International Journal of General Medicine & Surgery

Available Online: http://ijgms.edwiserinternational.com

Extracorporeal Shockwave Therapy is More Effective than Ultrasound on Osteoarthritis of the Knee: A Pilot Randomized Controlled Trial

Pawel Lizis[1], Wojciech Kobza[2], Grzegorz Manko[3], Barbara Para[4] and Jaroslaw Jaszczur-Nowicki[5]*

[1]Education and Health Protection Department, Holycross College, Kielce, Poland
[2]Physiotherapy Cabinet, Żywiec, Poland
[3]Ergonomics and Physiology of Physical Effort Department, Jagiellonian University, Cracow, Poland
[4]Health Protection Department, Med-On Company, Liszki, Poland
[5]Department of Tourism, Recreation and Ecology, Faculty of Environmental Sciences, University of Warmia and Mazury, Olsztyn, Poland

Article info

Received 11 October 2017
Revised 20 December 2017
Published 01 January 2018

*Corresponding author: Pawel Lizis, Education and Health Protection Department, Holycross College, Kielce, Poland, E-mail: pawel_lizis@poczta.onet.pl

Abstract

Objective: *The study intended to evaluate the extracorporeal shockwave therapy (ESWT) vs ultrasound (US) for patients with osteoarthritis (OA) of the knee.*
Methods: *A pilot randomized controlled trial (RCT) with concealed allocation, assessor blinding, and intention-to-treat analysis. The study occurred in the Physiotherapy Outpatient Department of the Regional Hospital in Zywiec, Poland. The participants were randomly assigned to an ESWT group, n=30 and a US group, n=30. The participants in both groups attended 5-week treatments. The ESWT group received 5 treatments once per week. The US group received 10 treatments twice per week. The primary outcome was physical function using Knee injury and Osteoarthritis Outcome Score (KOOS). The secondary outcome measured mobility, pressure pain threshold (PPT), and pain on visual analog scale (VAS).*
Results: *Post-intervention, the physical function improved on the KOOS for ESWT and US with regard to pain by a mean of 14 ± 10 and 7 ± 9 points ($p=0.003$), other symptoms and function in daily living by a mean of 12 ± 11 and 4 ± 7 points ($p<0.001$), function in sport/recreation by a mean of 22 ± 16 and 4 ± 14 points ($p<0.001$), knee-related quality of life by a mean of 20 ± 16 and 6 ± 6 points ($p<0.001$), pain on VAS by a mean of 2 ± 2 and 1 ± 1 points ($p<0.001$) respectively. The statistical significant between groups differences favouring the ESWT were found.*
Conclusion: *Patients with OA of the knee can achieve significantly better physical function caused by ESWT than by US.*

Keywords: Extracorporeal shockwave therapy; Ultrasound; KOOS; Mobility; Pain

Introduction

Osteoarthritis (OA) of the knee is a major musculoskeletal disorder affecting humankind and a major cause of disability and socioeconomic burden [1-4]. OA of the knee produces significant changes in health-related quality of life, particularly physical, mental and social components of health [5-8]. Currently several pharmacologic strategies are used in patients suffering from OA of the knee. Both paracetamol and nonsteroidal anti-inflammatory drugs (NSAIDs) are evidence-based drugs for symptom relief in OA. The

study of Verkleij et al. [9] indicated no significant difference between paracetamol versus diclofenac regarding KOOS pain and KOOS function. Over the 12-weeks follow-up KOOS pain in patients treated with paracetamol was with a mean of 34.8 ± 19.4 versus 37.4 ± 21.0 in patients treated with diclofenac. Estimated difference of –2.8 (95% CI=-10.7 to 5.1) with a small effect size (ES=0.01). Over the 12-weeks follow-up KOOS function in patients treated with paracetamol was with a mean of 28.4 ± 19.5) versus 31.4 ± 20.2 in patients treated with diclofenac. Estimated difference of –2.7 (95% CI=–10.6 to 5.0), but with a small improvement function (ES=0.02). Moreover, the authors found that patients more frequently reported minor adverse events after taking diclofenac (64%) than paracetamol (46%).

Zhang et al. [10] based on a meta-analysis concluded that paracetamol (acetaminophen) is effective for pain relief in OA, but with a small effect size (ES=0.21; 95% CI=0.02 to 0.41). Towheed et al. [11] based on the recent Cochrane review, reported that acetaminophen showed a statistically significant, but small reduction in pain (ES=0.13; 95% CI=0.04 to 0.22). However, there was no improvement in overall WOMAC, suggesting that it should not be expected to have a strong effect on stiffness or function. A meta-analysis concluded by Bannwarth [12] showed that NSAIDs, including COX-2 selective inhibitors, can reduce pain and functional disability in knee OA better than acetaminophen with a medium effect size (ES=0.32; 95% CI 0.24 to 0.39; ES=0.29; 95% CI 0.18 to 0.40, respectively).

Physiotherapy is a noninvasive intervention for patients with this disorder. Passive treatment (electrotherapy or manual therapy) has limited place in OA management, however, when combined with exercises, self-management, information/education, weight reduction can enhance the effectiveness of non-pharmacological intervention in people suffering from OA of the knee. Two meta-analysis conducted by Chodosh et al. [13] and Warsi et al. [14] assessed overall patient education about the objectives of treatment and the importance of changes in lifestyle, exercise, pacing of activities, weight reduction to decrease the symptoms of the knee OA. The authors reported that reduction of pain was small (ES=0.06 95% CI 0.02 to 0.10). Zhang et al. [15] recommend that patients with OA knee should be encouraged to undertake regular aerobic walking exercises and home-based quadriceps muscle strengthening exercises as a core recommendation in published guidelines and was supported by a systematic review and meta-analysis of 13 RCTs [14]. Pooled effect size's (ESs) for pain relief was in the medium range for both aerobic (ES=0.52, 95% CI 0.34 to 0.70) and muscle strengthening exercises (ES=0.32, 95% CI 0.23 to 0.42) and pooled ESs for self-reported disability (ES=0.46, 95% CI 0.25 to 0.67) for aerobic exercise (ES=0.32, 95% CI 0.23 to 0.41) for quadriceps strengthening exercises.

