

Comparative Efficacy of Quadriceps Strengthening, Infrared Radiation Therapy and Oral Diclofenac Sodium in the Management of Symptomatic Osteoarthritis of the Knee

Ebere Yvonne Ihegihu¹, Chima Collins Ihegihu², Egwuonwu Afamefuna Victor^{3,*}, Okonkwo Uchenna Prosper¹

¹Department of Physiotherapy, Nnamdi Azikiwe University Teaching Hospital, Nnewi

²Department of Orthopaedic and Trauma Surgery, Nnamdi Azikiwe University, Nnewi

³Department of Medical Rehabilitation, Nnamdi Azikiwe University, Nnewi

Abstract Background: Physiotherapy and non steroidal anti-inflammatory drugs form the bedrock of non surgical management of knee osteoarthritis (KOA) which focuses on reducing pain, maintaining or improving joint mobility, limiting functional impairment, and improving health-related quality of life. The purpose of this study was to compare the efficacy of quadriceps strengthening and infrared radiation alone; oral diclofenac sodium alone and the combination of quadriceps strengthening, infrared radiation and oral diclofenac sodium in the management of patients with symptomatic KOA. Knee pain intensity, quadriceps muscle strength and 30.4 metres walk-time were used as outcome measures. Methods: The research population comprised of patients with symptomatic KOA randomly assigned into four groups: group 1 (combination of quadriceps strengthening, infrared therapy and oral diclofenac sodium), group 2 (quadriceps strengthening and infrared therapy), group 3 (oral diclofenac sodium) and group 4 (control/placebo). The participants in groups 1 and 3 received one tablet of diclofenac sodium and one tablet of vitamin B complex twice daily while participants in the groups 2 and 4 received one tablet of vitamin B complex twice daily. In addition, the participants in groups 1 and 2 performed supervised quadriceps strengthening exercises and received infrared radiation therapy three times every week. Each participant was treated for seven consecutive weeks. Results: The participants comprised 43 (33.08%) males and 87 (66.92%) females. The male to female ratio was 1:2. At the end of seven weeks of intervention, there was reduction in the knee pain intensity in groups 1, 2 and 3, which was statistically significant ($p<0.05$). There was increase in the quadriceps strength in groups 1 and 2 which was statistically significant ($p<0.05$). There was reduction in the 30.4m walk-time in groups 1, 2 and 3, which was statistically significant ($p<0.05$). Conclusion: The combination of quadriceps strengthening, infrared radiation and oral diclofenac sodium was superior to oral diclofenac sodium therapy alone in all parameters used for comparison: knee pain intensity, quadriceps muscle strength and 30.4m walk-time. The combination of quadriceps strengthening, infrared radiation and oral diclofenac sodium was also superior to quadriceps strengthening and infrared radiation alone, only in reducing knee pain intensity. However quadriceps strengthening and infrared radiation alone was superior to diclofenac sodium therapy alone in all outcome measures except reducing knee pain intensity.

Keywords Comparative efficacy, Quadriceps strengthening, Infrared radiation therapy, Oral diclofenac sodium, Knee pain intensity, Quadriceps strengthening, 30.4m walk time

1. Introduction

Osteoarthritis (OA) of the knee is a chronic,

heterogeneous, complex degenerative joint disorder characterized by progressive destruction of articular cartilage with joint space narrowing, osteophyte formation, subchondral sclerosis and synovitis. [1] The knee is the most clinically significant site of primary osteoarthritis involvement [2] and by far the most common cause limiting the daily activities of the elderly population. [3] Clinically patients present with knee pain, knee stiffness, reduced knee joint range of motion, swelling, crepitation and disability. In the knee, OA radiographic abnormalities are present in

* Corresponding author:

vaegwuonwu@gmail.com (Egwuonwu Afamefuna Victor)

