Clinical Trial/Experimental Study

Medicine

OPEN

Integrative medicine in patients with degenerative arthritis of the knee

A pilot randomized control study

Sang Gyu Kwak, PhD[a], Hyun Jung Jung, MD[b], Won-Kee Choi, MD[c,*]

Abstract

Background: We aimed to comparatively analyze the effect of integrative medicine treatments (lifestyle change education, use of anti-inflammatory drugs, acupuncture, manual therapy-type massage) and conventional medical treatments (lifestyle change education and use of anti-inflammatory drugs) on pain control, knee function improvement, and quality of life improvement in patients with degenerative knee arthritis.

Methods: In this study, 30 patients were randomly divided into the control group (n = 15) and the experimental group (n = 15). Both groups were prescribed anti-inflammatory drugs and lifestyle change education for 12 weeks. The experimental group underwent acupuncture including electroacupuncture, moxibustion, and manual therapy-type massage 12 times during the first 6 weeks. Evaluations were performed at 3 visits: visit 1 (before treatment), visit 2 (6 weeks after initial treatment), and visit 3 (12 weeks after initial treatment). The effect of each treatment was measured using Visual Analog Scale (VAS, 0–10), Western Ontario and McMaster Universities index (WOMAC), and SF-36.

Results: From visit 1 to visit 2, the mean value of VAS decreased by 0.72 and 3.17 in the control and experimental groups, respectively. From visit 2 to visit 3, the mean VAS value decreased by 0.25 in the control group but increased by 0.87 in the experimental group. Among the sub-area of SF-36, the physical role restriction area and mental health area showed significant differences between the 2 groups over time ($P = .024$, $P = .006$).

Conclusion: Integrative medicine treatment has superior effects in pain control over conventional medical treatment. In integrative medicine treatment, pain control tends to decrease with time, but still superior over conventional medical treatment up to 6 weeks after treatment (12 weeks after initial treatment).

Abbreviations: K-L = Kellgren-Lawrence grade, MCS = mental component summary, PCS = physical component summary, VAS = Visual Analog Scale, WOMAC = Western Ontario and McMaster Universities.

Keywords: acupuncture, arthritis, integrative medicine, knee

1. Introduction

Degenerative arthritis of the knee is characterized by pain and deterioration of knee function in middle-aged and elderly patients, thereby affecting the quality of life.[1,2] With the aging population, the incidence of degenerative arthritis has been increasing, as well as its treatment cost.[3]

Various treatment methods are available. The most basic treatment starts with education for lifestyle changes and weight control. Anti-inflammatory drugs are also prescribed for pain control.[4–6] Non-surgical treatments include injection therapy, manual therapy, and acupuncture depending on the severity of the patient's symptoms. In East Asia, acupuncture has been used as a non-surgical treatment to control pain and severity of degenerative arthritis of the knee.[7–9] In addition, some meta-analyses reported that moxibustion treatment is more effective to manage degenerative arthritis of the knee than oral drugs or placebo.[10–12] However, studies on the non-surgical treatments have mostly focused on the effect of single treatment rather than an integrated medical treatment.[13–15] Integrative medicine treatment include conventional medical treatment, Korean traditional medical treatment and healing programs, and others. As various treatments are applied according to the patient's pain levels, we aimed to compare the therapeutic effects of conventional medical treatment service and integrative medicine treatment. In this study, we included a control group that

This research was supported by a grant of Comprehensive and integrative medicine R&D project through the Korea Health industry Development institute, funded by the Ministry of health & Welfare, Republic of Korea (grant number: HI20C1753)

The authors have no conflicts of interest to disclose.

The datasets generated during and/or analyzed during the current study are publicly available.

[a] Department of Medical Statistics, College of Medicine, Daegu Catholic University, Daegu, Republic of Korea, [b] Department of Diagnostics, College of Korean Medicine, Daegu Haany University, Daegu, Republic of Korea, [c] Department of Orthopaedic Surgery, College of Medicine, Daegu Catholic University, Daegu, Republic of Korea.

**Correspondence: Won-Kee Choi, Department of Orthopaedic Surgery, Daegu Catholic University Hospital, 3056-6, Daemyung-4-dong, Nam-gu, Daegu, Republic of Korea (e-mail: cwk1009@hanmail.net).*

How to cite this article: Kwak SG, Jung HJ, Choi W-K. Integrative medicine in patients with degenerative arthritis of the knee: A pilot randomized control study. Medicine 2022;101:34(e30385).

Received: 18 March 2022 / Received in final form: 20 July 2022 / Accepted: 22 July 2022

http://dx.doi.org/10.1097/MD.0000000000030385

received lifestyle change education and anti-inflammatory drugs in patients with degenerative knee arthritis and an experimental group that additionally received acupuncture and manual massage in combination.

Specifically, this study was conducted to analyze the following: first, the effect of integrative medicine treatment (lifestyle change education, use of anti-inflammatory drugs, acupuncture, manual therapy-type massage) and conventional medical treatment (lifestyle change education and use of anti-inflammatory drugs) on pain control, knee function improvement, and quality of life improvement in patients with degenerative arthritis of the knee; second, the short-term effect (6 weeks after treatment) after the end of the Integrative medicine treatment; and third, the compliance and safety of integrative medicine treatment.

