A Randomized, Controlled Trial to Assess the Efficacy of Arthroscopic Debridement in Combination with Oral Medication Versus Oral Medication in Patients with Gouty Knee Arthritis

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Abstract Gouty knee arthritis refers to a form of inflammatory diseases caused by deposits of needle-like crystals of uric acid in knee joint. The aim of this study was to assess the efficacy and safety of arthroscopic debridement in combination with oral medication versus oral medication alone for the treatment of gouty knee arthritis. A total of 60 patients with gouty knee

arthritis were randomized to receive either arthroscopic surgery in combination with oral medication or oral medication alone. Efficacy was assessed with the angle of motion, functions, and visual analog scale (VAS). These indices were measured prior to treatment and at 2, 4, 12, 24, and 48 weeks posttreatment. Surgery- and medication-related complications were observed. Significant differences in flexion and extension of the knee joint, lymphoma scores, and VAS were detected between the two groups at 2, 4, and 12 weeks posttreatment ($P < 0.05$) but not at weeks 24 and 48 posttreatment ($P > 0.05$). Significant differences in these indices were detected at different time points in each group ($P < 0.05$), except between weeks 24 and 48 ($P > 0.05$). Arthroscopic surgery in combination with oral medication is superior to single oral medication in the flexion and extension of the knee joint, lymphoma scores, and pain relief (VAS) before 24 weeks, although no statistical differences were detected in the efficacy after 24 weeks, and in medication-related safety between the two groups. Although arthroscopic debridement cannot replace systemic uric acid-lowering treatments such as medication and dietary control, it is still an effective approach.

Keywords Randomized controlled trial · Gouty knee arthritis · Arthroscopic debridement

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Introduction

Gouty arthritis is a common medical condition generally occurring at night and mainly presents with inflammation and joint swelling, high skin temperature, and sharp pain [1]. It most commonly affects the first metatarsophalangeal joint, followed by the dorsum of the foot, and then the ankle, knee, wrist, and elbow joints in sequence [2, 3]. It can even induce

extreme disability, seriously affecting the quality of life [4, 5]. Previously, medication or open surgery has been the most frequently used approach to the treatment of gouty arthritis of the knee, but with some limitations [6, 7]. In our local hospitals, arthroscopic debridement in combination with post-operative dietary therapy and medication has obtained favorable results. In the current study, we assessed the efficacy and safety of arthroscopic debridement combined with oral medication versus oral medication alone in patients with gouty arthritis of the knee.

Methods

Study Population

All subjects were ≥ 18 years old, met the criteria for the diagnosis of gouty arthritis defined by the American College of Rheumatology [8], and experienced pain in at least one knee joint. Patients were excluded from the study if the knee joint pain resulted from rheumatoid arthritis, bursitis, infection, or trauma.

Trial Design

The current study is a prospective, stratified, randomized and controlled clinical study. All patients were selected from the First Hospital and the Second Hospital of Lanzhou University from March 2008 to March 2012. These patients were randomized to receive either surgery in combination with oral medication or single oral medication. The study was conducted according to the ethical guidelines of the Declaration of Helsinki and the Good Clinical Practice. The local ethical committee reviewed the protocol and granted approval before the study. All patients provided written informed consent.

Randomization, Concealment of Allocation, and Masking

The random data form-generated randomization schedule was prepared by an individual independent of the study team. This team did not participate in the implementation of the clinical trials and the evaluation of results. Another team was in charge of patient assignment (1:1 ratio) to oral medicine or oral medicine plus surgery. The observers were masked to treatment assignment throughout the period.

Interventions

Arthroscopic Procedures All procedures were conducted by two experienced surgeons who had conducted more than 500 arthroscopic surgeries. Patients were placed in a supine position. Lumbar anesthesia was preferred; otherwise, laryngeal mask-assisted general anesthesia was given. A pneumatic tourniquet

was placed over the upper thigh at a pressure of approximately 37.32 to 39.99 kPa. The surgery was finished within 90 min. Routine infrapatellar anteromedial and anterolateral approaches were used. First, the turbid transudate inside the joint was rinsed. The suprapatellar bursa, patella, fossae medial and lateral of the knee joint, femoral trochlea, condylus medialis and lateralis femoris, intercondylar fossa, anterior and posterior cruciate ligament, tibial plateau, and meniscus were then checked in sequence. If necessary, posteromedial and posterolateral approaches were also applied to check the posterior joint capsule. As far as possible, urate crystals in the cartilage, ligament, and meniscus were removed with a curette. However, compression was not applied for complete removal of crystals that were firmly attached to the cartilage surface to prevent injury. To protect the anterior and posterior cruciate ligaments and meniscus, deep synovectomy was avoided. Postsurgery, a catheter was routinely placed into the joint cavity to rinse the cavity for 3 to 5 days.

