (244), calcium supplements 16.3% (172), multivitamins 16.5% (174). Ferrous sulfate, Pregabalin, Trypsin, Atorvastatin were the other drugs 3.9% (42) out of 1058 drugs used for OA patients [Table/Fig-3]. The common route of drug administration in OA patients was oral in 220 patients (85.9%) followed by intramuscular in 21 patients (8.2%) and topical in 15 patients (5.9%). There was statistically significant reduction in the pain, stiffness and physical function score in the follow-up visit when compared to first visit (p<0.0001) after a month of pharmacotherapy [Table/Fig-4]. Statistically significant reduction in WOMAC score was also observed in the follow-up visit when compared to first visit for Aceclofenac and Paracetamol, Diclofenac, Tramadol with Paracetamol, Etodolac with Paracetamol, Paracetamol (p<0.0001)

Demographic data	Number of patients N=256 (%)
Age (Years)	
<40	28 (10.9)
40-60	161 (62.9)
61-70	67 (26.2)
Gender	
Male	90 (35.2)
Female	166 (64.8)
Marital status	
Married	245 (95.7)
Unmarried	11 (4.3)
Duration of the disease	
<1 year	118 (46.1)
1-3 years	108 (42.2)
>3 years	30 (11.7)
Site of osteoarthritis	
Right knee	53 (20.7)
Left knee	53 (20.7)
Both knee	150 (58.6)

[Table/Fig-1]: Demographic details of study participants.

Number of drugs prescribed per patient	Number of patients (%)
2	21 (8.2)
3	52 (20.4)
4	89 (34.9)
5	67 (26.3)
6	20 (7.8)
7	6 (2.4)
9	1 (0.4)

[Table/Fig-2]: Frequency distribution of number of drugs prescribed per prescription.

Drugs	Number of prescriptions		Total	
	Monotherapy	Combination therapy	Number of prescriptions	Percent (%)
NSAIDS				
Paracetamol	19	192	211	82.4
Diclofenac	44	13	57	22.2
Aceclofenac	0	117	117	45.7
Etodolac	0	31	31	12.1
Ketorolac	0	2	2	0.8
Ibuprofen	1	0	1	0.4
Indomethacin	2	0	2	0.8
OPIOIDS				
Tramadol	0	32	32	12.5
Tapentadol	0	1	1	0.4
OTHERS				
Diacerein	9	5	14	5.4

[Table/Fig-3]: Frequency distribution of Monotherapy and Combination therapy in OA patients.

and Diacerein (p<0.01) [Table/Fig-5,6]. Percentage reduction in Womac score was calculated from first visit and follow-up visit scores using the formula P=a/b×100 where P is Percentage reduction, a is reduction difference between first and follow-up visit and b is original percentage value that was reduced. Based on this Pain, Stiffness and Physical function scores, reduction was 28%, 17%, 20%, respectively.

DISCUSSION

Two hundred and fifty six OA patients completed the present study with female preponderance (64.8%) as supported by Gupta R et al., and Poornima B et al., [1,16]. This female predominance was the major risk factor for OA and this could be due to their lack of physical activity, mobility and social issues. Majority of the patients (62.9%) were in the age group of 40 to 60 years which is similar to the study conducted by Gurung S et al., [17]. Dominance of knee OA with the duration of illness being 1 to 3 years (42.2%) was observed in the present study and this could be attributed with probable excessive use of squatting and cross-leg sitting positions

WOMAC scores	First visit scores	Follow-up visit scores	p-value
Pain score	13.1±2.4	9.4±2.5**	<0.0001
Stiffness score	2.3±1.5	1.9±1.4**	<0.0001
Function score	47.2±5.2	37.6±6.2**	<0.0001
Total score	62.7±7.9	48.9±8.9**	<0.0001

[Table/Fig-4]: WOMAC score for pain, stiffness, physical function during first and follow-up visits.
WOMAC: Western Ontario and McMaster Universities Arthritis Index Values are expressed as Mean±SD
**p<0.0001 as compared to first visit scores
Analysis was done using paired student t-test