2. Methods

2.1. Study design

This study is designed as a 2-group, parallel, single-center, randomized, controlled, assessor-blinded trial.

2.2. Subject

This study was conducted after institutional review board approval (approval number: CR-20-207-L). Patient information was registered in clinical research information service (Korean clinical trials 0006004). Lifestyle change education (weight control and knee weight-bearing posture correction) and anti-inflammatory drugs (cyclooxygenase-2 selective inhibitor)[16,17] were prescribed to patients with knee osteoarthritis who visited our joint center from January 2021 to December 2021. Informed consent was obtained from the participating patients.

The inclusion criteria were as follows: patients aged 20 years or older and <80 years old, those with knee pain for more than 1 month, and those with Kellgren-Lawrence (K-L) grades between 1 and 3 on X-rays.[18] K-L grade was determined with knee standing X-rays by one orthopedic surgeon. We excluded patients with mechanical pain due to abnormalities in internal structures during knee movement during initial physical examination, those with signs of infection, those with knee joint effusion, and those with a history of ipsilateral knee surgery within 1 year.

2.3. Sample size determination

This was a pilot study that focused on the preliminary confirmation of the prudence of the study and clinical results and the preparation of basic data before large-scale studies. Twelve patients were assigned to the experimental group (integrative medicine treatment) and control group (conventional medical treatment), from the initial requirement of 15 patients each in consideration of the 20% drop-out rate. Therefore, the total number of enrolled patients was 30.

2.4. Randomization and blinding

Simple randomization was performed, with an allocation ratio of control group: experimental group (1:1), resulting in 15 patients in the control group and 15 patients in the experimental group. The assignment code was sealed in an opaque envelope and was drawn in the order of subject enrollment. It was conducted with single blinding method, and only subjects who met the inclusion criteria, who did not meet the exclusion criteria and who gave voluntary consent were enrolled in this clinical trial.

2.5. Experimental group and control group

The treatment effects at weeks 6 and 12 were evaluated and compared between groups. Both groups were prescribed anti-inflammatory drugs and lifestyle change education for 12 weeks. The experimental group additionally received acupuncture and manual therapy-type massage were performed 12 times during the first 6 weeks.

In this study, the acupuncture points were selected to relieve pain in the knee joint as described in related previous studies.[7,19] Nine points were identified on the affected side: SP10, ST34, ST35, EX-LE5, SP9, GB34, GB33, ST36, and KI10. In case of pain in both knees, acupuncture points were considered from both sides. For acupuncture points for moxibustion, the location where the patient felt the most painful tenderness was selected. Needles were removed after 25 ± 5 minutes from puncturing, for 12 cycles in 6 weeks.

Approximately 9 to 18 disposable sterile 0.2 × 40 mm needles (Dongbang Acupuncture Manufacturing Co., Ltd., Korea) were used. The depth of puncture was 10 to 30 mm depending on the location of the acupoint. Precipitator stimulation was performed on GB33, GB34, SP9, and SP10, at 2 Hz for 25 minutes; the magnitude of the current was adjusted according to the patient's tolerance. The 30-minute manual therapy-type massage, which was a healing program, was performed 12 times in 6 weeks. Range of motion exercise was performed to improve the compressive force and load on the knee joint. Complex exercises required tools such as mats, gym balls, and sera bands, and some resistance exercises to maintain the mass of the sprawl quadriceps and hamstring, increase muscle strength and flexibility, minimize knee joint damage, and secure joint strength, alignment, and safety.[20]

2.6. Measurements

Demographic information including sex, age, height, and weight were collected, and K-L grade, Visual Analog Scale (VAS), Western Ontario and McMaster Universities index (WOMAC), and SF-36 were used.[21,22] Time points were visit 1 (before treatment), visit 2 (6 weeks after initial treatment), and visit 3 (12 weeks after initial treatment) to examine the treatment effect. VAS was measured to determine the degree of pain reduction of the treatment effect, in which the level of pain perceived by the subject was marked on a 10-cm straight line and the corresponding value was measured (0: none, 10: the most severe). To determine the knee function score, the 24-item WOMAC index questionnaire was used: 5 questions for pain, 2 questions for stiffness, and 17 questions for body function. To assess the quality of life, the 36-item SF-36 questionnaire was used with 8 sub-areas comprising the following: 10 questions for physical functioning, 4 questions for role limitations due to physical health, 2 questions for body pain, 5 questions for general health, 3 questions for role limitations due to emotional problems, 4 questions for energy/fatigue, 2 questions for social functioning, and 5 questions for emotional well-being. The first 4 sub-areas are called the physical component summary (PCS), and the latter 4 sub-areas are called the mental component summary (MCS). In the experimental group, compliance (%) to the additional treatments was calculated by dividing the number of acupuncture treatments and manual therapy-type massages by 12 (total times) and multiplying by 100.

