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CLINICAL RESEARCH

Effect of Qufeng Zhitong capsules supplemented with etocoxib tablets in the treatment of knee osteoarthritis and its effect on gait characteristics and inflammatory factors

Junfeng Kang[1] , Jinliang He[2#], Xuan Wang[2], Shixin Xing[1], Xilu Ren[1] , Xiaoyang Qiao[1] & Guozheng Lu[3*]

[1]Affiliated Hospital of Shanxi University of traditional Chinese Medicine

[2]Shanxi University of traditional Chinese Medicine

[3]Shanxi Provincial Hospital of traditional Chinese Medicine

Key words

Qufeng Zhitong capsules, Knee osteoarthritis, Gait characteristics, Inflammatory factors, Treatment effect

Correspondence

Guozheng Lu, Shanxi Province Hospital of Traditional Chinese Medicine, Taiyuan City, Shanxi Province. E-mail: 43332696@qq.com

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Abstract

Objective The effect of Qufeng Zhitong capsules supplemented with etocoxib tablets in the treatment of knee osteoarthritis and its effect on gait characteristics and inflammatory factors were evaluated in this research. **Methods** A total of 112 patients with knee osteoarthritis admitted to our hospital from April 2019 to January 2022 were selected and randomly divided into observation group (n=56) and control group (n=56). Patients in the control group were treated with etocoxib tablets, and patients in the observation group were treated with Qufeng Zhitong capsules on the basis of the control group. The Western Ontario and McMaster Universities (WOMAC) scale scores, gait characteristics, and inflammatory cytokines expression were compared between the two groups after treatment. **Results** The knee joint WOMAC scale scores of patients in the two groups were markedly lower than those before treatment, and those in observation group were apparently lower than those in control group (P<0.05). After treatment, the stride length and pace of patients in the two groups were significantly enhanced, and those in observation group were markedly higher than those in control group (P<0.05). After treatment, the levels of TNF-α, IL-1β and MMP-3 in the two groups were explicitly decreased, and the levels in observation group were obviously lower than those in control group (P<0.05). There was no significant difference in the incidence of adverse reactions between the two groups (P>0.05). **Conclusion** Qufeng Zhitong capsules supplemented with etocoxib tablets can improve the clinical symptoms of patients with knee osteoarthritis, promote step speed and step length and reduce the inflammatory response of patients, with relative safety.

Introduction

Knee osteoarthritis is a degenerative disease in the knee joint and a common chronic disease among orthopedic lesions [1]. Clinically, it is often accompanied by symptoms including joint pain, redness and stiffness. If effective treatment measures are not actively taken, the disease may develop into joint deformity or disability, which seriously affects the daily life of patients [2]. At present, corticosteroids and other hormonal drugs are often used in the clinical treatment of knee osteoarthritis, but these drugs bring more adverse reactions to patients [3]. Moreover, etocoxib is a non-steroidal anti-inflammatory drug, which has good anti-inflammatory, analgesic and antipyretic effects [4]. Besides, Qufeng Zhitong capsule is a Chinese patent medicine that can dispel wind, relieve pain and strengthen muscles and bones and it is suitable for osteoarthritis caused by wind-cold-damp arthralgia [5]. However, the combined treatment of etocoxib and Qufeng Zhitong capsules for arthritis has not been reported. Therefore, this study mainly explored the therapeutic effect of etocoxib combined with Qufeng Zhitong capsules for knee osteoarthritis.

Data and methods

General Information

A total of 112 patients with knee osteoarthritis admitted to our hospital from April 2019 to January 2022 were selected and randomly divided into observation group (n=56) and control group (n=56). There were no significant differences in gender, age, mean age, course of disease, mean course of disease, affected side and Kallgren-Lawrence grade between the two groups (P>0.05), as shown in Table 1. The study was approved by the Medical Ethics Committee, and the patients were informed and consented.

