Original Article

Effect of Glucosamine Hydrochloride Combined with Celecoxib on Inflammatory Response and Bone Metabolism in Patients with Knee Osteoarthritis

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Abstract

Background: Knee osteoarthritis is one of the common chronic degenerative joint diseases. The present study explored the efficacy of glucosamine hydrochloride combined with celecoxib in the treatment of knee osteoarthritis and its effect on inflammatory response and bone metabolism. **Material and Methods:** Ninety patients with knee osteoarthritis were randomly divided into the single treatment group and the combined treatment group, which received the treatment using single glucosamine hydrochloride and glucosamine hydrochloride combined with celecoxib for three months, respectively. **Results:** After treatment, compared with the single treatment group, in the combined treatment group the total effective rate was increased, the Visual Analogue Scale score was decreased, the Lysholm score was increased, the serum tumor necrosis factor-α, interleukin 6 and interleukin 1β levels were decreased, the serum β-C-telopeptides of type I collagen level was decreased, and the serum bone-specific alkaline phosphatase and osteocalcin levels were increased. The incidence of adverse reactions during treatment had no significant difference between two groups. **Conclusions:** Glucosamine hydrochloride combined with celecoxib has a good therapeutic efficacy for patients with knee osteoarthritis, and it can improve the bone metabolism and reduce the inflammatory response in patients.

Keywords: *Bone metabolism, celecoxib, glucosamine hydrochloride, inflammatory, knee osteoarthritis*

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Introduction

Knee osteoarthritis is one of the common chronic joint diseases. The main pathological manifestations of knee osteoarthritis are the articular cartilage destruction and bone hyperplasia. The incidence of knee osteoarthritis is high in the middle-aged and elderly population.[1] The patients of knee osteoarthritis may clinically present the symptoms such as joint pain, limited joint mobility, and joint swelling.[2] With the progress to the late stage, the knee osteoarthritis can cause the joint deformation or dysfunction, which seriously affects the normal work and life of patients.[3] The use of non-steroidal anti-inflammatory drugs, physical therapy, and intra-articular drug injection are the common methods for treatment of knee osteoarthritis.[1] These measures can alleviate the symptoms to a certain extent and delay the disease progression. However, if used for a long time, they will aggravate the patient's cartilage damage and gastrointestinal reactions, so the overall treatment effect is limited. Glucosamine hydrochloride is a commonly used drug for the treatment of knee osteoarthritis, which can promote the repair and reconstruction of chondrocytes, thus relieving the symptoms of joint pain, swelling and movement limitation caused by osteoarthritis. It protects the cartilage by stabilizing the cell membrane and intracellular collagen, and is not damaged by

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destructive enzymes.[4,5] Celecoxib is a cyclooxygenase-2 inhibitor that selectively inhibits the cyclooxygenase-2 activity and prevents the secretion of prostaglandin E2.[6] Celecoxib has significant anti-inflammatory and analgesic effects.[7,8] The aim of this study is to explore the efficacy of glucosamine hydrochloride combined with celecoxib in the treatment of knee osteoarthritis and its effect on inflammatory response and bone metabolism, for providing a clinical reference for the further application of this treatment strategy.

Patients and Methods

General information

Ninety patients with knee osteoarthritis admitted to our hospital from September 2021 to September 2023 were selected as the study subjects. They were randomly divided into the single treatment group and the combined treatment group, with 45 cases in each group. In the single treatment group, there were 28 males and 17 females. The age of patients ranged from 40 to 77 years, with average of 55.27 ± 6.10 years. The course of disease was 1-9 years, with average of 6.21 ± 1.44 years. There were 17 cases with lesion in left side and 28 cases with lesion in right side. In the combined treatment group, there were 24 males and 21 females. The age of patients ranged from 43 to 77 years, with average of 54.11 ± 7.29 years. The course of disease was 2-7 years, with average of 5.77 ± 1.23 years. There were 14 cases with lesion in left side and 31 cases with lesion in right side. There was no significant difference in general data between patients in two groups ($P > 0.05$). This study was approved by the ethics committee of Hospital of the 75th Group Army on 21 July, 2021.

