

Therapeutic efficacy of extracorporeal shock wave combined with hyaluronic acid on knee osteoarthritis

Shi-Chen Liu, MM^a, Xiao-Feng Qiao, MM^a, Qing-Xi Tang, MM^b, Xiao-Guang Li, MM^c, Jian-Hua Yang, MD^d, Tian-Qi Wang, MB^a, Ya-Jie Xiao, MB^a, Jian-Min Qiao, MB^{a,*}

Abstract

This retrospective study investigated the efficacy and safety of extracorporeal shock wave (EPSW) combined with hyaluronic acid (HA) for patients with knee osteoarthritis (KOA).

This retrospective study included 70 patients with KOA. Of those subjects, 35 of them received EPSW combined HA, and were allocated to a treatment group, while the other 35 participants received HA alone and were allocated to a control group. Patients in both groups were treated for a total of 8 weeks. The primary outcome was measured by visual analog scale (VAS). The secondary outcomes were measured by Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), and knee injury and osteoarthritis outcome score (KOOS). In addition, adverse events (AEs) were also evaluated. All outcomes were measured before and after the treatment.

After the treatment, patients in the treatment group exhibited better efficacy in VAS ($P < .01$), WOMAC scale (pain, $P < .01$; function, $P < .01$; and stiffness, $P < .01$), and KOOS scores (pain, $P < .01$; function in daily living, $P < .01$; symptoms, $P < .01$; sport and recreation, $P < .01$; and quality of life, $P < .01$), than patients in the control group. In addition, no significant differences regarding the AEs were found between 2 groups.

The findings of this study demonstrated that the efficacy of EPSW combined with HA is superior to the HA alone for patients with KOA.

Abbreviations: AEs = adverse events, EPSW = extracorporeal shock wave, HA = hyaluronic acid, KOA = knee osteoarthritis, KOOS = knee injury and osteoarthritis outcome score, VAS = visual analog scale, WOMAC = Western Ontario and McMaster Universities Osteoarthritis Index.

Keywords: efficacy, extracorporeal shock-wave therapy, hyaluronic acid, knee osteoarthritis

1. Introduction

Knee osteoarthritis (KOA) is one of most common inflammatory disorders for knee joint among the elderly population.^[1,2] It often manifests with severe pain, stiffness, limitation of joint

movement, and disability.^[3,4] Previous epidemiological studies have reported that the prevalence of KOA is about 16% to 75% in Asian females.^[5–7] The other studies also reported that more than 29.25% of female and 24.71% of males over 70 years old suffer from this disorder.^[8–10]

A variety of management are used to treat this condition effectively,^[11–17] especially for extracorporeal shock wave (EPSW) and hyaluronic acid (HA). A lot of previous clinical studies have assessed the efficacy of ESW or HA for the treatment of KOA.^[18–23] However, both of them has limited efficacy for some patients. Moreover, no clinical studies have reported to utilize the combination of EPSW and HA for the treatment of KOA. Thus, in order to achieve more promising outcome efficacy, this retrospective study aimed to explore the efficacy of EPSW combined with HA for the treatment of patients with KOA.

2. Methods/design

2.1. Hypothesis

The hypothesis of this study was that the efficacy of EPSW plus HA would be superior to the HA monotherapy in patients with KOA.

2.2. Ethical consideration

The present retrospective study has been approved by the Ethical Committee of First Affiliated Hospital of Jiamusi University. The

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S-C L and X-F Q contributed equally to this study.

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^a First Ward of Orthopedics Department, ^b Department of Emergency Surgery, First Affiliated Hospital of Jiamusi University, ^c Department of Orthodontics, Affiliated Stomatological Hospital of Jiamusi University, Jiamusi, ^d Department of Orthopedics, People's Hospital of Longgang District, Shenzhen, Guangdong, China.