Routine postoperative management included pressure dressing of the knee joint with an elastic stocking for 24 h, continuous ice compression for 24 h, diseased limb elevation, and suitable early postoperative functional exercises such as quadriceps femoris contraction, straight leg raising, and ankle and metatarsophalangeal joint flexion and extension to alleviate the lower limb swelling and prevent thrombosis.

In both groups, gout suppressants were orally administered (on postoperative day 2 in the surgery group): colchicine 0.5–1.5 mg for 14 days [9], followed by allopurinol (0.1 g, tid) for 3 months, and sodium bicarbonate tablet (0.9 g, tid) for 3 months [10]. A strict diet plan was also emphasized based on the avoidance of animal offal and bean products and high water intake [11].

Clinical Interview and Outcomes

All subjects were followed up at weeks 2, 4, 12, and 48 weeks postsurgery by four clinicians with more than 10 years of experience of gout diagnosis.

Clinical indices are as follows:

- Range of motion—knee joint flexion: refers to the maximal angle of autonomic flexion of the knee joint.
- Range of motion—knee joint extension: refers to the maximal angle of autonomic extension of the knee joint.
- Lysholm scores [12]: defined by Lysholm and Gillquist in 1982 and have been commonly applied in clinical practice to assess the joint function, with a total score of 100.
- Visual analog scale (VAS) [13]: In this scale, the pain attitude was represented with 11 digits, 0 as no pain and 10 as maximal pain. The patient selected a digit to describe the level of their pain.
- Oral medication-related complications resulted from orally taken colchicine and allopurinol. Surgery-related

complications resulted from arthroscopic surgery. Once adverse events were observed, hepatic and renal function was analyzed, and routine blood tests were conducted. In cases where no abnormalities were detected and patients were able to tolerate the events, the treatment was continued with periodical monitoring. In cases where abnormalities were detected, the treatment was discontinued immediately, and the patient was withdrawn from the study.

Statistical Analysis

SPSS 13.0 was used for statistical analysis. Continuous data were expressed as the mean $\pm$ standard deviation. Data between the two groups were compared with the *t* test of independent samples. Data within groups were compared with repetitive measure analysis of variance. Categorical data were compared with the chi-square test. $P < 0.05$ was considered statistically different.

Results

General Data

No significant differences were detected between the two groups in terms of age ($t = -0.28$, $P > 0.05$), sex ($\chi^2 = 0.39$, $P > 0.05$), knee joint flexion ($t = 0.43$, $P > 0.05$) and extension ($t = -0.27$, $P > 0.05$), Lysholm score ($t = 0.50$, $P > 0.05$), and VAS ($t = 0.52$, $P > 0.05$) (Table 1).

Thirty patients were included in each group. Patients who underwent surgery in combination with oral medication had disease in a single knee joint (left, 18; right 12). Twenty patients were new cases of this medical condition and 18 had recurrent attacks, with three to six episodes per year lasting for 1 to 2 weeks on each occasion. The course of disease ranged from 24 h to 5 years. Serum uric acid levels were found to be normal in nine cases and increased in 21 patients (average, 475.67 ± 132.37 $\mu\text{mol/L}$). Twenty-nine patients treated with oral medication alone had disease in a single knee joint (left, 14; right, 15). Seventeen patients were new

cases of this medical condition and 15 had recurrent attacks, with four to six episodes per year, lasting for 2 weeks on each occasion. The disease course ranged from 24 h to 6 years. Serum uric acid levels were found to be normal in 11 cases and increased in 19 patients (average, 468.70 ± 122.78 $\mu\text{mol/L}$).