Table 1 Comparison of general data of patients between the two groups

Group		The control group (n=56)	The observation group (n=56)	χ^2/Z/t	P
Gender (case)	Male	35	30	0.917	0.338
	Female	21	26		
Age (years old)		51.95 ±10.08	51.56 ± 9.67	0.197	0.844
Course of disease		4.07 ± 0.82	3.97 ± 0.92	0.607	0.545
Affected side	One knee	33	35	0.150	0.699
	knees	23	21		
Kallgren-Lawrence grade (case)	Grade Ⅰ	13	16		
	Grade Ⅱ	19	19	-0.698	0.485
	Grade Ⅲ	24	21		

Inclusion Criteria

(1) The symptoms of patients met the diagnostic criteria of treatment of knee osteoarthritis [6]. (2) The patient's hematuria routine was normal. (3) The electrocardiogram of patients was basically normal. (4) The morning stiffness time of patients was less than 30 minutes (min). (5) The data of patients were complete, and there was no history of drug allergy.

Exclusion criteria

(1) Patients with joint stenosis, osteoporosis, rheumatoid diseases and other bone diseases. (2) Patients who had suffered from fracture in the affected area in the past. (3) Patients with severe brain, liver, kidney and other important organ dysfunction. (4) Patients who were allergic to Qufeng Zhitong capsules and the etocoxib tablets. (5) Patients complicated with malignant tumor and mental system diseases. (6) Pregnant and lactating women. (7) Patients with severe joint deformity in the late stage, labor loss, disability or mental illness. (8) Patients who participated in other clinical researchers.

Treatment Methods

Patients in the control group were treated with etocoxib tablets 60 mg/once a day, which came from Hangzhou MSD Pharmaceutical Co., LTD (approval number of National Medical Products Administration: J20180059, specification: 0.12g*5s). On the basis of the control group, patients in observation group were orally given Qufeng Zhitong capsuless (1.8g/time, 2 times/d) that came from Shaanxi Buchang Pharmaceutical Co., LTD (approval number of National Medical Products Administration: Z10970038, specification: 0.3g*18*3plates). Besides, patients in the two groups were treated for 8 weeks.

Testing Indicators

(1) Western Ontario and McMaster Universities (WOMAC) score: after 8 weeks of treatment, the knee joint function was evaluated by WOMAC scale that mainly included pain, stiffness and dysfunction, with a total of 24 items. The higher the score, the more severe the patient's symptoms. (2) Serum inflammation index measurement: before and after treatment, 4-6 mL fasting venous blood was taken from the patients in the morning, which was centrifuged at 1000×g for 10 min, and the upper fluid was collected after static treatment. Subsequently, the levels of tumour necrosis factor alpha (TNF-α), interleukin (IL)-1β and matrix metalloproteinase-3 (MMP-3) were determined by enzyme-linked immunosorbent assay. (3) Observation of adverse reactions: patients' adverse reactions, including dizziness, nausea, fatigue and heartburn, were recorded in the two groups during the treatment. (4) Comparison of gait characteristics: hongtaisheng GAITviewAFA-50 gait analyzer was used to measure the gait (step speed and step length) of patients before and after treatment.

Statistical Methods

SPSS 20.0 was used for statistical analysis, the counting data were compared by χ^2 test, and the measurement data were expressed by mean ± standard deviation（$\bar{x}\pm s$）. Besides, independent sample *t* test was used for comparison between the two groups, and paired sample *t* test was used for comparison at different time points in the same group. Moreover, *P*-values less than 0.05 were deemed as statistically significance.

Results

Comparison on WOMAC score for knee joint of patients between the two groups

The indicators (pain, stiffness and dysfunction) in the WOMAC scale were evaluated before and after treatment in the two groups. The results showed that after treatment, the WOMAC score for knee joint of patients in the two groups was prominently declined, and the WOMAC score of knee join in observation group was clearly lower than that in control group (P<0.05), as shown in Table 2.

