

# Impact of Polypharmacy on Functional State in Patients with Symptomatic Knee Osteoarthritis

Goksen Goksenoglu<sup>\*</sup>, Mustafa Aziz Yildirim

Department of Physical Medicine and Rehabilitation, Istanbul Physical Medicine and Rehabilitation Education Research Hospital, Istanbul, Turkey

## Email address:

[goksenogkosenoglu@hotmail.com](mailto:goksenogkosenoglu@hotmail.com) (G. Goksenoglu), [mustafaaziz1907@hotmail.com](mailto:mustafaaziz1907@hotmail.com) (M. A. Yildirim)

<sup>\*</sup>Corresponding author

## To cite this article:

Goksen Goksenoglu, Mustafa Aziz Yildirim. Impact of Polypharmacy on Functional State in Patients with Symptomatic Knee Osteoarthritis. *Science Journal of Clinical Medicine*. Vol. 7, No. 3, 2018, pp. 25-29. doi: 10.11648/j.sjcm.20180703.11

**Received:** April 15, 2018; **Accepted:** May 2, 2018; **Published:** May 28, 2018

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**Abstract:** *Background:* Osteoarthritis (OA) is a degenerative, common and progressive inflammatory joint disease starting with disruption and corrosion of articular cartilage. Polypharmacy can be considered as use of multiple drugs. Objective: To investigate the correlation between polypharmacy for patients with symptomatic knee osteoarthritis and their function, pain, daily life activities and quality of life. Method: Fifty patients, diagnosed with knee osteoarthritis according to the American College of Rheumatology (ACR) classification criteria, were included in this study. Patient's demographic data, height, weight, body mass index, knee pain duration, number of painful knees, drugs used for treatment of comorbid diseases and knee osteoarthritis as well as drugs used for other diseases were recorded. Using 5 or more drugs were regarded as polypharmacy in this study. Characteristics of patients with polypharmacy were compared to those without polypharmacy. Kellgren-Lawrence Classification was used for radiological grading of knee osteoarthritis of the patients. Knee osteoarthritis related symptoms and functional state were evaluated by Knee Injury and Osteoarthritis Outcome Score (KOOS). Mini Mental State Examination (MMSE) was used for identifying the cognitive level. Result: Mean age of the patients included in the study was 64±13.7 years. 35 patients (70%) were female. Mean body mass index was 30.6±4.2 kg/m<sup>2</sup>. Mean knee pain duration was 4.9±3.8 years. 30 patients (60%) had bilateral knee involvement. Twenty-one patient (42%) had polypharmacy. While NSAIDs is the most frequently used drug, the most frequently observed comorbidity was hypertension. Kellgren Lawrence grade was significantly ( $p < 0.05$ ) higher in the group with polypharmacy than the group without polypharmacy. KOOS symptoms, pain, function-daily life, sport recreational acts, quality of life and total score and MMS total score were significantly ( $p < 0.05$ ) lower in the group with polypharmacy than the group without polypharmacy. Discussion: It has been observed that polypharmacy affects the functional state and quality of life negatively in patients with knee osteoarthritis. *Conclusion:* Attention must be paid to the training activities raising awareness for appropriate drug use, and awareness of the physicians as well as elderly people regarding the polypharmacy must be expanded.

**Keywords:** Polypharmacy, Osteoarthritis, Functional State

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## 1. Introduction

Osteoarthritis (OA) is a degenerative, common and progressive inflammatory joint disease starting with disruption and corrosion of articular cartilage. Pain and limitation of motion as well as additional complaints such as asthenia, insomnia and depression can be observed in this disease, affecting frequently loaded joints. Risk factors, prevalence and progression of disease vary by the joint affected. Bearing the

majority of body weight, knee joint is the joint that is most frequently exposed to osteoarthritis symptomatically [1-3]. With a prevalence increased by age, OA is a disease that can be observed in almost half of the population over 65 [4]. Drug use of the geriatric patients is increased as prevalence of the chronic diseases increases. Besides, pharmacokinetic properties of the drugs change by age. Thus, response to the drugs vary by different age groups [5].