Inclusion and exclusion criteria

Inclusion criteria were as follows: (1) the patients met the diagnostic criteria of knee osteoarthritis; (2) the knee osteoarthritis occurred on one side; (3) the patients had complete clinical data. Exclusion criteria were as follows: (1) the patients had severe abnormality in important organs; (2) the patients with knee joint deformities, bony ankylosis or joint cavity effusion; (3) the patients had malignant tumors or systemic immune system diseases; (4) the patients were undergoing the knee joint surgery; (5) the patients had mental abnormalities; (6) the patients were allergic to the drugs used in this study.

Treatment methods

Patients in the single treatment group were orally administered with glucosamine hydrochloride capsules (Zhejiang Chengyi Pharmaceutical Co., Ltd., Wenzhou, China) with dose of 750 mg, twice per day. The patients in the combined treatment group were orally administered glucosamine hydrochloride capsules (Zhejiang Chengyi Pharmaceutical Co., Ltd., Wenzhou, China) with a dose of 750 mg and celecoxib capsules (Jiangsu Chiatal Qingjiang Pharmaceutical Co., Ltd., Huaian, China) with a dose of 200 mg, twice per day. Both groups had a treatment period of three months.

Evaluation of clinical efficacy

At the end of treatment, the clinical efficacy of treatment was evaluated as follows: remarkably effect: the joint function was significantly improved, the joint pain had basically disappeared, and the clinical symptoms had disappeared; effective: the joint function, joint pain and clinical symptoms were all improved; ineffective: the joint function, joint pain and clinical symptoms were not improved. The total effective rate was calculated as follows: total effective rate (%) = [(number of remarkably effective cases + number of effective cases)/total case number] ×100%.

Pain scoring

Before and after treatment, the joint pain of patients was evaluated using Visual Analog Scale (VAS). The VAS score was 0-10 points. The 0 points presented no pain, and the 10 points presented the highest level of pain.

Knee joint function scoring

Before and after treatment, the knee joint function of patients was evaluated using the Lysholm Knee Scale. The Lysholm score was 0-100 points. The 0 point presented the worst knee joint function, and the 100 points presented the best knee joint function.

Determination of blood indexes

Before and after treatment, the venous blood was collected from the patients. The inflammatory factors including tumor necrosis factor-α (TNF-α), interleukin 6 (IL-6) and interleukin 1β (IL-1β) and bone metabolism indexes including β-C-telopeptides of type I collagen (β-CTX), bone-specific alkaline phosphatase (BALP) and Osteocalcin were determined using enzyme-linked immunosorbent assay. The determination operations followed the instructions of kits and instruments.

Observation of adverse reactions

During the treatment, the adverse reactions such as dizziness, nausea/vomiting, diarrhea and constipation in two groups were observed, and the incidence of adverse reactions was calculated. In addition, the renal function indexes of patients during the treatment were monitored.

Statistical analysis

SPSS 22.0 was adopted for the statistical analysis. The measurement variables (mean ± standard deviation) and enumeration variables (number or rate) between two groups were compared by using *t* test and

Chi-square test, respectively. $P < 0.05$ was considered as significantly different.

Results

Clinical efficacy

After three months of treatment, in the single treatment group, there were 20, 15 and 10 patients obtaining the remarkably effective, effective and ineffective treatment efficacy, respectively, with a total effective rate of 77.77%. In the combined treatment group, there were 24, 18 and 3 patients obtaining the remarkably effective, effective and ineffective treatment efficacy, respectively, with a total effective rate of 93.33%. The total effective rate had a significant difference between the two groups ($P < 0.05$) [Table 1].

VAS and Lysholm scores

Before treatment, there was no significant difference in VAS or Lysholm score between the two groups ($P > 0.05$). After treatment, compared with before treatment, in each group the VAS score was significantly decreased ($P < 0.05$), and the Lysholm score was significantly increased ($P < 0.05$). Compared with the single treatment group, in the combined treatment group the VAS score was further decreased ($P < 0.05$), and the Lysholm score was further increased ($P < 0.05$) [Table 2].

Inflammatory response indexes

Before treatment, there was no significant difference in serum inflammatory response indexes such as serum TNF-α, IL-6 or IL-1β levels between the two groups ($P > 0.05$). After treatment, each index in the two groups was significantly lower than before treatment, respectively ($P < 0.05$), and that in the combined treatment group was significantly lower than that in the single treatment group ($P < 0.05$) [Table 3].

