

Study on the importance of medical treatment and physical methods in recovering patients with knee osteoarthritis

Sinziana Calina Silisteanu^{1,2} Elisabeta Antonescu^{3,4*}, Maria Totan^{4,5}

Corresponding author: **Antonescu Elisabeta**, E-mail: bety_antonescu@yahoo.com.

All the authors have equal scientific contribution at this original article.

^{1,2} Railway Hospital Iasi - Specialty Ambulatory of Suceava - "Stefan cel Mare" University of Suceava FEFS-DSDU

³ Lucian Blaga University of Sibiu, Faculty of Medicine, Sibiu, Romania

⁴County Clinical Emergency Hospital, Sibiu, Romania

Abstract

Introduction. Etoricoxibum belongs to the group of non-steroidal anti-inflammatory inhibitors selective of cyclooxygenase-2. The non-steroidal anti-inflammatory drugs are used to treat acute musculoskeletal disorders as they result in pain-relieving therapeutical effect. Etoricoxibum intervenes by blocking cyclooxygenase-2 and by reducing the painful and inflammatory phenomena. **Material and method.** The trial focused on the evolution of patients diagnosed with knee osteoarthritis after making the treatment by etoricoxibum. This study was conducted in the ambulatory regime for a period of 6 months and included 77 patients. **Results and discussions** It was assessed the efficacy of the complex recovery treatment for the patients diagnosed by knee osteoarthritis with use of Etoricoxibum, in a dose of 60 mg/day, in order to improve the pain and the inflammation. The pursued objectives were: the assessment of the effects by using Etoricoxibum for the reduction of the pain and inflammation, the increase of the articular mobility and stability, the recovery of the walk and motor control, the decrease of the body weight, the increase of the quality of life. **Conclusions.** This trial show that, by making a combined treatment of medication and recovery, there was an reducing the pain and the inflammation as well as increasing the articular mobility.

Key words: *osteoarthritis, pain, ultrasound, recovery, disability,*

Introduction

The non-steroidal anti-inflammatory drugs (NSAIDs) are a class of medicines that belong to the category of the non-opioid analgesics. They have a high safety profile, a low risk of side effects and medicine interactions.

The NSAIDs inhibit reversibly the cyclooxygenase (COX), an enzyme that is involved in the synthesis of prostaglandin, at the central level and at the peripheral one. This enzyme can be found in two types, namely: cyclooxygenase 1 (COX-1-involved in the physiological secretion of prostaglandin, being a platelet antiaggregant and having the role to protect the intestinal mucosa) and the cyclooxygenase 2 (COX-2- having a role in the secretion of the prostaglandins that are involved in the painful and inflammatory processes).

The inhibition of COX-2 leads to the anti-inflammatory, analgic and antipyretic effect. The inhibitors of COX-2 are specific inhibitors, called coxibi (1), that have a low risk of digestive side effects towards other NSAIDs, but with a certain cardiovascular risk, that is why caution is imposed while giving it to certain patients.

The NSAIDs are greatly used in the treatment of the muscular-skeletal conditions. It is worth noting that over 80% of the population aged over 55 (2) presents radiologically modified joints. Such a modification is osteoarthritis, a progressive invalidating condition, having a degenerative and chronic character that affects the articular cartilage, the subchondral bone, the articular capsule, the hypertrophy of the marginal bone with the formation of osteophytes (3, 4).

The most frequent affected joint is the knee, involved in maintaining the static and dynamic balance, the walk and the orthostatic stability (5). The clinical and functional symptomatology includes pain, limitation of articular mobility, crepitating, deformation, instability, decreased of the functional capacity, affecting the walk and the posture (6, 7). Due to the functional deficit caused by the disease, the knee osteoarthritis is considered a health issue (8). In osteoarthritis are involved the cytokines -Interleukin 1 (it increases the protease release and it can inhibit the proteoglycan synthesis), Interleukin 17 (it stimulates the synthesis and enables the release of the pro-inflammatory cytokines), TNF-alpha that can deteriorate the cartilage. In order to have a good diagnose we have to take care of the quality of

biochemical parameters analysis and the correct interpretation of the results, respecting the reference limits (9).