Table 2 Comparison on WOMAC score for knee joint of patients between the two groups（$\bar{x}\pm s$, n=56）

Group	Pain (score)		Stiffness (score)		Dysfunction (score)		Total score	
	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Control group	21.06±6.17	17.97±2.84***	6.26±2.07	5.19±1.82**	55.29±9.25	39.97±9.01***	82.61±11.51	63.13±9.24***
Observation group	20.95±6.06	11.46±2.79***	6.28±2.12	3.45±1.74***	55.24±9.21	29.94±8.89***	82.47±11.29	44.85±9.67***
t	0.095	12.240	0.051	5.171	0.029	5.930	0.065	10.230
P	0.924	<0.001	0.960	<0.001	0.978	<0.001	0.948	<0.001

Note: compared with the data before treatment in the same group: $^{*}P$<0.05, $^{**}P$<0.01, $^{***}P$<0.001.

Comparisons of gait characteristics between the two groups before and after treatment

After treatment, the step length and step speed of patients in the two groups were notably increased, and the step length and step speed of patients in observation group were obviously higher than those in control group (P<0.05), as described in Table 3.

Comparisons of inflammatory factors between the two groups

After treatment, the TNF-α, IL-1β and MMP-3 levels of patients in the two groups were markedly decreased, and the levels of TNF-α, IL-1β and MMP-3 in observation group were obviously lower than those in control group (P<0.05), as listed in Table 4.

Table 3 Comparisons of step speed and step length between the two groups before and after treatment（$\bar{x}\pm s$, n=56）

Group	Step speed (cm/s)		Step length (cm)	
	Before treatment	After treatment	Before treatment	After treatment
Control group	87.96±9.72	95.12±10.96***	51.13±3.27	54.45±4.12***
Observation group	87.25±9.38	106.69±13.82***	50.96±3.15	58.08±5.29***
t	0.393	4.909	0.280	10.230
P	0.695	<0.001	0.780	<0.001

Note: compared with the data before treatment in the same group: *P<0.05, **P<0.01, ***P<0.001.

Table 4 Comparisons on TNF-α, IL-1β and MMP-3 levels between the two groups before and after treatment（$\bar{x}\pm s$, n=56）

Group	TNF-α (pg/mL)		IL-1β (pg/mL)		MMP-3 (μg/L)	
	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Control group	86.15±15.23	46.34±9.08***	12.45±3.18	8.87±2.11***	325.22±84.87	211.32±56.79***
Observation group	85.82±15.35	29.97±9.13***	12.89±3.12	6.17±1.95***	327.86±83.37	150.22±47.25***
t	0.114	9.514	0.739	7.033	0.166	6.189
P	0.909	<0.001	0.461	<0.001	0.868	<0.001

Note: compared with the data before treatment in the same group: *P<0.05, **P<0.01, ***P<0.001.

Comparisons of adverse reactions between the two groups

In the control group, there were 2 cases of dizziness and 4 cases of nausea, and the incidence of adverse reactions was 10.71%. In the observation group, there were 2 cases of fatigue, 1 case of dizziness, 3 cases of nausea and 1 case of heartburn, and the rate of adverse reactions was 12.5%. There was no significant difference in the incidence of adverse reactions between the two groups (P>0.05).

Discussion

The clinical symptoms of osteoarthritis mainly include knee pain, swelling, degeneration, and limited movement. If patients were not treated in time, the joint function of patients will be damaged and the patients' quality of daily life will be affected. Traditionally, Western medicine is often used for the treatment of knee osteoarthritis, with oral drugs such as salicylic acid, aspirin and indomethacin, or injection drugs such as sodium hyaluronate intracavitary injection as the mainstream [7-10]. However, due to the high cost of treatment and adverse reactions including gastrointestinal reactions, liver and kidney toxicity and other factors, Western medicine treatment is limited to some extent. In this study, etocoxib, a kind of Western medicine, was selected to treat knee osteoarthritis, which could reduce the secretion of cyclooxygenase, thromboxane and prostaglandin, thus playing a powerful anti-inflammatory and analgesic role. Compared with traditional non-steroidal anti-inflammatory drugs, etocoxib has higher safety as well as tolerance and lower adverse reactions. It is found that etocoxib tablets can be combined with other Western medicines or traditional Chinese medicines to improve the clinical efficacy of patients with knee osteoarthritis.