2.7. Statistical analysis

We used SPSS (Win. Ver. 19.0, IBM [IBM SPSS version 19.0 software (SPSS Inc., Chicago, IL, USA)]) for statistical analysis, and the significance level was set to 5%, and 2-sided test was used for all tests. In the descriptive statistical analysis of the demographic characteristics of subjects, we summarized the mean, standard deviation for quantitative data, and frequency and percentage. To test the homogeneity of demographic and clinical characteristics according to the control and experimental group, 2-sample t test or Mann–Whitney U test was performed for quantitative data depending on

normality, and chi-square test for qualitative data. Repeated-measure 2-factor analysis was performed to determine the difference between the 2 groups for VAS, WOMAC index, and SF-36 according to time points, between time points, between groups, and between time points according to groups. Multiple comparisons were performed using contrast based on the Bonferroni correction.

The chi-square test was used to compare the number of occurrences of adverse events related to acupuncture treatment and healing programs in each group and the proportion of study subjects who experienced one or more adverse events.

3. Results

3.1. General characteristics

A total of 30 patients who met the inclusion/exclusion criteria participated in this study. Of the 15 subjects assigned to the experimental group, 3 dropped out (follow-up failure, n = 2; inappropriate participation, n = 1), and 12 subjects (3 male, 9 female) were finally enrolled in this study. Of the 15 subjects in the control group, 1 dropped out (lost to follow-up), and 14 subjects (2 male, 12 female) were finally enrolled (Fig. 1). The mean ± standard deviation of age was 60.33 ± 7.90 years and 64.86 ± 6.61 years in the experimental and control groups, respectively (Table 1), without significant difference between 2 groups ($P = .125$). Body mass index, K-L grade, and sex were also not significant different between groups (all $P > .05$).

3.2. Compliance and safety

In the experimental group, compliance with acupuncture treatment and manual therapy-type massage was as follows: for both, 11 out of 12 patients showed 100% compliance (12 participations/total 12 times) and 1 patient with 92% compliance (11 participations/total 12 times), indicating a very high compliance rate. No adverse events were reported, thus confirming safety.

3.3. Hange of VAS in experimental and control group

The mean ± standard deviation of VAS was 5.13 ± 0.8, 1.96 ± 0.94, and 2.83 ± 1.23 at visits 1, 2, and 3, respectively, in the experimental group and 4.29 ± 1.33, 3.57 ± 1.6, and 3.32 ± 1.9 at visits 1, 2, and 3, respectively, in the control group (Table 2). In the comparison by visit, excluding the effect between groups, the VAS significantly improved over time ($P < .001$), but the patterns of change were significantly different between groups over time ($P < .001$). From visit 1 to visit 2, the mean value of VAS decreased by 0.72 and 3.17 in the control and experimental groups, respectively. From visit 2 to visit 3, the mean VAS value decreased by 0.25 in the control group but increased by 0.87 in the experimental group (Fig. 2). As the time point changed, the pattern of change between groups was different.

3.4. WOMAC index change

The mean ± standard deviation of WOMAC index for pain was 6.92 ± 3.63, 3.42 ± 2.47, and 5.25 ± 2.86 at visits 1, 2, and 3, respectively, in the experimental group and 6.00 ± 3.44, 5.86 ± 2.38, and 4.93 ± 4.03 at visits 1, 2, and 3, respectively, in the control group (Table 2). The patterns of change based on the WOMAC index for pain were not significantly different between groups over time according to the time of visit ($P = .099$). The mean ± standard deviation of WOMAC index for stiffness was 4.00 ± 1.91, 2.42 ± 1.62, and 2.25 ± 1.42 at visits 1, 2, and 3, respectively, in the experimental group and 3.07 ± 1.77, 2.57 ± 1.65, and 2.43 ± 1.91 at visits 1, 2, and 3, respectively, in the control group (Table 2). The WOMAC index for stiffness by group and between groups were not significantly different over time ($P = .705$, $P = .261$), except at each time point ($P = .005$). The mean ± standard deviation of WOMAC index for body function was 30.25 ± 12.41, 16.08 ± 8.74, and 16.83 ± 7.78 at visits 1, 2 and 3, respectively, in the experimental group and 23.57 ± 11.20, 19.07 ± 8.69, and 18.29 ± 9.88 at visits 1, 2, and 3, respectively, in the