Today, definition of polypharmacy can be considered as use of multiple drugs although it is not clearly defined [6]. Minor

polypharmacy is defined as using more than two drugs while using more than four drugs is defined as major polypharmacy [7]. Advanced age as well as functional and cognitive disorders, visual problems, low level of education might be considered among the issues leading to polypharmacy [8]. Long term and multiple drug use due to pathogeny of chronic diseases causes both undesired side effects of the drugs and interaction of the drugs to be observed [9].

Upon analysis of the previous researches, the most frequently observed chronic diseases in elderly people are hypertension, osteoarthritis, coronary failure, diabetes, coronary heart disease, osteoporosis and cerebrovascular accidents. Polypharmacy has been increased as a result of high prevalence of these diseases at older ages [5].

In this study, the impact of polypharmacy was investigated, resulting from pathogeny of chronic diseases, on the function, pain, daily life activities and quality of life in patients diagnosed with knee Osteoarthritis.

## 2. Method

This study includes 50 patients in total, diagnosed with knee osteoarthritis per the American College of Rheumatology (ACR) classification criteria, aged 50-80 and literate, and applied to the polyclinic due to knee pain. Patients without sufficient cognitive functions to express symptoms and findings were excluded from the study. Patients' demographic data, height, weight, body mass index, knee pain duration, number of painful knees, drugs used for treatment of comorbid diseases and knee osteoarthritis as well as drugs used for other diseases were recorded. Using 5 or more drugs were regarded as polypharmacy in this study. Characteristics of patients with polypharmacy were compared to those without polypharmacy.

Anteroposterior weight-bearing radiography of the knee was applied to all patients directly, and their Kellgren-Lawrence (KL) radiographic score was calculated. Accordingly, grades are considered as follows: KL grade 1 - doubtful joint space narrowing (JSN) and possible osteophytic lipping, grade 2 - definite osteophytes and possible JSN on anteroposterior weight-bearing radiograph, grade 3 - multiple osteophytes, definite JSN, sclerosis, possible bony deformity, grade 4 - large osteophytes, marked JSN, severe sclerosis and definite bony deformity. KL is a classification method used for grading the knee osteoarthritis. Graded between 0-4, the grading system is commonly used in grading knee and hip osteoarthritis [10].

Knee osteoarthritis related symptoms and functional state were evaluated by Knee Injury and Osteoarthritis Outcome Score (KOOS). It has 5 sub-groups: pain, other symptoms, daily life activities related functional state, sports and recreational acts related functional state, and knee related quality of life. It comprises 42 questions. Each sub-scale is scored by 0-100 (0 means a serious problem while 100 means no problem. A change by 10 or more points indicates a clinically significant change [11].

Mini Mental State Examination (MMSE) was used for identifying the cognitive level. This test comprises 11 questions and scored out of 30 points. Following points are compatible with the following level of dementia: Twenty-four to thirty points - normal, 18 to 23 points - light, 17 or less points - serious. It tests orientation, memory, attention, calculation, recognition, language, motor function and perception, visuospatial abilities [12].

Mean, standard deviation, median lowest, highest, frequency and ratio values were used for descriptive statistics of the data. Distribution of variables was measured via Kolmogorov Simirnov test. Mann-Whitney U test was used for analysis of quantitative independent data. Chi-square test, and Fischer test where conditions for chi-square test cannot be met were used for analysis of qualitative independent data. The SPSS 22.0 program was used for analyses.

## 3. Result

Twenty-one (42%) in 50 patients included in the study with polypharmacy and mean age of the patients in this group was  $69.5 \pm 10.2$  years. 35 in all patients (70%) were female. Mean body mass index was  $30.6 \pm 4.2$  kg/m<sup>2</sup>. Mean knee pain duration was  $4.9 \pm 3.8$ . 30 patients (60%) had bilateral knee involvement. Comparative demographic data and clinical properties of the patients with and without polypharmacy are indicated in Table 1.

