



Original Article

Comparative Observational Study on the Effects of Intra-articular Hominis Placenta Pharmacopuncture and Acupoint Hominis Placenta Pharmacopuncture for Knee Osteoarthritis Patients



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ABSTRACT

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The aim of this case report was to observe the effects of intra-articular hominis placenta pharmacopuncture (HPP). Based on the medical records patients who received intra-articular treatment or received acupoint pharmacopuncture treatment, a comparison was made. There were 35 patients who were hospitalized for degenerative osteoarthritis of the knee joint from the 1st October 2019 to 26th September 2020. There were 14 patients who were treated with HPP in the intra-articular joint space (Group A), and 14 patients who were treated with HPP at specific acupoints (Group B). The outcome effects were measured using the Korean Western Ontario and Mc (KWOMAC) the visual analog scale (VAS) before the first treatment, and after the fifth treatment. The KWOMAC ($p < 0.001$) and the VAS scores ($p < 0.001$) in Groups A and B significantly improved after treatment compared with before treatment. When comparing Group A improvement with Group B improvement using the KWOMAC there was no statistically significant difference however, when using the VAS scores, Group A treatment was statistically more effective compared with Group B ($p = 0.002$). This study indicated that HPP may be an effective treatment for knee osteoarthritis. Moreover, intra-articular HPP may be more effective than acupoint HPP for knee osteoarthritis.

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Introduction

Osteoarthritis (OA) of the knee is a degenerative condition within the joint [1]. OA is a disorder of movable joints causing pain and stiffness, and is characterized by deterioration of articular cartilage, osteophyte formation and bone remodeling, changes in periarticular tissues, and a low-grade, non-purulent inflammation of varying severity [2], and it is a common clinical condition of aging [3].

Treatments for degenerative knee OA include acupuncture, pharmacopuncture, moxibustion, herbal medicine, and Miniscalpel-Acupuncture [4,5]. In pharmacopuncture, hominis placenta is used for joint diseases [6-8]. According to the criteria

of Korean medicine, hominis placenta has both sweetness and saltiness, but it does not dry out, and it enters 3 meridians: lungs, liver, and kidney. It tonifies qi, replenishes blood, and tonifies and replenishes kidney essence, so it is used to treat conditions such as weakness caused by old age, constitutional insufficiency, insufficiency of qi and blood, and insufficiency of kidney essence [9]. It is used for pulmonary tuberculosis, nervous breakdowns, anemia, and bronchial asthma. Hominis placenta is used for pharmacopuncture [10]. Pharmacologically, hominis placenta contains several cell growth factors, various interferons, interleukins, and colony-forming stimulating factors [11].

Treatment of degenerative knee OA has been investigated using intra-acupoint, intramuscular, and intra-articular injections using

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bee venom pharmacopuncture and results showed that intra-articular bee venom pharmacopuncture was slightly more effective [12,13]. In the case of hominis placenta, intra-acupoint injection treatment and acupuncture treatment were reported to have similar effects [6]. The effectiveness of intra-articular injections has not been reported.

Therefore, in order to observe the effects of intra-articular hominis placenta pharmacopuncture (HPP), inpatients diagnosed with degenerative knee OA who received HPP treatment, were compared with patients who received acupoint HPP to determine meaningful treatment effects.

Case Report

Patients

A total of 35 patients were hospitalized for degenerative knee OA at the Samse Korean Medicine Hospital between October 1st, 2019 and September 26th, 2020. Patients who met the study selection criteria were included in the study population. The effects of treatment were retrospectively analyzed in 14 patients treated with intra-articular HPP and 14 patients treated with acupoint HPP.

This study is a retrospective chart review approved for exemption from deliberation by the Institutional Review Board of the Dong-eui Korean Medicine Hospital (IRB no.: DIRB-202010-HR-E-46).

Selection criteria

- ① Aged $\geq 40 < 80$ years.
- ② Knee OA diagnosed by an orthopedist, using criteria based on the American College of Rheumatology classification.
- ③ Knee pain in 1 or both knees rated ≥ 4 on the visual analog scale (VAS).

