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Therapeutic Efficacy of Dexamethasone Phonophoresis on Symptomatic Knee Osteoarthritis in Elderly Women

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Abstract

Objectives: The knee joint osteoarthritis is one of the important causes of disability and is more frequent in menopausal women. Phonophoresis is a therapeutic method using ultrasound to enhance percutaneous absorption of drugs. This study was aimed at evaluating the therapeutic efficacy of dexamethasone phonophoresis in the management of knee osteoarthritis in elderly women.

Materials and Methods: 55 women aged 56.03±5.7 years who had mild or moderate knee osteoarthritis were randomly allocated into 3 groups. First group (n=18) received ultrasound (as control group), second group (n=18) received phonophoresis of 4mg dexamethasone ampoule and third group (n=19) received phonophoresis of 0.4% dexamethason gel. All groups were treated with an ultrasound program using stroking technique, pulse mode, 1.5 W/cm2, 5 minutes per session for 10 sessions. Visual Analog Scale (VAS) for pain severity and Western Ontario and McMaster universities Osteoarthritis Index (WOMAC) and the time up and go test (TUG) were evaluated before and after treatment in all groups.

Results: The VAS, total WOMAC and TUG scores were significantly improved after treatment in all groups ($P<0.001$). The group receiving phonophoresis of dexamethasone ampoule showed more significant effects in reducing pain and improving function and mobility among three groups.

Conclusion: Our results indicated that both ultrasound and phonophoresis of dexamethasone are effective methods in pain relief and improving function in mild and moderate knee osteoarthritis but phonophoresis of dexamethasone ampoule is better than the other treatments and it is suggested as an available method for treatment of knee osteoarthritis symptoms.

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Introduction:

Osteoarthritis (OA) is one of the most common articular diseases. Knee joint is the most sensible joint to degenerative changes. Knee Osteoarthritis causes reduction of patient function due to articular pain, stiffness and movement restriction.(1,2) This disease is more common in women than men .The prevalence rate and frequency of OA increase in menopause age. Many researchers focus on imbalance or deficiency of estrogen during and after menopause as a risk factor for osteoarthritis.In some studies, long-term estrogen therapy in postmenopausal women caused a decline in the incidence of osteoarthritis(3). Long term osteoarthritis causes dysfunction, debilitating pains in joints and disuse of them leads to peri-articular muscular weakness and high costs for treatment such as joint replacement, so it is essential to improve therapeutic techniques. In addition to medical treatment, using rehabilitation methods and physiotherapy has main role in pain relief and improvement of patient function (4). One of the efficient methods in order to rehabilitate osteoarthritis patients is to use ultrasound. Ultrasound is a deep heating modality that is widely used for relieving pain in patients with osteoarthritis of the knee. Ultrasound acts by converting electrical energy into sound waves, then sound energy is converted to heat as it passes through the various tissues. Biologic responses to ultrasound therapy via thermal and non-thermal effects include increased pain threshold, tissue regeneration, muscular relaxation and decrease in inflammation (5,6). The use of intra-articular glucocorticoid injection can be helpful in relieving pain and improving function in patients(7). This class of drugs acts by inhibiting cartilage catabolism and preventing the formation of osteophytes (8). Articular infection and septic arthritis are complications of intra-articular corticosteroid injection(9). Although there are more advantages with drug transport through the skin than other common methods, such as orally or by injection, low skin permeability to topical drugs is one of the problems with these drugs . In order to resolve this problem, different techniques are used with topical medications that one of them is phonophoresis. Phonophoresis is the use of ultrasound waves (US) to enhance the absorption of topically applied drugs by increasing skin permeability to topical medications (10). Few studies have been done on phonophoresis of topical corticosteroids in reducing the symptoms of articular degenerative diseases and comparison between the efficiency of these treatments on reduction of inflammation diverse regions. With regard to high prevalence of knee osteoarthritis and its debilitating pain in patients, it is essential to explore new methods of osteoarthritis treatment .Therefore, in order to improve therapeutic methods, reduce health care costs, and reduce OA symptoms in menopausal women, the effect of phonophoresis of dexamethasone on the treatment of knee OA was assessed and compared with ultrasound therapy.