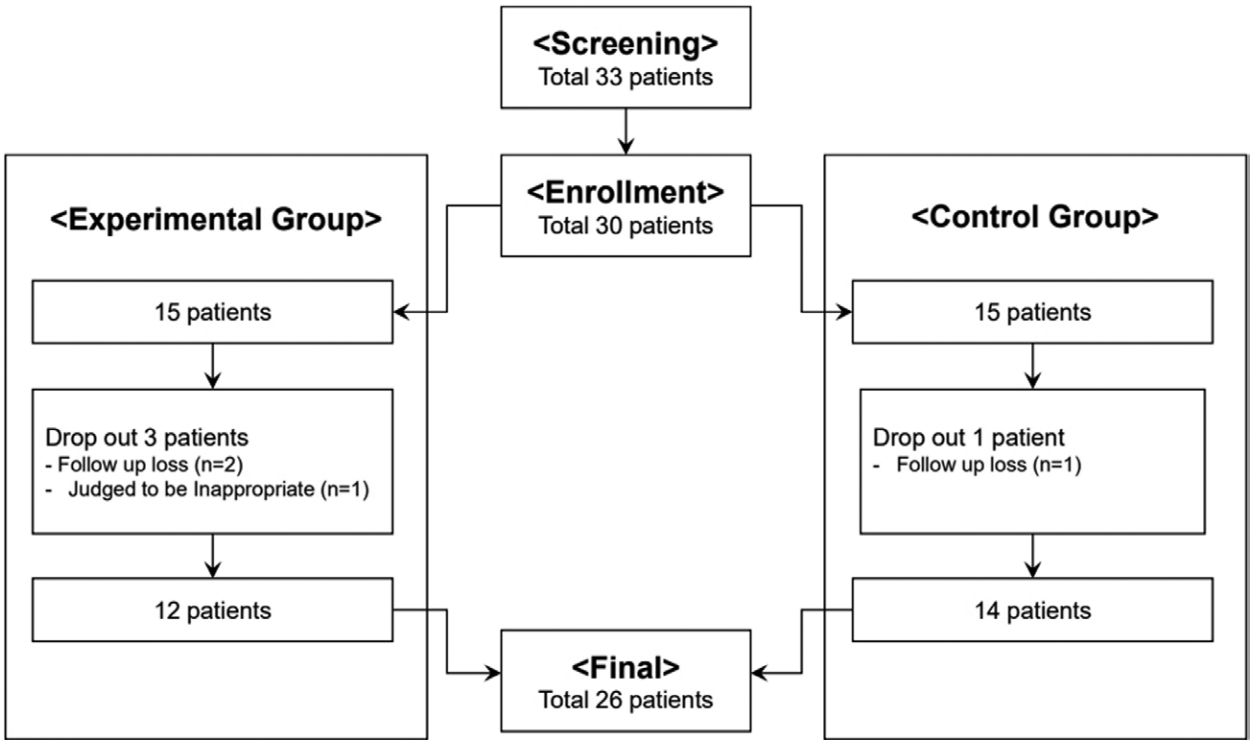

Figure 1. Patient flow chart including the number of screening, enrollment, dropout, and final patient count.

Table 1

Demographic characteristics between experimental group and control group.

Variable		Experimental group (n = 12)	Control group (n = 14)	*P* value
Age (yr)		60.33 ± 7.9	64.86 ± 6.61	.125
BMI (kg/m^2)		25.73 ± 1.79	25.9 ± 3.77	.890
K-L grade	1	4 (33.3)	2 (14.3)	.479
	2	6 (50)	8 (57.1)	
	3	2 (16.7)	4 (28.6)	
Sex	Male	3 (25)	2 (14.3)	.490
	Female	9 (75)	12 (85.7)	
Medical history	No	11 (91.7)	11 (78.6)	.356
	Yes	1 (8.3)	3 (21.4)	
Detail	Eye	0	1	-
	Endocrine	0	1	
	Cardiovascular	1	1	
	Digestive	0	1	
	etc	0	1	

Values were presented by mean ± standard deviation or frequency (percent).
BMI = body mass index, K-L = Kellgren-Lawrence.

Table 2

Comparison for VAS and functional outcomes between experimental group and control group.

		Visit, mean ± SD			*P* value		
Variable	Group	V1 (pre)	V2 (6 weeks)	V3 (12 weeks)	V	G	V*G
VAS	Exp	5.13 ± 0.80	1.96 ± 0.94	2.83 ± 1.23	<.001*	.340	<.001*
	Con	4.29 ± 1.33	3.57 ± 1.60	3.32 ± 1.90			
WOMAC pain	Exp	6.92 ± 3.63	3.42 ± 2.47	5.25 ± 2.86	.076	.639	.099
	Con	6.00 ± 3.44	5.86 ± 2.38	4.93 ± 4.03			
WOMAC stiffness	Exp	4.00 ± 1.91	2.42 ± 1.62	2.25 ± 1.42	.005*	.705	.261
	Con	3.07 ± 1.77	2.57 ± 1.65	2.43 ± 1.91			
WOMAC body function	Exp	30.25 ± 12.41	16.08 ± 8.74	16.83 ± 7.78	<.001*	.794	.094
	Con	23.57 ± 11.20	19.07 ± 8.69	18.29 ± 9.88			
WOMAC total	Exp	41.17 ± 16.62	21.92 ± 11.97	24.33 ± 10.59	<.001*	.890	.093
	Con	32.64 ± 15.06	27.5 ± 11.82	25.64 ± 15.14			

P values were obtained by repeated-measure 2 factor analysis.
Con = control, Exp = experimental, G = group, SD = standard deviation, V = visit, VAS = Visual Analog Scale, WOMAC = Western Ontario and McMaster Universities.
*Statistically significant with $P < .05$.