Ages, drug use of the patients in the group with polypharmacy were significantly higher ( $p < 0.05$ ) than the group without polypharmacy. There is not any significant ( $p > 0.05$ ) difference between distributions of gender in the groups with and without polypharmacy. There is not any significant ( $p > 0.05$ ) difference between height, weight and BMI values in the groups with and without polypharmacy. There is not any significant ( $p > 0.05$ ) difference between knee pain side and knee pain duration values in the groups with and without polypharmacy. Kellgren Lawrence grade in the group with polypharmacy was significantly higher ( $p < 0.05$ ) than the group without polypharmacy (Table 1).

**Table 1.** Demographic data and clinical properties of the patients with and without polipharmacy.

		Drug Use 0-4			Median	Drug Use $\geq 5$			P	
		Mean	$\pm$	s.s./n%		Mean	$\pm$	s.s./n%		
Age		57.3	$\pm$	15.0	59.0	69.5	$\pm$	10.2	71.0	0.002 <sup>m</sup>
Gender	Female	13		61.9%		22		75.9%		0.288 <sup>x<sup>2</sup></sup>
	Male	8		38.1%		7		24.1%		
Height (m)		162.0	$\pm$	8.4	162.0	159.0	$\pm$	6.9	156.0	0.052 <sup>m</sup>
Weight (kg)		76.1	$\pm$	8.7	78.0	77.6	$\pm$	8.4	78.0	0.609 <sup>m</sup>
Body Mass Index(kg/m <sup>2</sup> )		29.2	$\pm$	4.3	28.0	30.5	$\pm$	3.9	31.0	0.052 <sup>m</sup>
Painful Knee	Right	6		28.6%		8		27.6%		0.911 <sup>x<sup>2</sup></sup>
	Left	3		14.3%	May	3		10.3%		

		Drug Use 0-4			Median	Drug Use ≥5			p
		Mean	±	s.s./n%		Mean	±	s.s./n%	
Knee Pain Duration	Bilateral	12		57.1%	3.0	18		62.1%	0.118 <sup>m</sup>
		3.8	±	2.6		5.7	±	4.4	
Kellgren Lawrence	Grade I	1		4.8%		0		0.0%	0.000 <sup>x²</sup>
	Grade II	9		42.9%		0		0.0%	
	Grade III	7		33.3%		15		51.7%	
	Grade IV	4		19.0%		14		48.3%	

<sup>m</sup> Mann-Whitney u test / <sup>x²</sup> Chi-square test

While NSAII (88%) is the most frequently used drug among the drugs used for pain, it was observed that anti-hypertensives (70%) are the most frequently used drugs other

than the drugs used for knee osteoarthritis. The most frequently observed comorbidities were respectively hypertension (70%) and heart failure (50%). (Table 2).

Table 2. Comorbidities and drug use.

	N	%
<b>Drug use</b>		
Paracetamol	33	66.0%
NSAIDs	43	86.0%
Steroid	15	30.0%
Topical Opioid	5	10.0%
Antihypertensive	35	70.0%
Diabetics	17	34.0%
Thyroid Drug	14	28.0%
Osteoporosis Drug	10	20.0%
Antilipidemic	11	22.0%
Cardiac Drug	23	46.0%
Anticoagulant	20	40.0%
Stomach Drug	21	42.0%
<b>Comorbidities</b>		
Hypertension	35	70.0%
Diabetes Mellitus	16	32.0%
Heart failure	25	50.0%
Stomach disease	21	42.0%
Thyroid disease	10	20.0%
Parkinson disease	1	2.0%
Other comorbidity	26	52.0%

KOOS symptoms, pain, ADL, sport recreational Act, QOL, Global score were significantly lower in the group with polypharmacy than the group without polypharmacy. (Table 3)

MMS total score in the group with polypharmacy was significantly lower (p < 0.05) than the group without polypharmacy. (Table 3)

Table 3. Knee Injury and Osteoarthritis Outcome Score (KOOS) and Mini Mental State (MMS) scores of patients.