Material & Methods:

Inclusion and exclusion criteria :

In a randomized clinical trial, 55 women with mild to moderate knee osteoarthritis confirmed by clinical and radiological studies were randomly selected from physical medicine and rehabilitation outpatient clinic of Shohada and Imam Reza Hospitals of Tabriz during a17- months period from May 2012 to September 2013. Patients over 50 years with mild to moderate knee osteoarthritis on the basis of the American College of Rheumatology criteria (ACR) (11) and the Radiological criteria (Kellgren-Lawrence grade I-III) (12) were included in this study.(fig 1) Patients with rheumatologic problems such as rheumatoid arthritis, previous surgery on the knee joint, previous fracture of the lower extremity with knee joint involvement, severe knee osteoarthritis, those with electronic implants such as pacemakers, history of heart block, people with epilepsy, those with thrombosis of the lower limbs, people who are not able to cooperate in order to complete the questionnaire for any reason, people with a history of injections in knee joint in the last 6 months, patients with

balance disorders, people with neuropathy and sensory disorders, those with skin damage around the knee, any contraindications or precautions for the use of corticosteroids (e.g. high blood pressure, and diabetes) any contraindications or precautions for the use of ultrasound (e.g. malignancy) were excluded. The samples were randomly selected and 55 patients were asked about the duration of treatment and duration of follow up. The sample size was similar to sample size of studies done in other countries. 55 patients selected randomly by selecting one of 3 pockets named in order 1, 2 and 3 were divided into three groups. The first group (n = 18) underwent ultrasound therapy (as control group), second group (n = 18) underwent phonophoresis of dexamethasone ampoule (as experimental group) and third group (n = 19) underwent phonophoresis of dexamethasone gel (as experimental group). The person responsible for the assessment of patients was assistant of physical medicine and rehabilitation; however, patients were unaware of the type of treatment. This study as a clinical trial at the IRCT site has been registered under No. 201210011292 N3.

After obtaining written informed consent for all patients, VAS (Visual Analog Scale) and WOMAC (Western Ontario and McMaster Universities Osteoarthritis Index) questionnaires were completed and mobility test (Timed Up and Go Test) was conducted. VAS tool is a scale ruler from zero to ten that patients based on pain severity showed minimal point to the greatest extent of the numbers on the ruler. WOMAC Questionnaire was designed to measure patients' pain and dysfunction in associated with osteoarthritis of the lower extremities so this questionnaire assesses 24 items divided into 3 subscales: 17 items of physical function, 5 items of activity-related pain and 2 items related to articular stiffness. The rating scale of this Questionnaire is between zero which represent the best case and 96 that is severe osteoarthritis (13). The Timed Up and Go Test (TUG) was also administered to patients in this way; it uses the time that a person takes to rise from a chair, walk three meters, turn around, walk back to the chair, and sit down(14). This test is performed three times and mean values of them were recorded. In the third group to prepare a 0.4% dexamethasone gel , 0.4 g of dexamethasone powder was dissolved in 5 ml of propylene glycol and also 0.3 g disodium hydrogen phosphate powder separately was dissolved in 5 ml of distilled water and these two solutions were added to 100 ml of ultrasound gel. Thereafter, this solution was put in a magnetic stirrer for 24 hours to prepare a uniform gel. Then the resulting solution was passed through filter and hold in dark glass with a volume of 100 ml maintenance kit (15). The second group underwent Phonophoresis of dexamethasone ampoule (in each session with half of 8mg vial and 35 g ultrasound gel). The first group just underwent treatment with ultrasound that was considered as control group. The interventional treatment consisted of 10 sessions of physical therapy three times a week. Therapeutic modalities were applied in the maximum pain point in the medial compartment of the knee in all patients. All groups were treated with an ultrasound program using stroking technique, pulse mode, 1.5 W/cm2, 5 minutes per session for 10 sessions (10). For all patients (three groups) during sessions of physiotherapy treatment, common physical modalities were used in osteoarthritis of the knee uniformly, including superficial heat for 20 min, exercises to strengthen the muscles around the knee, stretch of hamstring tendons and heel Cord. All patients during study were benefited by routine treatment of knee osteoarthritis, including Glucosamine and Acetaminophen. After treatment for each group, in the last treatment session, VAS, WOMAC questionnaires were completed and testing of mobility (Timed Up and Go Test) was done. Data obtained in each group before and after treatment were compared between groups. The person responsible for the statistical analysis of the data was unaware of the applied interventions on the groups.