Drugs	Number of patients	First visit scores	Follow-up visit scores	p-value
T. Aceclofenac+Paracetamol	117	63.92±6.9	50.09±7.9**	<0.0001
T. Diclofenac	57	60.57±8.1	46.76±10.3**	<0.0001
T. Tramadol+Paracetamol	32	64.86±6.8	50.93±7.2**	<0.0001
T. Etodolac+Paracetamol	29	60.17±8.7	46.55±9.6**	<0.0001
T. Paracetamol	19	62.11±9.5	49.74±8.4**	<0.0001
T. Diacerein	9	59.14±9.1	43.29±12.8*	<0.001

[Table/Fig-5]: Comparison of WOMAC score among NSAIDS, Opioids and Diacerein users.
WOMAC: Western Ontario and Universities Arthritis McMaster Index Values are expressed as Mean±SD
*p<0.001 as compared to first visit scores
**p<0.0001 as compared to first visit scores
Analysis was done using paired student t-test

in Indian customs. The present study results were comparable with the study conducted by Poornima B et al., and Venkatachalam J et al., where knee joint was commonly involved in OA [16,18]. The most frequent co-morbid conditions were hypertension, diabetes, CAD, asthma and hypothyroidism which was similar to study done by Gurung S et al., [17].

Pharmacological treatment is aimed to relieve the signs and symptoms and indeed, to reduce the disease progression with improvement in QoL. Based on this, the most frequently prescribed drug class was NSAIDs similar to the study done by Sahayam JSA et al., where NSAIDs were commonly prescribed [19]. Gastro protective agents were commonly prescribed in OA patients to prevent non-selective NSAIDs induced Gastrointestinal adverse effects and also calcium supplements were prescribed to increase bone strength in the OA patients which was in accordance with study done by Poornima B et al [16]. Paracetamol was most frequently prescribed as combination therapy along with Aceclofenac, Tramadol and Etodolac whereas Diclofenac was commonly used as monotherapy. In contrast to present study, Poornima B et al., study showed Etoricoxib and Aceclofenac were the frequently prescribed drug as monotherapy and among the combination therapy, Paracetamol was prescribed with Aceclofenac, Diclofenac and Tramadol as compared with present study observation [16]. Tramadol combined with paracetamol has been used in only 32 patients (12.5%) in the present study.

A	Drugs	Number of patients	Pain score		p-value	Stiffness score		p-value	Physical function score		p-value
			First visit	Follow-up visit		First visit	Follow-up visit		First visit	Follow-up visit	
1	T. Aceclofenac+Paracetamol	117	13.34±2.2	9.59±2.4**	<0.0001	2.51±1.4	2.10±1.4**	0.0001	48.08±4.3	38.40±5.6**	0.0001
2	T. Diclofenac	57	12.57±2.6	8.78±2.7**	<0.0001	2.16±1.7	1.80±1.5	0.002	45.84±5.1	36.18±7.1**	0.0001
3	T. Tramadol+Paracetamol	32	13.90±1.9	10.14±2.3**	<0.0001	2.45±1.4	2.03±1.5	0.005	48.52±4.5	38.76±4.8**	0.0001
4	T. Etodolac+Paracetamol	29	12.83±2.8	9.07±2.7**	<0.0001	2.14±1.6	1.55±1.5*	0.007	45.21±5.4	35.93±6.8**	0.0001
5	T. Paracetamol	19	12.63±2.3	9.16±2.2**	<0.0001	1.79±1.4	1.63±1.4	0.268	47.68±6.8	38.95±6.1**	0.0001
6	T. Diacerein	9	11.86±3.6	7.86±3.8*	0.001	1.57±1.1	1.43±1.5	0.805	45.86±5.3	33.86±7.7*	0.001

[Table/Fig-6]: Change in WOMAC score (pain, stiffness and physical function) during first and follow-up visits among NSAIDs, Opioids And Diacerein Users
Values are expressed as Mean±SD. * p<0.01 as compared to first visit scores. . ** p<0.0001 as compared to first visit scores.
Comparison was done by student paired 't' test
WOMAC: Western ontario and mcmaster universities arthritis index; T: Tablet

