Department of Orthopedics, Faculty of Medicine, University of Szeged, Hungary
Clinical Medicine Doctoral School

# CLINICAL EFFECTIVENESS OF CERTAIN PHYSIOTHERAPIES IN MUSCULOSKELETAL DISORDERS

PhD thesis

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Clinical and Experimental Research in Reactivating and Organ-Saving Surgery. Evidence based physiotherapy

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# INTRODUCTION

Physiotherapy is the most ancient medical discipline. It uses physical energy aimed at prevention, treatment and rehabilitation; although its modes of action are still left unknown.

The division of physiotherapy is heterogeneous in the world. In Hungary, we used to group it according to the energy used, but in the past few decades it has been divided according to the physiological effects caused.

Shockwave therapy is a kind of mechanotherapy as mechanical energy transforms into biochemical and biological sign. It has been applied since the 1980s in musculoskeletal diseases.

Light Amplification by Stimulated Emission of Radiation (Laser) therapy can be reckoned as phototherapy. It causes photobiostimulation, enhances tissue regeneration, cell metabolism and preserves homeostasis.

During ultrasound therapy electrical energy is converted into mechanical energy and heat. It can be reckoned among electro-, mechano- and thermotherapy.

Balneotherapy deals with the effects and medical use of natural mineral waters, gases and peloids. Pelotherapy is a considerable part of balneotherapy. Medical muds/peloids have a high heat retention and low heat conduction capacity; therefore, they can provoke endogen heat formation and can be reckoned as thermotherapy.

In the treatment of musculoskeletal disorders physiotherapy has been used empirically for ages. The emergence of evidence-based medicine (EBM) enabled us to evaluate and verify the biological effects and modes of action of physiotherapy. It has important role in the treatment of chronic degenerative and also chronic inflammatory disorders. Physiotherapeutic modalities have been investigated mainly in combination with each other. It is hard to compare the numerous study designs and their conclusions due to the non-uniform treatment techniques and parameters (intensity, frequency, dose). It is desirable that the number of randomized controlled clinical trials (RCT) are arising, which can support meta-analysis and evidences in therapeutic recommendations.

Beside fibromyalgia, physiotherapy is not recommended in the therapeutic guideline of chronic soft tissue disorders. There are some evidences about the effects of physiotherapy in myofascial pain syndrome (MPS), but there is still not enough controlled trials.

In the treatment of autoimmune and immun-mediated chronic inflammatory disorders pharmacotherapy is still in the first line, although there are some favourable clinical data about physiotherapy either.

The new OARSI (Osteoarthritis Research Society International) guideline, updated in 2014, recommends balneotherapy besides intra-articular corticosteroids and oral non-steroidal anti-inflammatory drugs (NSAIDs) for the treatment of multiple-joint osteoarthritis (OA) with relevant comorbidities. Therapeutic recommendations of the American College of Rheumatology (ACR) in 2012 with regard to the treatment of hip osteoarthritis include both drug and non-drug therapies. Among physiotherapies, exercise is ranked number one, however, there is also evidence of manualtherapy, TENS, laser and ultrasound therapies being effective combined with exercise.

The aim of my PhD work was to evaluate the effects of certain physiotherapies in musculoskeletal disorders in order to contribute to the evidence-based data and the appropriate use of physiotherapy.

AIMS OF THE THESIS

*I. To evaluate the effects of mechanotherapy and phototherapy in musculoskeletal disorders, especially in regional pain syndrome.*

*I./1.* The efficiencies of soft laser therapy and shockwave therapy in myofascial pain syndrome on pain and function are reported in medical literature to various extents. Both therapies were investigated compared to other physiotherapies but only one literature report is known to compare shockwave therapy and laser therapy in neck myofascial pain syndrome.

Our aim was to compare the effects of shockwave therapy and laser therapy on pain tolerances, neck functionality, and quality of life in patients suffering from myofascial pain syndrome of the trapezius.

*II. To evaluate the effects of thermotherapy in musculoskeletal disorders*

*II./1.* Previous research results have already confirmed the effects of US therapy on pain and function in a range of musculoskeletal disorders, but there has not been any evidence that ultrasound treatment can alter inflammation.

