

Importance of Rehabilitation in Primary Knee Osteoarthritis

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ABSTRACT. In our observational study, we aim to highlight the role of rehabilitation program in the control and maintaining of the clinical and functional status of people with primary knee osteoarthritis and co-morbidities. We established that the complete rehabilitation program (diet, symptomatic medication and herbal products, electrotherapy measures and kinetic exercises) will give the optimal healthcare for this type of patients.

KEYWORDS: Primary knee osteoarthritis, co-morbidities, rehabilitation program

Introduction

Osteoarthritis (OA), is a low-grade inflammatory disease affecting all components of synovial joints (cartilage, subchondral bone, joint capsule and synovial) [1], one of the most prevalent reasons in both adolescents and elderly individuals for physical disability [2].

OA is among the ten most disabling chronic diseases in developed countries and one of the diseases with the highest cost, exceeding other forms of joint disease, including rheumatoid arthritis [3].

The knee joint, the intermediate pivot and a very important biomechanical segment of the lower limb, is the major location of OA. Medical data mentioned the increase of incidence of osteoarthritis for the knee (KOA) in the last decades (83% of the global disease burden for OA) [4].

Its global prevalence was approximately 4% in the last five years [5].

Severe pain, a hallmark symptom of KOA in the aging patients, affects activities of daily living and is a major predisposing factor for loss of function and increased fall risk with major dysfunctional impact on the body [6].

It is accepted that KOA is a heterogenic and multifactorial condition with a multitude of pathophysiologic drivers (articular cartilage loss, local inflammation, and remodeling of subchondral bone) leading to multiple phenotypes [7].

The multifactorial KOA pathogenesis involves mechanical transduction, the interplay between metalloprotease (MMP3, MMP13), cartilage degradation and cartilage repair processes include protease inhibitor and cytokines. [8].

KOA's natural history is highly variable, with diseases improving in certain patients, stable in others, and progressively deteriorating in others, apart from patient-aged correlations. Each OA phenotype (OA in the knee without any other diseases, KOA with associated diseases, multi-joint OA without associated pathology, multi-joint OA with co-morbidities) may be targeted and potentially be treated differently [9].

Some of these phenotypes will be acquiescent to pharmacologic involvement but others are less likely to respond to drugs, especially in elderly people [10].

Medical care in osteoarthritis is provided by a multidisciplinary team and may be challenging because of the presence of co-morbidities that coexist with KOA in adults and elderly people.

The Osteoarthritis Research Society International (OARSI) rules require that non-surgical therapy of KOA is the first choice and can include both physical exercise and intra-articular corticosteroid injections. [5].

The last recommendations of Technical Expert Panel (TEP) of The American College of Rheumatology (ACR) are that the choice is

individualized and based on the patient preferences and capacity to conduct exercise.

All patients with KOA symptoms should be registered in the training program according to their capacity for performing these tasks.

In addition, the TEP highly proposes the use of tramadol, duloxetine or hyaluronan injections for people over 70 years of age, and topical rather than oral anti-inflammatory drugs [11].

In this study, we purpose to underline the role of an adapted rehabilitation program based on physical exercise for achieving regaining of KOA patients clinical and functional status, more exactly patients with KOA and multi-joint OA with associated pathology.

We chose our rehabilitation measures in accordance with actual international (OARSI and ACR) management recommendations for KOA.

Patients and Methods

The approval from Craiova University of Medicine and Pharmaceutical Ethics Committee was obtained and all subjects participant in our study signed an informed consent.

Our study included 70 patients, diagnosed with primary knee osteoarthritis. We conducted our study in 2018 in the Rehabilitation Department of the "Filantropia" Hospital Craiova.

The groups were designed with the following criteria in mind:

- age over 40;
- disease progression of at least 5 years;
- knee pain that lasts at least 48 hours after physical exercise;
- no knee injuries in the last 6 months;
- no major disturbances of the knee's frontal plane alignment;
- patients with other co-morbidities, but well controlled, like: arterial hypertension, dyslipidemia and mellitus diabetes type II; a history of a symptomatic or complicated upper gastro-intestinal ulcer;
- compliance with physical exercise during the healthcare program.