Published online at <http://journal.sapub.org/health>

Copyright © 2018 The Author(s). Published by Scientific & Academic Publishing

This work is licensed under the Creative Commons Attribution International

License (CC BY). <http://creativecommons.org/licenses/by/4.0/>

more than 30% of people aged 65 years and above and approximately 40% are symptomatic [4] affecting more women than men. [5] The current treatments for knee OA focus on ameliorating the illness not cure, since there is presently no pharmacologic agent that modifies the structural changes that occur in OA joints. Reducing knee pain, maintaining or improving knee joint mobility, limiting functional impairment, and improving health-related quality of life (QOL) are the objectives of most knee OA (KOA) treatment protocols. Several guidelines have been recommended for managing OA of the knee. [6, 7, 8, 9] Analgesics, non-steroidal anti-inflammatory drugs (NSAIDs), opioids, weight loss and physiotherapy form the bedrock of management before joint replacement.

Physiotherapy is a health care profession that provides a range of non-pharmacological interventions for knee OA. It is frequently recommended in addition to NSAIDs to increase the efficacy of treatment. [6, 7] Physiotherapy encompasses numerous treatment modalities such as quadriceps strengthening exercises, infrared radiation therapy, short-wave diathermy therapy, ultrasound therapy, transcutaneous electrical nerve stimulation (TENS) and interferential therapy. [10, 11] Two studies; such as that by Roddy et al [12] Imoto et al [13] have reported that strengthening the quadriceps muscles can be beneficial in the management of osteoarthritis of the knee. The benefits include improved knee joint range of motion, improved knee function and reduced joint pain. Infrared radiation therapy is frequently used to ameliorate symptoms of osteoarthritis of the knee. Heat from infrared radiation relieves pain by increasing the pain threshold, increasing blood flow and washing away pain producing metabolites. [14] It enables collagen to deform easily causing an increase in the extensibility of the connective tissue [15]. Some researchers have reported that superficial heat decreases joint pain and stiffness, while increasing joint range of motion and improving disability in patients with OA of the knee. [16, 17]

Diclofenac sodium a non steroidal anti-inflammatory drug is among the medications most widely used worldwide in the treatment of OA. It has been shown to decrease pain and stiffness while improving function. [18, 19] Diclofenac sodium prevents prostaglandin synthesis at both the peripheral and central levels by inhibiting Cyclo-oxygenase 1 and 2 (COX-1 and COX2) enzymes non-selectively. [20] It possesses analgesic, anti-inflammatory and antipyretic properties and following administration passes into the synovial fluid where maximum concentrations are measured 2-4 hours after peak plasma values have been obtained. [20] However Diclofenac therapy is associated with undesirable side effects such as gastro-intestinal (GIT) ulcers and bleeding. [21] Other undesirable side effects of diclofenac sodium therapy include destabilization of blood pressure, renal function impairment and an increased risk of cardiovascular events. [22, 23] B vitamins are a class of water-soluble vitamins that play important roles in cell metabolism. Each B vitamin is either a coenzyme for key

metabolic processes or is a precursor needed to make one. They have not been reported to have any relieving effect in the treatment of symptomatic OA of the knee.

The purpose of this study was to compare the efficacy of the combination of quadriceps strengthening, infrared therapy and oral diclofenac sodium with quadriceps strengthening and infrared therapy alone and oral diclofenac sodium alone in the management of patients with symptomatic OA of the knee using reduction in knee joint pain intensity, increase in quadriceps muscle strength and reduction in 30.4 metres walk-time as outcome measures.

2. Methods

The research population comprised of patients who had confirmed diagnosis of symptomatic osteoarthritis of the knee according to the criteria established by the American College of Rheumatology. [24] Ethical approval was obtained from Nnamdi Azikiwe University Teaching Hospital Ethical Committee. All patients gave written informed consent for participation. A total of 130 patients aged 45yrs and above were consecutively recruited into the study. Patients who had any form of inflammatory arthropathy, recent injury in the knee, history of peptic ulcer, congestive heart disease, pregnant or lactating were excluded from the study. Patients participating in other clinical trials were also excluded from the study. The sample size for the study was determined using 19.6% prevalence as reported by Brandt. [25] The participants were randomly distributed into four groups: group 1 (combination of quadriceps strengthening, infrared radiation and oral diclofenac sodium); group 2 (quadriceps strengthening and infrared radiation alone); group 3 (oral diclofenac sodium alone) and group 4 (control).