Flexion and Extension of the Knee joint, Lysholm Score, and VAS

The results of the intent-to-treat analysis (Table 2) were consistent with those of the per-protocol analysis (Table 3). Significant differences in flexion ($t_{2w} = 9.33$, $t_{4w} = 2.68$, $t_{12w} = 2.57$) (Fig. 1a) and extension of the knee joint ($t_{2w} = -11.87$, $t_{4w} = -7.83$, $t_{12w} = -3.52$) (Fig. 1b), Lysholm score ($t_{2w} = 39.76$, $t_{4w} = 13.09$, $t_{12w} = 4.06$) (Fig. 1c), and VAS ($t_{2w} = -16.92$, $t_{4w} = -18.73$, $t_{12w} = -27.25$) (Fig. 1d) were detected between the two groups at weeks 2, 4, and 12 ($P > 0.05$). However, no significant differences in flexion ($t_{24w} = -1.636$, $t_{48w} = -0.957$) and extension of the knee joint ($t_{24w} = -0.50$, $t_{48w} = -0.98$), Lysholm score ($t_{24w} = 1.52$, $t_{48w} = 1.38$), and VAS ($t_{24w} = 0.26$, $t_{48w} = 1.30$) were detected between the two groups at weeks 24 and 48 ($P > 0.05$).

Within each group, significant differences in the flexion of the knee joint (surgery plus oral medication: $F = 1,111.07$, $P < 0.05$; oral medication alone: $F = 725.80$, $P < 0.05$), extension of the knee joint (surgery plus oral medication: $F = 522.88$, $P < 0.05$; oral medication alone: $F = 521.27$, $P < 0.05$), Lysholm score (surgery plus oral medication: $F = 2,240.54$, $P < 0.05$; oral medication alone: $F = 2,795.38$, $P < 0.05$), and VAS (surgery plus oral medication: $F = 8,775.06$, $P < 0.05$; oral medication alone: $F = 1,468.24$, $P < 0.05$) were detected at two time points at least.

Least significant difference tests were used for multiple comparisons within each group. Results revealed significant differences in these indices at different time points in each group (pretreatment vs. posttreatment week 2; pretreatment vs. posttreatment week 4; pretreatment vs. posttreatment week 12; pretreatment vs. posttreatment week 24; pretreatment vs. posttreatment week 48; posttreatment week 2 vs. week 4; posttreatment week 2 vs. week 12; posttreatment week 2 vs. week 24; posttreatment week 2 vs. week 48; posttreatment week 4 vs. week 12; posttreatment week 4 vs. week 24; posttreatment week 4 vs. week 48; posttreatment week 12 vs. week 24; and posttreatment week 12 vs. week 48) (all $P < 0.05$, except between weeks 24 and 48 where $P > 0.05$).

Complications

Surgery-related complications occurred only in the arthroscopic debridement group. All incisions healed primarily without joint infection and nerve and blood vessel injuries. Joint hematoma was observed in two patients, which healed with aspiration and pressure dressing.

Table 1 Baseline demographic and clinical characteristics of the study patients

	Surgery + oral medication ($n = 30$)	Oral medication ($n = 30$)
General (mean, n (%))	28 (93.33)	26 (86.67)
Age (year, mean (SD))	42.00 (6.91)	42.57 (8.82)
Knee flexion (mean (SD))	92.60 (5.95)	91.97 (5.57)
Knee extensor (mean (SD))	25.03 (3.01)	25.23 (2.74)
Lysholm score (mean (SD))	45.77 (2.45)	45.47 (2.16)
VAS (mean (SD))	6.75 (0.18)	6.73 (0.17)

Table 2 Per-protocol analysis of the effectiveness of outcome indicators

Time	Knee flexion		Knee extensor		Lysholm score		VAS	
	Surgery + oral medication	Oral medication	Surgery + oral medication	Oral medication	Surgery + oral medication	Oral medication	Surgery + oral medication	Oral medication
Before	92.60±5.95	91.97±5.57	25.03±3.01	25.23±2.74	45.77±2.45	45.47±2.16	6.75±0.18	6.73±0.17
2 weeks	115.87±2.32**	105.93±5.35***	11.03±3.01**	17.30±2.00***	75.23±2.31**	57.03±0.96***	3.70±0.12**	4.34±0.17***
4 weeks	125.82±2.55***	122.85±5.35***	7.37±1.27***	10.53±1.81***	84.35±2.89***	76.65±1.43***	2.48±0.16***	3.33±0.19***
12 weeks	140.93±4.29***	137.90±4.83***	5.97±1.43***	7.07±0.94***	87.40±2.62***	84.60±2.72***	0.78±0.17***	1.99±0.18***
24 weeks	143.61±3.61***	145.04±4.20***	4.68±1.22***	5.00±1.39***	91.04±2.03***	89.08±2.63***	0.36±0.13***	0.37±0.18***
48 weeks	144.21±3.80***	144.85±4.19***	4.57±1.32***	4.85±1.79***	90.71±2.31***	90.11±3.14***	0.40±0.12***	0.36±0.15***