Statistical analysis

The results were expressed as mean ± standard deviation (Mean ± SD), frequency

and percentage. SPSS™ version 16 was used as statistical software program.

In order to compare results, Independent Sample T-test and Repeated measured ANOVA were used for quantitative variables and Qui-square was used for qualitative variables. P-values less than 0.05 were considered significant and are written in the parentheses.

Results:

All participants of this study were women. Overall mean age of patients, 56.03 ±5.70 years have been in the range of 50 to 71 years so we named them as elderly women. The mean age of patients was 56.95±7.33 years in the ultrasound group, 56.55±2.28 years in the group receiving phonophoresis of dexamethasone ampoule and 54.60±6.23 years in the group receiving phonophoresis of dexamethasone gel. The differences between the age of three groups studied were not statistically significant (P= 0.428). Description of the basic data of patients and comparisons among groups, such as height, weight indicators, the type and severity of deformity conflict with the stated numerical value of P is given in Table 1. The mean reduction in VAS values were 2.45±1.95 in group receiving ultrasound, 4.35±2.25 in group receiving phonophoresis of dexamethasone ampoule, and 2.88±2.07 in the group receiving phonophoresis of dexamethasone gel respectively, reduction in VAS value was significantly in ampoule group than the other groups (P=0.013). The mean reduction in VAS index in the phonophoresis of dexamethasone gel didn't have significant difference as compared with ultrasound group (P=0.66). The mean reduction in WOMAC values has been in the group receiving ultrasound 16.30±2.8, in the group receiving dexamethasone ampoule phonophoresis 24.05 ±15.31 and in the group receiving dexamethasone gel phonophoresis 22.8±9.08 respectively. Reduction in WOMAC index in the group receiving phonophoresis of dexamethasone ampoule dexamethasone ampoule was significantly higher than the other groups (P=0.02). The mean reduction in WOMAC index in the group receiving phonophoresis of dexamethasone gel as compared with ultrasound group was not significantly different (P=0.65). The mean reduction in the Timed Up and Go test in the group receiving ultrasound, was 1.40±1.1 sec, in the group receiving phonophoresis of dexamethasone ampoule 7.45 ±2.98 sec and in the group receiving phonophoresis of dexamethasone gel 1.7±1.2 sec respectively. Reduction in Timed Up and Go test in the group receiving dexamethasone ampoule phonophoresis were significantly higher than the other groups (P=0.01). There was no significant difference in average decline in the Timed Up and Go index, in the group receiving phonophoresis of dexamethasone gel as compared with ultrasound group (P=0.125).

Variables described and compared among the three groups before the intervention in greater details and P-values have been given in Table 2.

Variables were compared in the groups before and after mentioning and the numerical P-value have been given in Tables 3, 4 and 5 and Variables changes were compared among the three groups, as well as changes in more details and mention the numerical value of P is given in Table 6.

Discussion:

According to previous studies, knee Osteoarthritis increases in prevalence throughout the elderly years that is more common in women than in men. Females have more severe OA with involvement of more number of joints. Hand osteoarthritis is more common in women near menopause that observations confirmed estrogen deficiency is responsible for polyarticulars osteoarthritis. Evidence of OA in women that experienced hysterectomy or gynecological surgery confirm association between hormonal effect and OA (3). In this study, the effects of treatment with phonophoresis of dexamethasone gel, phonophoresis of dexamethasone ampoule and ultrasound in patients with osteoarthritis of the knee were evaluated in relieving pain and increasing patient function and the results of each treatment were compared with the results of the other treatments. In this study, three groups in terms of age, sex, disease, history of treatment for osteoarthritis of the knee,