3. Materials

Diclofenac sodium tablets each containing 50mg of diclofenac sodium (manufactured by Merckle GmbH, Blaubeuren-Weiler, Germany for Mepha LLC, Aesch-Basel, Switzerland) were used for NSAID therapy while vitamin B complex tablets (Manufactured by Emzor Pharmaceutical Industries Isolo-Lagos, Nigeria) each containing 1mg of vitamin B1, 1mg of B2 and 15mg of Nicotinamide were used as the placebo drug. Sand bags of different weights were used to increase resistance during quadriceps strengthening exercises while Infra-red Lamp (Infraphil, Philips model, 150watts) was used for infrared radiation therapy. A Stadiometer (SECA model) was used to measure the weights and heights of the participants and Stop watch (Nokia model, 8850) was used to record walk time. Water Marker was used to mark out anatomical land marks on the participants whilst a masking tape was used to mark out the distance for walk time. An inelastic measuring tape (Bouncing Rabbit, made in China) was used to measure out the 30.4metres walk distance and the quadriceps muscle strength of the affected limbs

were obtained using the Oxford grading Scale. [26] Box Numerical Pain Scale (BNPS) of 1-10 was used to assess knee joint pain intensity. [27]

The sex, age, occupation, duration of knee pain, family history, social history and radiology reports of weight bearing plain radiographs of the knee(s) of the participants were documented. Baseline knee pain intensity score, quadriceps muscle strength and 30.4m walk-time for each participant were recorded at the beginning of the study. The height, weight and 30.4m walk time of the participants were measured and recorded in metres (m), kilograms (kg) and seconds (sec) respectively. The participants in groups 1 and 3 received one tablet of diclofenac sodium and one tablet of vitamin B complex twice daily (morning and evening) taken before a meal without chewing, together with a glass of water while participants in groups 2 and 4 took one tablet of vitamin B complex only twice daily (morning and evening) before a meal without chewing, together with a glass of water. The drugs were taken by each participant for seven consecutive weeks. In addition the participants in groups 1 and 2 performed supervised quadriceps muscle strengthening exercises (isotonic and isometric) and received infrared radiation therapy [28] three times every week for seven consecutive weeks. The infrared radiation therapy was administered for 15 minutes during each treatment session. During the study period, participants were not allowed to have any additional therapies such as topical NSAIDS, intra-articular corticosteroid injections and other analgesics. At the end of seven weeks, the knee joint pain intensity score; quadriceps muscle strength and 30.4m walk time were measured and recorded for each participant.

4. Data Analysis

The Statistical Package for Social Sciences (SPSS) version 20 software package was used for the data entry and analysis. Descriptive statistics of mean and standard deviation were calculated for measurements taken. Analysis of variance (ANOVA) was used to compare the baseline characteristics across the four groups. Paired t-test was used to compare pre and post mean test score changes for each

parameter (knee pain intensity score, quadriceps strength and 30.4m walk-time) in each treatment group. Alpha level for all statistical analysis employed was set at $p < 0.05$.

5. Results

One hundred and thirty participants completed the study. They comprised 43 (33.08%) males and 87 (66.92%) females. The male to female ratio was 1:2. The participants were within the age range of 45 and 68 years, with a mean age of 52.35 ± 5.81 years. The mean weight, height and body Mass Index (BMI) of the participants were 86 ± 8.19 kg, 1.73 ± 0.03 m, 28.05 ± 2.17 kg/m² respectively. The mean length of time since onset of condition was 2.79 ± 1.33 years. More participants (38) in the quadriceps strengthening and infrared radiation group completed the study when compared with the other three groups (Table 1). The result revealed that least number of patients (26) who completed the study was in the control group. The mean age of 54.23 ± 5.68 years of the participants in the control group was more than the mean age of participants in the other groups. The participants in the quadriceps strengthening and infrared radiation group had a higher mean BMI (30.05 ± 1.60 kg/m²) and weighed more (89.52 ± 5.78) than the participants in the other groups. The difference in the mean weight and mean BMI were statistically significant ($p < 0.05$).