* Correspondence: Jian-Min Qiao, First Ward of Orthopedics Department, First Affiliated Hospital of Jiamusi University, No.348 Dexiang Street, Xiangyang District, Jiamusi 154002, China (e-mail: jianmin2007@yeah.net).

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written informed consent from individual patient has been waived because all the data of this study were collected from the completed medical records.

2.3. Design

All cases were collected between December 2016 and November 2018 at the First Affiliated Hospital of Jiamusi University. A total of 70 patients with KOA were included and were divided into a treatment group (n=35, received EPSW and HA) and a control group (n=35, received HA alone) according to the different treatments they received. All patients in both groups were treated for a total of 8 weeks. All outcomes were measured before and after the treatment. All patients, researchers, and outcomes were not blinded in this retrospective study. However, the data analyst was masked to the group allocation and treatment

2.4. Patients

Patients were included if they aged from 50 to 85 years old and were clinically diagnosed as KOA.^[24] In addition, all of them had average pain intensity of knee visual analog scale (VAS) ≥ 4 over the past 6 months. Patients were excluded if they were pregnant, breastfeeding, history of knee surgery, local knee tumors, and trauma. In addition, they were also excluded if they received other therapies, such as acupuncture, moxibustion, or medications for KOA during the study period, except the EPSW and HA.

2.5. Intervention schedule

All patients in both groups received an injection of HA in the attacked knee joint (2.5 ml of 1% HA solution), once for a period of 4-week within a total of 8-week treatment period. Additionally, the patients in the treatment group also received EPSW (0.25 mJ/mm² for 4000 pulses in total and a frequency of 15 Hz/s) by using EPSW Device (Sonothera, Hanil Tm Co Ltd, Korea), once weekly for a total of 8 weeks.

2.6. Outcome measurements

Primary outcome was measured by using 0 to 10 cm VAS scale, with 0 of no pain, and 10 of severest pain.^[25] The secondary outcomes were assessed by the Western Ontario and McMaster Universities Arthritis Index (WOMAC),^[26] and self-reported knee injury and osteoarthritis outcome score (KOOS).^[27] WOMAC tool consists of 3 subscales of pain, function, and stiffness.^[26] KOOS tool includes 5 subscales with a total of 42 items. Each subscale is transformed to a 0 to 100 scale.^[27] In addition, adverse events (AEs) were also assessed. All outcomes were evaluated before and after the treatment.

2.7. Statistical analysis

All outcome data were analyzed by a professional statistician using SAS package (Version 9.1; SAS Institute Inc, Cary, North Carolina). All continuous data were analyzed by using *t* test or Mann–Whitney rank sum test. All categorical data were analyzed by using Fisher exact test. The value of $P < .05$ was considered as the statistically significant (2-side).

Sample size was calculated based on the change of VAS score with $\alpha = 0.5$, $\beta = 0.8$, and with an assumed 15% drop-out rate.

Table 1

Comparison of characteristics before the treatment.

Characteristics	Treatment group (n=35)	Control group (n=35)	P
Mean age, yr	66.8 (9.1)	68.2 (10.3)	.55
Sex			
Male	13 (37.1)	15 (42.9)	.63
Female	22 (62.9)	20 (57.1)	.63
Race (Chinese Han)	35 (100.0)	35 (100.0)	–
BMI, kg/m ²	25.9 (3.1)	26.4 (3.4)	.52
Duration of disease, yr	14.0 (3.8)	15.2 (4.2)	.21
VAS scale	6.5 (1.6)	6.8 (1.9)	.47
WOMAC score			
Total	52.0 (11.1)	53.9 (11.8)	.49
Pain	12.6 (3.2)	13.0 (3.4)	.61
Stiffness	4.5 (1.6)	4.7 (1.8)	.62
Function	34.8 (7.9)	36.1 (8.3)	.50
KOOS score			
Pain	66.1 (9.6)	67.9 (10.4)	.45
Function in daily living	70.3 (12.0)	72.7 (13.5)	.43
Symptoms	64.4 (10.7)	66.2 (12.2)	.51
Sport and recreation	34.8 (9.3)	36.1 (10.0)	.57
Quality of life	44.7 (15.5)	46.6 (16.1)	.61
Previous treatment			
Medications	34 (97.1)	35 (100.0)	.49
Physical therapy	20 (57.1)	18 (51.4)	.63
Acupuncture	21 (60.0)	15 (42.9)	.15

Data are present as mean \pm standard deviation or number (%).