the severity of osteoarthritis were similar. In this study, all the patients were women. Based on the results of our study, all three methods, ultrasound, phonophoresis of dexamethasone ampoule and phonophoresis of dexamethasone gel have been effective to reduce the VAS, WOMAC and Timed Up and Go tests. This means that there was statistically significant differences in findings of these tests in the three groups before the intervention and after that were significant differences (in all cases the difference before and after intervention with a P value of less than 0.001). However, reduction in pain, reduction in WOMAC index and the Timed Up and Go test time in the group receiving phonophoresis of dexamethasone ampoule were significantly higher than the other two treatment groups. This study characterized by comparing between effects of dexamethasone ampoule with dexamethasone gel. According to the results, phonophoresis of dexamethasone ampoule which is a simple and most practical method , has more advantageous effects than phonophoresis of dexamethasone gel. However, more studies appear to be necessary to more assess and evaluate this difference.

The results of our study are comparable with the results of other studies in this area. Akinbo et al. in their study compared the effects of phonophoresis and iontophoresis of dexamethasone on patients with osteoarthritis of the knee, it was reported both methods are effective (16). Accordingly, in our study also phonophoresis of dexamethasone ampoule, phonophoresis of dexamethasone gel and ultrasound have been able to be effective in reducing pain and improving function in patients. However, phonophoresis of dexamethasone ampoule is much better than the other treatments maybe due to the difference in absorption rate. In the study of Erkan kozanoglu et al. ibuprofen phonophoresis and ultrasound both were reported effective equally (17). Another study by Luksurapan et al. was done to assess the phonophoresis of piroxicam and comparison of phonophoresis of piroxicam with ultrasound therapy on symptomatic knee osteoarthritis. The results indicated that the use of phonophoresis has been able to improve the patients' function and reduce the patients' WOMAC index and VAS. This study has also shown that the maximum effect of phonophoresis in patients with grade 2 osteoarthritis (18). This is also similar to the findings of our study significantly. In our study, 13 patients (23/6%) had mild disease and 42 patients (76/3 percent) had moderate disease. Therefore, it can be demonstrated that phonophoresis of dexamethasone gel and ampoule are effective in moderate knee osteoarthritis. In the study of Hsieh et al. phonophoresis of diclofenac was effective in reducing pain and increasing patients' function (19). In the study of Ganidağlı et al., using ultrasound to treat pain and improve function in patients with osteoarthritis of the knee has been reported efficient significantly(20). In our study, the use of ultrasound was effective in reducing pain and increasing performance of patients. In the study of Tascioglu, the use of pulse mode ultrasound was with high efficiency in the reduction of pain measured using VAS (21). These findings are also similar to the results and methods of our study. Studies of Boyaci et al. demonstrated phonophoresis of ketoprofen significantly decreases pain and increases function in patients with osteoarthritis of the knee. This study is comparable with the results of our study, the overall use of phonophoresis is effective in improvement of symptoms of knee osteoarthritis(22). In reviewing the available literature and articles on databases, there are few studies on phonophoresis of steroid in the treatment of knee osteoarthritis.

The limitations of this study could be mentioned the number of samples, no follow-up of patients after treatment and the lack of evaluation of variables in patients during therapy sessions. In order to better generalize the results of this study, a multi-center study with a larger sample size appears to be necessary. Furthermore, it is essential more studies to compare phonophoresis of dexamethasone ampoule with phonophoresis of diclofenac and piroxicam injections, to assess the reliability of therapeutic effects after the last meeting

of treatment, and to assess probable cause of more effect of dexamethasone ampoule than dexamethasone gel.

Conclusion :

Based on the results of evaluation of pain intensity and physical function parameters and the Timed Up and Go test, three methods of using ultrasound, phonophoresis of dexamethasone gel and phonophoresis of dexamethasone ampoule in reducing pain and increasing performance and efficiency were effective. However, the effect of phonophoresis of dexamethasone ampoule has been far greater.

Conflicts of interest:

Authors declare that there is no any conflict of interest.

Acknowledgments:

This is a report of a database from thesis entitled Efficiency of dexamethasone phonophoresis in compare to ultrasond therapy in knee osteoarthritis registered in Tabriz University of Medical Science.