Table 2 shows the means of the knee pain intensity scores of the participants in the four groups at the beginning and at the end of the study. At the end of seven weeks of treatment, the result revealed that there was significant reduction in the knee pain intensity of the participants in groups 1, 2 and 3, ($p < 0.05$). The control group did not show any significant reduction in knee joint pain intensity, ($p > 0.05$).

The values of the means of the quadriceps strength at beginning and end of study are presented in Table 3. The result revealed that there was significant increase in the quadriceps strength of the participants in groups 1 and 2 at the end of seven weeks of treatment ($p < 0.05$). There was no significant increase in the quadriceps muscle strength in groups 3 and 4 ($p > 0.05$).

Table 1. The baseline physical characteristics of the participants in the four groups

Characteristics	Groups				f-value	p-value
	combined	quadriceps Strengthening & infrared	diclofenac	control		
Number	34	38	32	26		
Male/Female	12/22	12/26	10/22	9/17		
Mean duration of Condition (years)	2.7 ± 1.33	2.82 ± 1.16	3.03 ± 1.28	2.5 ± 1.24	3.667	0.067
Mean age (years)	52.35 ± 5.81	52.89 ± 5.74	53.166 ± 5.93	54.23 ± 5.68	1.776	0.088
Mean height (m)	1.73 ± 0.05	1.72 ± 0.03	1.73 ± 0.03	1.75 ± 0.04	3.774	0.053
Mean weight (kg)	87.76 ± 10.19	89.52 ± 5.78	83.69 ± 7.96	85.27 ± 7.74	4.321	0.049*
Mean BMI (kg/m ²)	29.23 ± 2.47	30.05 ± 1.60	27.79 ± 2.18	27.88 ± 2.13	4.423	0.033*

Table 2. Means of the knee pain intensity scores of the participants at the beginning and at the end of seven weeks of study

Treatment Groups	PIS beginning	wk7 PIS	t-value	p-value
Combined	7.24±1.46	3.12±2.09	9.309	0.000*
Quadriceps	7.74±1.46	4.84±2.64	6.73	0.045*
Strengthening and Infrared				
Diclofenac sodium	7.03±1.43	5.59±2.34	3.749	0.001*
Control	7.08 ± 1.09	6.92+ 1.47	0.57	0.574

Values are presented as the Mean ± Standard Deviation

*means $p < 0.05$ is significant.

PIS means knee pain intensity score

Wk7 means end of the seventh week

Table 3. Mean quadriceps muscle strength of participants in the four groups at beginning and end of the study

Treatment Group	Muscle strength at beginning	Muscle strength at Wk7	t-value	p-value
Combined	3.12±0.33	4.00±0.00	-15.632	0.000*
Quadriceps	3.13±0.34	3.95±0.23	-12.30	0.000*
strengthening and infrared				
Diclofenac sodium	3.41±0.50	3.59±0.50	-1.982	0.056
Control	3.15±0.37	3.19±0.40	-1.000	0.33

Wk7 means end of the seventh week

Values are represented as the mean ± Standard deviation

*means $p < 0.05$ is significant.

Table 4. Mean 30.4m walk –time of the participants in the four groups at the beginning and end of study

Treatment Groups	Mean Walk time at beginning	Mean Walk time at Wk7	t-value	p-value
Combined	40.63±6.27	32.73±3.1	7.537	0.000*
Quadriceps	41.92±6.22	37.00±5.64	5.47	0.000*
strengthening and infrared				
Diclofenac sodium	42.02±7.52	37.76±5.56	2.700	0.011*
Control	40.45±6.76	40.47±7.30	0.014	0.984

Wk7 means end of the seventh week

Values are presented as the mean ± Standard deviation

*means $p < 0.05$ is significant.