All patients were completely assessed.

We conducted etiopathogenic, clinical, lab screening and functional evaluation (lab-screening, x-raying and ultrasound).

The *etiopathogenic* and *clinical assessment* included:

- patient history was taken in order to establish pain baseline and accompanying symptoms;

- general physical examination (including sensory assessment);
- skeletal muscle examination (testing)-somatoscopic examination, range of movement evaluation (we evaluated the knee flexion) and manual leg muscle testing, particularly knee muscles, patellar shock evaluation;
- bipodal, unipodal and seated position load examination;
- gait assessment, speed and dynamics, analyzes of pain (on flat floor and stairs) during walking.

During the examination, we performed a laboratory and radiological examination of the knee and also an ultrasound examination to highlight synovial knee modifications to properly diagnosed all co-morbidities in our patients; screening laboratory test, lipid profiles.

The Kellgren and Lawrence Radiographic KOA (K&L) scoring is often measured in grades 0 to 4 based on spatial narrowing and structural bone modifications.

In order to assess the functional parameters we used the Visual Analogue Scale (VAS) where 0 means the patient has no pain and 10 represents maximal pain.

Values from 0 to 10 are directly proportional to the pain intensity and individual acceptability. Lequesne Functional Index and the WOMAC scale were used for determining the effect the disease has in performing daily living activities.

In the WOMAC scale the 0 score is equivalent to maximal functional status and 96 indicates a minimum status, with high disruption in day to day tasks.

For the Lequesne Index 0 is indicative of maximum functional status while 24 is the minimum.

Lower limb dysfunction is indicated from 0 (none), 4 (mild), 5-7 (moderate), 8-10 (severe), 11-13 (very severe and more than 14 is characteristic for extremely severe limiting and dysfunction.

Patients assessment was performed on three levels-first (T1), after 14 days (T2) and after another 12 weeks (T3) in the outpatient environment-during which the in-hospital rehabilitation program was carried out.

Patients followed a home-workout program between T2-T3 (individuals learned during hospitalization) and continued pharmacological treatment with a natural adjuvant treatment consisting of *Boswellia serrata*, *Commiphora wightii*, *Glycyrrhiza glabra*, *Alpinia galanga*,

Tinospora cordifolia, Tribulus terrestris and Zingiber officinale, 2 tbs per day.

The healthcare objectives were:

- pain management;
- inflammatory process control;
- correction of the abnormal system of walking, with ordinary restoration;
- knee functionality as a biomechanical part of the limb;
- motor control recovery, optimum function of the knee;
- preserving quality of life.

Healthcare in both patient groups has been complicated based on non-surgical interventions and included:

- non-pharmacological measures: education, diet and hygiene, pose, physiotherapy, massage and kinetic measures (thermotherapy-paraffin-electrotherapy-magnetodiaffluss, TENS, ultrasound);
- pharmacological measures-the optimal daily medication for each co-morbidity and the natural adjuvant treatment-2 tablets per day were given for 3 months.

The kinetic program was implemented only to physical exercise-compliant patients. This program was intended for upgrading the all muscles around knee joint and was characterized by the following aspects:

- personalized, depending on knee stability and patient resources and on pain severity;
- Structured-posture, load less activity practice (mobilization and active expansion), isometry, progressive loaded isotonic exercises (pedaling on a heavy saddle cyclo-ergometer), balancing exercises and kinetic gait coordination exercises (pedaling);
- complete, with patient compliance tactics-setting realistic goals, patient explanations, gradually initiating and slowing progress,

optimal time planning and group physical therapy.

A series of drills (home-training) were suggested for the patients at the time of their release. Three primary forms of physical therapy and home-trained workouts for the research group are included.