Figure 1. Flow diagram of enrolled participants of ultrasound versus phonophoresis of dexamethasone ampule and phonophoresis of dexamethasone gel in knee OA

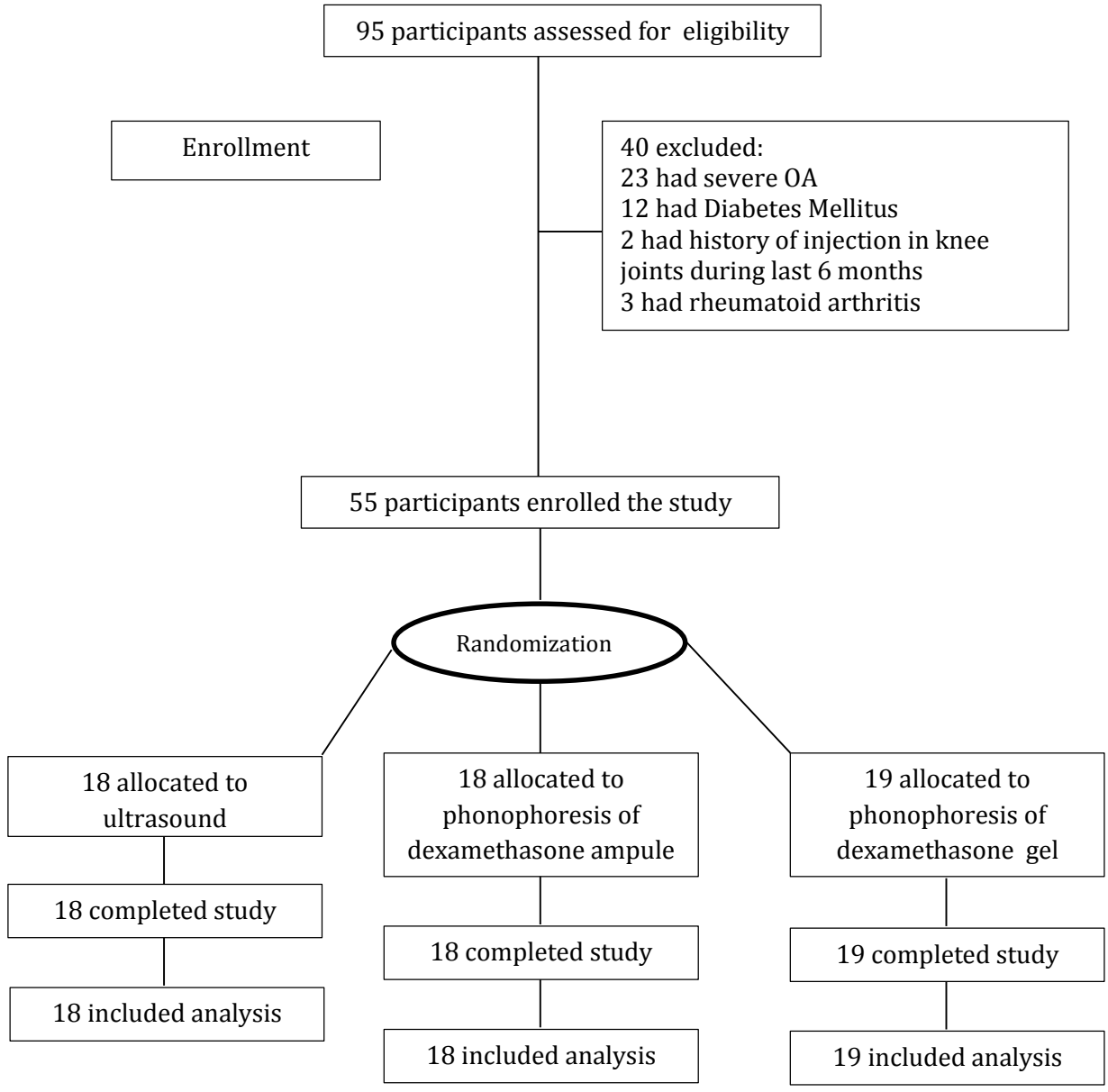

Table 1. Comparison of basic data among three groups.