According to the revised ACR criteria, the physical exercise is very important in the recovery, beside the use of NSAIDs. There are trials which show that, by making a combined treatment of medication and recovery (5), there was an attempt at reducing the pain and the inflammation as well as increasing the articular mobility.

A trial of 2011 (10) focused on the evolution of 39 patients with knee osteoarthritis who made physiotherapy and were evaluated according to WOMAC and Lequesne scales, to the “stand up and walk” test and the 6 minutes’ walk test. Except for the WOMAC scale, all the other results were significant. The recovery treatment is supposed to have modern physiotherapy techniques that prevent, fight and recover the redness in the joints, the faulty precarious and tissular regeneration as well as the functional deficit (11). The electrical therapy techniques (low frequency currents - galvanic, diadynamic, Trabert, TENS, average frequency -interferential) are some of the most used methods of physiotherapy (12). Its purpose is to obtain antalgic and anti-inflammatory effects. It is very efficient when associated to other procedures (e.g. ultrasound) (12, 13).

The ultrasound treatment enables the transmission of the pendular mechanic vibrations, their penetration and absorption in the human body. The ultrasound has the qualities of being fibrinolytic and muscle relaxant (14, 15). The pathogenesis of osteoarthritis refers to the excessive loading of the joints and to the modification of the biomechanics models together with the deregulation of the hormones and of the cytokines (16, 17). The kinetic therapy has the purpose of preventing the muscular atrophy of the bilateral quadriceps, to tonify the musculature, to repair the dynamic control for a good static posture but also for the walk, to repair the articular mobility (18, 19). Moreover, at the psychical level, the physical activity, by the synthesis of neurotrophins and the improvement of neuroplasticity can have a beneficial contribution in the neurodegenerative diseases, respectively in the slight cognitive disorder (20). Cochrane showed in 2015 the importance of the physical activity in order to improve the pain and the functional condition for persons with knee osteoarthritis (21). Nevertheless, the small number of trials does not point out the minimal intensity of the

physical exercise programs necessary to demonstrate the clinical effect.

Another trial (22) points out that the physical exercise is one of the non pharmacological methods recommended by international guidelines. The data were taken from 54 trials related to pain, physical function and quality of life. The proofs of the trials show that therapeutic exercise can be beneficial for a short term of 2-6 months, in comparison to the treatment by NSAIDs. Yet, in the chronic therapy made systematically, there have been numerous adverse reactions at the gastrointestinal, cardiovascular, pulmonary and renal levels (23, 24). It is preferred to use NSAIDs in the topic form instead of the oral administration but, in case of using topic NSAIDS, the level of the active substance in the blood is very low in comparison to the one of the oral administration (25, 26).

According to the recommendations of ACR/RACGP, the administration of non-selective NSAIDs or specific COX-2 is indicated in the moderate or severe osteoarthritis, in efficient minimal doses, taking into account that osteoarthritis has an undulating slowly progressive evolution, with acutisation periods.

According to the recommendations of ACR/RACGP, the optimal management of osteoarthritis is made by associating the non-pharmacological treatment to the pharmacological one. We tried this association in our trial, too (27).

The indications by Cochrane are for the administration of specific NSAID (Etoricoxibum) for patients who are at gastrointestinal risk (20). It is considered that Etoricoxibum has a more reduced power than the other NSAIDS, but it is preferred as it has fewer side effects (28). Etoricoxibum (5-chloro-6'-methyl3- [4- (methylsulfonyl) phenyl] -2.3'-bipyridine) belongs to the group of non-steroidal anti-inflammatory inhibitors selective of cyclooxygenase-2 (COX-2). Etoricoxibum intervenes by blocking COX-2 and by reducing the painful and inflammatory phenomena (29).

Objective

The trial focused on the evolution of patients diagnosed with knee osteoarthritis after making the treatment by etoricoxibum beside the complex recovery one.

