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ORIGINAL ARTICLE

Prescribing Pattern for Osteoarthritis In A Tertiary Care Hospital

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ABSTRACT

Background: Treatment of osteoarthritis aims at reducing pain and improving mobility. NSAIDs are widely prescribed for symptomatic relief despite well-known adverse effects. Paracetamol with its better safety profile is recommended as the initial analgesic of choice. SYSADOA is a generic term used for **sy**mptomatic **s**low **a**cting **d**rugs for **o**steo**a**rthitis, and includes glucosamine sulphate and related compounds, chondroitin sulphate, and diacerein. SYSADOA when compared to NSAIDs, are safer, comparable in symptomatic efficacy and better in structure modifying efficacy in osteoarthritis. A drug utilization study is considered to be one of the most effective methods to assess and evaluate the prescribing attitude of physicians. Despite the considerable socio-economic impact of OA, not many studies have established the drug-prescribing trend in India. Hence we decided to study the prescribing pattern of SYSADOA, paracetamol and NSAIDs in OA vis-à-vis the standard recommendations and in the process provide constructive feedback to prescribing clinicians.

Methods: Prescriptions for osteoarthritic patients collected cross-sectionally for six months from an orthopaedic outpatient unit in a tertiary care hospital, were analysed.

Results: Out of 154 prescriptions analysed, 7% were prescribed glucosamine and chondroitin, while 4% received diacerein. Paracetamol was prescribed in 17% cases. NSAIDs were prescribed in 84%, with 27% receiving two or more NSAIDs simultaneously.

Conclusion: SYSADOA and paracetamol were under-prescribed while NSAIDs were probably over-prescribed.

Key Message

- The prescribing pattern for osteoarthritis in the study setup differs from the guidelines recommended by the Osteoarthritis Research International and European League against Rheumatism.
- Gastrointestinal adverse effects of NSAIDs requiring the use of gastro-protectives can be minimized by increasing the use of paracetamol and SYSADOA

Key words: SYSADOA, glucosamine sulphate, chondroitin sulphate, diacerein, osteoarthritis

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Introduction

Osteoarthritis (OA) is becoming increasingly recognized in both developed and developing countries as a major cause of chronic pain and disability among the elderly [1]. Its high prevalence and moderate-to-severe impact on daily life pose a significant public health problem [2]. Today, the management of OA is largely palliative, focusing on the alleviation of symptoms. Current recommendations for the management of OA include a combination of non-pharmacological interventions (weight loss, education programs, exercise, and lifestyle changes), pharmacological treatments (paracetamol, nonsteroidal anti-inflammatory drugs [NSAIDs], topical medication) and invasive interventions (intra-articular injections, lavage, arthroplasty) [3, 4]. Among the pharmacological treatments, NSAIDs remain the most widely prescribed drugs for OA, despite the fact that they provide only symptomatic relief and do not prevent progression of the disease [5]. Moreover, NSAIDs cause serious adverse effects, especially on long term use, accounting for over 16,500 deaths and over 103,000 admissions to hospital each year in the United States [6]. It is for this reason that paracetamol due to its better gastrointestinal safety profile has been recommended as the initial drug of choice for symptomatic relief in OA [3], [4]. NSAIDs should be considered only in patients unresponsive to paracetamol [3]. In this context, there is a need for safe and effective alternative treatments which would provide both symptomatic improvement and disease modifying effects in OA. SYSADOA may provide an answer, as many clinical trials have proven their safety and efficacy for symptom relief and possible structure-modifying effects [7], [8], [9], [10]. SYSADOA is a generic term used for **sy**mptomatic **s**low **a**cting **d**rugs for **OA**, and includes glucosamine sulphate and related compounds, chondroitin sulphate, and diacerein [3]. Glucosamine sulphate is the sulphate derivative of the natural aminomonosaccharide, glucosamine. Glucosamine is a normal constituent of glycosaminoglycans in cartilage matrix and synovial fluid. Chondroitin is a highly hydrophilic, gel-forming polysaccharide macromolecule. Its hydrocolloid properties convey much of the compressive resistance of cartilage, preventing cartilage loss. Diacerein or diacetylrhein is an anthroquinone which probably acts by inhibiting IL1beta induced nitric oxide production and metalloproteinases [11]. The recent EULAR (The European League Against Rheumatism) and OARSI (Osteoarthritis Research Society International) recommendations have laid down the importance of use of these disease modifying drugs in OA of hip and knee [3], [4]. However there still seems to be some reservation and a lot of confusion regarding the effectiveness of these drugs in OA. A drug utilization study is considered to be one of the most effective methods to assess and evaluate the prescribing attitude of physicians [12]. Despite the considerable socio-economic impact of OA, not many studies have established the drug-prescribing trend in India. Hence this drug utilization review was carried out to study the prescribing pattern of SYSADOA, paracetamol and NSAIDs in OA vis-à-vis the standard recommendations and in the process provide constructive feedback to prescribing clinicians.