Variable	Ultrasound Group	Dexamethasone Ampule Phonophopresis	Dexamethasone Gel Phonophopresis	P value
Age	56.95±7.33	56.55±2.28	54.6±6.23	0.428
Sex	18 (100%) persons women	18 (100%) persons women	19 (100%) persons women	0.804
Height	163.22±6.13	159.94±9.04	163.22±5.73	0.141
Weight	75.8±22.19	78.4±9.32	75.35±11.4	0.064
Body mass index(BMI)	26.79±3.44	30.44±3.70	28.26±3.05	0.06
Severity of disease	(33.3%)6 persons mild 12 persons (66.7%)moderate	2 persons (11.2%)mild 16 persons (88.8%)moderate	(31.6%)6 persons mild (68.4%)13 persons moderate	0.095
Type of deformity	2 persons with Genu valgum 3 persons with Genu varum	1 person with Genu valgum 6 persons with Genu varum	1 person with Genu valgum 1 person with Genu varum	0.50

Table 2 Comparison the variables (VAS, WOMAC and Timed up and go test) among three groups before treatment.

Variable	Ultrasound Group	Dexamethasone Ampule Phonophopresis	Dexamethasone Gel Phonophopresis	P value
VAS, 0-10	6.75±1.58	7.95±1.35	6.71±2.79	P=0.95
WOMAC subscales				
Pain	11.65±2.92	11.2±3.62	11.65±1.65	P=0.11
Stiffness	2.4±1.93	4±1.45	5.05±1.1	P=0.59
Physical function	33.7±11.02	36.3±12.23	37.6±15.6	P=0.18
Total	47.75±13.8	51.5±17.04	54.3±12.3	P=0.69
Timed up and go test, second	11.45±2.1	19.8±2.9	12.05±3.64	P=0.30

Table 3. Comparison of variables before and after treatment in the ultrasound group (control).

Variable	Pre Trial	Post Trial	P value
VAS	6.75±1.58	4.3±1.78	P=0.0001
WOMAC subscales			
Pain	11.65±2.92	7.05±3.93	P=0.0001
Stiffness	2.4±1.93	1.5±1.39	P=0.0001
Physical function	33.7±11.02	22.9±11.53	P=0.0001
Total	47.75±13.8	31.45±15.41	P=0.0001
Timed up and go test, second	11.45±2.1	10.05±2.7	P=0.0001

Table 4. Comparison of variables before and after treatment in the group receiving phonophoresis of dexamethasone ampoule.

Variable	Pre Trial	Post Trial	P value
VAS	7.95±1.35	3.6±2.72	P=0.0001
WOMAC subscales			
Pain	11.2±3.62	6.2±4.9	P=0.0001
Stiffness	4±1.45	1.95±1.87	P=0.0001
Physical function	36.3±12.23	19.3±15	P=0.0001
Total	51.5±17.04	27.45±11.3	P=0.0001
Timed up and go test, second	19.8±2.9	12.35±1.78	P=0.0001

Table 5. Comparison of variables before and after treatment in the group received phonophoresis of dexamethasone gel.

Variable	Pre Trial	Post Trial	P value
VAS	6.71±2.79	3.83±2.71	P=0. 001
WOMAC subscales			
Pain	11.65±1.65	7.9±6.75	P=0.0001
Stiffness	5.05±1.1	2.3±1.97	P=0.0001
Physical function	37.6±15.6	21.3±12.21	P=0.009
Total	54.3±12.3	31.5±12.25	P=0.001
Timed up and go test, second	12.05±3.64	10.35±1.78	P=0.001

Table 6. Comparison of variables changes (VAS, WOMAC and Timed up and go test) among three groups.

VariableChanges	Ultrasound Group	Dexamethasone Ampule Phonophopresis	Dexamethasone Gel Phonophopresis	P value
VAS, 0-10	2.45±1.95	4.35±2.25	2.88±2.07	0.013
WOMAC subscales				
Pain	4.6±2.1	5±1.2	3.75±1.7	P=0.23
Stiffness	0.9±0.2	2.05±1.1	2.75 ±1.8	P=0.41
Physical function	10.8±2.1	17±3.4	16.3±5.6	P=0.13
Total	16.3±2.8	24.05±15.31	22.8±9.08	P=0.02
Timed up and go test, second	1.4±1.1	7.45±2.98	1.7±1.2	P=0.01

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