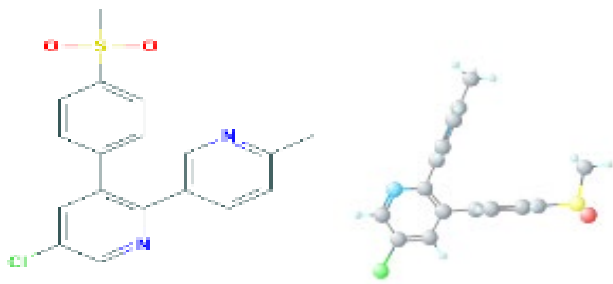


Fig. 1. The chemical formula for Etoricoxibum.
C18H15ClN2O2S
 (PubChempubchem.ncbi.nlm.nih.gov)

Material and methods

The trial was conducted in the ambulatory regime for a period of 6 months and included 77 patients. They were informed about the trial and gave their consent. The trial complied with the valid ethics norms and with the deontological ones.

The exclusion criteria were: the chronic rheumatologic diseases (ankylosing spondylitis, rheumatoid arthritis, gut), the traumatic issues of the knee (fracture, luxation, sprain), younger than 45, neurological disorders present at the level of the lower limbs, decompensate cardiovascular and pulmonary disorders, persons who did not agree to participate in the trial. The inclusion criteria were: older than 45, diagnosis of bilateral knee osteoarthritis, minimum one-year-old disease, compliance with the treatment, return for the medical check-up, persons who did not receive physical treatment in the past 5 months, patients who gave their consent to participate in the trial. It was important to calculate the body weight index with the formula $\text{mass (kg) / height (cm)}^2$. The treatment was complex: hygiene-diet (diet, movement and posture), pharmacological (administration of NSAIDs) and recovery. The patients received indications on how to follow the daily calorie regime according to their age, how to do activities aimed at keeping / reducing the body weight, the daily walking program (walk, going up/down the stairs), the correct posture from a static and dynamic point of view, to avoid standing up for too long, too many household/ professional activities as well as the wrong postures. From a pharmacological point of view, according to the same recommendations (to administrate NSAIDs in an efficient dose), the patients received treatment by Etoricoxibum in a daily dose of 60 mg. The used electrical therapy procedures were: the Trabert current (the fixed frequency of 140 Hz, the length of

the impulse 2ms and the pause of 5ms), the current frequency average (the frequency de 80-100 Hz) for the anti-inflammatory/antalgic purpose. The applied ultrasounds had the frequency of 1 MHz and a power of 0.3W/cm², a pulsatile form, by using an acoustic gel, without the active pharmacological substance, by applying it with circular movements, by using the applicator with the diameter of 5 cm. The recovery program included isometric exercises (with a ball and an elastic band), insisting especially on quadriceps and adductors. The assessment was made at the beginning and at the end of the treatment, but also at the control of 3 months. It consisted of a clinical examination, radiological investigations and knee ultrasound. Clinically the following were considered: the bilateral knee issue, the presence of the spontaneous pain the articular mobility, the inflammatory modifications at the level of the knee joint, the stability of the knee – static and dynamic, the alignment of the lower limbs, nutrition status, and muscular status.

Radiologically (*Kellegren Lawrance scale*) and by ultrasound the following were pointed out: a narrower articular space, frequently medial, marginal and posterior osteophytose, the subchondral sclerosis, deviations of the biomechanical axis of the sick lower limb.

The pain was assessed according to the VAS scale, the functional index and the articular redness were assessed according to the WOMAC scale whereas the articular mobility was assessed by means of the goniometer.

Before the beginning of the trial, the participants were informed and gave their participation consent.

The pursued objectives were: the assessment of the effects by using Etoricoxibum for the reduction of the pain and inflammation, the increase of the articular mobility and stability, the recovery of the walk and motor control, the decrease of the body weight, the increase of the quality of life.