Methods

Prescriptions of patients diagnosed with OA were collected from an orthopaedic outpatient unit in a tertiary care hospital, for a period of six months. Relevant data (including age, sex, duration of disease, drugs prescribed and doses) were recorded and the prescribing pattern of SYSADOA, paracetamol and NSAIDs analyzed. Drugs accounting for drug utilization 90% (DU 90%) segment were noted. DU 90% segment is the number of drugs accounting for 90% of drug use [13]. This method is inexpensive, flexible and simple for assessing the quality and quantity of drug use in routine health care. The study was approved by the Institutional Ethics

Committee. Descriptive statistical analysis was done.

Results

One hundred and fifty four patients with the diagnosis of OA visited the orthopaedic outpatient unit during the six months in which data was collected. Prescriptions of all 154 patients were analyzed, out of which 66 (43%) were male and 88 (57%) female. [Table/Fig 1] shows the demographic characteristics of the patients. One hundred and fifty three (99%) patients were affected with osteoarthritis of the knee alone, either unilateral or bilateral. In one patient along with the knees, the right wrist was also involved. Thirty nine patients were newly diagnosed cases of OA, 115 were old cases.

(Table/Fig 1) Demographic characteristics of patients

Characteristic	n=154
Male : Female	66 : 88
Mean Age (±SD)	62.3 (±7.8)
Newly diagnosed (%)	39 (25.4%)
Old cases (%)	115 (74.6%)

[Table/Fig 2] shows the details of the drugs used. Only ten (7%) patients were prescribed glucosamine; nine received a combination of glucosamine and chondroitin while one received glucosamine alone. Six (4%) patients were prescribed diacerein.

(Table/Fig 2) Frequency of drugs prescribed in osteoarthritis

Drug		N* (%)
Diclofenac	Topical	31
	Systemic monotherapy	17
	Combinations:	20
	Diclofenac + Rabeprazole	10
	Diclofenac + Serratiopeptidase	5
	Diclofenac + Paracetamol	3
	Diclofenac + Paracetamol + Serratiopeptidase	1
	Diclofenac + Paracetamol + Dextropropoxyphene	1
	Total	68 (44)
Paracetamol	Monotherapy	5
	Combinations:	21
	Paracetamol + Aceclofenac	8
	Paracetamol + Tramadol	7
	Paracetamol + Ibuprofen	1
	Total	26 (17)
Naproxen	Monotherapy	21 (14)
Aceclofenac	Monotherapy	13
	Combinations	8
	Total	21 (14)
Nimesulide	Topical	1
	Systemic	18
	Total	19 (12)
Etoricoxib		10 (7)
Piroxicam	Topical	1
	Systemic	7
	Total	8 (5)
Ibuprofen	Monotherapy	1
	Combination	1
	Total	2 (1)
Glucosamine + Chondroitin sulphate		10 (7)
Diacerein		6 (4)
Anti-ulcer agents	Pantoprazole	13
	Rabeprazole	10
	Omeprazole	1
	Ranitidine	5
	Total	29 (19)

***N- number of prescriptions**

A total of 174 NSAIDs were used. Forty two (27%) prescriptions contained more than one NSAID. Twenty four (16%) patients were not prescribed any NSAID. In 5 (3%) patients only topical NSAIDs were prescribed. In 28 (18%) patients both topical and systemic NSAIDs were prescribed simultaneously. Diclofenac, paracetamol, naproxen and aceclofenac accounted for the DU 90% segment. The most common NSAID used was diclofenac, totaling to 68 (44%). Paracetamol was prescribed in 26 (17%) cases, either alone or in combination with NSAIDs. Etoricoxib, the only COX – 2 inhibitor used, was prescribed in 10 (7%) patients. Various gastroprotective agents were used along with the oral NSAIDs in 29 (19%) patients, pantoprazole being the most preferred one.