* $P<0.05$, statistically significant difference between the two groups; ** $P<0.05$, statistically significant difference between pretreatment and posttreatment groups; *** $P<0.05$, statistically significant difference between pretreatment and posttreatment groups at week 2; # $P<0.05$, statistically significant difference between pretreatment and posttreatment groups at week 4; ## $P<0.05$, statistically significant difference between pretreatment and posttreatment groups at week 12

Table 3 Intention-to-treat analysis of the effectiveness of outcome indicators

Time	Knee flexion		Knee extensor		Lysholm score		VAS	
	Surgery + oral medication	Oral medication	Surgery + oral medication	Oral medication	Surgery + oral medication	Oral medication	Surgery + oral medication	Oral medication
Before	92.60±5.95	91.97±5.57	25.03±3.01	25.23±2.74	45.77±2.45	45.47±2.16	6.75±0.18	6.73±0.17
2 weeks	115.87±2.32**	105.93±5.35***	11.03±3.01**	17.30±2.00***	75.23±2.31**	57.03±0.96***	3.70±0.12**	4.34±0.17***
4 weeks	125.82±2.55***	122.85±5.35***	7.37±1.27***	10.53±1.81***	84.35±2.89***	76.65±1.43***	2.48±0.16***	3.33±0.19***
12 weeks	140.93±4.29***	137.90±4.83***	5.97±1.43***	7.07±0.94***	87.40±2.62***	84.60±2.72***	0.78±0.17***	1.99±0.18***
24 weeks	143.64±3.50***	145.23±4.05***	4.73±1.20***	4.90±1.37***	91.47±2.56***	90.29±2.56***	0.37±0.12***	0.36±0.17***
48 weeks	144.17±3.73***	145.19±4.08***	4.60±2.13***	5.00±1.76***	91.18±2.98***	90.17±3.00***	0.39±0.13***	0.35±0.19***

* $P<0.05$, statistically significant difference between the two groups; ** $P<0.05$, statistically significant difference between pretreatment and posttreatment groups; *** $P<0.05$, statistically significant difference between pretreatment and posttreatment groups at week 2; # $P<0.05$, statistically significant difference between pretreatment and posttreatment groups at week 4 (P<0.05); ## $P<0.05$, statistically significant difference between pretreatment and posttreatment groups at week 12

Fig. 1 Indicators from baseline to 48 weeks of follow-up. **a** Knee flexion. **b** Knee extension. **c** Lysholm scores. **d** VAS scores

Oral medication-related complications included nausea ($n=2$), anorexia ($n=2$), vomiting ($n=1$), and diarrhea ($n=1$) in the combination group and nausea ($n=3$), anorexia ($n=2$), vomiting ($n=2$), and abdominal pain ($n=2$) in the oral medication group.

The incidence of complications was not significantly different between the two groups ($\chi^2=0.341$, $P>0.05$). All patients continued the treatment, and no patients withdrew from the study due to complications.

Recurrence

In patients treated with surgery combined with oral medication, two patients experienced recurrence, with an incidence of 6.67 % and at a frequency of once a year. In patients treated with oral medication alone, seven patients experienced recurrence, with an incidence of 26.67 % and at a frequency of once to twice a year. The incidence of recurrence was significantly different between the two groups ($\chi^2=5.46$, $P<0.05$).

Lost to Follow Up

Two and three patients were lost to follow up in the group with combined oral medication (3.33 %) and in the group with oral medication alone (10.00 %), respectively.

Discussion

In recent years, the incidence of gout has grown steadily from year to year due to lifestyle changes and an aging population [14]. The disease generally occurs in males aged over 40 years with a male-to-female ratio of 20:1 [15]. Gouty knee arthritis, which refers to the condition in which gout involves the knee joint, results from the deposition of urate crystals in the joint synovium, ligaments, articular cartilage, and meniscus, causing damage to these tissues and joint dysfunction and even disability. Normal articular cartilage collagen is destroyed and followed by cartilage or synovial proliferation, which presents predominantly as joint pain, swelling, and deformation [16].