The statistical analysis

The data were recorded in folders in Microsoft Excel; the average, the median, the standard deviation and the t-student test in order to compare the obtained results and in order to see whether the work hypothesis was confirmed. Thus, after calculating the t-student test, there was considered the value of the p index that shows the possibility of an occurring error related to the hypothesis.

Results and discussions

The participants to the trial were divided into 2 groups, namely: group 1 who received low frequency currents (the Trabert current), frequency average (interferential), ultrasound and

kinetic therapy (n= 40) and group 2 (n=37) who also received (in comparison to group 1) treatment by NSAIDs selectively, respectively Etoricoxibum of 60 mg/day for 14 days. For these groups, the characteristics are found in Table 1.

	GROUP 1		GROUP 2	
AGE	58.5±8.45		59±8.78	
AGE GROUP	women	men	women	men
(45-54) years	8	3	3	4
(55-64) years	11	6	9	6
(65-74) years	7	2	6	5
>75 years	2	1	2	2
TOTAL patients	28	12	20	17
	40		37	
BODY WEIGHT INDEX	28.88±3.05		28.24±2.99	

Table 1. A presentation of the trial groups

It is found in both trial groups that the most affected age group was 55-64 years, whereas the female patients were the most affected ones (28 in group 1 and 20 in group 2), in comparison to the male patients (12 in group 1 and 17 in group 2). The pain assessment led to the analysis of the obtained

results after using the VAS scale, but also the pain assessment segment in the WOMAC scale.

The visual analogue scale for the pain assessment (VAS) quantifies pain from 0 (the absence of pain) to 10 (the maximal score for pain). By using this scale the patient can observe pain in the assessment moments (Table 2).

VAS	GROUP 1			GROUP 2		
Moment	Initial/Final	Final/Control	Initial/Control	Initial/Final	Final/Control	Initial/Control
T-student test	0.0111	0.0027	0.0009	0.0143	0.0276	0.0065

Table 2. The value of the p index calculated for the analysed moments (VAS scale)

For group 1 the pain was reduced by 21.5% at the end of the treatment, by 9.82% between the end of the treatment and control, and by 28.58% between the beginning of the treatment and control after 3 months. In group 2 the pain was reduced by 25% at the end of the treatment, by 33.4% between the end

of the treatment and control, and by 50% 3 months after the beginning of the treatment. Thus it was found a reduction of the pain assessed by means of VAS scale, for both trial groups, significant in group 2, especially at the control moment versus final moment, $p < 0.05$ (Table 3) (Fig.2, Fig .3).

		GROUP 1			GROUP 2		
SCALE	Moment	Initial	Final	Control	Initial	Final	Control
VAS	Median/dev.std	7±1.23	5.5±1.31	5±1.56	8±1.31	6±1.01	4±0.79
WOMAC	Median/dev.std	14.5±3.61	111±2.68	7±0.49	15±2.06	10±2.39	8±0.53

Table 3. The evolution of the pain assessed by VAS and WOMAC scales

The WOMAC scale is used especially for the assessment of the impact that the disease has upon the patients in relation to 3 important elements: pain, articular redness and daily activities. The pain quantification is made from 0 (lack of pain) to 4

(the maximal value for pain), being assessed while standing up, sitting down or on the back, during the sleep, while going upstairs and walking.