Table 1: Clinical efficacy in two groups

Group	*n*	Remarkably effective (*n*)	Effective (*n*)	Ineffective (*n*)	Total effective rate (%)
Single treatment	45	20	15	10	77.77
Combined treatment	45	24	18	3	93.33
χ^2					4.406
P					0.036

Table 2: VAS and Lysholm scores in two groups (*n*=45)

Index	Group	Before treatment	After treatment	*t*	*P*
VAS	Single treatment	7.21±1.56	4.88±0.88	8.727	0.000
	Combined treatment	7.11±1.32	3.04±0.56	18.994	0.000
	t	0.361	11.833		
	P	0.719	0.000		
Lysholm	Single treatment	60.34±21.37	72.06±16.37	2.921	0.004
	Combined treatment	62.62±18.22	81.21±19.28	4.701	0.000
	t	0.545	2.427		
	P	0.587	0.017		

VAS, Visual Analog Scale

Table 3: Inflammatory response indexes in two groups (*n*=45)

Index	Group	Before treatment	After treatment	*t*	*P*
TNF-α (ng/ml)	Single treatment	97.73±20.27	62.43±14.73	9.450	0.000
	Combined treatment	96.18±21.32	56.29±12.38	10.854	0.000
	t	0.353	2.141		
	P	0.725	0.035	9.450	0.000
IL-6 (pg/ml)	Single treatment	536.52±123.68	420.05±69.44	5.508	0.000
	Combined treatment	516.66±156.14	382.31±75.31	5.199	0.000
	t	0.669	2.472		
	P	0.505	0.015		
IL-1β (pg/ml)	Single treatment	166.29±34.52	78.62±21.94	14.384	0.000
	Combined treatment	158.31±32.72	66.36±16.68	16.793	0.000
	t	1.127	2.984		
	P	0.263	0.004		

TNF-α, tumor necrosis factor-α; IL-6, interleukin 6; IL-1β, interleukin 1β

Table 4: Bone metabolism indexes in two groups (*n*=45)

Index	Group	Before treatment	After treatment	*t*	*P*
β-CTX (pg/ml)	Single treatment	0.93±0.21	0.62±0.12	8.598	0.000
	Combined treatment	0.89±0.18	0.55±0.08	11.579	0.000
	t	0.970	3.256		
	P	0.335	0.002		
BALP (U/L)	Single treatment	41.28±7.95	56.19±9.32	8.165	0.000
	Combined treatment	39.36±6.70	61.63±11.62	11.152	0.000
	t	1.239	2.452		
	P	0.219	0.016		
Osteocalcin (μg/L)	Single treatment	4.59±0.85	5.27±1.31	2.937	0.004
	Combined treatment	4.53±0.98	6.03±1.52	5.564	0.000
	t	0.310	2.549		
	P	0.757	0.013		

β-CTX, β-C-telopeptides of type I collagen; BALP, bone-specific alkaline phosphatase

Table 5: Adverse reactions in two groups

Group	*n*	Dizziness (*n*)	Nausea/vomiting (*n*)	Diarrhea (*n*)	Constipation (*n*)	Incidence (%)
Control	45	1	2	1	2	13.33
Study	45	2	3	1	3	20.00
χ^2						0.720
P						0.396

Bone metabolism indexes

Before treatment, the bone metabolism indexes showed no significant difference between two groups, respectively ($P > 0.05$). After treatment, compared with before treatment, in each group the serum β-CTX level was significantly decreased ($P < 0.05$), and the serum BALP and osteocalcin levels were significantly increased, respectively ($P < 0.05$). Compared with the single treatment group, in the combined treatment group the serum β-CTX level was further decreased ($P < 0.05$), and the serum BALP and osteocalcin levels were further increased, respectively ($P < 0.05$) [Table 4].

Adverse reactions

In the whole treatment, there were some adverse reactions such as dizziness, nausea/vomiting, diarrhea and constipation in the patients. The incidence of adverse reactions had no significant difference between the two groups ($P > 0.05$) [Table 5]. In addition, the renal function indexes had no obvious change in each group, indicating that both glucosamine hydrochloride and celecoxib had no obvious renal toxicity to the patients.