BMI=body mass index, KOOS=knee injury and osteoarthritis outcome score, VAS=visual analog scale, WOMAC=Western Ontario and McMaster Universities Osteoarthritis Index.

Therefore, the required sample size of for this study was 70 patients in total and 35 subjects in each group.

3. Results

The characteristic values of all patients in both groups before the treatment are showed in Table 1. The comparison of all these values did not differ significantly between the 2 groups (Table 1).

After treatment, patients in the treatment group exerted better outcomes either in VAS ($P < .01$, Table 2), WOMAC (pain, $P < .01$; stiffness, $P < .01$; function, $P < .01$, Table 3), or in KOOS (pain, $P < .01$; function in daily living, $P < .01$; symptoms, $P < .01$; sport and recreation, $P < .01$; and quality of life, $P < .01$, Table 4) scores, than patients in the control group.

After treatment, the comparison of AEs did not differ significantly between 2 groups (Table 5). No severe AEs were documented in either group. No death related to the treatment occurred in either group.

4. Discussion

Numerous clinical studies have reported the efficacy of HA for the treatment of KOA, and have achieved exciting efficacy.^[21–23]

Table 2

Comparison of VAS after treatment (change from pretreatment).

Outcome	Treatment group (n=35)	Control group (n=35)	Difference	P
VAS	−1.9 (−3.3, −1.0)	−4.1 (−5.9, −2.8)	−2.2 (−2.9, −1.4)	<.01

Data are present as mean \pm standard deviation.

VAS=visual analog scale.

Table 3**Comparison of WOMAC after treatment (change from pretreatment).**

WOMAC	Treatment group (n = 35)	Control group (n = 35)	Difference	P
Total	-33.1 (-41.2, -20.5)	-26.0 (-36.4, -15.2)	-7.1 (-8.3, -5.4)	<.01
Pain	-3.2 (-4.8, -1.7)	-8.4 (-11.5, -5.8)	-5.2 (-7.6, -3.8)	<.01
Stiffness	-3.4 (-4.6, -2.2)	-2.1 (-3.3, -1.0)	-1.3 (-1.8, -0.6)	<.01
Function	-26.4 (-34.5, -17.7)	-15.5 (-23.8, -9.1)	-10.9 (-15.4, -4.6)	<.01

Data are present as mean \pm standard deviation.

WOMAC = Western Ontario and McMaster Universities Osteoarthritis Index.

Table 4**Comparison of KOOS after treatment (change from pretreatment).**

KOOS score	Treatment group (n = 35)	Control group (n = 35)	Difference	P
Pain	-52.4 (-65.3, -39.8)	-28.1 (-41.0, -16.2)	-24.3 (-28.8, -17.3)	<.01
Function in daily living	-55.9 (-67.5, -41.7)	-36.6 (-48.9, -22.3)	-19.5 (-27.7, -10.4)	<.01
Symptoms	-50.7 (-63.8, -37.4)	-33.1 (-45.5, -21.0)	-17.6 (-26.6, -8.8)	<.01
Sport and recreation	-26.1 (-38.3, -15.5)	-11.7 (-18.6, -7.4)	-14.2 (-19.3, -7.9)	<.01
Quality of life	-34.8 (-46.7, -22.7)	-20.3 (-33.5, -8.9)	-14.5 (-24.7, -8.7)	<.01

Data are present as mean \pm standard deviation.

KOOS = knee injury and osteoarthritis outcome score.