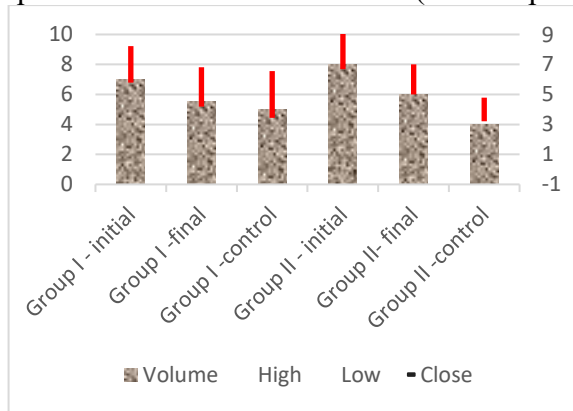


Fig. 2. The evolution of the pain for the two groups assessed by VAS scale

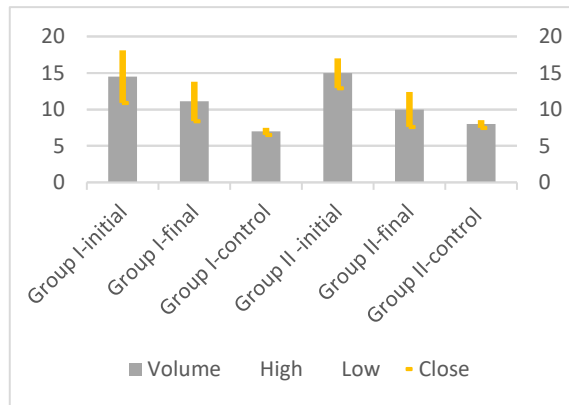


Fig. 3. The evolution of the pain for the two groups assessed by WOMAC scale

WOMAC pain	GROUP 1			GROUP 2		
	Initial/ Final	Final/ Control	Initial/ Control	Initial/ Final	Final/ Control	Initial/ Control
t-student test	0.0168	0.0414	0.0109	0.0273	0.0157	0.0062

Table 4. The value of the p index calculated for the analysed moments (WOMAC pain)

The pain assessed by the WOMAC scale was reduced at the final moment of the treatment by 24.14% in group 1 and 33.34% in group 2. Between the final moment of the treatment and the control of 3 months, the pain was reduced by 36.36% in group 1 in comparison to 20% in group 2. Between the initial moment of the treatment and the control of 3 months, the pain was reduced by 52.73% in group 1 in comparison to 46.67% in group 2.

As for the value recorded on the WOMAC scale - pain, it is found that the value of this parameter was reduced in the two trial groups, whereas the values were more significant in group 2, especially at the control of 3 months after the beginning of the treatment, the values for $p < 0.05$. The pain and the inflammation were reduced, as well as the

prostaglandine, due to the administration of etoricoxibum in the daily dose of 60 mg.

According to the WOMAC scale, the articular redness was assessed in the morning while waking up and during the day, while sitting down or lying on the back. The minimal value was 0 whereas the maximal one was 8.

In our trial the WOMAC scale showed a statistical evolution for the two groups and at all the moments, except for group 1 at the final moment when the obtained result is not significant. This can be explained by the fact that the patients of group 2 received NSAIDs with an analgic and anti-inflammatory effect, by contributing to the reduction of the pain and inflammation, thus of the articular redness (Table 5).

WOMAC redness	GROUP 1			GROUP 2		
	Initial/ Final	Final/ Control	Initial/ Control	Initial/ Final	Final/ Control	Initial/ Control
T-student test	0.0232	0.0629	0.0156	0.0438	0.0138	0.0148

Table 5. The value of the p index calculated for the analysed moments (WOMAC redness)

The assessment of the articular redness recorded a diminution at the end of the treatment by 38.58% in group 1 in comparison to 42.86% in group 2, by 40% in group 1 and 25% in group 2 at the control

of 3 months, and in an equal percent of 57.15% in the 2 groups at the assessment between the beginning of the treatment and the control made by patients after 3 months (Table 6).

WOMAC redness	GROUP 1			GROUP 2			
	Moment	Initial	Final	Control	Initial	Final	Control
median/ standard dev.		7±1.15	5±1.64	3±0.48	7±0.91	4±0.59	3±0.51

Table 6. The evolution of the articular redness

Another discussed parameter is the daily activities quantified on the WOMAC scale. Some of the daily activities are: going upstairs/downstairs, getting on the car/getting out of it, walking on a flat road, doing easy/hard household activities,

dressed/naked. The obtained results were significant at all the moments, especially at the control of 3 months, for both trial groups, whereas the value of p was lower than 0.05 (Table 7).