The values of the means of the 30.4 meter walk-time at beginning and end of the study showed that there was a significant reduction ($p < 0.05$) in the 30.4m walk-time in all the groups except for the participants in the control group (Table 4). However, participants in groups 1 and 2 demonstrated superior reduction in 30.4m walk time to those in group 3.

6. Discussion

The results of the study revealed that there was significant reduction in knee pain intensity in all the groups except the control group suggesting that quadriceps strengthening and infrared radiation alone and diclofenac sodium alone reduced knee pain intensity. The pain relieving effects of diclofenac sodium is documented in the literature by two researchers and this is as a result of its analgesic and anti-inflammatory properties. [18, 19] The pain relieving effect of infrared radiation therapy has also been reported in other studies. [16, 17] Quadriceps strengthening exercises are effective in improving pain, function and quality of life in patients with

osteoarthritis of the knee as reported by Imoto et al. [29] Roddy et al [30] and Lankhorst et al [31] in their studies that quadriceps weakness is common in patients with OA of the knee which correlates with pain and strengthening the quadriceps muscles reduced pain intensity as confirmed in this study. Infrared radiation therapy and quadriceps strengthening exercises increase blood flow and tissue metabolism, relax the muscles and improve stability in the knee joint; properties capable of significantly contributing to reduction in pain intensity. In essence, the sum of the effects of the three therapies on pain could then be a reason for the superior reduction in knee joint pain intensity score in the combined group when compared to the other groups. This further supports the recommendation by the American College of Rheumatology [6] that the medical management of OA of the knee should include a combination of NSAIDs, quadriceps strengthening exercises and other physical modalities. Although the three modalities of treatment significantly reduced knee joint pain intensity in the participants, the results showed that the combination of the three therapies was superior to oral diclofenac sodium alone and quadriceps strengthening and infrared radiation alone.

However participants in the diclofenac group showed superior improvement when compared with participants in the quadriceps strengthening and infrared radiation therapy group. There was no significant reduction in knee joint pain intensity in the control group.

The participants in groups 1 and 2 demonstrated increased quadriceps muscle strength after performing supervised quadriceps muscle strengthening exercises for seven weeks. The stability and the functional capacity of the knee joint are largely dependent on the quadriceps muscle strength. [32] Thus the affected quadriceps muscles were put through a strengthening exercise regimen during the study in the two groups and increased in strength. This is consistent with the findings of other researchers [30, 33]; that judicious quadriceps strengthening exercises to an osteoarthritic knee improved the quadriceps muscle strength. Participants in the diclofenac sodium group had no significant improvement in quadriceps muscle strength. The study showed that oral diclofenac sodium did not have any significant effect on quadriceps muscle strength. To the best of the researchers' knowledge, there are no previous studies that have reported on the effect of NSAIDs on quadriceps strength. There was also no significant change in muscle strength in the participants in the control group.

There was reduction in the 30.4m walk-time in all the groups except in the placebo group. This could be due to the fact that reduction in pain intensity and increased muscle strength all contributed to improved function and performance of the affected joints. This is consistent with previous studies by Shekelle et al [34] and Barnes [35] and corroborates the findings of Stiskal [36] that exercises improve functional capacities of patients with symptomatic OA of the knee. The reduction in walk-time in the diclofenac group was mainly due to the reduction in pain intensity as a result of its anti-inflammatory and analgesic properties. This is consistent with findings in previous studies by Walker-Bone et al, [37] and Moore et al. [38] however the result also revealed that the combined group and quadriceps strengthening and infrared radiation therapy group showed superior reduction in 30.4m walk-time when compared with the diclofenac group. Quadriceps strengthening exercises and infrared radiation therapy enhance dynamic stability of knee OA joints as reported by Hicks et al. [39] Thus including quadriceps muscle strengthening exercise program and infrared radiation therapy in the management of patients with OA of the knee lead to better functional outcome.