	Drug Use 0-4			Median	Drug Use ≥5			p	
	Mean±s.d./n%				Mean±s.d./n%		Median		
KOOS									
Symptoms	57.1	±	21.3	57.1	37.5	±	17.3	35.7	0.002 <sup>m</sup>
Pain	55.8	±	20.8	52.8	34.1	±	15.7	36.1	0.001 <sup>m</sup>
Function in daily living	58.3	±	17.4	55.9	33.9	±	15.3	33.8	0.000 <sup>m</sup>
Function in sport and recreation	39.0	±	22.1	35.0	21.2	±	12.8	20.0	0.003 <sup>m</sup>
Knee related Quality of life	55.1	±	17.3	56.3	33.6	±	16.5	31.3	0.000 <sup>m</sup>
Global score	54.9	±	18.2	53.6	32.8	±	14.2	31.5	0.000 <sup>m</sup>
Mini Mental State Total Score	26.8	±	2.7	27.0	23.5	±	2.6	23.0	0.000 <sup>m</sup>

### 4. Discussion

In this study, it has been observed that functional state, quality of life and daily life activities were reduced in patients with symptomatic knee osteoarthritis and polypharmacy. While the prevalence changes in the studies where polypharmacy is investigated, it is observed that polypharmacy increases as people get older. A study carried

out by Ramage reveals that 63% of the elderly people use five or more drugs and that 30% of such patients are over 85 and get extra drugs for this reason [13]. In a study carried out in United States, it was observed that 37.1% of the male and 36% of the female, aged between 75 and 85, were prescribed five or more drugs [14]. In this study, the mean age of the patients with polypharmacy was significantly higher and the ratio of patients with polypharmacy was 58%. In a study carried out widely in Turkey, it was observed that 38.2% of

the patients use four or more drugs [15]. Even if this study was carried out with a limited number of patients with osteoarthritis, the ratio of patients with polypharmacy were found to be in compliance with the literature.

Presence of chronic and multiple diseases in the elderly people increases the prevalence of polypharmacy. In the studies carried out, it is reported that CVS diseases and musculoskeletal diseases are the most common diseases and accordingly, CVS drugs, NSAIDs, basic analgesics and anxiolytics are the most common drugs used, in the advanced age group [16].

Acetaminophen is suggested as the first option in many OA treatment guides. In cases where paracetamol is ineffective for symptomatic knee OA, NSAII use is listed in almost all suggestions or guides [17]. As the primary complaint by most of the patients with OA is pain, ratio of the patients using NSAII and paracetamol, which are frequently used for pain, was identified to be 86% and 66%, respectively. Symptomatic treatment oriented polypharmacy, particularly for pain complaint or to remove side effects of other drugs are common. Therefore, painkillers and drugs for gastrointestinal system are used frequently [18]. One out of two patients in this study was taking gastro protective drugs.

In this study, age and Kellgren Lawrence grade were significantly higher in the group with polypharmacy than the group without polypharmacy. This situation might be associated with the fact that osteoarthritis is a chronic degenerative disease observed as people get older, physical incapacities and increased pain.

With reduced cognitive and functional capacity in elderly people, certain problems arise in drug use. These problems include reduced communication with doctors, misused drugs as a result of memory problems of the patients, increased expectations of the patients [19]. In this study, the fact that pain, function-daily life, sports-recreational acts and quality of life values are significantly lower in the group with polypharmacy than the group without polypharmacy indicates that polypharmacy reduces the functional state and quality of life. In a study, it was identified that 79.1% of the elderly people are independent in their daily life activities. However, it was observed that daily functions performance of those with lower MMSE scores are low [20]. Also in this study, MMS total score in the group with polypharmacy was significantly lower than the group without polypharmacy.

Limitations of this study might be considered as limited number of patients included, non-distribution of the group without polypharmacy into sub-groups, non-classification of the group with polypharmacy by ages.

## 5. Conclusion

As a result, elderly individuals need to take higher number of drugs due to chronic diseases. We think that patients with knee osteoarthritis might have pain, reduced functional state, daily life activities and quality of life as a result of both drug interactions and reduced cognitive level as the number of drugs taken for other diseases as well as osteoarthritis

increases. To prevent that, attention must be paid to the training activities raising awareness for appropriate drug use, and awareness of the physicians as well as elderly people regarding the polypharmacy must be expanded.

## Funding

The research received no grant from any funding agency in the public, commercial or not-for-profit sectors.

## Conflict of Interest

The authors declare that they have no competing interests.

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