control group (Table 2). The WOMAC index for physical function by group and between groups over time were not significantly different ($P = .794$, $P = .094$), except by each time point ($P < .001$). The mean ± standard deviation of the total WOMAC 41.17 ± 16.62, 21.92 ± 11.97, 24.33 ± 10.59 at visits 1, 2, and 3, respectively, in the experimental group and 32.64 ± 15.06, 27.5 ± 11.82, and 25.64 ± 15.14 at visits 1, 2, and 3, respectively, in the control group (Table 2). The total WOMAC by group and between groups over time were not significantly different ($P = .794$, $P = .094$), except for each time point ($P < .001$). The WOMAC index measured to determine the knee function score was significantly decreased in both group as the time point was changed, but there was no difference in the change pattern between the 2 groups.

3.5. SF-36 change

The mean ± standard deviation of PCS was 45.42 ± 12.85, 61.28 ± 8.86, and 55.44 ± 9.32 at visits 1, 2, and 3, respectively, in the experimental group and 45.07 ± 12.87, 49.22 ± 12.08, and 50.69 ± 13.83 at visits 1, 2, and 3, respectively, in the control group (Table 3). PCS was not significantly difference between groups and between groups over time ($P = .107$, $P = .112$), except at each time point ($P = .002$). The mean ± standard deviation of MCS 56.05 ± 12.01, 67.76 ± 9.79, and 64.12 ± 11.29 at visits 1, 2, and 3, respectively, in the experimental group and 56.62 ± 11.85, 60.08 ± 13.07, and 62.79 ± 13.93 at visits 1, 2, and 3, respectively, in the control group (Table 3). MCS was not significantly different in the pattern of change between groups over time ($P = .107$, $P = .112$), except at each time point ($P = .002$). Among the sub-area of SF-36, the physical role restriction area and mental health area showed significant differences between the 2 groups over time ($P = .024$, $P = .006$), confirming that the mean of the 2 sub-areas in the experimental group increased significantly compared to the control group when the time point was changed from visit 1 to visit 2 (Fig. 3A and B). SF-36, measured to determine the quality of life, showed differences in change patterns between the 2 groups in the domain of physical role restriction and the domain of mental health. However, there was no difference in the change patterns between the 2 groups for PCS and MCS.

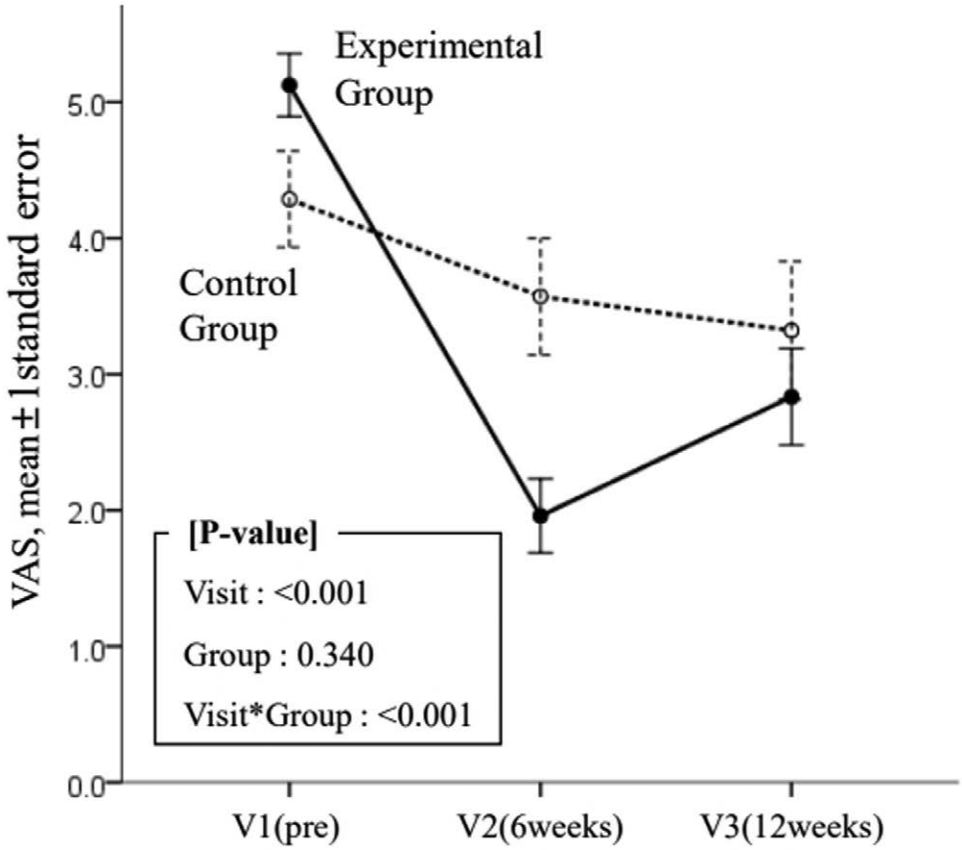

Figure 2. Result of VAS by 3 visits (pre, 6 weeks, and 12 weeks) between groups (experimental group and control group). VAS = Visual Analog Scale.