Exclusion criteria

- ① Those who have undergone surgery on the knee(s) due to degenerative OA or other trauma.
- ② Those who have received intra-articular injections such as prolotherapy or steroids or hyaluronic acid within the past 3 months.
- ③ Those who received intra-articular injections such as prolotherapy, steroids, or hyaluronic acid during inpatient treatment.
- ④ Patients with degenerative knee OA secondarily induced after trauma.
- ⑤ Those who are receiving treatment with corticosteroid drugs or other nonsteroidal anti-inflammatory drugs for other diseases.

Treatment method

Acupuncture

Treatment was performed with sterilized disposable steel needles 0.20 mm \times 30 mm (Dongbang Medical). The EX-LE2, EX-LE4, ST35, ST34, SP9, SP10, GB34, and Ashi points were used [14]. The depth of needling was 10–30 mm, depending on the point location. Needles were stimulated manually for 10 seconds to achieve de qi. Patients were treated twice a day for 15 minutes.

The acupuncturists were required to be licensed Korean medical doctors who had been qualified for at least 3 years.

HPP

The hominis placenta used for HPP was supplied by Jaseng,

a Korean medical materials supplier in Namyangju, Gyeonggi Province.

1. Intra-articular HPP

In order to perform a medicinal acupuncture injection into the pocket above the patella that is connected to the synovial membrane, needles were inserted 2 mL from the depression point, just above the patella outer pole, toward the pocket above the patella [15] to a depth of 20 mm. The doctors were equipped with 30 G \times 25 mm sterilized injection needles (Sungsim Medical, Inc.) attached to 3 mL disposable syringes (Sungsim Medical Inc.) before the procedure, while wearing sterile surgical gloves (DS Enterprise Inc.). Before and after injection, disinfection was performed with 10% povidone-iodine. Afterwards, 3 passive joint flexion exercises were performed. HPP treatment was performed using 2 mL each time, 2–3 times/week, 5 times in a 2-week period. In addition, the patient was informed that contact with water at the treatment site should be avoided on the day of the procedure, and education related to infection control was provided.

2. Acupoint HPP

Acupoint HPP treatment was performed using 31 G \times 8 mm needles, and 1 mL disposable insulin syringes (Sungsim Medical Co., Ltd.), EX-LE2, EX-LE4, ST35, ST34, SP9, SP10, and GB34 at each acupoint with 0.2 mL of HPP with a total of 2 mL used.

Herbal medicine

The primary herbal medicine prescription was for Gamihwalhyeol-tang and Dokhwalkigisaeng-tang according to the patients' condition. Patients took 2 herbal medicines, 3 times a day (each 120 mL), 1 hour after meals (Tables 1 and 2).

Physiotherapy

Transcutaneous electrical nerve stimulation treatment was

Table 1. Composition of Gamihwalhyeol-tang.

Scientific name	Amount (g)
Cyperi Rhizoma	6
Rehmanniae Radix	6
Linderae Radix	6
Angelica gigatis Radix	6
Paeoniae Radix	6
Cnidii Rhizoma	6
Ponciri Fructus	6
Rhei Undulati Rhizoma	6
Persicae Semen	6
Caesalainiae Lignum	4
Carthami Flos	2
Total amount	60

Table 2. Composition of Dokhwalkigisaeng-tang.

Scientific name	Amount (g)
Araliae Continentalis Radix	2.8
Angelicae Gigantis Radix	2.8
Paeoniae Radix	2.8
Loranthus parasiticus	2.8
Rehmanniae Radix Preparata	2
Cnidii Rhizoma	2
Ginseng Radix	2
Poria Sclerotium	2
Achyranthis Radix	2
Eucommiae Cortex	2
Gentiana macrophylla	2
Asiasari Radix et Rhizoma	2
Saposhnikoviae Radix	2
Cinnamomi Cortex	2
Glycyrrhizae Radix et Rhizoma	1.2
Total amount	32.4

performed once a day, for 20 minutes, under the patella of the knee with OA.