In the next study Elerian et. al. [16] reported the significant improve of the shockwave therapy (SWT) group than of the corticosteroid injection group where p was 0.000 for pain on visual analog scale (VAS), range of motion of the knee (ROM) and quality of life (WOMAC). At 6 months post-intervention the severity of pain on VAS in patients treated with SWT was 4.08 ± 1.75 and in patients treated with corticosteroid injection was 6.91 ± 1.55. The ROM of the knee flexion was 130.67 ± 5.67 and 102.97 ± 8.56 and the WOMAC was 23.05 ± 4.93 and 53.07 ± 1.92 respectively. However, the authors didn't show the effect size (ES) between the related treatments. Another study of Mascarin et al. [17] reported that ultrasound (US), transcutaneous electrical nerve stimulation (TENS), and kinesiotherapy (KIN) were effective for reducing pain on VAS and improving ROM, the quality of life on WOMAC. At the end of the intervention (12 week) the severity of pain on VAS in the right knee in US group was 4.5 ± 3.7 in TENS was 2.6 ± 2.9 in KIN was 2.3 ± 2.7 where the authors identified small or medium therapeutic effect size (ES=0.41; 0.76, 0.70) within groups respectively. In the left knee the severity of pain in US was 3.8 ± 3.1 in TENS was 2.3 ± 2.5 in KIN was 2.4 ± 2.8 where the effect sizes were medium (ES=0.54; 0.53; 0.68) within groups respectively. No significant differences were observed between the groups for the right and the left knees after the treatment period. ROM of the flexion in the right knee in US group was 76 ± 7 in TENS was 76 ± 10 in KIN was 73 ± 12. In the left knee the values were 75 ± 8, 79 ± 7 and 69 ± 12 respectively. ROM of the extension in the right knee in US group was 175 ± 7 in the TENS was 178 ± 3 in the KIN was 177 ± 4. In the left knee the values were 173 ± 7, 176 ± 4 and 178 ± 3 respectively. Unfortunately, the authors didn't show the effect size between the related treatments. The protocols adopted by the present study did not cause improvements in flexion for any of the knees. For extension, increases in ROM were found in the KIN and TENS groups for the both knees. However, no significant differences were observed for flexion and extension between the groups in the right and the left knees after the treatment period. Regarding WOMAC total score in the US was 28.8 ± 14.8 in the TENS was 14.2 ± 11.0 and in the KIN was 7.0 ± 8.1. A medium or a large therapeutic effect size (ES=0.67, 0.81 and 0.73)

on WOMAC was observed within the groups respectively. Despite on, the improvement in the patients treated with US was significantly less pronounced than that in the patients from the KIN and TENS groups, were $p<0.05$.

Despite pharmacologic and non-pharmacologic treatment, people with OA of the knee continue to experience pain and disability although they receive the best evidence-based therapies, and further researches are necessary to improve the treatment.

The systematic review showed, that no one examined the effectiveness of extracorporeal shockwave therapy (ESWT) vs. ultrasound (US) in patients with OA of the knee. Therefore, the research team consequently conducted a pilot randomized controlled trial (RCT) to compare the effects of ESWT and US on physical function in patients with OA of the knee. The research question was:

Do five weeks of the ESWT improve physical function in patients with OA of the knee more than the US?

Table 1: Characteristics of the participants.

Characteristic	Group ESWT (n=30)	Group US (n=30)
Females/males, (n)	10/20	8/22
Age *(yr)*, mean (SD)	59.8 (3.9)	60.7 (4.8)
Height *(m)*, mean (SD)	1.76 (0.05)	1.77 (0.06)
Mass *(kg)*, mean (SD)	72.6 (5.1)	74.2 (5.7)
BMI *(kg/m^2)*, mean (SD)	24.18 (0.69)	23.78 (0.66)
Level of education		
Primary school graduates, (n)	10	9
Secondary school graduates, (n)	13	10
University graduates, (n)	7	11
Occupation		
Physical worker/white-collar worker, (n)	16/14	17/13
Affected knee right/left, (n)	10/20	13/17
Duration of complaints *(yr)*, mean (SD)	8.0 (2.0)	7.4 (2.4)
ESWT: Extracorporeal shockwave therapy, US: Ultrasound.		

Methods

Study design

This study was a pilot RCT with concealed allocation, assessor blinding, and intention-to-treat analysis conducted according to the guidelines for Good Clinical Practice, and the Consolidated Standards of Reporting Trials (CONSORT) Statement guidelines [18]. This study was designed with the respect for the rules of conducting experimental studies with humans after the approval by the Bioethical Committee at the Holycross College in Kielce (approval number 06/152016KB of 8th June 2016), and were consistent with the Helsinki Declaration of 1975 as revised in 2000. The study was conducted at the Physiotherapy Outpatient Department of the Regional Hospital in Zywiec, Poland. The participants were patients of the department in the hospital. All the participants signed consent forms knowingly the participation in the study. Seventy prospective participants were assessed for eligibility by an independent physician not involved into the study between August 1st and September 1st, 2016. Ten of them met the exclusion criteria. Finally, sixty participants were randomly assigned either to an intervention group that received ESWT, or to a control group that received US. The participants were assigned to the groups in a 1:1 ratio using a simple-computerized random-number generator [19]. The allocator did not know the type of the intervention assigned to each group and was not involved in the participants' recruitment. The group allocator kept the allocation list and no one else had access to it. The same physiotherapist, with a postgraduate degree in physiotherapy and 10 years' experience, provided all the treatments to both groups and remained blinded as to the primary and the secondary outcome measures.

Table 2: Mean (SD) of groups, mean (SD) difference within groups, and mean (95% CI) difference between groups for all outcomes.

