



Pisco Med Publishing

Clinical Study of Compound Duzhong Jianggu Granules Combined with Glucosamine Sulfate in the Treatment of Knee Osteoarthritis

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Abstract: Objective: To investigate the clinical effects of a compound Du Zhong Jianggu granules combined with glucosamine sulfate capsules in the treatment of knee osteoarthritis. **Methods:** A total of 104 patients with knee osteoarthritis who visited and were hospitalized in the hospital between January 2020 and March 2020 were selected and randomly divided into two groups of 52 patients: the control group patients received oral glucosamine sulfate capsules, 2 capsules / time, 3 times / D on a daily basis. Patients in the study group received compound Du Zhong Jianggu granules at 12 g / time for 3 times / D daily on the basis of oral glucosamine sulfate capsule therapy. After the two groups were consecutively treated for 6 weeks, the clinical outcomes of patients in the two groups were observed and compared, and the serological parameters including: Serum Hypersensitivity C-Reactive Protein (hs CRP), cyclooxygenase-2 (COX-2), cartilage oligomeric matrix protein (COMP) and matrix metalloproteinase-3 (MMP-3) were collected before and after treatment, respectively, and the above data were collected and compared. the above data were collected and subjected to comparative analysis. The visual analog scale (VAS) scores and Lysholm knee scores before and after treatment in the two groups were collected for comparative analysis. **Results:** After 6 weeks of treatment, the therapeutic response rate of the control group was 80.77%, which was significantly lower than that of the study group (94.23%, $P < 0.05$). The levels of hs CRP, COX-2, comp, and MMP-3 were significantly lower in both groups, and the values of the same groups were significantly different before and after treatment ($P < 0.05$, $P < 0.05$), both of which were significantly lower than the control group ($P < 0.05$). After treatment, the VAS scores of both groups were significantly lower, but the Lysholm scores were significantly higher ($P < 0.05$). After completion of the 6-week treatment, the Lysholm scores of the study group were higher than those of the control group, and the VAS scores were significantly lower than those of the control group ($P < 0.05$). **Conclusion:** The compound Du Zhong Jianggu granules combined with glucosamine sulfate capsules can achieve good efficacy in the treatment of knee osteoarthritis, and this method has better clinical efficacy than glucosamine sulfate capsules alone.

Keywords: Compound Duzhong Jianggu Granules; Glucosamine Sulfate; Knee Osteoarthritis; Hs CRP; COX-2; COMP; MMP-3

Introduction

Knee OA is a degenerative and structurally disordered condition of cartilage in the knee that results from long-term physical activity performed by affected individuals, which subsequently leads to joint wear and destruction, cartilage denudation, osteoproliferation, and even deformity, ultimately leading to functional disability of the knee. 1 the main clinical manifestations of OA are: tenderness and swelling of the knee, with effusion in the knee, and during knee activity

Rhabdomyolysis or soreness cause distress to the daily work and life of patients, greatly affecting the quality of life of the patients. Currently, for knee osteoarthritis disease, the clinical treatment is mainly based on glucosamine sulfate capsules as the first-line drug, with significant clinical effects.^[1] In recent years, domestic scholars have widely adopted traditional Chinese medicine (TCM) pathways combined with glucosamine sulfate capsules for the treatment of knee OA, including TCM moxibustion, resazurin, needle knife, and traditional Chinese medicine preparation, etc., and clinical investigations have shown that the clinical effect of treating patients with TCM preparation assisted by glucosamine sulfate capsules is higher than that of using sulfate based glucose capsules alone^[2]. The compound Du Zhong Jianggu granule is a commonly used traditional Chinese medicine (TCM) formulation in clinical practice, which is mainly used to treat disorders such as knee dysfunction and swelling pain caused by knee osteoarthritis, and it has the efficacy of tonifying liver and kidney, relieving collaterals, and supplementing blood flexor tendons.

1. Data and methods

1.1 Patient data

All 104 patients enrolled in the study were patients with knee OA who visited the hospital and were hospitalized between February 2020 and April 2020, and all 104 met the disease diagnostic criteria for knee OA^[3]. The control group consisted of 27 males and 25 females; age range 47-65 years, mean (54.63 ± 5.22) years; disease duration 1-6 years, mean (3.78 ± 0.64) Years; were graded using radiographic grading criteria: 19 knees in patients with grade I, 28 knees in patients with grade II, and 23 knees in patients with grade III. In the study group, there were 29 males and 23 females; age, 46-68 years [mean (57.14 ± 6.22)] years; disease duration, 1-7 years [mean (4.27 ± 0.83) Years; graded by radiographic grading scale: 24 knees in patients with grade I, 30 knees in patients with grade II, and 22 knees in patients with grade III). There was no significant difference between the two patient data groups ($P > 0.05$).