This study utilised modified WOMAC index-CRD Pune version to assess the QoL which showed significant reduction in the pain, stiffness and physical function scores in the follow-up visit when compared to first visit with 28% reduction in pain score, 17% reduction in stiffness score and 20% reduction in physical function score, after a month of pharmacotherapy which is the supporting evidence for the efficacy of the NSAIDs being used globally. Jadhav MP et al., reported using WOMAC score that there were 20%, 30% and 16% reduction in pain subscale, stiffness and physical function, respectively after 12 weeks of pharmacotherapy in their study [12]. This reduction was in the all three domains in WOMAC score with 12 weeks of pharmacotherapy as compared with 4 weeks of therapy in the present study.

It was also observed that combination of Aceclofenac with Paracetamol had caused significant reduction in all the three subscales of WOMAC score during follow-up visit when compared to first visit ($p<0.0001$). The study result was in accordance with Kanaki AR et al., who observed that Aceclofenac treated patients had statistically significant reduction ($p<0.0001$) in WOMAC scores when compared to Diclofenac group at the end of third month [20]. The improvement in WOMAC score with Aceclofenac therapy is attributed to its easy penetration into inflammatory tissue, such as joints and effectively suppressing prostaglandin production by the inhibition of cyclooxygenase (COX-1 and COX-2) enzyme with moderate selectivity for COX-2 inhibition. It also possesses inhibiting action on IL-β which in-turn has stimulatory effect on synthesis of cartilage matrix. Invitro studies have shown that, Aceclofenac causes stimulation of glycosaminoglycan synthesis in human osteoarthritic cartilage and protects chondrocytes. The anti-inflammatory effect of Aceclofenac could also be due to inhibition of various mediators like IL-6 and tumour necrosis factor in human osteoarthritic synovial cells and articular chondrocytes. It was also found that inhibition of reactive oxygen species ion and expression of cell adhesion molecules in human neutrophils ascribed to the action of Aceclofenac [21]. Paracetamol, a simple analgesic with minimal anti-inflammatory action was frequently recommended as a first line drug in the treatment of OA. This study also showed that Paracetamol significantly improved the pain and physical function score ($p<0.0001$) during follow-up when compared to first visit. However, reduction in stiffness score was not significant ($p=0.268$) in Paracetamol during follow-up visit [Table/Fig-6]. Paracetamol acts by inhibiting the COX isoenzymes and exhibits poor anti-inflammatory action [22]. Animal studies have shown that paracetamol modulates descending serotoninergic pathways involved in inhibition of pain sensation. It was also found that paracetamol inhibit L-Arginine/NO pathway in the nociceptive processes of the spinal cord that are activated by Substance P and N-methyl-D-aspartate receptors [23]. Surprisingly, this study also indicated that Coxibs were not prescribed in any of the patients with OA which could be due to their adverse effects. In addition to pharmacotherapy, patient's education about the disease and beneficial role of other non-pharmacological measures like exercise should also be emphasised.

Limitation(s)

Though this study had demonstrated the improvement of QoL by pharmacotherapy, the OA patients were followed-up for one month only which has become the constraint of the present study. Moreover, present study was a hospital based study and not a community based with limited sample size. Regular prescription analysis should be recommended in larger sample size with repeated follow-ups in order to improve the awareness and enable suitable modification in the prescription of OA patients to increase the therapeutic benefits.

CONCLUSION(S)

The study indicates that there is a significant improvement in QoL of the patients determined by WOMAC score (pain, stiffness and physical function) after a month of pharmacotherapy. Aceclofenac with paracetamol combination therapy and Diclofenac monotherapy were most frequently prescribed among the NSAIDs. Safety is the proven concern in treating chronic conditions in OA, hence Aceclofenac and Paracetamol is recommended as combination therapy. To infer, this study indicates that oral NSAIDs when promptly used could provide promising relief of pain, improve physical function and QoL.

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