Table 3

Comparison for quality of life between experimental group and control group.

		Visit, mean ± SD			*P* value		
Variable	**Group**	**V1 (pre)**	**V2 (6 weeks)**	**V3 (12 weeks)**	**V**	**G**	**V*G**
PCS	Exp	45.42 ± 12.85	61.28 ± 8.86	55.44 ± 9.32	.002*	.107	.112
	Con	45.07 ± 12.87	49.22 ± 12.08	50.69 ± 13.83			
MCS	Exp	56.05 ± 12.01	67.76 ± 9.79	64.12 ± 11.29	.006*	.465	.237
	Con	56.62 ± 11.85	60.08 ± 13.07	62.79 ± 13.93			
PF	Exp	46.67 ± 14.51	63.33 ± 18.38	56.67 ± 14.67	.017*	.653	.533
	Con	47.5 ± 22.08	55.36 ± 17.81	56.79 ± 19.77			
RPH	Exp	52.08 ± 24.76	78.65 ± 11.45	72.4 ± 18.36	.003*	.051	.024*
	Con	50.45 ± 26.23	53.13 ± 25.68	54.02 ± 24.10			
BP	Exp	39.17 ± 8.00	50.63 ± 16.72	46.88 ± 12.84	.047*	.291	.629
	Con	39.46 ± 14.94	45.18 ± 11.16	41.61 ± 11.71			
GH	Exp	43.75 ± 18.96	52.50 ± 19.25	45.83 ± 18.07	.484	.667	.303
	Con	42.86 ± 12.36	43.21 ± 13.53	50.36 ± 19.56			
REP	Exp	60.42 ± 25.90	83.33 ± 17.41	75.69 ± 22.04	.008*	.320	.268
	Con	60.71 ± 24.11	67.86 ± 23.99	67.86 ± 27.32			
EF	Exp	51.25 ± 8.01	50.42 ± 8.38	49.58 ± 10.54	.863	.018*	.570
	Con	53.57 ± 8.19	56.79 ± 7.50	56.07 ± 6.84			
SF	Exp	63.54 ± 19.55	73.96 ± 19.55	71.88 ± 12.07	.066	.510	.348
	Con	61.61 ± 17.99	63.39 ± 22.18	73.21 ± 18.90			
EWB	Exp	49.00 ± 9.96	63.33 ± 7.78	59.33 ± 9.47	.000*	.107	.006*
	Con	50.57 ± 8.09	52.29 ± 9.60	54.00 ± 10.50			

P values were obtained by repeated-measure 2 factor analysis.

BP = body pain, C = control, EF = energy/fatigue, EWB = emotional well-being, Exp = experimental, G = group, GH = general health, MCS = mental component score, PCS = physical component score, PF = physical functioning, REP = role limitations due to emotional problems, RPH = role limitations due to physical health, SD = standard deviation, SF = social functioning, V = visit.

*Statistically significant with $P < .05$.

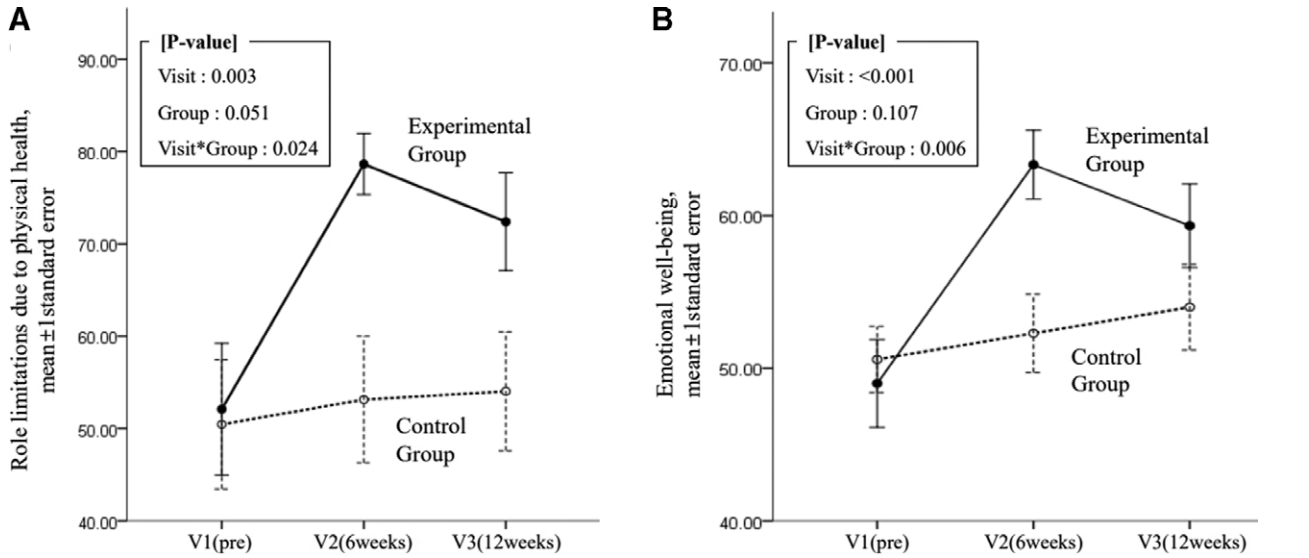

Figure 3. Result of 2 subdomains of SF-36, role limitations due to physical health (A) and emotional well-being (B) by 4 visits (pre, 2 weeks, 6 weeks, and 12 weeks) between group (experimental group and control group).