1.2 Inclusion and exclusion criteria

Inclusion criteria: (1) the diagnosis of knee osteoarthritis was clear and met the diagnostic criteria; (2) He has not taken relevant drugs or received physical therapy and local surgery of knee joint in recent two months; (3) The clinical data are perfect.

Exclusion criteria: (1) combined with other knee diseases, such as osteoporosis, psoriatic arthritis, bone tumor and so on; (2) There are severe liver and kidney insufficiency, autoimmune diseases, cardiovascular diseases, etc.; (3) Allergic to compound Duzhong Jiangu granule or glucosamine sulfate capsule; (4) Pregnant and lactating women; (5) Mental cognitive abnormalities. All the above subjects had informed consent and signed the informed consent form.

1.3 Therapeutic drugs

Both groups were treated with glucosamine sulfate capsules (produced in Zhejiang Hisun Pharmaceutical Co., Ltd., specification 0.314g/pellet), 2 pellets / time, 3 times /.

The study group was treated with compound Du Zhong Jianggu granules punch (generously provided by Huarun ChangShi Pharmaceutical Co., Ltd., specification 12g / bag.), 12g / time, 3 times / d.

Patients in both groups continued treatment for 6 weeks with unscheduled patient follow-up visits occurring 1-6 months after treatment.

1.4 Efficacy evaluation criteria^[4]

Remarkable effect: symptoms such as knee pain, tenderness, morning stiffness, knee stiffness and unfavorable knee flexion and extension basically disappeared; Effective: the knee movement has been significantly improved, but there is still a slight sense of pain and stiffness; Ineffective: knee tenderness and morning stiffness are obvious, and the range of motion of knee joint has not been significantly improved, which seriously affects normal life. Effective rate = (markedly effective + effective) / total number of cases.

1.5 Observation indicators

1.5.1 Serological

Take 5ml of blood from an antecubital vein was drawn in the fasting state from the patient in the early morning before treatment and after the end of 6 weeks of treatment, respectively, and serum from the upper layer was collected for further use after centrifugation and the levels of serum hs-CRP, COX-2,COMP, and MMP-3 were measured as described previously.

1.5.2 VAS and Lysholm knee scores were compared

1.5.2 Comparison of visual analogue score and Lysholm knee score

The VAS^[5] was used to score the pain degree of the two groups before and after treatment. The VAS score was 0 ~ 10 points: 0 ~ 2 points were excellent, 3 ~ 5 points were good, 6 ~ 8 points were fair, and more than 8 points were poor. The lower the score, the less obvious the pain. Lysholm knee score scale^[6] was used to evaluate the recovery of knee function, including support, claudication, noose, pain, dyskinesia, joint instability, swelling and other aspects. The score was 0 ~ 100. The higher the score, the better the recovery of knee function.

1.6 Observation of adverse reactions

The gastrointestinal symptoms and allergies such as nausea and vomiting during treatment were recorded.

1.7 Statistical treatment

Spss26.0 software was used for data statistics and analysis. The measurement data were expressed as mean ± standard deviation (). The data were compared by t-test, and the efficiency was compared by χ^2 test. $P < 0.05$ was regarded as the difference between the groups, which was statistically significant.

2. Results

2.1 Comparison of clinical efficacy between the two groups

After 6 weeks of treatment, 10 cases in the control group were ineffective, 17 cases were effective and 25 cases were markedly effective. The total effective rate was 80.77%; In the study group, 3 cases were ineffective, 21 cases were effective and 28 cases were markedly effective. The total effective rate was 94.23%. There was significant difference in the total effective rate between the two groups ($P < 0.05$). See Table 1.

Table 1 Comparison of clinical efficacy between the two groups [n (%)]

group	n/case	Invalid / case	Effective / case	Remarkable effect / case	Total effective rate/%
control group	52	10	17	25	43(80.77)
Research Group	52	3	21	28	49(94.23)
χ^2					4.308
P					0.038

2.2 Comparison of serological indexes between the two groups

After 6 weeks of treatment, the levels of hs CRP, COX-2, comp and MMP-3 in the two groups were significantly lower than those in the same group before and after treatment ($P < 0.05$). After treatment, the serological indexes of the study patients were significantly lower than those of the control group, and the difference was statistically significant ($P < 0.05$). See Table 2.