The aim of this randomized, double-blinded, controlled clinical trial was to determine the effects of underwater US therapy in patients with RA; analgesic and anti-inflammatory effects (primary endpoint), and effects on joint function and quality of life (secondary endpoint). In case of the controll group, the US device was not turned on.

*II./2.* In the last 20 years, several organizations have made therapeutic recommendations with regard to the treatment of hip osteoarthritis; some of them also contain physiotherapy. Based on RCTs high evidence exists for the efficiency of exercise therapy and low evidence for the efficiency of ultrasound therapy in OA. There are two trials, that compared the continuous and pulsed modes in the treatment of OA, both have different results.

The aim of our study was to compare the effects of various types of ultrasound therapy on pain relief and quality of life in patients with moderate (Kellgren II-III stage) hip osteoarthritis.

*II./3.* Several studies have confirmed the effectiveness of peloids in knee osteoarthritis (OA). The effects of Kolop peloid in knee OA have been evaluated by Hungarian authors in a randomised, controlled, follow-up study.

Next to the production of Kolop peloid in Tiszasüly, another mud deposit was found. As the production of the two peloids is next to each other, thus their composition is similar; it is within a natural fluctuation.

In our non-inferiority study, we postulated that the clinical effectiveness of the two very similar peloids are alike.

## I./1. COMPARATIVE STUDY OF SHOCK WAVE THERAPY AND LOW LEVEL LASER THERAPY EFFECTS IN PATIENTS WITH MYOFASCIAL PAIN SYNDROME OF THE TRAPEZIUS.

*Methods*

In this randomized, assessor-blinded, follow-up study we evaluated the effects of soft laser therapy and shockwave therapy on myofascial pain syndrome of the neck.

The study was conducted at the Physiotherapy Devision of Petz Aladár County Teaching Hospital's Rheumatology Outpatient Clinic. Soft laser treatment (Group 1) was administered once daily, altogether 15 times (on 15 work days) on the trapezius muscle and on trigger point (PR999 4W scanning laser; Medical Italia; regions around the trigger point were treated with 2000 Hz (800 mW), 3 J/cm$^2$ for 2 min; the palpable trigger point was treated with 5000 Hz (2000 mW), 9 J/cm$^2$, for 2 min). In the shockwave arm (Group 2), patients received therapy once weekly, altogether three times to the trigger point and its vicinities (BTL-6000 SWT Topline Power; 1000 impulses in the region of the trigger point, 1.5 bar, 10 Hz, energy density: 0.25 mJ/mm$^2$, 15 mm treating head diameter, followed by 1000 impulses, 2 bar, 10 Hz, energy density: 0.25 mJ/mm$^2$, using a 15 mm treating head diameter to the trigger point).

Outcome measures were recorded by a rheumatologist before therapy (Week 0), after the last treatment session (Week 3), and at the end of the follow-up period, at Week 15. During each visit, we applied a 100 mm visual analogue scale to assess rest/spontaneous pain level, we measured the functional impairment (Neck Disability Index - NDI), quality of life using SF-36, and the need for painkiller medication. At the start of the study, we applied a dolorimeter [BASELINE (Fabrication Enterprises, Inc.)] to determine pain

tolerance in the upper parts of both trapezius muscles [pressure value in kg/cm$^2$, whereby a maximal (VAS:100 mm) pain is signalled by the patient]. In subsequent visits, by applying the same standarized pressure as at the baseline visit, we asked the patients to indicate their pain on 100 mm VAS. At Week 3 and Week 15 visits patients also evaluated their status/subjective well-being in a 4-grade Likert scale (1: significantly improved; 2: improved; 3: unchanged; 4: worsened).