Assessment methods

The assessments were performed before the first treatment and after the fifth treatment. Before and after the treatment values of each group were checked and the changes were compared. Assessments were made by Korean medical doctors with more than 1 year of clinical experience other than the procedures.

WOMAC

WOMAC is an evaluation tool developed for the purpose of evaluating the pain and condition of patients with OA in the hip or knee joint. It consists of 24 questions including 5 pain items, 2 stiffness items, and 17 body functions. Functional disorders related to knee pain and the degree of limitation during specific tasks can be combined and evaluated. The total sum of each item was marked on a 5-point Likert scale which displayed values between 0 and 96. A higher score indicated more severe symptoms and a higher limitation of activity. In this study, KWOMAC [16], a Korean version of WOMAC was applied.

VAS

A state of no pain and no gait disorder would result in a VAS

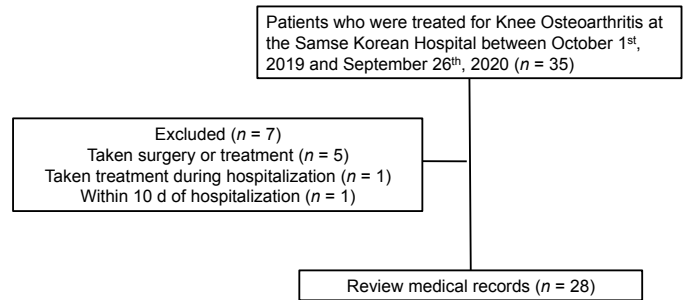


Fig. 1. Flow chart of patient selection.

score of 0, and a state of being unable to walk would be indicated by a VAS score of 10.

Data analysis

The experimental results were statistically processed using IBM SPSS statistics for windows Version 18.0. For the nominal variables, gender and lesion, the Chi-square test was used. In the case of not following the normal curve the Mann-Whitney U-test was performed (age, duration of knee OA), and VAS, and an Independent 2 sample *t*-test were performed on the KWOMAC scores. With normally distributed data, a comparison within (intra) each group was performed using the paired *t*-test, and an independent 2 sample *t*-test was used for comparison between (inter) the 2 groups. For data not normally distributed, a Wilcoxon signed rank test was used to compare results within (intra) each group, and a Mann-Whitney U-test was used for comparison between (inter) the 2 groups. The value for the nominal variable was expressed as a number, the variable following normality was expressed as mean \pm SD, and the variable not following normality was expressed as the median (Fig. 1).

Results

The intra-articular HPP treatment group (Group A) was comprised of 14 patients, and the acupoint HPP treatment group (Group B) also included 14 patients. Of the 14 patients in Group A, 2 were affected on 1 side, and 12 on both sides, and out of the 14 patients in Group B, 3 were affected on 1 side and 11 on both sides. There was no statistically significant difference in sex or lesions between groups A and B ($p = 1.000$). The mean age of all patients was 60.11 ± 6.47 years; the mean age of Group A was $60.50 (51.75-64.75)$ years, and in Group B the mean age was $60 (57.25-63.25)$ years, with no statistically significant difference between groups ($p = 0.550$). The mean duration of knee OA in all patients was 3.09 ± 2.83 years, the mean duration in Group A was $1.75 (0.73-3.25)$ years, and in Group B was $3.00 (0.73-6.00)$ years, and there was no statistically significant difference between groups ($p = 0.344$). The age of patients and duration of knee OA were determined to be the same in Groups A and B. There was no statistically significant difference between Groups A and B using the KWOMAC and the VAS scores before treatment, indicating that Groups A and B were homogeneous.

The pre- and post-treatment assessment using the KWOMAC in Group A showed a significant improvement ($p < 0.001$) from 61.14 ± 11.06 before treatment to 40.86 ± 16.06 after treatment

Table 3. Improvement of KWOMAC in Group A (Before-After).

	Before	After	<i>p</i>
KWOMAC*	61.14 ± 11.06	40.86 ± 16.06	< 0.001 [‡]
Pain	12.64 ± 3.00	8.21 ± 3.64	< 0.001 [‡]
Stiffness [†]	5.00 (4.00-6.25)	3.00 (2.00-4.25)	0.005 [§]
Function	43.57 ± 9.39	29.36 ± 11.61	0.001 [‡]

Data are presented as mean ± SD or median (range).