However, it still has limited efficacy for some patients, and also accompanied a couple of AEs.^[22,23] Thus, it would be great if an alternative therapy with fewer AEs can be used as adjunctive therapy to HA for the treatment of KOA. Fortunately, EPSW is a new alternative therapy that also can be used to treat a variety of pain conditions with great effect and fewer AEs. Additionally, no study has reported the efficacy of EPSW combined with HA for the treatment of KOA.

Presently, to our best knowledge, this study first investigated the efficacy and safety of the combination of EPSW and HA for the treatment of patients with KOA. In this study, we compared the efficacy and safety of EPSW plus HA with HA alone. The results of this study showed that patients who received EPSW plus HA showed better efficacy in VAS, WOMAC, and KOOS, than patients who received HA only. In addition, both groups had a similar safety profile. It indicated that the efficacy of EPSW plus HA for the treatment of KOA is much better than HA alone.

This retrospective study has 4 limitations. First, all patients and researchers were not blinded to the treatment and group allocation, because this study just analyzed the data from the completed medical records. Thus, it may increase the selection risk of bias. Second, all the outcome assessors were also not masked to the group allocation, which may increase the detection risk of bias in this study. Third, no randomization was applied in this study, which may affect patient selection in this study, thus, may increase the selection risk of bias. Fourth, this study did not include follow-up period visits after the treatment. Therefore,

Table 5**Comparison of injection sites reactions.**

Adverse events	Treatment group (n = 35)	Control group (n = 35)	P
Joint pain	4 (11.4)	5 (14.3)	.72
Joint swelling	1 (2.9)	0 (0)	.49
Joint stiffness	2 (5.7)	3 (8.6)	.64
Joint puffiness	0 (0)	1 (2.9)	.49
Infection	0 (0)	1 (2.9)	.49

Data are present as number (%).

long term efficacy of EPSW plus HA for the treatment of KOA is still needed to be explored in future studies.

5. Conclusion

The results of this study demonstrated that the efficacy of EPSW and HA is superior to the HA alone for the treatment of patients with KOA.

Author contributions

Conceptualization: Shi-Chen Liu, Xiao-Feng Qiao, Qing-Xi Tang, Xiao-Guang Li, Jian-Hua Yang, Jian-Min Qiao.

Data curation: Shi-Chen Liu, Xiao-Feng Qiao, Qing-Xi Tang, Xiao-Guang Li, Jian-Hua Yang, Tian-Qi Wang, Ya-Jie Xiao, Jian-Min Qiao.

Formal analysis: Shi-Chen Liu, Ya-Jie Xiao.

Funding acquisition: Jian-Min Qiao.

Investigation: Xiao-Feng Qiao, Xiao-Guang Li.

Methodology: Shi-Chen Liu, Jian-Hua Yang, Ya-Jie Xiao.

Project administration: Tian-Qi Wang, Jian-Min Qiao.

Resources: Shi-Chen Liu, Qing-Xi Tang, Xiao-Guang Li, Tian-Qi Wang, Ya-Jie Xiao.

Software: Shi-Chen Liu, Jian-Hua Yang.

Supervision: Qing-Xi Tang, Jian-Min Qiao.

Validation: Xiao-Feng Qiao, Qing-Xi Tang, Jian-Hua Yang, Tian-Qi Wang, Jian-Min Qiao.

Visualization: Xiao-Feng Qiao, Qing-Xi Tang, Xiao-Guang Li, Jian-Hua Yang, Tian-Qi Wang, Jian-Min Qiao.

Writing – original draft: Shi-Chen Liu, Xiao-Feng Qiao, Tian-Qi Wang, Ya-Jie Xiao, Jian-Min Qiao.

Writing – review and editing: Shi-Chen Liu, Qing-Xi Tang, Xiao-Guang Li, Jian-Hua Yang, Tian-Qi Wang, Ya-Jie Xiao, Jian-Min Qiao.

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