The statistical analysis was processed with IBM SPSS 24 software. The data are expressed as the mean ± SD. Data distribution was investigated with the Kolmogorov-Smirnov test. We found a normal distribution for age and NDI; here we used the independent patterned t test and paired t test. Other data were calculated by Mann-Whitney and Wilcoxon test. The measurements of differences between groups were carried out by either an independent t test or Mann-Whitney test. The difference between the groups was expressed using mean differences, with a 95% confidence interval (95% CI). Chi-squared test and Fisher's exact test were used for categorical data. Missing data were imputed using the last observation carried forward (LOCF) method. P values < 0.05 were considered significant. We did not use an intention to treat analysis (ITT) approach.

*Results*

Altogether, 70 patients were included and 61 patients were randomized. Following randomization, 61 patients were grouped to treatment with soft laser (n=31, mean age: 62.62 ± 9.62-years; male/female: 4/27) or shockwave (n=30, mean age 57.26 ± 14.31-years, male/female: 3/27) There were no significant differences among the two groups in age or gender proportions.

Both groups demonstrated similar changes during the study in all parameters.

Resting and pressure pain, neck disability significantly decreased in both groups after therapy and at a 15 weeks follow-up (p<0,001). The SF-36 QoL questionnaire domains of physical function, energy, and pain showed significant improvements in the laser group immediately after therapy (p<0,05) and at Week 15 (p<0,001). Shockwave therapy patients improved significantly in all eight parameters in all visits (p<0,05). When comparing changes between the two groups, improvement in the shockwave therapy group was significantly higher, except for emotional wellbeing on week 3 and physical health at week 15.

In both groups 86.6% of patients improved, and less than 25% of patients needed medication (analgesics, antirheumatics, or muscle relaxants) during the study. No adverse events were noted or recorded during this study.

## II./1. EFFECTS OF UNDERWATER ULTRASOUND THERAPY ON PAIN, INFLAMMATION, HAND FUNCTION AND QUALITY OF LIFE IN PATIENTS WITH RHEUMATOID ARTHRITIS - A RANDOMIZED CONTROLLED TRIAL.

*Methods*

In this randomized, double-blinded, controlled, follow-up study we evaluated the effects of underwater ultrasound in patients with moderately active rheumatoid arthritis.

The study was conducted at the Physiotherapy Division of the Rheumatology Outpatient Clinic of Petz Aladár County Teaching Hospital in Hungary.

Patients in the ultrasound group received 10 applications (10 working days) of continuous underwater US therapy (35-36 Celsius degree tap water; with the transducer at a distance of 2 cm from the treated surface) intensity of 0.7 $W/cm^2$ SATA (spatial average - temporal average [continuous]), for 7 min to the palmar and dorsal aspects of each hand and wrist using a 830 kHz ULTRON home OE-302 device with treatment head size of 4.2 $cm^2$ (BNR: max.5:1, energy: 1234.8J, power: 2.94W). At inclusion, the age and gender of patients as well as duration of the disease and DMARD therapy (in years) were recorded. Inflammatory laboratory parameters (i.e. ESR, CRP), disease activity (measured using DAS28), quality of life (measured using Health Assessment Questionnaire - HAQ), number of painful and swollen joints, severity of pain at rest recorded on a 100 mm VAS, and duration of morning joint stiffness (in minutes) were assessed at each visit. Physical function was assessed by measuring range of motion in the wrists (in degrees), degree of fist making (based on nail tilting, 3 grades were used: 0: insufficient, 1: incomplete, 2: complete); and hand grip strength (in kg) was measured with a JAMAR dynamometer. At the end of treatment period and at the Month 3 follow-up visit, patients evaluated their own condition on a 4-grade scale (1: significantly improved, 2: improved, 3: unchanged, 4: worsened).

Statistical analysis was performed by using the IBM SPSS 20 software. The statistical power was 60%. Normality was verified with the Kolmogorov-Smirnov test. The

difference between the groups was expressed using mean differences and 95% confidence interval (95% CI). Chi-squared test was used for categorical data. Missing data was imputed using the Last Observation Carried Forward (LOCF) method. We did not use an intention to treat analysis (ITT) approach. P values < 0.05 were considered significant.

*Results*

Sixty patients were screened and 50 patients were randomized to the US group and the control group. Forty-eight patients completed the study i.e. attended at least 80% of the treatment sessions; 25 patients in the US group (mean age: 63.24±11.04 years) and 23 patients in the control group (mean age: 62.83±7.25 years). Regarding demographic data, disease duration, and background therapy duration, the groups were similar at baseline.