* Using Paired *t*-test.

† Using Wilcoxon signed rank test.

‡ Using Paired *t*-test, *p* < 0.05.

§ Using Wilcoxon signed rank test, *p* < 0.05.

Table 4. Improvement of KWOMAC in Group B (Before-After).

	Before	After	<i>p</i>
KWOMAC*	51.64 ± 16.18	36.29 ± 17.09	< 0.001 [‡]
Pain	10.64 ± 3.54	6.93 ± 3.12	< 0.001 [‡]
Stiffness [†]	4.00 (3.00-5.25)	3.00 (2.00-4.00)	0.002 [§]
Function	36.93 ± 12.02	26.43 ± 13.09	< 0.001 [‡]

Data are presented as mean ± SD or median (range).

* Using Paired *t*-test.

† Using Wilcoxon signed rank test.

‡ Using Paired *t*-test, *p* < 0.05.

§ Using Wilcoxon signed rank test, *p* < 0.05.

(*p* < 0.001). Pre- and post-treatment assessments for pain, stiffness, and function showed statistically significant improvements *p* < 0.001, *p* = 0.005, *p* = 0.001, respectively (Table 3). The pre- and post-treatment assessment using the KWOMAC in Group B showed a significant improvement (*p* < 0.001) from 51.64 ± 16.18 before treatment to 36.29 ± 17.09 after treatment (*p* < 0.001). Pre- and post-treatment assessments for pain, stiffness, and function showed statistically significant improvements *p* < 0.001, *p* = 0.002 and *p* < 0.001, respectively (Table 4).

The pre- and post-treatment assessment using the VAS scores in Group A showed a significant improvement (*p* = 0.001) from 8.00 (7.00-8.00) before treatment to 3.00 (2.75-4.25) after treatment. The pre- and post-treatment assessment using the VAS scores in Group B showed a significant improvement (*p* = 0.001) from 7.00 (6.00-8.00) before treatment to 4.50 (3.00-5.00) after treatment.

The improvement between the 2 groups was compared according to the amount of change in the KWOMAC before and after treatment in Groups A and B. The KWOMAC data for pain, stiffness, and function, did not show improvement (*p* = 0.28, *p* = 0.484, *p* = 0.248, and *p* = 0.324, respectively). The improvement in the VAS scores before and after treatment was compared between Group A (-4.00) [(-5.00)-(-3.00)] and Group B (-2.50) [(-3.25)-(-2.00)]. The degree of change in Group A was significantly greater than in Group B (*p* = 0.002).

Discussion

Degenerative OA is characterized by local degenerative changes in articular cartilage, hypertrophy of the subchondral bone, excessive bone formation in surrounding osteochondral parts, and deformation of joints. Early symptoms of degenerative knee OA are pain and abnormal sound in the knee joint, and as the disease progresses, it may show symptoms such as muscle atrophy, limited movement, and joint lock [17].

Hominis placenta contains cell proliferation factors that generate various hepatocytes, epithelial cells and nerve cells, various types of interferons that inhibit viruses, and interleukins and corona formation stimulating factors. It also contains various hormones and their precursors, nucleic acid-related substances involved in nucleic acid formation, various amino acids, and vitamins [18]. In addition, Kim et al [19] reported on the protective effect of cartilage degradation in the synovial membrane by inhibiting the activities of the proteolytic enzymes MMP-2 and MMP-9 in the synovial membrane when administered to the cartilage.

Yeom et al [20] reported experimental results showing that hominis placenta herb-acupuncture is effective for joint diseases in white rats, and Lee et al [7] reported that hominis placenta herb-acupuncture is effective in treating ankle disease. In addition, Park et al [6] reported that hominis placenta herb-acupuncture is effective for degenerative OA. Song et al [8] reported that HPP megadose is effective for spinal canal stenosis, confirming that

HPP is effective in treating joint disease.