Discussion

Knee osteoarthritis is closely related to the factors such as endocrine disorders, long-term joint weight-bearing, and abnormal cartilage metabolism in patients, with the bone hyperplasia and joint swelling and pain as the main clinical features.[9] Knee osteoarthritis is not only a medical issue, but also a social issue that is increasingly attracting people's attention. It is particularly important to adopt timely and effective methods for treatment of knee osteoarthritis. Glucosamine is an amino monosaccharide that easily penetrates into proteoglycan molecules. It is extremely beneficial for proteoglycans, cations, and bound water, forming a mucinous elastic layer that has cushioning and lubricating effects.[10] In addition, glucosamine has good effect on the rehabilitation and metabolic function of joint chondrocytes, which can stimulate the production of proteoglycans by joint chondrocytes, and protect the morphology and structure of joint cartilage matrix.[11] Celecoxib is a specific inhibitor that can alleviate joint pain and is less likely to induce the adverse symptoms.[12] Celecoxib can also enhance the activity of superoxide dismutase, reduce the content of lipid peroxides, delay the cartilage degeneration, and promote the cartilage repair.[13] This study explored the efficacy of glucosamine hydrochloride combined with celecoxib in treatment of knee osteoarthritis. After three months of treatment, compared with the single treatment group, in the combined treatment group, the total effective rate was significantly increased, the VAS score was significantly decreased, and the Lysholm score was significantly increased. This indicates that, compared with the single use of glucosamine hydrochloride, the combination of glucosamine hydrochloride and celecoxib is more effective for treatment of knee osteoarthritis. In addition, during the treatment, the incidence of adverse reactions

had no significant difference between two groups, which suggesting the good safety of the combined treatment strategy.

TNF-α is a type of peptide hormone, and is mainly generated by the monocytes and macrophages. It can effectively the inhibit osteoblasts and has a stimulating effect on the osteoclasts.[14] In addition, TNF-α is an extremely strong inflammatory factor. It can promote the osteoblasts to form the osteoclast-activating factors, thereby inhibiting the formation of cartilage collagen and proteoglycans and preventing the formation of chondrocytes, which causes the rapid destruction of chondrocytes and damages the joint cartilage.[15] IL-6 and IL-1β are considered the amplification factors of inflammatory response, with a certain degree of multifunctionality. They mediate the key factors in cartilage damage, which can cause the chondrocytes to migrate, proliferate, and form the proteoglycans.[16] At the same time, they can induce an autoimmune response in cartilage, causing the progressive damage to joint cartilage.[17] The level of these inflammatory mediators is directly proportional to the incidence of inflammation.[18] The results of this study showed that, after treatment, the serum TNF-α, IL-6 and IL-1β levels in the combined treatment group were significantly lower than those in the single treatment group. This indicates that, compared with the single use of glucosamine hydrochloride, the combination of glucosamine hydrochloride and celecoxib can further reduce the inflammatory response, so further alleviate the knee osteoarthritis.

Bone metabolism is closely related to the onset of knee osteoarthritis. β-CTX is a bone resorption marker, and its concentration change is positively correlated with the joint swelling and pain in knee osteoarthritis.[19] BALP mainly comes from the osteoblasts, and its change can effectively reflect the activity of osteoblasts.[20] Osteocalcin is mainly synthesized and secreted by the hypertrophic chondrocytes, odontoblasts, and bone cells. When the bone resorption and formation are coupled, the osteocalcin can effectively reflect bone formation.[21] Our study found that, after treatment, compared with the single treatment group, in the combined treatment group the serum β-CTX level was further decreased, and the serum BALP and osteocalcin levels were further increased. This indicates that the combination of glucosamine hydrochloride and celecoxib can improve bone metabolism by increasing the β-CTX level and increasing the BALP and osteocalcin levels.

Conclusion

In conclusion, glucosamine hydrochloride combined with celecoxib has a good therapeutic efficacy on patients with knee osteoarthritis, and can improve the bone metabolism and reduce the inflammatory response in patients. This combined treatment strategy is better than the single use of glucosamine hydrochloride. However, the comparison between the single use of celecoxib and combined use of glucosamine hydrochloride and celecoxib has not been performed. This is a limitation of our study. In the next study, the efficacy and mechanism between single celecoxib and glucosamine hydrochloride combined with celecoxib should be performed for obtaining more findings.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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