Pain decreased in both groups, while inflammatory parameters decreased in the US group at each successive visit compared to baseline. Decrease of pain and CRP was significantly better in the ultrasound group. No substantive changes were observed in the duration of morning joint stiffness, the number of tender and swollen joints in any of the groups at any visits, and no difference was found between the groups.

Disease activity index decreased in both groups at the end of treatment and at Week 14 compared to baseline, but the difference between the groups was not significant. Extension and flexion of the wrists improved non-significantly from baseline in the US group and did not change in the control group. In the ultrasound group, only left wrist extension showed a significant improvement at Week 2 when compared to the control group (mean between-group difference visit 2-1 = 4.35, 95% CI = 1.09 to 7.60). The degree of fist making did not show any changes in any of the groups. Hand grip strength slightly increased in the US group, but the difference between the two groups was not statistically significant.

Quality of life measured using HAQ improved in the US group, but the difference between the two groups was not significant.

Patients of both the US group and the control group considered their own condition improved at the end of treatment and at the Week 14 follow-up visit. No adverse events were observed during the study.

## II./2. EFFECTS OF VARIOUS TYPES OF ULTRASOUND THERAPY IN HIP OSTEOARTHRITIS - A DOUBLE-BLINDED, RANDOMIZED, CONTROLLED, FOLLOW-UP STUDY

*Methods*

In this double-blinded, randomized, controlled, follow-up study we evaluated and compared the effects of various types of ultrasound therapy (continuous, pulsed, ultrasound combined with electrotherapy).

The study was conducted at the Department of Rheumatology in Petz Aladár County Teaching Hospital, Győr, and at the Musculoskeletal Rehabilitation Department in Zsigmondy Vilmos Harkány Spa Hospital. The patients in each group received conventional treatment (exercise, massage, balneotherapy) every working day for two weeks, on a total of 10 occasions. The exercise included standardized hip exercises, Swedish massage techniques were used during the massage therapy, and the balneotherapy was performed in thermal water at 34 °C. In addition to the conventional therapy, patients in group 1 received continuous ultrasound therapy with moving head in three fields – inguinal, gluteal, trochanteric – for 3 minutes pro field, altogether 9 minutes every working day for two weeks, on a total of 10 occasions (calibrated BTL-4825S Premium device, head size of 5 cm, 3 MHz frequency, 1.5 W/cm$^2$ intensity); patients in group 2 received pulsed ultrasound therapy (1.5 W/cm$^2$ intensity, 3 MHz frequency, 50% duty cycle). Patients in group 3 received sonotens therapy for 10 minutes per day (US: 0.5 W/cm$^2$ intensity, 3 MHz carrier frequency; TENS: 100 Hz frequency, 100 μs impulse, constant frequency); patients in group 4 received sham ultrasound therapy (the device was switched off).

When including the patients in the study, their age, sex, weight, and Body Mass Index were recorded. In addition, the severity of hip pain at rest/spontaneous hip pain (on a 100mm VAS) was evaluated at baseline, after the treatment sessions, and 3 months later. The function was measured using the WOMAC VA 3.0 index and the 6-minute walking test, and the quality of life was documented (RAND 36-Item Health Survey (Version 1.0)) during each visit.

After the treatment (Week 2) and during the control examination in the third month (Week 14), the patients evaluated their own condition on a 4-point scale (1:extremely improved; 2:improved; 3:no change; 4:became worse). In accordance with the

internationally accepted practice, the need of analgesic or anti-inflammatory medication during the treatment or the follow-up period was documented on the outpatient forms.

Statistical analysis was performed using the IBM SPSS 25 statistical software. The statistician was an independent person. Last observation carried forward (LOCF) method was used to handle missing data. As for the baseline values, normality was assessed by using the Kolmogorov-Smirnov test. Differences among the 4 groups were calculated by Kruskal-Wallis test, while post-hoc test was performed by using Mann-Whitney test. The changes between endpoints and baseline data were compared by using Wilcoxon test.