In Japan, it has been reported that intra-articular injection therapy is effective in patients with chronic knee OA [21], but there have been no reports in Korea comparing intra-articular HPP and acupoint HPP.

The authors reviewed the medical records of 35 patients who were hospitalized and treated for degenerative knee OA at the Samse Korean Medical Hospital between October 1st, 2019 and September 26th, 2020. Of the 35 patients, 28 patients, excluding 5 patients who had undergone surgery and procedures, 1 who received a hyaluronic acid intra-articular injection during the hospitalization period, and 1 who had been severely discharged, were reviewed. Patients were treated with intra-articular or acupoint HPP, and through this, the effect of HPP as a treatment method was evaluated.

The 28 patients received HPP treatment 2-3 times per week for a total of 5 treatments during the 2-week hospitalization period. In the intra-articular HPP group, 2 mL of hominis placenta was injected in the intra-articular cavity, that is, the patellar sac. In the acupoint HPP group, points among EX-LE2, EX-LE4, ST35, ST34, SP9, SP10, and GB34 [14] were added and subtracted, and with 0.2 mL used at each acupoint, a total of 2 mL of pharmacopuncture was performed.

The initial homogeneity between the 2 groups was confirmed. The *p* values for sex, lesion, age, duration of knee OA, KWOMAC, pain, stiffness, function, and VAS were 1.000, 1.000, 0.550, 0.344, 0.081, 0.119, 0.196, 0.115 and 0.156, respectively. There were no statistically significant differences between the groups.

In the case of the intra-articular HPP group, the pain, stiffness, and function of KWOMAC, along with VAS scores all showed a significant decrease. In the case of the acupoint HPP group, the pain, stiffness, and function of KWOMAC, together with VAS scores showed significant decreases.

Hominis placenta reduces inflammatory cytokines (TNF, IL-1 β , and IL-6) [20], remarkably inhibits the production of nitrogen oxides, TNF, and oxidase, and is effective in the proliferation of chondrocytes [22]. It has been reported that the sensitivity to pain is decreased by raising the pain threshold [23]. Therefore, for a short-term inpatient treatment course of 2 weeks, it is thought that hominis placenta played a slightly greater role in controlling pain than its effect on the proliferation of chondrocytes. There is a continuing need for future research to examine changes in chondrocytes through long-term observation. From the above results, it can be observed that a course of treatment combining Korean Medicine with HPP for degenerative knee arthritis patients during a 2-week hospitalization is effective in controlling pain, improving daily life movements, and reducing the degree of disability.

When comparing the 2 treatment groups, the difference in the amount of change in KWOMAC was greater in the intra-articular HPP group. Although there appeared to be a greater effect, but there was no statistically significant difference. In the VAS scores, there was a statistically significant greater difference in the amount of change in the intra-articular HPP group. In view of this, it is estimated that intra-articular HPP treatment will be more clinically effective.

Additionally, the patients did not complain of great discomfort after receiving pharmacopuncture treatments. No adverse reactions, excessive bleeding or swelling, redness, pain, or hot sensations were reported after pharmacopuncture.

The limitations of this study are that in addition to pharmacopuncture treatment, other additional treatments such as acupuncture, drug treatment, and physical therapy were performed together, that follow-up was limited to a short period of 2 weeks,

and that the number of patients was small.

Therefore, in order to more clearly confirm the effectiveness of HPP, a systematic study such as a randomized control clinical trial securing a larger number of samples, a more comprehensive period and the use of additional evaluation tools is required.

In summary, among the patients who were hospitalized between October 1st, 2019 and September 26th, 2020 for degenerative knee arthritis at the Samse Korean Medicine Hospital, 14 were treated with intra-articular HPP, and 14 were treated with acupoint HPP. As a result of a comparative observation of the medical records of the patients, it was determined using the KWOMAC and VAS scores that following treatment, Groups A and B significantly improved. The VAS scores, of Group A showed intra-articular HPP was significantly more effective than acupoint HPP treatment received by Group B, and therefore may be more effective than acupoint HPP for knee OA.

Conflicts of Interest

The authors have no conflicts of interest to declare.

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