Table 2 Comparison of serological indexes between the two groups before and after treatment ($\bar{x} \pm s$)

	control group (52)		Research Group (52)		<i>t/P</i> 值 (Between groups after treatment)
	Before treatment	After treatment	Before treatment	After treatment	
hs-CRP/(mg·L ⁻¹)	14.12±1.41	8.22±1.35	14.02±1.38	6.56±1.32	6.154/0.000
COX-2/(ng·L ⁻¹)	721.25±28.2	440.65±13.1	722.56±27.5	318.57±12.8	47.806/0.000
COMP/(μg·L ⁻¹)	4.63±0.38	2.43±0.19	4.61±0.41	1.11±0.14	40.332/0.000
MMP-3/(ng·L ⁻¹)	26.78±5.32	15.86±3.18	26.54±5.42	11.27±3.29	7.234/0.000

2.3 Comparison of visual analog score and Lysholm knee score

After 6 weeks of treatment, the VAS score of the two groups decreased significantly, while the Lysholm score increased significantly. The difference between the same group before and after treatment was statistically significant ($P < 0.05$). After treatment, the VAS score of the study group was significantly lower than that of the control group, while the Lysholm score was significantly higher than that of the control group ($P < 0.05$). See Table 3.

Table 3 Comparison of VAS score and Lysholm knee score ($\bar{x} \pm s$)

	Control Group (52)		Research Group (52)		<i>t/P</i> (Between groups after treatment)
	Before treatment	After treatment	Before treatment	After treatment	
VAS	8.12±2.41	6.24±1.17	8.27±1.95	3.84±1.52	9.023/0.000
Lysholm	29.85±5.49	64.23±5.32	30.18±4.84	81.07±5.74	15.516/0.000

2.4 Comparison of adverse reaction rates between the two groups

There were no drug-related adverse reactions in both groups during treatment.

Discussion

Knee osteoarthritis is common in middle-aged and elderly patients. It is a common disease in clinic. The main clinical manifestations are knee swelling and pain, limited activity and morning stiffness. Some patients have joint bounce and effusion. If not properly treated, it is very easy to cause joint deformity and even disability. The main component of glucosamine sulfate capsule is glucosamine sulfate, which is an amino-monosaccharide existing in articular cartilage. After taking glucosamine sulfate capsule, patients will increase the plasma concentration of glucosamine and proteoglycan^[7], so as to protect and repair the cartilage matrix and reduce the stenosis of joint space. It can stimulate articular chondrocytes to form proteoglycan, stabilize cell membrane, and inhibit the production of oxygen free radicals, so as to play an anti-inflammatory role and inhibit cartilage injury, so as to relieve pain and improve the condition^[8]. Compound Duzhong Jiangu granule is a traditional Chinese medicine preparation made of *Eucommia ulmoides*, *Radix Paeoniae Alba*, *Dipsacus Dipsacus*, *astragalus*, *wolfberry fruit*, *Achyranthes bidentata*, *Panax notoginseng*, *Caulis Spatholobi*, *ginseng*, *Angelica sinensis*, *Cortex Phellodendri*, *Clematis* and other traditional Chinese medicines. It is mainly used to treat knee swelling, pain, knee dysfunction and other symptoms caused by knee osteoarthritis. It can nourish liver and kidney, blood and soften tendons the effect of dredging collaterals and relieving pain.

In this study, after 6 weeks of treatment, the effective rates of the two groups were 94.23% in the study group and 80.77% in the control group; In addition, after treatment, the VAS score of the two groups decreased significantly, while the Lysholm score increased significantly, suggesting that compound Duzhong Jiangu granule combined with glucosamine sulfate capsule in the treatment of knee osteoarthritis can significantly improve the degree of pain and joint function. After treatment, the expressions of serum hs CRP, COX-2, comp and MMP-3 decreased significantly in the two groups, especially in the study group. It shows that compound Duzhong Jiangu granule combined with glucosamine sulfate capsule can obtain good curative effect in the treatment of knee osteoarthritis.

In conclusion, compound Duzhong Jiangu granule combined with glucosamine sulfate capsule has good clinical efficacy and high safety in the treatment of knee osteoarthritis. It can significantly alleviate knee pain and improve knee activity, and has good clinical application value.

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