Outcome	Groups				Difference within groups		Difference between groups	P*	ES (Cohen d)
	Week 0		Week 5		Week 5 minus Week 0		Week 5 minus Week 0		
	ESWT (n=30)	US (n=30)	ESWT (n=30)	US (n=30)	ESWT	US	ESWT minus US		
KOOS (0 to 100 pts)									
Pain	74(12)	76(12)	88(11)	83(9)	14(10)	7(9)	7(3 to 13)	0.003	0.75
Other symptoms	78(10)	81(15)	90(9)	85(14)	12(11)	4(7)	8(3 to 16)	<0.001	0.87
Function in daily living	79(10)	81(15)	90(9)	85(14)	11(11)	4(7)	8(4 to 13)	<0.001	0.81
Function in sport/recreation	64(11)	69(22)	86(14)	73(19)	22(16)	4(14)	18(10 to 26)	<0.001	1.20
Knee-related quality of life	64(12)	69(11)	84(16)	75(11)	20(16)	6(6)	14(7 to 20)	<0.001	1.16
Mobility (s)									
Walk 15 meters	16(4)	13(4)	11(2)	12(4)	-5(4)	-1(1)	-4(-6 to -3)	<0.001	1.37
Get up and Go	14(3)	13(3)	10(3)	12(2)	-4(3)	-1(1)	-3(-4 to -2)	<0.001	1.34
Walk upstairs	11(4)	10(4)	6(3)	8(3)	-4(3)	-1(1)	-3(-4 to -2)	<0.001	1.34
Walk downstairs	13(5)	10(5)	6(1)	8(5)	-7(5)	-2(2)	-5(-7 to -3)	<0.001	1.31
Pressure Pain Threshold (kgf/cm^2)									
Superior patellar extremity	4.1(1.4)	4.1(1.4)	5.5(1.5)	4.4(1.2)	1.4(1.9)	0.3(1.2)	1.1(0.2 to 1.9)	0.021	0.69
Inferior patellar extremity	4.6(1.5)	4.3(1.5)	6.5(1.7)	5.0(1.3)	1.9(2.0)	0.7(1.9)	1.2(0.2 to 2.2)	0.032	0.61
Lateral patellar extremity	3.6(1.2)	3.6(1.2)	5.5(1.9)	4.2(1.2)	1.9(1.6)	0.6(0.9)	1.3(0.7 to 2.1)	<0.001	1.00
Medial patellar extremity	3.6(1.2)	3.3(0.9)	5.0(1.4)	3.8(0.8)	1.4(1.5)	0.5(0.9)	0.9(0.2 to 1.5)	0.020	0.73
Lateral knee region	2.9(1.3)	2.5(0.6)	4.3(1.5)	2.7(0.6)	1.4(1.6)	0.2(0.8)	1.2(0.5 to 1.9)	<0.001	0.95
Medial knee region VAS (0 to 10 cm)	2.3(0.9)	2.0(0.9)	3.5(1.1)	2.4(0.5)	1.2(1.1)	0.4(1.0)	0.8(0.3 to 1.4)	0.016	0.76
Pain	5(1)	5(2)	3(2)	4(2)	-2(2)	-1(1)	-1(-2 to -1)	<0.001	0.63

ESWT: Extracorporeal shockwave therapy, US: Ultrasound, ES: Effect size, KOOS: Knee injury and osteoarthritis outcome score, VAS: Visual analog scale.
*P: P value obtained by Mann-Whitney U-test.

Table 3: Number of participants (%) post-intervention (Week 5) for clinically improvement difference in KOOS, mobility, pressure pain threshold and VAS by treatment groups.

	Groups				P*	Odds ratio (95% CI)
	ESWT (n=30)	US (n=30)	ESWT (n=30	US (n=30)		
	improved ≥ 30% n(%)		improved <30% n(%)			
KOOS (0 to 100 pts)						
Pain	25(83)	14(47)	5(17)	16(53)	0.003	5.45(1.71 to 20.19)
Other symptoms	25(83)	17(57)	5(17)	13(43)	0.002	6.21(1.95 to 23.11)
Function in daily living	24(80)	16(53)	6(20)	14(47)	0.003	3.39(1.09 to 11.57)
Function in sport/recreation	23(77)	16(53)	7(23)	14(47)	0.019	3.63(1.22 to 11.78)
Knee-related quality of life	24(80)	14(47)	6(20)	16(53)	0.009	4.39(1.43 to 15.06)
Mobility (s)						
Walk 15 meters	23(77)	12(40)	7(23)	18(60)	0.005	4.74(1.59 to 15.55)
Get up and Go	23(77)	14(47)	7(23)	16(53)	0.012	3.63(1.22 to 11.78)
Walk upstairs	20(67)	9(30)	10(33)	21(70)	0.005	4.49(1.54 to 14.16)
Walk downstairs	25(83)	14(47)	5(17)	16(53)	0.003	5.45(1.71 to 20.19)
Pressure Pain Threshold (kgf/cm^2)						
Superior patellar extremity	21(70)	12(40)	9(30)	18(60)	0.023	3.40(1.18 to 10.42)
Inferior patellar extremity	23(77)	15(50)	7(23)	15(50)	0.037	3.19(1.06 to 10.32)
Lateral patellar extremity	25(83)	15(50)	5(17)	15(50)	0.007	4.78(1.49 to 17.70)
Medial patellar extremity	22(73)	14(47)	8(27)	16(53)	0.040	3.06(1.05 to 9.52)
Lateral knee region	23(77)	12(40)	7(23)	18(60)	0.005	4.74(1.59 to 15.55)
Medial knee region	25(83)	13(43)	5(17)	17(57)	0.002	6.21(1.95 to 23.11)
VAS (0 to 10 cm)						
Pain	24(80)	15(50)	6(20)	15(50)	0.018	3.86(1.26 to 13.19)

ESWT: Extracorporeal shockwave therapy, US: Ultrasound, KOOS: Knee injury and osteoarthritis outcome score, VAS: Visual analog scale.
*P: P value obtained by Fisher's exact mid-p test.