Discussion

As has been reported in the existing medical literature, [14], [15] in this study too, OA was found to be overwhelmingly more common in the knee than in other joints and was more common in females than in males. Despite the huge international hype and claims of recent increase in consumption of drugs like glucosamine in OA [16], this

study found that SYSADOA (glucosamine, chondroitin and diacerein) have been used sparingly, despite these drugs being very safe and so far the only ones having both symptom modifying and structure modifying effects in OA. Many reports including the recent EULAR and OARSI recommendations have favoured their use [3], [4],[7], [8], [9], [10], especially in early OA. Their under-prescription probably reflects the lack of faith in the clinical effectiveness and cost effectiveness of these drugs. Large scale randomized clinical trials are needed to clear the air regarding the benefits of using these drugs. In the meantime, SYSADOA should be welcomed if the patient can afford them, even if they only marginally delay the progression of this chronic disabling disease while safely improving the symptoms.

Paracetamol has been recommended as the oral analgesic to be used first and if effective, for long durations owing to its gastrointestinal safety. Analgesic efficacy of paracetamol has been found to be comparable to that of ibuprofen and naproxen [17], [18]. NSAIDs are to be started only if the patient is unresponsive to paracetamol. However, paracetamol too was under-prescribed, with only 17% patients receiving it, and only 3% receiving it as monotherapy. This could be because the symptom-modifying efficacy of paracetamol in OA is suspect, as found in some studies [19], and as perceived by most physicians.

As against the use of SYSADOA and paracetamol, NSAIDs were prescribed in 84% of patients, with 27% patients receiving two or more NSAIDs at the same time. Simultaneous use of two or more NSAIDs, which essentially act by the same mechanism, defies logic. Inspite of the disturbing statistics of the adverse effects of oral NSAIDs and their limited disease modifying efficacy, these drugs have been found to be the most preferred. Diclofenac was the most common NSAID used (44%). Though ibuprofen has been rated as the safest conventional NSAID [20], only two prescriptions contained it. Selective COX-2 inhibitors (used in 7% patients) seem to have lost the race, probably owing to reports of associated cardiovascular risks. Topical NSAIDs were used in only 21% of patients, either alone or in combination with systemic NSAIDs. There is growing evidence that topical and oral NSAIDs have equivalent efficacy; moreover, topical NSAIDs display better gastrointestinal safety than their systemic counterparts [21]. With doubts about the analgesic efficacy of paracetamol in OA, and concerns about cardiovascular effects of selective COX-2 inhibitors, topical NSAIDs should be used more often for symptomatic relief in OA. However, this study found that in patients with gastrointestinal risk, conventional NSAIDs combined with gastroprotective agents (19%), mainly proton pump inhibitors were preferred instead. Results of similar drug utilization studies in OA have been tabulated in [Table/Fig 3]. Only one study [25] found the management of OA being followed was satisfactorily close to the standard guidelines.

(Table/Fig 3) Summary of similar studies

Study	Relevant results: drugs used			Remarks
	NSAIDs	Paracetamol	SYSADOA	
Present study	84%	17%	11%	NSAIDs most frequently used; paracetamol and SYSADOA underprescribed
OA: medication & health service utilization study[22]	Unselective COXI– 38.7% COX-2I- 2.6%	1.0 %	13.34%	NSAIDs used most frequently; paracetamol and SYSADOA only marginally prescribed
Prescription pattern in OA at PUHC[23]	Unselective COXI- 40% COX-2I- 36%	24%	Not in DU 90%	Nimesulide over-used
HERAS survey[24]	38.7%	26.7%	Not available	only 42.1% of the OA patients had a guideline adequate treatment
Drug treatment modalities in OA at Royal London and Newham University Hospitals[25]	40%	76%	39%	paracetamol and complementary therapy well utilized

In conclusion, this study has found that in the treatment of osteoarthritis NSAIDs, especially oral diclofenac is the most preferred drug. Paracetamol, SYSADOA and topical NSAIDs are being under-prescribed.

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