WOMAC-daily activities	GROUP 1			GROUP 2			
	Moment	Initial/ Final	Final/ Control	Initial/ Control	Initial/ Final	Final/ Control	Initial/ Control
T-student test		0.0064	0.0176	0.0021	0.0092	0.0165	0.0027

Table 7. The value of the p index calculated for the analysed moments (WOMAC daily functionality)

As for the assessed daily activities done by the patients of the two groups, it was found that the articular mobility increased at the end of the treatment by 19.68% in group 1 in comparison to 22.81% in group 2. These values were relatively close during the

control, of 30.62% in group 1 versus 29.55% in group 2, whereas the values at the initial assessment control were increased, of 44.27% in group 1 and 45.62% in group 2 (Table 8).

WOMAC-daily activities	GROUP 1			GROUP 2			
	Moment	Initial	Final	Control	Initial	Final	Control
median/ standard dev.		61±2.25	49±3.08	34±1.69	57±3.23	44±3.26	31±1.26

Table 8. The evolution of the daily functionality

The articular balance at the knee level represented another parameter assessed during the trial. It was also found that all the results were significant with $p < 0.05$, for all the trial groups and at all the moments, with more significant results at the

control moment in comparison to the final moment of the treatment, which can be explained by the effects of using electrical therapy, kinetic therapy and NSAIDs (Table 9).

Groups	Moment	Flexion of the right knee			Flexiegenunchistang		
		Initial	Final	Control	Initial	Final	Control
Group 1	median/ std.dev.	79±17.76	87±17.25	93±18.07	80.5±17.0	90±15.58	98±16.15
Group 2	median/ std.dev.	86±12.35	96±13.46	110±14.96	80±15.97	93±14.72	110±15.26

Table 9. The evolution of the knee flexion

The increase of the knee mobility assessed by the articular balance recorded different increase for the two knees. As for the right knee, the values were higher in group 2 with 11.63% in comparison to 10.12% in group 1 at the end of the treatment, of 14.58% in group 2 in comparison to 6% in group 1 at control, and significantly higher at the initial-control assessment of 27.91% in group 2 in comparison to 17.7% in group 1.

As for the left knee, group 2 has recorded values of 16.25% in comparison to 12.5% in group 1 at the end of the treatment, of 18.28% in group 2 in comparison to 9.45% in group 1 at the control, whereas at the initial-control assessment the values were 37.5% in group 2 and 22.36% in group 1.

This trial assessed the efficacy of the complex recovery treatment for the patients diagnosed by knee osteoarthritis and the use of Etoricoxibum, in a dose of 60 mg /day, in order to improve the pain and the inflammation. It is hereby easy to find modifications of the parameters assessed at the three assessment moments, especially at the control.

These results are similar to the ones in the specialty literature which show that it is possible to obtain significant benefits in the patients with knee osteoarthritis by using kinetic therapy, ultrasound or TENS (8, 30).

In the future, we are also looking for other modern therapy techniques. Raman spectroscopy will become a standard technique in osteoarthritis treatment. Raman spectroscopy is used for drop-coating deposition in osteoarthritis (31).

Conclusions

Osteoarthritis is the commonest form of articular disease and the main cause of the pain and of the physical disability in the elderly. The pain and the inflammation were reduced due to the administration of non-steroidal anti-inflammatory drugs but also due to the electrical therapy procedures (currents of low and average frequency, the use of ultrasound) with analgesic and anti-inflammatory character. The articular mobility as well as the static and dynamic stability improved due to the individualized program of kinetic therapy. An issue of the current trial would be the low number of patients but the results can be the starting point for future trials.

Abbreviations

NSAID -The non-steroidal anti-inflammatory drugs

COX - cyclooxygenase

VAS scale - Visual Analog Scale for Pain

WOMAC scale - Western Ontario and McMaster Universities Osteoarthritis Index

RACGP - The Royal Australian College Of General Practitioners

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This study, being a retrospective one, did not require a written consent from the patients involved. All authors have read and approved this publication and had equal scientific contribution in publishing this material.

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