Qufeng Zhitong capsule is composed of seven kinds of traditional Chinese medicines: radix angelicae pubescentis, flos carthami, radix dipsaci, radix aconiti kusnezoffii preparata, mistletoe, herba geranii, and radix clematidis. It has the effects of dispelling wind and removing dampness, dredging channels and activating collaterals, nourishing liver and kidney, and strengthening tendons and bones, which targets at the pathogenesis of knee osteoarthritis. A previous study has shown that Qufeng Zhitong capsules combined with etocoxib tablets can improve the clinical efficacy of patients with knee osteoarthritis, and reduce the morning stiffness time, NRS score and inflammatory response of patients [11]. In this study, we also chose Qufeng Zhitong capsules combined with etocoxib tablets to explore the effect of this combination on the curative effect, gait characteristics and inflammatory factors of patients with knee osteoarthritis. First of all, we used WOMAC scale to evaluate the joint pain, stiffness and dysfunction of patients, and the results showed that the scores of WOMAC scale of patients treated with combination therapy were apparently lower than those of patients treated with etocoxib tablets alone. In addition, it was found that the step speed and step length of patients with combined therapy were notably higher than those of patients treated with etocoxib tablets alone. According to the research, Qufeng Zhitong capsules combined with etocoxib tablets can obviously improve the pace and step length of patients with knee osteoarthritis compared with the impact of etocoxib tablets alone [12], which indicated that Qufeng Zhitong capsules can improve the therapeutic effect of Western medicine.

Similar to the research of Mingqi Chen, we found that the combined treatment of Qufeng Zhitong capsules and etocoxib tablets can obviously improve the inflammatory response of patients [13]. Qufeng Zhitong capsules combined with etocoxib tablets obviously reduced the levels of inflammatory factors (TNF-α, IL-1β and MMP-3), as compared with etocoxib tablets alone.. Serving as an important inflammatory mediator in human body, TNF-α can also degrade cartilage matrix, and the increased secretion of TNF-α is able to lead to the proliferation of synovial fiber cells to promote cartilage degradation, resulting in the destruction of edge bone [14]. Moreover, IL-1β is a key pro-inflammatory factor, which can promote cartilage matrix degradation and induce cartilage destruction [15]. Besides, MMP-3 has the ability to promote the degradation of articular cartilage matrix, destroy the synthesis of collagen II and collagen III of cartilage, and then lead to the destruction of cartilage [14]. Therefore, the decrease of TNF-α, IL-1β and MMP-3 levels in patients with knee osteoarthritis indicated the improvement of the disease, which manifested that the combined treatment of Qufeng Zhitong capsules and etocoxib tablets could improve the inflammatory response of patients. In addition, after treatment, in the combination group, two patients had fatigue, one patient had dizziness, three patients had nausea, and one patient had heartburn. Although the adverse reaction rate in the combination group was not statistically significant compared with that in the

etocoxib group, the number of cases was relatively small, which showed that Qufeng Zhitong capsules supplemented with etocoxib tablets in treating knee osteoarthritis had less adverse reactions to patients.

Generally speaking, Qufeng Zhitong capsules supplemented with etocoxib tablets could improve the clinical symptoms of patients with knee osteoarthritis, promote the pace and step length, and reduce the inflammatory response of patients, and the medication is safer.

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Declaration of conflict-of-interest

The authors declare no conflict-of-interest.

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