The statistical processing was carried out using Microsoft Excel (Microsoft Corp.) (Redmond, WA, U.S.A.) and IBM SPSS Statistics 20.0 (IBM Corporation, Armonk, NY, USA), together with the XLSTAT Add-on MExcel (Addinsoft SARL, Paris) for data management.

We used Z test for proportions to investigate the statistical significance of the difference between the frequency of binary variables in general population and the observed frequency p in our sample group.

Because the study involved numerical comparisons between 3 sets of data from the same patients, recorded during 3 different visits, that did not have normal (Gaussian) distributions, we used the median, quartiles and minimum-maximum to describe the numerical data, and the nonparametric Friedman test, followed by post-hoc comparisons to detect significant differences between pairs of groups.

Results

Our study group consisted of 70 patients, aged 41 to 82 (Table 1), diagnosed with mild (27 patients) and moderate (43 patients) KOA, in accordance with Kellgren and Lawrence (K&L) score.

The sex repartition was 81.43% females and 18.57% males, which shows a highly significant difference from the sex repartition in the general population (z score for proportions <0.001).

Table 1. Demographic data of studied patients

Biographic data						Total
Residence	Urban=50%		Rural=50%			70
Sex	Female=81.43%		Male=18.57%			70
Age	40-49 years	50-59 years	60-69 years	70-79 years	80-89 years	70=100.00%
	4.29%	20.00%	42.86%	28.57%	4.29%	
Weight	Normal	Overweight	Obese I	Obese II	Obese III	70=100%
	8.57%	41.43%	31.43%	15.71%	2.86%	

The urban: rural ratio was 1, which means there is no influence of the area of residence on the studied condition.

Age distribution was almost normal (Anderson-Darling test for normality $p=0.477>0.05$), but we have to mention that the condition appears after 40 years of age.

Weight distribution was not normal (Anderson-Darling test for normality $p=0.0276<0.05$), with weights skewed towards higher values, meaning this condition is associated with overweight status.

As comorbidities, we found that there are 27.14% of patients with Diabetes mellitus, 57.14% patients with hypertension, and 64.29% patients with hypercholesterolemia.

Taking into consideration the mean values for studied parameters in our patients we considered that the rehabilitation program and the natural adjuvant treatment had optimal effect on the clinical and functional status.

Comparing the values recorded for the flexion angle among the three visits (Table 2), we observe a steady increase in the values, the overall differences being highly significant (Friedman $p<0.001$) (Fig.1).

Performing post-hoc analysis, we found the values from the second visit to be greater than the initial values, and the values from the last visit being significantly greater than the intermediate values.

Table 2. The study variables-median and spread values

Variable	Flexion angle			VAS		
Parameter	T1	T2	T3	T1	T2	T3
Mean value and SD	80.57±15.84	89.64±11.01	97.78±9.95	7.62±1.29	5.21±1.23	3.57±1.23
Minimum	40.00	55.00	70.00	4	2	1
1st Quartile	70.00	85.00	90.00	6.25	4	3
Median	90.00	90.00	100.00	8	5	4
3rd Quartile	90.00	100.00	100.00	9	6	4
Maximum	100.00	100.00	120.00	9	7	6
Variable	WOMAC			Lequesne functional index		
Parameter	T1	T2	T3	T1	T2	T3
Mean value	55.07±10.48	44.80±11.18	35.98±10.31	14.80±3.59	11.77±2.71	8.89±2.56
Minimum	25	19	11	8	5.5	1.5
1st Quartile	50.25	37.25	30	12	10	1.5
Median	56	44.5	37	16	11	7.5
3rd Quartile	60.75	50.75	42	17	14	9
Maximum	76	91	56	21	18	10