Minimal Clinically Important Improvement (MCII) at Week 14 was defined as ≥21,1% relative improvement in a normalized WOMAC function score. Improvement compared to the placebo group was measured by binary logistic regression and expressed with ODDS value. A p value <0.05 was considered significant for the statistical analysis.

*Results*

The study involved 80 patients, and 71 patients were randomized. Out of the 71 patients, 21 of them (mean age: 67.95 years; male/female:4/17) were randomized into group 1, 17 patients (mean age: 65.82 years, male/female:4/13) into group 2, 15 patients into group 3 (mean age: 65.93 years; male/female:2/13), and 18 patients into group 4 (mean age: 65.72 years; male/female:4/14). There were no differences among the groups in terms of age, sex ratio and Body Mass Index (BMI). Out of the 71 randomized patients, 1 only attended the baseline visit, and another 1 attended only the first two visits. Based on BMI, the patients were overweight or obese. The baseline pain intensity at rest measured on the VAS was similar across all four groups by Week 2 and Week 14, the intensity of pain decreased significantly in all four groups; there was no significant difference among the groups during either visit.

The distance walked in the 6-minute walking test increased significantly after the treatment in all four groups, and it continued to increase until the control examination in the third month. The difference among the groups was not significant at either measurement time. The total score of the three dimensions (pain, stiffness, and physical function) of the WOMAC index increased significantly in each group after the treatment (Week 2), which was maintained until the third month in group 2, 3, and 4. Pain during movement significantly decreased by the 3. month in all groups (p<0,05). Stiffness improved significantly by the Week 2 in all of the groups, and by the 3. month in group 2, 3, 4. Improvement in physical function was significant after the treatment in group 1., 2.,

4, and at Week 14 in group 2., 3., 4. The highest number of patients achieving Minimal Clinically Important Improvement (MCII) at Week 14 was in the sonotens group (73%), but the difference compared to the placebo group was not significant. In Group 1 only 38% of patients showed MCII, which is less, than in the placebo group.

Out of the eight domains of SF-36, 6 domains (role physical, vitality, mental health, social functioning, bodily pain, and general health) improved significantly in group 3; 4 domains (role emotional, vitality, bodily pain, and general health) in group 4; 3 domains (physical functioning, bodily pain, and general health) in group 2; and only 1 domain (bodily pain) in group 1 for a moderately long term, by the third month. All four groups showed significant improvement in the bodily pain domain, and the improvement in the general health domain was significant in three groups.

More than 60% of patients in each group reported improvement in condition (measured on a 4-point Likert scale) immediately after the treatment. This tendency continued until Week 14, the majority of patients in each group reported improvement.

Almost 2/3 of patients took non-steroidal anti-inflammatory or analgesic drugs at baseline. After the treatment, the proportion of those taking medicine slightly decreased (by about 20%), and by the third month the initial proportion was observed.

At the start of the study, the majority of patients in all four groups did exercise only occasionally, but during the control examination in the third month, most of them reported doing exercise on a daily base.

## II./3. THE EFFECTS OF TISZASÜLY AND KOLOP MUD PACK THERAPY ON KNEE OSTEOARTHRITIS: A DOUBLE-BLIND, RANDOMISED, NON-INFERIORITY CONTROLLED STUDY

*Methods*

In this randomized, double-blinded, controlled, non-inferiority study we evaluated and compared the effects of Tiszasüly and Kolop mud pack therapy on pain, function and quality of life in patients with knee osteoarthritis.

The study was conducted at the Physiotherapy Devision of Petz Aladár County Teaching Hospital’s Rheumatology Outpatient Clinic.