To keep the assessors blinded, the participants were reminded before each measurement not to reveal the nature of their treatments. They were unaware of their group allocations and were informed only about the existence of the 2 groups but not about the study's hypothesis. The measurements were obtained at baseline and 5 weeks later, post-intervention (Figure 1). The baseline characteristics of the participants are shown in Table 1.

Participants

The participants who were included into the study by the physician didn't suffer from comorbidities diseases, they were 40-60 years of age (our participants were relatively young, because at the time of our research the Regional Hospital in Zywiec organized screening for early prevention of the knee OA, so we united our efforts), they had duration of complaints ≥ 1 year, met on Xray medial or lateral femoro-tibial OA localization reported by a radiologist; met the severity of knee (OA) grade 1 according Kellgren and Lawrence classification; met the American College of Rheumatology (ACR) clinical criteria for OA of the knee [20], which includes knee pain plus presentation of at least five of the following: morning joint stiffness that usually resolved within 30 minutes, crepitus with active motion of the knee, bony tenderness, bony enlargement, or no palpable warmth of the synovium.

The subjects were excluded if they had bilateral knee OA, had previous knee joint surgery and any surgical procedure of the lower limbs, had received an intra-articular injections or physiotherapy intervention for their knee during the preceding 3 months, had skin changes, had inability to comprehend and complete study assessments or comply with the study instructions.

Intervention

The intervention group received ESWT − 1000 pulses during the first treatment, 1500 during the second and the third treatments, and 2000 during the fourth and the fifth treatments, respectively (pressure, 2.5 bar; frequency, 8 Hz; energy density, 0.4 mJ/mm2). The patients received 5 ESWT treatments, once per week. The treatments were performed using a Rosetta ESWT (CR Technology, Korea). The patients were placed in a supine position with the affected knee flexed at 90 deg, and an acoustic gel that did not contain any pharmacologically active substance was applied. The shockwave probe was held stationary on a trigger point such as: the base and apex of the patella, collateral tibial ligament (MTL), collateral fibular ligament (LCL), avoiding direct placement on the peroneal nerve or vessel. Each treatment session did not exceed 10 minutes. The control group received continuous US waves: intensity, 0.8 W/cm^2; 100% fill; carrier frequency, 1 MHz. The patients received 10 treatments, twice per week. The treatments were performed using a US 13 EVO Cosmogamma (Emildue, Italy). The patients lied in a supine position with the affected knee flexed at 90 deg. The applied acoustic gel did not contain any pharmacologically active substance. The same trigger point as in ESWT were treated with US applied in circular movements. To ensure the best absorption of the energy the probe was put at right angles. Each treatment session did not last longer than 10 minutes. All of the treatments were performed at the Physiotherapy Outpatient Department of the Regional Hospital in Zywiec, Poland. The same physiotherapist with a postgraduate degree in physiotherapy and 10 years' experience provided all the interventions to both (intervention and control) groups and remained blind to the primary and the secondary outcome measures throughout the trial. The application of ESWT and US are shown in Figure 2 and Figure 3.

Outcome measures

The outcomes were assessed at baseline (Week 0) and post-intervention (Week 5).

Primary outcome was

Physical function: It was assessed using a simple translation of the KOOS. It is an instrument used to assess patients' opinions about their knee and the associated problems. It is a modification of the Western Ontario and McMaster Universities (WOMAC) Osteoarthritis Index consisting of 41 questions arranged in 5 subscales: pain, other symptoms, function in daily living, function in sport and recreation, knee-related quality of life. Standardized answer options are given in 5 Likert boxes and each question gets a score from 0 to 4. A normalized score where 100 indicates no symptoms and 0 indicates extreme symptoms was calculated for each subscale. The participants marked each of the domains after their usual daily activities. Each domain's results in points were recorded for the statistical analysis [21,22].

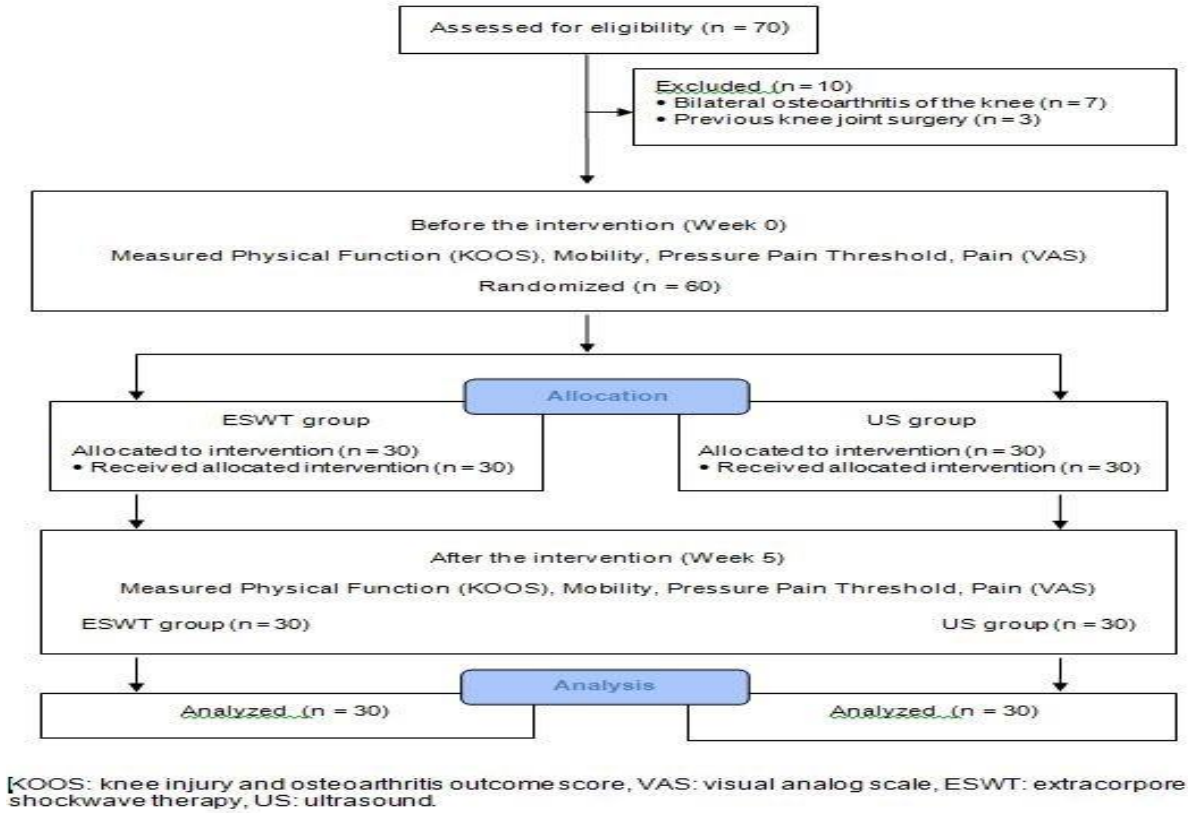

Figure 1: Flowchart of the study.