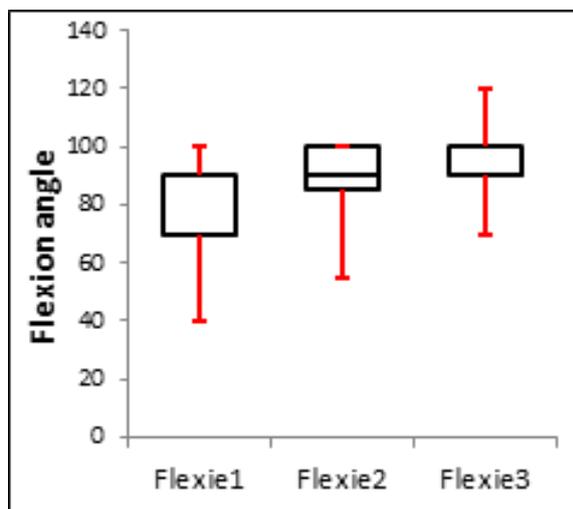


Fig.1. Flexion angle values

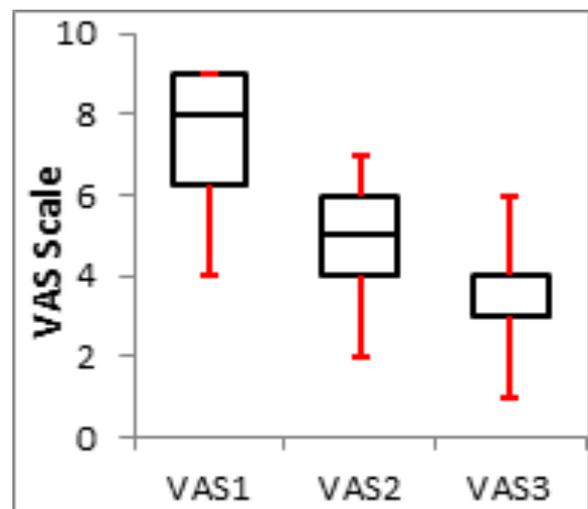


Fig.2. VAS Scale values

Analyzing the visual-analog scale recordings, we found highly significant differences among the three visits, the values decreasing over time (Friedman $p < 0.001$); the post-hoc analysis showed the values from the first visit being lesser than the values from the second visit, which were significantly lesser than the values from the third visit (Fig.2). The finding for the WOMAC scale values (Fig.3) and the Lequesne functional index values (Fig.4) are similar to those for VAS, showing a highly significant decrease over time (Friedman $p < 0.001$) (Table 2).

Analyzing the correlation between the increase in flexion angle and decrease of the perceived pain or discomfort in performing day to day functions, using Spearman's rho correlation coefficient, we found the Lequesne functional index to show the greatest correlation to flexion angle ($\rho = -0.298$), followed by WOMAC scale ($\rho = -0.278$) and VAS ($\rho = -0.210$) (Table 2).