7. Conclusions

The combination of quadriceps strengthening, infrared radiation and oral diclofenac sodium was superior to oral diclofenac sodium alone in all parameters used for comparison. The combination of quadriceps strengthening, infrared radiation and oral diclofenac sodium was superior to quadriceps strengthening and infrared radiation alone in reducing knee joint pain intensity. However quadriceps

strengthening and infrared radiation alone was superior to diclofenac sodium alone in all outcome measures except reduction in knee pain intensity. The placebo group did not show any significant improvement in all the outcome measures at the end of seven weeks of treatment. It is recommended that quadriceps strengthening exercises and infrared radiation therapy be routinely combined with oral diclofenac sodium in the management protocol of patients with symptomatic osteoarthritis of the knee but when oral diclofenac sodium is contraindicated, quadriceps strengthening exercises and infrared radiation therapy may be prescribed.

REFERENCES

- [1] Felson DT, Zhang Y, Hannan MT, Naimark A, Weissman BN, Aliabadi P, Levy D. The incidence and natural history of knee osteoarthritis in the elderly. The Framingham Osteoarthritis Study. *Arthritis Rheum.* 1995 Oct; 38(10): 1500-5.
- [2] Felson DT, Lawrence RC, Dieppe PA, Hirsch R, Helmick CG, Jordan JM, Kington RS, Lane NE, Nevitt MC, Zhang Y, Sowers M, McAlindon T, Spector TD, Poole AR, Yanovski SZ, Ateshian G, Sharma L, Buckwalter JA, Brandt KD, Fries JF. Osteoarthritis: new insights. Part 1: the disease and its risk factors. *Ann Intern Med.* 2000 Oct 17; 133(8): 635-46.
- [3] Verbrugge LM, Patrick DL. Seven chronic conditions: their impact on US adults' activity levels and use of medical services. *Am J Public Health.* 1995 Feb; 85(2): 173-82.
- [4] Lawrence RC, Felson DT, Helmick CG, Arnold LM, Choi H, Deyo RA, Gabriel S, Hirsch R, Hochberg MC, Hunder GG, Jordan JM, Katz JN, Kremers HM, Wolfe F; National Arthritis Data Workgroup. Estimates of the prevalence of arthritis and other rheumatic conditions in the United States. Part II. *Arthritis Rheum.* 2008 Jan; 58(1): 26-35. doi: 10.1002/art.23176.
- [5] Felson DT, Naimark A, Anderson J, Kazis L, Castelli W, Meenan RF. The prevalence of knee osteoarthritis in the elderly. The Framingham Osteoarthritis Study. *Arthritis Rheum.* 1987 Aug; 30(8): 914-8.
- [6] Hochberg MC, Altman RD, April KT, Benkhalti M, Guyatt G, McGowan J, Towheed T, Welch V, Wells G, Tugwell P; American College of Rheumatology. American College of Rheumatology 2012 recommendations for the use of nonpharmacologic and pharmacologic therapies in osteoarthritis of the hand, hip, and knee. *Arthritis Care Res (Hoboken).* 2012 Apr; 64(4): 465-74.
- [7] Jordan KM, Arden NK, Doherty M, et al. EULAR recommendations 2003: an evidence based approach to the management of knee osteoarthritis. Report of a Task Force of the Standing Committee for International Clinical Studies Including Therapeutic Trials (ESCISIT). *Ann Rheum Dis.* 2003; 62(12): 1145-1155 [PMC free article] [PubMed].
- [8] Zhang W, Moskowitz RW, Nuki G, et al. OARSI recommendations for the management of hip and knee osteoarthritis: part II OARSI evidence-based, expert consensus guidelines. *Osteoarthritis Cartilage.* 2008; 16(2): 137-162 [PubMed].