Participants

The participants who were included into the study by the physician didn't suffer from comorbidities diseases, they were 40-60 years of age (our participants were relatively young, because at the time of our research the Regional Hospital in Zywiec organized screening for early prevention of the knee OA, so we united our efforts), they had duration of complaints ≥ 1 year, met on Xray medial or lateral femoro-tibial OA localization reported by a radiologist; met the severity of knee (OA) grade 1 according Kellgren and Lawrence classification; met the American College of Rheumatology (ACR) clinical criteria for OA of the knee [20], which includes knee pain plus presentation of at least five of the following: morning joint stiffness that usually resolved within 30 minutes, crepitus with active motion of the knee, bony tenderness, bony enlargement, or no palpable warmth of the synovium.

The subjects were excluded if they had bilateral knee OA, had previous knee joint surgery and any surgical procedure of the lower limbs, had received an intra-articular injections or physiotherapy intervention for their knee during the preceding 3 months, had skin changes, had inability to comprehend and complete study assessments or comply with the study instructions.

Intervention

The intervention group received ESWT − 1000 pulses during the first treatment, 1500 during the second and the third treatments, and 2000 during the fourth and the fifth treatments, respectively (pressure, 2.5 bar; frequency, 8 Hz; energy density, 0.4 mJ/mm^2).

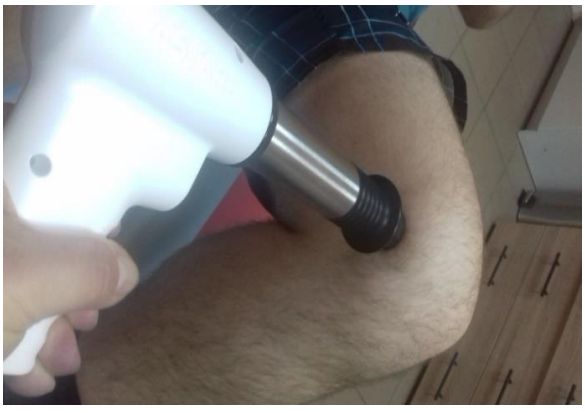

Figure 2: Application of ESWT.

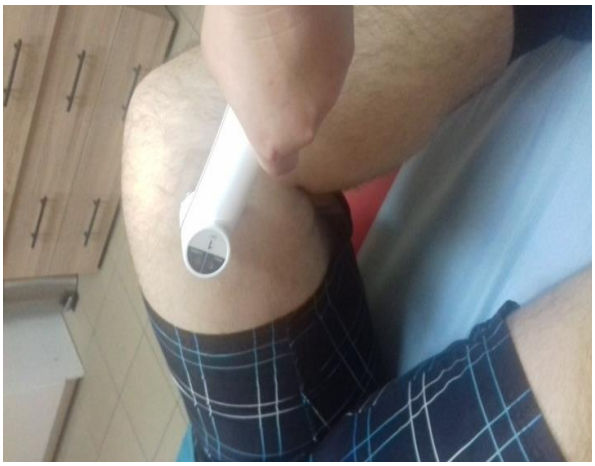

Figure 3: Application of US.

The patients received 5 ESWT treatments, once per week. The treatments were performed using a Rosetta ESWT (CR Technology, Korea). The patients were placed in a supine position with the affected knee flexed at 90 deg, and an acoustic gel that did not contain any pharmacologically active substance was applied. The shockwave probe was held stationary on a trigger point such as: the base and apex of the patella, collateral tibial ligament (MTL), collateral fibular ligament (LCL), avoiding direct placement on the peroneal nerve or vessel. Each treatment session did not exceed 10 minutes. The control group received continuous US waves: intensity, 0.8 W/cm^2; 100% fill; carrier frequency, 1 MHz. The patients received 10 treatments, twice per week. The treatments were performed using a US 13 EVO Cosmogamma (Emildue, Italy). The patients lied in a supine position with the affected knee flexed at 90 deg. The applied acoustic gel did not contain any pharmacologically active substance. The same trigger point as in ESWT were treated with US applied in circular movements. To ensure the best absorption of the energy the probe was put at right angles. Each treatment session did not last longer than 10 minutes. All of the treatments were performed at the Physiotherapy Outpatient Department of the Regional Hospital in Zywiec, Poland. The same physiotherapist with a postgraduate degree in physiotherapy and 10 years' experience provided all the interventions to both (intervention and control) groups and remained blind to the primary and the secondary outcome measures throughout the trial. The application of ESWT and US are shown in Figures 2 and 3.

Outcome measures

The outcomes were assessed at baseline (Week 0) and post-intervention (Week 5).

Primary outcomes were:

Physical function: It was assessed using a simple translation of the KOOS. It is an instrument used to assess patients' opinions about their knee and the associated problems. It is a modification of the Western Ontario and McMaster Universities (WOMAC) Osteoarthritis Index consisting of 41 questions arranged in 5 subscales: pain, other symptoms, function in daily living, function in sport and recreation, knee-related quality of life. Standardized answer options are given in 5 Likert boxes and each question gets a score from 0 to 4. A normalized score where 100 indicates no symptoms and 0 indicates extreme symptoms was calculated for each subscale. The participants marked each of the domains after their usual daily activities. Each domain's results in points were recorded for the statistical analysis [21,22].