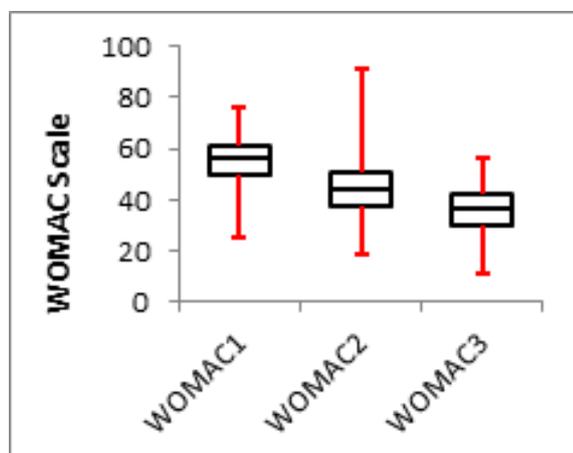


Fig.3. WOMAC Scale values

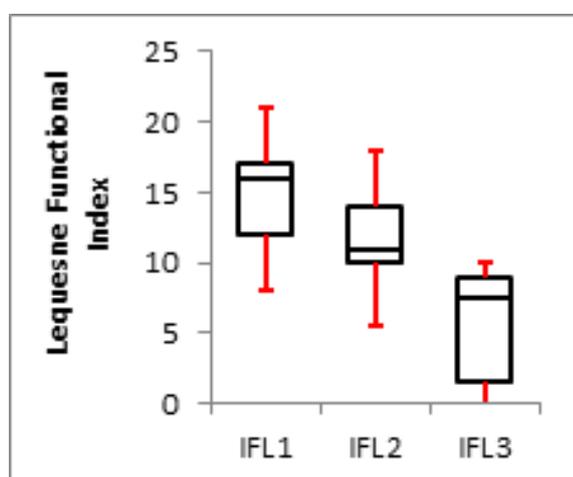


Fig.4. Lequesne Functional Index values

Discussions

This is Romania's first clinical study to evaluate effectiveness of a natural adjuvant treatment in patients with co-morbidities and mild or moderate degree KOA. More exactly our patients are included in the second (KOA with associated diseases-28 patients) and fourth (multi-joint OA with associated pathology-42 patients) sub-phenotypes of four sub-phenotypes OA stratification (KOA without any associated diseases, KOA with associated pathology, multi-joint OA without any associated diseases, multi-joint OA with associated pathology) [10].

The fourth sub-phenotype patient number is higher than the second one because the mean age is also higher and the correlation between age and multi-joint OA is recognized. The studied patients were previously diagnosed with the subsequent moderate associated health conditions: type 2 diabetes, high blood pressure, depression, obesity and with one high co-morbidity risk-history of gastrointestinal (GI) bleeding. The most frequent co-morbidity in our patients is hypercholesterolemia, followed by the hypertension, especially in patients with age over 60 years. We didn't take into consideration the physical impairment limiting activity as co-morbid concern because this aspect defines the functional status of each patient.

We did not obtain a significant correlation between mean values of studied parameters (VAS, WOMAC scale and Lequesne index) and the type of co-morbidities. So, the results were presented only through mean values, in all three times of assessment.

Since 2000, the European League Against Rheumatism (EULAR), the Osteoarthritis Research Society International (OARSI) and the American College of Rheumatology (ACR) and the American Academy of Orthopedic Surgeons (AAOS) have released a series of professional organizations' hand, hip and knee management suggestions for the OA. These recommendations were based on the evidence and on the informal consensus approach following an extensive systematic literature reviews.

We applied these recommendations (2012 ACR osteoarthritis guidelines and OARSI) in our study. All enrolled patients received optimal pharmacologic treatment (stratification for appropriate co-morbidities and OA in joints other than knee) participated in self-management program, received walking aids (as needed), were instructed in the use of transcutaneous electrical stimulation (TENS)

and ultrasound and the use of thermal agents [11,14].

In accordance with OARSI non-surgical management guidelines for OA knee, the rehabilitation program of our patients included only biomechanical interventions, kinetic measures and walking cane, topical NSAIDs (associated with ultrasound) without intra-articular corticoids, COX2 inhibitors (selective NSAIDs) and duloxetine [15,16].

The role of physical training in maintaining and regaining functional status in KOA patients is mentioned in a lot of studies worldwide. Our findings represent the information observed in medical literature, which demonstrate that pain relief and functional enhancement are accomplished in patients with ankle OA in the application of an individualized kinetic program based on illness severity, age, gender, and functional status of the individual. The parameters of kinetic exercises (intensity, duration and frequency) are in accordance with mild or moderate type of KOA [17,18].

In many other earlier research, the period of the kinetic program is roughly 8 weeks, including strength training, proprioception (equilibrium) and flexibility, knee bracing, and patient education [19].

It is important to include in physical training in symptomatic OA of the knee patients the active motion of all lower limb joints (range of motion and flexibility exercises) and strength exercises, analytic (quadriceps strengthening) and global scheme [20,21,22]. Also balance training is very important for functional gait scheme. All in-patient exercises have to continue at home (home-training) [23].