Group 1 received Tiszasüly hot mud pack (42 °C), group 2 received Kolop hot mud pack (42 °C) on the painful knee once a day for 30 min on 10 occasions (2 weeks). The two

mud packs had similar package and physical properties. Neither the testing investigators and assistants nor the patients were aware of the treatment assignments both at the start and the end of the study. Before the start of the therapy (Week 0), immediately after the therapy series (Week 2) and 3 months later (Week 12) range of motion, tenderness or swelling, rest/spontaneous pain level using a 100m VAS were assessed. Functional impairment was measured by 3 different questionnaires: (1) the WOMAC VA 3.0, (2) the KOOS and (3) Lequesne Algofunctional Index. Quality of life was measured by EuroQoL-5D and EQ VAS questionnaires. EQ-5D was valued based on a standardised time trade-off (TTO) for the general population in the United Kingdom (UK).

The statistical analysis was processed by the IBM SPSS 25 software. Data distribution was investigated with the Kolmogorov-Smirnov test. We found a non-normal distribution; the data were calculated by the Mann-Whitney and Wilcoxon test and are represented as the mean ± SD. The measurements of differences between groups were carried out by the Mann-Whitney test. We handled missing data using the last observation carried forward (LOCF) method. P values < 0.05 were considered significant. We did not use an intention to treat analysis approach. The power analysis done by the G power 3.1.9.2 programme was calculated from VAS pain values at week 2 using the Mann-Whitney nonparametric test. The power proved to be 84% in case of 29 and 31 sample sizes.

*Results*

Altogether, 75 patients were included and 60 patients were randomised into two groups. Twenty-nine patients out of 60 (mean age, 65.03 ± 8.56 years; male/female, 10/19) were assigned to group 1 and 31 patients (mean age, 66.67 ± 7.62 years; male/female, 8/23) to the Group 2.

Both groups demonstrated similar changes during the study in all parameters. Spontaneous pain, WOMAC pain, stiffness, function and total score, the Lequesne index and EQ-5D improved significantly in both groups right after treatment and at Week 12 ($p<0,001$). Immediately after therapy, the Tiszasüly mud pack group (group 1) showed better improvement ($p = 0.009$) compared with group 2 (Kolop mud pack).

The KOOS score showed decreasing impairment in both groups, but significant changes were demonstrated only in the Kolop mud pack group ($p0\text{-}1=0,046$ $p0\text{-}2=0,039$).

## ETHICS

Study participants were informed verbally about the protocol, received written information and they signed the Informed Consent Form before the initiation of the study. The study was approved by the Regional Research Ethics Committee of Petz Aladár County Teaching Hospital

## CONCLUSIONS, DISCUSSION, NEW RESULTS

I./1. According to the results of our study both low level laser therapy and shockwave therapy have a beneficial effect on the clinical parameters and quality of life of patients with myofascial pain syndrome of the trapezius.

Outcome parameters in the shockwave group improved significantly better, than in the laser group. We cannot currently find an exact reason for the higher analgesic effect using shockwave therapy, but we can postulate that the painful effects of therapy could have a role in that. Pressure pain was sensed differently in the left and right trapezius muscles in patients of the shockwave therapy, which we attribute to random variation or the small patient number. Physical functioning, vitality, social role functioning, and bodily pain improved the most among QoL domains in both groups in our study. This can be attributed to pain relief and trigger point inactivation effects of laser and shockwave therapies. In our study, less than 25% of patients were taking medication for analgesia and muscle relaxation. As the constitution of patients taking medication, there was a difference in each follow-up visit, and the duration of pharmacotherapy was short. We cannot declare a relationship between changes in patient numbers, and the efficiency of therapy.

Our study is the second in the literature that compares shockwave therapy and laser therapy in neck myofascial pain syndrome. In our study, higher laser power and higher energy density shockwaves were applied.

Patient number is one of the limitations of our study; increasing the number of study participants would be desirable in further studies. Literature reports are ambiguous as to the frequency and duration of therapy sessions; although a three times ESWT was efficient, increasing frequency could increase the clinical efficiency even further. In laser therapy, one parameter (power) was taken into account, while a power increase and multi-local irradiation of trigger points could also increase the effect.
We can conclude, that both laser and shockwave therapy are possible therapeutic options in the treatment of myofascial pain syndrome of the upper trapezius.