- [9] Zhang W, Nuki G, Moskowitz RW, et al. OARSI recommendations for the management of hip and knee osteoarthritis: part III. Changes in evidence following systematic cumulative update of research published through January 2009. *Osteoarthritis Cartilage*. 2010; 18(4): 476-499 [PubMed].
- [10] Cetin, Aytar and Ataky 2008. Comparing hot pack, short-wave diathermy, ultrasound, and TENS on isokinetic strength, pain, and functional status of women with osteoarthritic knees: a single-blind, randomized, controlled trial. *Am J Phys Med Rehabil*. 2008 Jun; 87(6): 443-51. doi: 10.1097/PHM.0b013e318174e467.
- [11] Doi T, Akai M, Fujino K, Iwaya T, Kurosawa H, Hayashi K, Marui E. Effect of home exercise of quadriceps on knee osteoarthritis compared with nonsteroidal antiinflammatory drugs: a randomized controlled trial. *Am J Phys Med Rehabil*. 2008 Apr; 87(4): 258-69. doi: 10.1097/PHM.0b013e318168c02d.
- [12] Roddy E., Zhang W., Doherty M., Arden N.K., Barlow J., Birrell F., et al. (2005) Evidence-based recommendations for the role of exercise in the management of osteoarthritis of the hip or knee—the MOVE consensus. *Rheumatology*44: 67–73 [PubMed].
- [13] Imoto AM, Peccin MS, Trevisani VF. Quadriceps strengthening exercises are effective in improving pain, function and quality of life in patients with osteoarthritis of the knee. *ActaOrtop Bras*. 2012; 20(3): 174-9. doi: 10.1590/S1413-78522012000300008.
- [14] Berliner MN, Maurer AI. Effect of different methods of thermotherapy on skin microcirculation. *Am J Phys Med Rehabil* 2004; 83: 292–7.
- [15] Lentell G, Heatherington T, Eagan J, Morgan M. The use of thermal agents to influence the effectiveness of a low-load prolonged stretch. *J Orthop Sports Phys Ther* 1992; 16: 200-7.
- [16] McCarberg W, Erasala G, Goodale M, Grender J, Hengehold D, Donikyan L. Therapeutic benefits of continuous low-level heat wrap therapy (CLHT) for osteoarthritis (OA) of the knee. 24th Annual Scientific Meeting of the American Pain Society. Boston (MA); 2005.
- [17] Stelian J, Gil I, Habet B, Rosenthal M, Abramovici I, Kutok N, Khahil A. Improvement of pain and disability in elderly patients with degenerative osteoarthritis of the knee treated with narrow-band light therapy. *J Am Geriatr Soc*. 1992 Jan; 40(1): 23-6.
- [18] Ward JR. Efficacy of diclofenac in osteoarthritis. *Am J Med*. 1986; 80 (Suppl 4B): 53-7. [IDIS 215385] [PubMed 3518434].
- [19] Germain BF. A placebo-controlled study of diclofenac sodium for the treatment of osteoarthritis of the hip and knee. *Curr Ther Res*. 1985; 37:259-68.).
- [20] Scholer DW, Ku EC, Boettcher I et al. Pharmacology of diclofenac sodium. *Am J Med*. 1986; 80 (Suppl 4B): 34-8. [IDIS 215381] [PubMed 3085490]
- [21] Straube S, Tramèr MR, Moore RA, Derry S, McQuay HJ. Mortality with upper gastrointestinal bleeding and perforation: effects of time and NSAID use. *BMC Gastroenterol*. 2009 Jun 5; 9: 41. doi: 10.1186/1471-230X-9-41.
- [22] Valat JP, Deray G, Héloire F. Are there any differences in the cardiovascular tolerance between classical NSAIDs and coxibs? *Presse Med*. 2006 Sep; 35Suppl 1: 25-34.
- [23] Graham DJ. COX-2 inhibitors, other NSAIDs, and cardiovascular risk; the seduction of common sense. *JAMA*. 2006; 296:1653-6. [PubMed 16968830]
- [24] Altman R, Asch E, Bloch D, Bole G, Borenstein D, Brandt K, et al. (1986) Development of criteria for the classification and reporting of osteoarthritis: classification of osteoarthritis of the knee. *Arthritis Rheum* 29:1039–1049.