Currently, there is no radical cure for gouty knee arthritis. The current treatments including medication, surgery, and dietary control aim to delay the onset and ameliorate the symptoms of disease.

Previously, oral medication alone has been the most common approach, with the objective of timely control of the onset of acute gouty knee arthritis. However, in spite of effective pain relief, this approach is limited to the improvement of symptoms and functions of joints [17]. Calcium carbonate is sustainably present, and uric acid enters the blood under cold damp conditions and as a result of exertion, causing frequent acute inflammation. Thus, the quality of life is seriously affected. Improper usage of drugs such as colchicine may also induce multiple complications [18].

Traditional surgery often requires large incisions and does not allow accurate assessment of articular disease severity. As a result, some tissues, such as ligaments, are easily damaged in surgery, and infection easily occurs, resulting in a high incidence of side effects and complications. Therefore, traditional surgery is not an ideal approach in clinical practice.

The arthroscopic technique allows the removal of the pathogenic factor (urate crystals) under microinvasive conditions, thus inhibiting the urate crystal-induced inflammatory reaction at the level of pathogenesis [19]. Consequently, this procedure has been increasingly adopted by clinicians. However, the clinical evidence is still insufficient to prove that the benefits of medication in combination with arthroscopic surgery outweigh those of the traditional medication.

In the current study, oral medication alone and oral medication combined with arthroscopic surgery were compared for efficacy. Results showed that oral medication combined with arthroscopic surgery was superior to oral medication alone in terms of improved range of motion and joint junction scores at weeks 2, 4, and 12. This demonstrated that oral medication combined with arthroscopic surgery improves symptoms and restores joint function because the first-line uric acid-lowering drugs (colchicine and sodium bicarbonate tablets) have limited effects. Another drug, allopurinol, inhibits xanthine oxidase, resulting in reduced synthesis of uric acid in the blood and deposition in the bone and joint. However, it may dissolve the calcium carbonate surface due to the sharp drop of uric acid in the blood. Thus, small amounts of uric acid enter the blood, preventing significant relief of the symptoms in the early stages. Therefore, this drug is not suitable for use in the early stages of gout. Considering the aforementioned disadvantages, allopurinol was administered at weeks 2 in the current study, which may be the cause of the reduced efficacy in the group with single oral medication compared with that in the group with medication combined with surgery in the early stages (weeks 2, 4, and 12).

At weeks 24 and 48, the range of motion and function scores were not statistically different between the two groups and among different time points in the same groups. These observations demonstrated equivalent long-term efficacy in the two groups and, furthermore, that arthroscopic surgery represents a local treatment method which can significantly relieve joint pain and swelling, decrease the damage to joint structures caused by urate crystals and improve the joint deformation and dysfunction but cannot alleviate the purine metabolism abnormality. Therefore, surgery alone cannot replace oral medication and is not superior in terms of long-term efficacy. Consequently, for gouty arthritis, arthroscopic surgery combined with oral medication produces persistent efficacy.

Postsurgery, disease recurrence was observed in the group with medication combined with surgery ($n=2$) and the group with medication alone ($n=7$). The rate of recurrence was

statistically lower in the group with medication combined with surgery. These results may be related to the fact that surgery removes urate crystals in the joint and stimulates massive recruitment of leucocytes and inflammatory mediators to the symposium [20], while the disease in the joint is not treated in medication alone group. Therefore, the development of gout may be blocked by oral medication combined with arthroscopic surgery. Our study demonstrates that arthroscopic debridement plays an important role in blocking the local pathogenesis of gouty knee arthritis and promotes joint function restoration.

In the group with oral medication alone, three patients experienced adverse gastrointestinal events within 3 months, which were relieved by gastric mucosal protective drug treatment. In the group with medication combined with surgery, two patients reported adverse gastrointestinal events. No infections were reported among the patients who underwent surgery, and only two patients developed joint hematomas, which gradually disappeared in response to pressure dressing. No patients withdrew from the study due to complications, and there was no difference in the safety of oral medication between the two groups.

It should be noted that interpretation of the results of the current study are limited by the small sample size and the design, which was not blinded to patients and participants. Furthermore, the follow-up period of 1 year is relatively short and should be prolonged to fully evaluate the stability of long-term efficacy.

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