Secondary outcomes were:

Mobility: It was measured as the time required to perform four activities in seconds (walking along a level unobstructed corridor for 15 meters, rising from chair and walking 15 meters [get up and go], walking up 11 stairs, and walking down 11 stairs). The values in seconds were recorded for the statistical analysis [23].

Pressure pain threshold: It was assessed with a pressure algometer (EMG System do Brasil, model EMG230C, Sao Paulo, Brazil). The participant was seated with knees flexed to 90 deg and progressive pressure was applied perpendicular to the skin. The participants were instructed to report immediately when the sensation of pressure was accompanied by pain. The amount of pressure at that moment was recorded and considered as the pressure pain threshold (PPT). The pressure was applied and recorded at six points around the knee in a random order: the base and apex of the patella, the lateral and medial extremities of the patella, and the lateral and medial aspects of the knee joint line. Each point was assessed once after one familiarisation trial at each point. The values in kgf/cm^2 were recorded for the statistical analysis [24].

Pain: It was measured with the patient's indicating his/her current level of pain by marking a point on a 10-centimeters VAS, in which 0 represents no pain and 10 represents the unbearable pain. The participants marked the scale of their current pain level after their usual daily

activities. The values in centimeters were recorded for the statistical analysis.

Statistical analysis

To determine the required sample size, 16 participants were tested to determine the standard deviation of pain subscale of the KOOS. We sought an effect on pain of about 10 points on KOOS subscale. Using the standard deviation of 15 points from our test data, a significance level of 5% and a test power of 80%, the research team calculated that the study needed a minimum of 22 participants in each group. Therefore, as we anticipated a possibility that some patients would not complete the study, we included 30 patients in each group. The data analysis provided the mean and standard deviation (SD) of the two groups, the mean and SD for the within-group differences, and a 95% confidence interval (CI) for the mean between-group differences, using inferential techniques. A mean between-group difference (95% CI) was calculated for each of the outcomes based on the change scores, ie, week 5 minus week 0 scores. The Shapiro-Wilk test identified the non-normal distribution of the KOOS, mobility, pressure pain threshold, and VAS data. To compare the differences between the groups, the Mann-Whitney U test was used. To describe the differences in related treatments, the effect size between groups differences was calculated using Cohen's d, and classified as small ($d \geq 0.20$ and<0.50), medium ($d \geq 0.50$ and <0.80) and large ($d \geq 0.80$) [25]. The comparison of the proportion of the clinically important differences at Week 5 (improved percentage $\geq$ 30% or<30% for KOOS, mobility, pressure pain threshold, and VAS) between ESWT and US treatments were tested by Fisher's exact test with mid-p correction (2x2 contingency table), and odds ratio with 95% CI [26,27]. The level of statistical significance was set at a two-tailed p value of 0.05. The analysis was performed by a blinded and independent statistician according to a pre-specified statistical analysis plan on an intention-to-treat basis.

Results

Compliance with the study protocol

During the treatments, all the participants (n=60) did not receive any anesthetic or other physical methods of relief. The used ESWT doses were painless, and minor pain during the intervention did not produce any unpleasant sensation in patients. As a result, the patients did not report any adverse events. Therefore, we think that the applied doses are safe and friendly for the patients.

Effect of intervention

After the intervention, the physical function improved on the KOOS within both groups. The research team found the significant differences between the groups post-intervention on the KOOS scores. The greatest between-groups differences were identified for the function in sport/recreation, knee-related quality of life subscales with a mean difference in points of 18 (95% CI 10 to 26, effect size=1.20), and 14 (95% CI 7 to 20, effect size=1.16) respectively, in favor for the ESWT group, all p<0.001. The smallest differences were observed for the pain, function in daily living, and other symptoms subscales, with a mean of 7 points (95% CI 3 to 13, p=0.003, effect size=0.75), 8 (95% CI 4 to 13, p<0.001, effect size=0.87), and 9 (95% CI 3 to 16, p<0.001, effect size=0.81) respectively, but better results were in the ESWT group (Table 2).

After the intervention, the research team identified the improvement in mobility within both groups. They also found the significant differences between the groups post-intervention. The ESWT group had significantly better scores than the US group for 15 meters walk, with a mean difference in seconds of -4 (95% CI -6 to -3, effect size=1.37), get up and go, walk upstairs, with a mean of -3 (95% CI -4 to -2, effect size=1.34) and walk downstairs, with a mean of -5 (95% CI -7 to -3, effect size=1.31), all p<0.001 (Table 2).

After the intervention, the pressure pain threshold (PPT) increased and pain severity reduced on the VAS within both groups. The research team found the significant differences between the groups post-intervention. The greatest between-groups differences were identified for the pressure pain threshold at lateral patellar extremity, lateral knee region, with a difference in kgf/cm2 of 1.3 (95% CI 0.7 to 2.1, effect size=1.00), and 1.2 (95% CI 0.5 to 1.9, effect size=0.95) respectively, in favor for the ESWT group, all p<0.001. The smallest differences were observed for the pressure pain threshold at medial patellar extremity, medial knee region, with a mean of 0.9 kgf/cm2 (95% CI 0.2 to 1.5, p=0.020, effect size=0.73), 0.8 (95% CI 0.3 to 1.4, p=.016, effect size=0.76) respectively, but better results were in the ESWT group. That group also had significantly lower scores than the US group on the VAS scale, with a mean difference in centimeters of -1 (95% CI -2 to -1, p<0.001, effect size=0.63), as presented in Table 2.