**II./1.** Our randomized, double-blinded, placebo-controlled study showed, that underwater ultrasound therapy has beneficial effect on the hand function and qualitiy of life of patients with rheumatoid arthritis. All measured parameters showed significant improvement in the short term. Pain measured on a VAS also decreased, although to a lesser extent, in the control group, which could be due to placebo effect. The anti-inflammatory effect could be supposedly partly due to vasodilation caused by the thermal effect and partly due to mechanical effect, which stimulated nitrogenmonoxid production resulting in vasodilation. Decrease of CRP in the control group could have been due to the normal tissue repair, which was enhanced by the therapy in the ultrasound group. There wasn't any statistically significant difference between the groups in tender and swollen joint count, DAS28 score and morning stiffness.
Wrist extension improved more than flexion, which is explained by the nature of the disease. Improvement in quality of life was also in short term. The weakness of our study was the small sample size and lack of intention to treat analysis. Based on our study, underwater ultrasound therapy is a possible therapeutic option treating the hands of rheumatoid arthritis patients.

**II./2.** According to our double-blinded, randomized, controlled, follow-up study, conventional treatment (exercise, massage, balneotherapy) has positive effects on pain, function and quality of life in hip OA. No significant differences were found among the effects of different modes of US (continuous, pulsed, combined with electrotherapy, placebo US). As in the placebo group significant improvement was noticed and there wasn't any inter-group difference, we can assume, that ultrasound does not increase the effects of conventional treatment. Based on our results, ultrasound therapy could be an adjunctive therapy in the treatment of hip OA beside other physiotherapy.

One of the limitation is the low patient number. Based on the power analysis, the ideal number of study patients would have been 20 patients in each group (80 patients altogether). We chose the transcutaneous electrical nerve stimulation in the group US combined with electrotherapy. However, comparison of ultrasound monotherapy with other combination therapy (ultrasound plus other impulse electrotherapy, e.g. interferential current) could be interesting as well.

Based on our results, ultrasound therapy could be an adjunctive therapy in the treatment of hip OA beside other physiotherapy.

**II./3.** In our randomized, double-blinded, controlled non-inferiority study we confirmed that Kolop mud pack decreases pain, improves function and quality of life in knee OA. We proved, that the clinical effects of Tiszasüly and Kolop muds are basically the same, there was no significant difference between them, though Tiszasüly mud-pack showed better improvement in one parameter right after treatment.

Increasing the number of patients would power our study, though this number was enough to draw conclusions. We are planning to extend the follow-up period to 6 and 9 months.

We can conclude, that not only Kolop mud, but also Tiszasüly mud could be a therapeutic option in knee osteoarthritis.

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ACKNOWLEDGEMENTS

First and foremost, I would like to thank my supervisor, Professor Tamás Bender for his unstinting, continued support, professional guidance and great encouragement in my research work, not to mention his gentle humour and ever-positive attitude.

I also wish to thank Ferenc Szanyó for his invaluable institutional support and encouragement.

My thanks also go to my previous superiors, Péter Temesvári, László Hodinka and Judit Ortutay, for providing me with edification and their exemplariness.

I am very much obliged to Katalin Hodosi for her expert help with the statistical calculations.

I am also grateful to my colleague Péter Bálint for his professional support in our joint work.

Many thanks to my close colleagues, especially Edina Gömöri and Eszter Kővári for their collaboration, cooperation and professional help.

My special thanks go to the head assistant of the Department of Physiotherapy at the Petz Aladár County Teaching Hospital, Ildikó Horváth Geyerné and also to our physiotherapists, Edit Ravai Raufiné, Katalin Kovacsics Siposné, Mihályné Szalay and Ágnes Péntek Tóthné for their unwavering support in performing physiotherapy.

I am immensely thankful to my dear colleague and friend, Ildikó Katalin Tefner for the invaluable professional and human support she has given me throughout my PhD project.

I am extremely grateful to my parents, grandparents for giving me guidance and for their help and simply for loving me during my studies and work. I would also like to thank my brother for his love and support.

Many thanks to my late husband, who never ceased to encourage me and always placed great trust in me.

I also thank my dear son, Zoli for his love, patience and endurance while he was forced to spend less time with his mother all along my doctoral studies.