- [25] Brandt KD. Osteoarthritis. In D L Kasper, E Braunwald, A Fauci, S Hauser (edition). *Harrison's Principles of Internal Medicine*, 16th Edition Chapter 312, New York; McGraw Hill: 2005.
- [26] Porter, S. *Musculoskeletal Assessment*, in Porter's (ed) *Tidy's Physiotherapy*, 13th edition, Oxford, Elsevier publishers; 2004. Pages 60-69.
- [27] McDowell, I. & Newell, C. Pain measurements. In *Measuring Health: A Guide to Rating Scales and Questionnaires* 2nd edition, New York, Oxford University Press, 1996. Pages 335 – 337.
- [28] *Schreiber JW* (1981). *Infrared and Luminous Radiation*. In *manual of Electrotherapy* (4th edition), Henry Kimpton Publishers; London, 23-37.
- [29] Imoto AM, Peccin MS, Trevisani VF¹. Quadriceps strengthening exercises are effective in improving pain, function and quality of life in patients with osteoarthritis of the knee. *ActaOrtop Bras*. 2012; 20(3): 174-9. doi: 10.1590/S1413-78522012000300008.
- [30] Roddy E, Zhang W, Doherty M. Aerobic walking or strengthening exercise for osteoarthritis of the knee? A systematic review. *Annals of the Rheumatic Diseases* 2005; 64: 544–8).
- [31] Lankhorst GJ, Van de Stadt RJ, Van der Korst JK. The relationships of functional capacity, pain, and isometric and isokinetic torque in osteoarthrosis of the knee. *Scand J Rehabil Med*. 1985; 17(4): 167-72.
- [32] Slemenda C, Brandt KD, Heilman DK, Mazucca S, Braunstein EM, Katz BP, Wolinsky FD. Quadriceps weakness and osteoarthritis of the knee. *Ann Intern Med*. 1997 Jul 15; 127(2): 97-104.
- [33] Bennell KL, Hinman RS, Metcalf BR, Buchbinder R, McConnell J, McColl G, Green S, Crossley KM. Efficacy of physiotherapy management of knee joint osteoarthritis: a randomised, double blind, placebo controlled trial. *Ann Rheum Dis*. 2005 Jun; 64(6): 906-12.
- [34] Shekelle PG, Morton SC, Suttrop MJ, Buscemi N, Friesen C; Agency for Healthcare Research and Quality. Challenges in systematic reviews of complementary and alternative medicine topics. *Ann Intern Med*. 2005 Jun 21; 142(12 Pt 2): 1042-7. Bennell KL1, Hinman RS, Metcalf BR, Buchbinder R, McConnell J, McColl G, Green S, Crossley KM. Efficacy of physiotherapy management of knee joint osteoarthritis: a randomised, double blind, placebo controlled trial. *Ann Rheum Dis*. 2005 Jun; 64(6): 906-12.
- [35] Barnes PM, Powell-Griner E, McFann K, Nahin RL. Complementary and alternative medicine use among adults: United States, 2002. *Adv Data*. 2004 May 27; (343): 1-19.

- [36] Stiskal, D. The role of the Arthritis Foundation in the treatment of osteoarthritis (patient education, self-management, and exercise programs). *Phys Med Rehabil State Art Rev.* 2001; 15: 15–32.
- [37] Walker-Bone K, Javaid K, Arden N, Cooper C. Regular review: medical management of osteoarthritis. *BMJ.* 2000 Oct 14; 321(7266): 936-40.
- [38] Moore RA, Tramèr MR, Carroll D, Wiffen PJ, McQuay HJ. Quantitative systematic review of topically applied non-steroidal anti-inflammatory drugs. *BMJ.* 1998 Jan 31; 316(7128): 333-8. Erratum in: *BMJ* 1998 Apr 4; 316(7137): 1059.
- [39] Hicks JE, Perry MB, Gerber LH: Rehabilitation in the management of patients with osteoarthritis. In: Moskowitz RW, Howell DS, Altman RD, Buckwalter JA, Goldberg VM, eds. *Osteoarthritis, Diagnosis and Medical/Surgical Management.* Philadelphia: WB. Saunders; 413-446.