In our study, we recommended the continuance of home exercises and orthopedic knee hygiene rules for 12 weeks for patient compliant with the kinetic program as a reason for subjects to be used to this program for the further distance in order to maintain their normal life and to retain their functional gain. In comparison with the proportion on the WOMAC functional scale and the Lequesne index, an improvement in the proportion of pain is clarified by the complicated functional conditions, in particular in older patients [19,24].

The original aspect of our study is the pharmacological agent used in all patients-a natural adjuvant treatment consisting of *Commiphora wightii*, *Boswellia serrata*, *Glycyrrhiza glabra*, *Alpinia galangal*, and *Zingiber officinale*. In the last years, it was

mentioned in medical literature the major role of herbal care for OA patients. This type of treatment is in accordance with actual mentioned challenges in treating OA (limited effective therapy contraindications due to medical co-morbidities of current therapies, lack of access or availability to treatments, difficulties with patients adhering to treatments). Our research shows that symptoms such as pain, inflammation, joint malfunction and movement in OA patients have improved significantly owing to the natural adjuvant treatment combined with the complex rehabilitation program. None of the patients that received the natural adjuvant treatment revealed severe adverse events during the 3-month trial period, also they were diagnosed with various metabolic co-morbidities. The laboratory parameters of the studied natural adjuvant therapy patients did not alter, like in other literature data that shows numerous clinical benefits of the natural adjuvant treatment, without age limits and supervised rehabilitation program [25].

There were no patient side effects reported. The natural adjuvant treatment appear to have been both secure and efficient medicine for the OA patients, and the effects of it in relieving pain, inflammation, free mobility and safety in OA patients can be compared by a double-blind, placebo-controlled trial. [26].

The specimens of the natural adjuvant treatment: *Boswellia serrata*, *Alpinia galanga*, *Commiphora wightii*, *Glycyrrhiza glabra*, *Tinospora cordifolia* and *Tribulus terrestris* could explain all the beneficial impacts of the pharmaceutical measure used. These components demonstrated that they are anti-inflammatory, anti-arthritis, immune modulatory, relaxing muscle and analgesic. [27].

Another argument to use the herbal product in our patients is theirs various co-morbidities. The whole health sector is aware that non-steroidal anti-inflammatory drugs (NSAIDs) are becoming more and more susceptible to gastrointestinal bleeding and vascular side effects. Second-line (according to EULAR) medications, including glucosamine sulfate, glucosamine hydrochloride, Chondroitin sulfate, Hyaluronic acid, Avocado soybean unsaponifiables (ASU) and diacerein (Interleukine-1B Inhibitor), and herbal medicines (other medical trials) may be suggested for this condition. This may be considered for use in other studies. [28].

We considered that the natural adjuvant treatment was the optimal choice in pharmacological measure in mild and moderate

KOA patient with co-morbidities because other glucosamine/chondroitin derivatives have cautions in patients with diabetes (may increase glucose levels) and have possible interaction with warfarin (increased INR) [29].

We have chosen and carried out all rehabilitation efforts for OA patients as "a moving joints disease, marked by cell stress and extracellular degradation of matrix caused by micro and macro injury, activating maladaptive repair reactions including pro-inflammatory mechanisms of inborn immunity". The disease first manifests as a molecular distortion (abnormal joint tissue metabolism) followed by anatomic and/or physiological changes (which can culminate in cartilage degradation, osteophytic formation, joint swelling, loss of ordinary joint function) [30].

Conclusions

This investigation demonstrated the potency of the natural adjuvant therapy in the treatment of osteoarthritis, so it is the better pharmacological treatment choice for knee osteoarthritis sub-phenotypes with co-morbidities and multi-joint affected.

Complete rehabilitation program (education on symptom control, diet, physical therapy, stretching and exercise) in accordance with new osteoarthritis definition and limited effectiveness of existing therapies offers the better control of complex disability and quality of life.

In the next years, controlled studies may be conducted to evaluate the complex role of natural adjuvant treatments in the complete management of all sub-phenotypes KOA patient, in line with global medical osteoarthritis guidelines and changes to lifestyles.

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