4. Discussion

Non-surgical treatment of degenerative arthritis of the knee is very diverse, and acupuncture has been commonly performed in Northeast Asian countries including Korea,[4–9] where its effectiveness has been proven.[7–9] In addition, simultaneous anti-inflammatory treatment and acupuncture result in superior pain relief than with single treatment.[8,23] The main treatment for osteoarthritis of the knee is currently focused on the patient's pain control. In that diversity of treatments according to the degree of pain, the present study aimed to examine the effectiveness of combining integrated medical treatment in comparison with conventional treatment alone to control pain.

Our results revealed the following: First, for patients with degenerative knee arthritis, the results of comparative analysis of the therapeutic effects of integrative medicine treatment and conventional medical treatment service showed that CIM treatment had a significantly superior effect on pain control than conventional medical treatment. When the minimal clinical important difference of VAS was 1.8 points,[24] 6 weeks after the start of integrative medicine treatment, the decrease of VAS was greater than that of conventional medical treatment, and the difference between the 2 treatments was larger than 1.8 points. Even after 6 weeks from the end of treatment, the integrative medicine treatment showed superior results in pain relief compared to the conventional medical treatment, but the difference was smaller in VAS than the minimal clinical important difference of 1.8. There was no statistical difference between the 2 treatments in terms of knee function improvement. Based on the results of SF-36 used to evaluate quality of life, integrative medicine treatment showed significantly superior effect than conventional medical treatment in role limitations due to physical health and emotional well-being. Second, the superiority of pain control of integrative medicine treatment was maintained until 6 weeks after the end of integrative medicine treatment. Third, compliance with the Korean traditional medicine treatment and healing program, which was conducted 12 times over 6 weeks, was very high. In addition, no adverse events were reported, thus confirming safety.

Most of the studies on the effects of acupuncture on knee degenerative arthritis pain have investigated the effects of acupuncture during and short-term after treatment,[7,23,24] suggesting that the short-term effect persists even after completion of treatment.[23,24] In the results of this study, the integrative medicine treatment showed superior treatment effect than conventional medical treatment in pain relief, role limitations due to physical health, and emotional well-being. However, common in all 3 questions, the magnitude of the effect gradually decreased after the end of treatment.

VAS, WOMAC index, and SF-36, which were used as evaluation indicators after each treatment, showed a clear difference between the 2 groups in the change pattern according to time point. Immediately after the end of integrative medicine treatment, the collected indicators showed a rapid treatment effect. However, the effect of integrative medicine treatment decreases after 6 weeks after the end of treatment. In contrast, the evaluation index after conventional medical treatment shows an increasing treatment effect over time, suggesting that the effect of integrative medicine treatment is maximized during the treatment period but weakened over time after treatment.

This study is a pilot study, and more extensive research is needed based on the derived results. The clinical information and result of this study expected to be utilized in large-scale clinical research. As a result of post hoc analysis of the power for VAS change, the primary efficacy evaluation variable between the 2 groups, it showed a high power of 0.94. Also, in this study, only a short-term (6 weeks after termination) effect was analyzed after integrative medicine treatment. Since acupuncture and manual massage therapy were omitted from integrative medicine treatment, the effects tended to decrease immediately. Analysis of the effects of the middle and long term will be essential in future studies.

5. Conclusion

Integrative medicine treatment has superior effects in pain control over conventional medical treatment. In integrative medicine treatment, pain control tends to decrease with time, but still superior over conventional medical treatment up to 6 weeks after treatment (12 weeks after initial treatment).

Author contributions

Conceptualization: Sang Gyu Kwak, Hyun Jung, Won-Kee Choi.
Data curation: Sang Gyu Kwak, Hyun Jung, Won-Kee Choi.
Formal analysis: Sang Gyu Kwak, Won-Kee Choi.
Funding acquisition: Sang Gyu Kwak, Won-Kee Choi.
Investigation: Sang Gyu Kwak, Won-Kee Choi.
Methodology: Won-Kee Choi.

Project administration: Sang Gyu Kwak, Won-Kee Choi.
Supervision: Sang Gyu Kwak.
Validation: Sang Gyu Kwak, Won-Kee Choi.
Visualization: Sang Gyu Kwak, Hyun Jung, Won-Kee Choi.
Writing – original draft: Sang Gyu Kwak, Won-Kee Choi.
Writing – review & editing: Sang Gyu Kwak, Hyun Jung, Won-Kee Choi.