After the intervention, the research team identified a better success rate in all outcomes in the ESWT group. The ESWT group had a greater success rate than the US group on KOOS outcome. The ESWT group outcomes

ranged from 83% for pain and other symptoms to 77% for function in sport/recreation vs 57% for the other symptoms, and 47% for pain, knee-related quality of life in the US group. The ESWT group had also a greater success rate than the US group in mobility. The ESWT outcomes ranged from 83% for walking downstairs to 67% for walking upstairs vs 47% for getting up and going, walking downstairs to 30% for walking upstairs in the US group. The success rate in PPT for the ESWT group ranged from 83% for lateral patellar extremity, medial knee region to 70% for superior patellar extremity vs 50% for the inferior patellar extremity, lateral patellar extremity, and 40% for the superior patellar extremity, lateral knee region in the US group. The success rate on VAS for the ESWT group was 80% vs. 50% for the US group. The odds ratio and 95% CI for all the parameters that were statistically significantly different between the groups tested with Fisher's exact test with mid-p were shown in Table 3. So, there are the relationships between a kind of the treatment and health benefits among the people suffering from OA of the knee.

Discussion

The results following 5 weeks of the treatment showed that KOOS, mobility, pressure pain threshold improved (PPT), and pain (VAS) in knees decreased in both the intervention (ESWT) and the control (US) groups. However, post-intervention the significant results were obtained by the participants treated with ESWT. The significant clinical effects were found in function, in sport/recreation and knee-related quality of life on KOOS. In the three dimensions of KOOS, such as pain, other symptoms, and function in daily living improvement was statistically significant, however smaller, that showed rather absence of important clinical effects. The similar results were observed in pain on PPT or VAS. Only for PPT in a lateral patellar extremity the significant clinical effect was found. The treatment effects sizes were moderate or large, ranged from 0.61 for PPT in the inferior patellar extremity to 1.37 for mobility (walk 15 meters). The odds ratio was also always more far-reaching in the patients treated with ESWT, than those ones in the patients treated with US.

The usefulness of the ESWT was reported to the treatment of OA in animals, which improved motor dysfunction and ameliorated pain. ESWT improved the walking ability of rats on a treadmill [28]. The degree of lameness in the horses receiving ESWT significantly improved compared with the horses treated with placebo or polysulfated glycosaminoglycan [29].

The study of Zhao et al. [30] in humans confirmed those findings. The authors used a medium-energy ESWT to treat OA of the knee and compared it with a placebo treatment. In the ESWT group, the patients received 4000 pulses of shockwave at 0.25 mJ/mm^2 a week for 4 weeks. In the placebo group the patients got shockwave at 0 mJ/mm^2 in the same area for the same time. The authors reported clinically significant reduction of pain severity on VAS and perceived of health on WOMAC, both at $p=0.01$ after 1, 4 and 12 weeks post-intervention. However, they didn't show the therapeutic effect size. Kim et al. [31] found that 3-weeks of a medium-energy ESWT with an impulse energy flux density of 0.093 mJ/mm^2, significantly greater improved the VAS, ROM, WOMAC, and the Lequesne index than a low-energy ESWT with an impulse energy flux density of 0.040 mJ/mm^2, when $p<0.001$, but the authors didn't describe the therapeutic effect size either.

In our study we used an alternative treatment protocol, comparing with other authors. The new approach was based on a longer than 5-week treatment period during which a high-energy ESWT of 8000 pulses in total with an impulse energy flux density of 0.4 mJ/mm2 were greater than the doses used by other authors. Despite on, our findings were in line with the results of other authors. Therefore, the patients treated with medium-energy ESWT or high-energy ESWT can achieve health benefits, which decreased progression of knee OA and improved their quality of life. Moreover, the main point is to apply safe and friendly ESWT doses for the patients. The used ESWT doses in our study were painless, and minor pain during the interventions did not produce any unpleasant sensations in patients. As a result, the patients did not report any adverse events.

The randomization conducted in this pilot study complied with the standard of a scientific study and assured the both groups' compatibility. The research tools used in the study were easy for the application and understandable for the patients. Therefore, the possibility of making a measurement error was minimal. So, all of those aspects caused the results of our study and they can increase the practical knowledge useful for practitioners and patients to obtain the most appropriate health benefits in people suffering from OA of the knee.

It is unlikely that the differences of the results between the groups can be explained in terms of a spontaneous remission or through natural resolution, because one of the requirements of the study was to be in a chronic stable condition.

So, the main physiological benefit of ESWT over US can probably explain that the shockwaves involve microdestructions − the application of ESWT causes microbreaks in avascular or poorly vascularised tissue, thus stimulating appropriate revascularization and stem cell growth. It also induces the release of enzymes, which affect nociceptors, resulting in localized analgesia, giving the significant reduction of activity limitations and short duration of the treatment [32].

The study has some limitations. The participants were relatively young (at the time of our research the Regional Hospital in Zywiec organized screening for early prevention of the knee OA), therefore they suffered with simple knee pain. So, to confirm the present results, the future study should be performed with older participants. The limitation is also a self-assessed health by the participants on KOOS and that a simple translation, a non-validated version of KOOS was used. Therefore, the reliability and repeatability of the test should be examined in the future studies, which may provide more accurate results. The next limitation was the short follow-up period. Therefore, the future study ought to be a minimal follow up of 1–2 years for all the subjects, it would significantly increase the impact of this kind of the study, unfortunately, we had no chances to prolong the study. The last limitation is the small sample size. Therefore, future long-term studies with a larger sample size are needed to confirm these results.

Conclusion

Among the people, who were treated for OA of the knee, at the short term ESWT led to greater physical function, than a protocol which included US. The obtained results may be valuable for doctors, physiotherapists and patients with OA of the knee in choosing the most appropriate types of treatment based on the patients' preferences and convenience.

Acknowledgment

Thanks to all the participants in this study for the contribution in the development of the research in this area.

Conflict of Interest

The authors declare that there is no conflict of interest.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not for profit sectors.