References

[1] Wan RCW, Fan JCH, Hung YW, et al. Cost, safety, and rehabilitation of same-stage, bilateral total knee replacements compared to two-stage total knee replacements. Knee Surg Relat Res. 2021;33:17.
[2] Lee DH, Kim SJ, Kim SA, et al. Past, present, and future of cartilage restoration: from localized defect to arthritis. Knee Surg Relat Res. 2022;34:1.
[3] Peat G, McCarney R, Croft P. Knee pain and osteoarthritis in older adults: a review of community burden and current use of primary health care. Ann Rheum Dis. 2001;60:91–7.
[4] Arden NK, Perry TA, Bannuru RR, et al. Non-surgical management of knee osteoarthritis: comparison of ESCEO and OARSI 2019 guidelines. Nat Rev Rheumatol. 2021;17:59–66.
[5] Bannuru RR, Osani MC, Vaysbrot EE, et al. OARSI guidelines for the non-surgical management of knee, hip, and polyarticular osteoarthritis. Osteoarthr Cartil. 2019;27:1578–89.
[6] DeRogatis M, Anis HK, Sodhi N, et al. Non-operative treatment options for knee osteoarthritis. Ann Transl Med. 2019;7(Suppl 7):S245.
[7] Li J, Li YX, Luo LJ, et al. The effectiveness and safety of acupuncture for knee osteoarthritis: an overview of systematic reviews. Medicine. 2019;98:e16301.
[8] Liu SC, Qiao XF, Tang QX, et al. A retrospective study of acupuncture as an adjunctive therapy to topical ibuprofen for chronic knee pain due to osteoarthritis. Medicine. 2019;98:e15308.
[9] Selfe TK, Taylor AG. Acupuncture and osteoarthritis of the knee: a review of randomized, controlled trials. Fam Community Health. 2008;31:247–54.
[10] Choi TY, Lee MS, Kim JI, et al. Moxibustion for the treatment of osteoarthritis: an updated systematic review and meta-analysis. Maturitas. 2017;100:33–48.
[11] Yuan T, Xiong J, Wang X, et al. The effectiveness and safety of Moxibustion for treating knee osteoarthrotis: a PRISMA compliant systematic review and meta-analysis of randomized controlled trials. Pain Res Manag. 2019;2019:265792.
[12] Li A, Wei ZJ, Liu Y, et al. Moxibustion treatment for knee osteoarthritis: a systematic review and meta-analysis. Medicine (Baltim). 2016;95:e3244.
[13] Lin L, Cheng K, Tan MT, et al. Comparison of the effects of 10.6-mμm infrared laser and traditional moxibustion in the treatment of knee osteoarthritis. Lasers Med Sci. 2020;35:823–32.
[14] Suarez-Almazor ME, Looney C, Liu Y, et al. A randomized controlled trial of acupuncture for osteoarthritis of the knee: effects of patient-provider communication. Arthritis Care Res. 2010;62:1229–36.
[15] Tillu A, Tillu S, Vowler S. Effect of acupuncture on knee function in advanced osteoarthritis of the knee: a prospective, non-randomised controlled study. Acupunct Med. 2002;20:19–21.
[16] Nakata K, Hanai T, Take Y, et al. Disease-modifying effects of COX-2 selective inhibitors and non-selective NSAIDs in osteoarthritis: a systematic review. Osteoarthr Cartil. 2018;26:1263–73.
[17] Jevsevar DS. Treatment of osteoarthritis of the knee: evidence-based guideline. JAAOS-J Am Acad Orthop Surg. 2013;21:571–6.
[18] Kohn MD, Sassoon AA, Fernando ND. Classifications in brief: Kellgren-Lawrence classification of osteoarthritis. Clin Orthop Relat Res. 2016;474:1886–93.
[19] Lee YJ, Han CH, Jeon JH, et al. Effectiveness and safety of polydioxanone thread-embedding acupuncture (TEA) and electroacupuncture (EA) treatment for knee osteoarthritis (KOA) patients with postoperative pain: an assessor-blinded, randomized, controlled pilot trial. Medicine. 2020;99:e21184.
[20] Moon SH, Lee S, Bae DK. History and concept of manual therapy. J Korean Orthop Assoc. 2020;55:29–37.
[21] McConnell S, Kolopack P, Davis AM. The Western Ontario and McMaster Universities osteoarthritis Index (WOMAC): a review of its utility and measurement properties. Arthritis Rheum. 2001;45:453–61.
[22] Webster KE, Feller JA. Comparison of the short form-12 (SF-12) health status questionnaire with the SF-36 in patients with knee osteoarthritis who have replacement surgery. Knee Surg Sports Traumatol Arthrosc. 2016;24:2620–6.
[23] Zhang L, Yuan H, Zhang L, et al. Effect of acupuncture therapies combined with usual medical care on knee osteoarthritis. J Tradit Chin Med. 2019;39:103–10.
[24] Wu SY, Lin CH, Chang NJ, et al. Combined effect of laser acupuncture and electroacupuncture in knee osteoarthritis patients: a protocol for a randomized controlled trial. Medicine. 2020;99:e19541.