References

1. Corti MC, Rigon C. Epidemiology of osteoarthritis: prevalence, risk factors, and functional impact. Aging Clin Exp Res 2003; 15: 359-363.
2. Felson DT, Zhang Y, Hannan MT, et al. The incidence and natural history of knee osteoarthritis in the elderly: the Framingham Osteoarthritis Study. Arthritis Rheum 1995; 38: 1500-1505.
3. Jackson BD, Wluka AE, Teichtahl AJ, et al. Reviewing knee osteoarthritis: A biomechanical perspective. J Sci Med Sport 2004; 7: 347-357.
4. Wu CW, Kalunian KC. New developments in osteoarthritis. Clin Geriatr Med 2005; 21: 589-601.
5. Du H, Chen SL, Bao CD, et al. Prevalence and risk factors of knee osteoarthritis in Huang-Pu District, Shanghai, China. Rheumatol Int 2005; 25: 585-590.
6. Lachance L, Sowers MF, Jamadar D, et al. The natural history of emergent osteoarthritis of the knee in women. Osteoarthritis Cartilage 2002; 10: 849-854.
7. Pearle AD, Warren RF, Rodeo SA. Basic science of articular cartilage and osteoarthritis. Clin Sports Med 2005; 24: 1-12.
8. Salaffi F, Carotti M, Stancati A, et al. Health-related quality of life in older adults with symptomatic hip and knee OA: a comparison with matched healthy controls. Aging Clin Exp Res 2005; 17: 255-263.
9. Verkleij SP, Luijsterburg PA, Willemsen SP, Koes BW, Bohnen AM, Bierma-Zeinstra SM. Effectiveness of diclofenac versus paracetamol in knee osteoarthritis: a randomised controlled trial in primary care. Br J Gen Pract 2015; 65: 530-537.
10. Zhang W, Jones A, Doherty M. Does paracetamol (acetaminophen) reduce the pain of osteoarthritis? A meta-analysis of randomised controlled trials. Ann Rheum Dis 2004; 63: 901-907.
11. Towheed TE, Maxwell L, Judd MG, et al. Acetaminophen for osteoarthritis. Cochrane Database Syst Rev 2006; 25: 4257.

12. Bannwarth B. Acetaminophen or NSAIDs for the treatment of osteoarthritis. Best Pract Res Clin Rheumatol 2006; 20: 117-129.
13. Chodosh J, Morton SC, Mojica W, et al. Meta analysis: chronic disease self-management programs for older adults. Ann Intern Med 2005; 143: 427-438.
14. Warsi A, LaValley MP, Wang PS, Avorn J, Solomon DH. Arthritis selfmanagement education programs: A meta-analysis of the effect on pain and disability. Arthritis Rheum 2003; 48: 2207-2213.
15. Zhang W, Moskowitz RW, Nuki G, et al. OARSI recommendations for the management of hip and knee osteoarthritis, Part I: Critical appraisal of existing treatment guidelines and systematic review of current research evidence. Osteoarthritis Cartilage 2007; 15: 981-1000.
16. Elerian AE, Ewidea TM, Ali N. Effect of shock wave therapy versus corticosteroid injection in management of knee osteoarthritis. Int J Physiother 2016; 3: 246-251.
17. Mascarin NC, Vancini RL, Andrade ML, et al. Effects of kinesiotherapy, ultrasound and electrotherapy in management of bilateral knee osteoarthritis: prospective clinical trial. BMC Musculoskelet Disord 2012; 22: 182.
18. Schulz KF, Altman DG, Moher D. CONSORT Group. CONSORT 2010 statement: Updated guidelines for reporting parallel group randomised trials. BMJ 2010; 340: 332.
19. http://www.randomizer.org/
20. Altman RD, Asch E, Bloch DA, et al. Development of criteria for the classification and reporting of osteoarthritis: classification of osteoarthritis of the knee. Arthritis Rheum 1986; 29: 1039-1049.
21. Roos EM, Toksvig-Larsen S. Knee injury and Osteoarthritis Outcome Score (KOOS)–validation and comparison to the WOMAC in total knee replacement. Health Qual Life Outcomes 2003; 1: 17.
22. Roos EM, Lohmander LS. The knee injury and osteoarthritis outcome score (KOOS): From joint injury to osteoarthritis. Health Qual Life Outcomes 2003; 1: 64.
23. Hurley MV, Scott DL, Rees J, et al. Sensorimotor changes and functional performance in patients with knee osteoarthritis. Ann Rheum Dis 1997; 56: 641-648.
24. Wylde V, Palmer S, Learmonth I, et al. Test-retest reliability of quantitative sensory testing in knee osteoarthritis and healthy participants. Osteoarthritis Cartilage 2011; 19: 655-658.
25. Cohen J. A power primer. Psychol Bull 1992; 112: 155-159.
26. Freeman JV, Julious SA. The analysis of categorical data. Scope 2007; 16: 18-21.
27. Berry G, Armitage P. Mid-P confidence intervals: A brief review. The Statistician 1995; 44: 417-423.
28. Ochiai N, Ohtori S, Sasho T, et al. Extracorporeal shock wave therapy improves motor dysfunction and pain originating from knee osteoarthritis in rats. Osteoarthritis Cartilage 2007; 15: 1093-1096.
29. Frisbie DD, Kawcak CE, McIlwraith CW. Evaluation of the effect of extracorporeal shock wave treatment on experimentally induced osteoarthritis in middle carpal joints of horses. Am J Vet Res 2009; 70: 449-454.
30. Zhao Z, Jing R, Shi Z, et al. Efficacy of extracorporeal shockwave therapy for knee osteoarthritis: a randomized controlled trial. J Surg Res 2013; 185: 661-666.
31. Kim JH, Kim JY, Choi CM, et al. The dose-related effects of extracorporeal shock wave therapy for knee osteoarthritis. Ann Rehabil Med 2015; 39: 616-623.
32. Wang CJ, Wang FS, Huang CC, et al. Treatment for osteonecrosis of the femoral head: comparison of extracorporeal shock waves with core decompression and bone-grafting. J Bone Joint Surg Am 2005; 87: 2380-2387.

Citation: *Lizis P, Kobza W, Manko G, et al. Extracorporeal shockwave therapy is more effective than ultrasound on osteoarthritis of the knee: A pilot randomized controlled trial. Int J Gen Med Surg 2018; 2: 112.*

This manuscript was peer-reviewed
Mode of Review: Single-blinded
Academic Editor: Dr. Suguru Ohsawa