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Effect of Prednisolone Therapy on Hand Osteoarthritis Patients with Synovitis

Xue Han[1,*], Jianjun Li[2], Ningning Liu[2]

[1] Operation room, Binzhou People's Hospital, Binzhou, Shandong, China, 256600.
[2] Orthopaedics, Binzhou People's Hospital, Binzhou, Shandong, China, 256600.
**Binzhou People's Hospital, No. 515, Huanghe 7th Road, Binzhou, Shandong, China, 256600.*

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Abstract: Objective: To study the clinical effect of short-term prednisolone therapy on patients with hand osteoarthritis accompanied by synovitis. Methods: From December 2017 to December 2019, 80 patients with synovitis diagnosed with hand osteoarthritis were randomly divided into 2 groups according to different treatment schemes, 40 cases in each group: Prednisone treatment group (group P: 5 mg/ mL /time/day, 2 ml, oral) and placebo group (group C: 2 mL /time/day, placebo, oral) continued this regimen for 6 weeks. The patients in group P were changed to 5 mg/mL/time/day, and after 1 week of continuous medication, the dosage was changed to 2.5 mg/day and continued to be used for 1 week, and the medication was stopped. Group C changed the placebo dosage according to group P. Observed from the 9th to the 14th week, a total of 6 weeks. The joint swelling, visual analogue score (VAS score), salvage analgesic drug use, joint function score, and serum C-reactive protein (CRP) levels were recorded in both groups. Results: All patients completed the 14-week trial and follow-up. The recorded results are as follows: the VAS scores of the hand bone joints of the two groups were compared with those before treatment (T0). The VAS scores were 6 weeks (T1) and 8 weeks (T2). The pain was relieved, and the difference was statistically significant ($P<0.05$). After receiving prednisolone treatment, the swelling of the hand joints in group P was reduced at T1 and T2, and the joint function score was decreased at T1 and T2. Serum CRP level was reduced at T1 and T2, the difference was statistically significant ($P<0.05$). Compared with group C, the pain in group P was reduced at T1 and T2, the degree of joint swelling was reduced at T1 and T2, the joint function score was decreased at T1 and T2, and the serum CRP level was reduced at T1 and T2. The difference was statistically significant ($P<0.05$); the use of salvage analgesics in group P was 1 and 2 at T1 and T2, respectively, and the use of salvage analgesics in group C was 7 and 12 at T1 and T2, respectively, the difference between the two groups was statistically significant ($P<0.05$). One case of gastrointestinal discomfort occurred in group C (2.50%); one case of gastrointestinal discomfort occurred in group P(2.50%), two cases of elevated

blood glucose(5.00%), and one case of rash(2.50%). There was no significant difference in the occurrence of adverse reactions between the two groups (P>0.05). Conclusion: The short-term treatment of prednisolone can significantly improve the pain symptoms of hand osteoarthritis, reduce the synovitis reaction, and there are no obvious adverse events, which can effectively improve hand joint function.

1. Introduction

Osteoarthritis (OA) is a common and chronic clinical degenerative osteoarthritic disease [1], with middle-aged and elderly patients being the most prevalent group for the disease. The prevalence of hand osteoarthritis (HOA) is 8%-10%, and the small joints of the hand are often affected, with the distal interphalangeal joints being the most commonly affected [2]. The main clinical manifestations of HOA are deformity, pain and limited movement of the hand joints. Due to pain and limited finger movement, it causes many inconveniences to patients' life and work [3]. At present, NSAIDs are widely used in clinical practice, but they can only obtain short-term relief of pain symptoms and do not fundamentally alleviate the further development of the disease [4], and the long-term application of NSAIDs may lead to digestive complications. Numerous studies in recent years have confirmed that the inflammatory pain and imaging changes that occur in osteoarthritis are not only caused by mechanical injury, but local inflammatory responses also play a role [5,6]. Glucocorticoids, as a multi-targeted anti-inflammatory drug, can effectively inhibit the inflammatory response, so our hospital has obtained good clinical results by giving prednisolone to some patients with hand arthritis associated with synovitis, which is now reported as follows:

2. Information and methodology

2.1 2.1 General information.

One hundred patients who visited our outpatient clinic between December 2017 and December 2019, who were diagnosed with osteoarthritis of the hand with synovitis were selected, of which 20 patients were excluded and finally a total of 80 patients were included in the study. Patients were randomly divided into 2 groups of 40 patients according to different treatment regimens: the prednisolone treatment group (group P) and the placebo group (group C).The mean age of group P was 62.62±1.81 years, with 4 males and 36 females, and the mean duration of the disease was 2.42±1.32 years. The mean age of group C was 65.63±1.54 years, with 5 males and 35 females, and the mean duration of the disease was 2.21±1.12 years. Both groups were high in female patients, but there was no statistical difference in age, sex, BMI, disease duration or pre-treatment VAS score between the two groups (P>0.05), see Table 1:

Table 1 Comparison of the general condition of the two groups of patients (n=40)

index	Group P	Group C
year(y, x±s)	62.62±1.81	65.63±1.54
sex ratio(Female/Male)	36/4	35/5
BMI(kg/m^2, x±s)	23.41±2.32	22.82±1.21
course of disease(y, x±s)	2.42±1.32	2.21±1.12
VAS(score, x±s)	6.43±0.21	6.36±0.19

2.2 Criteria for selection.

Patients selected for clinical treatment were required to meet the following criteria: meeting the diagnostic criteria for osteoarthritis of the hand established by the Osteoarthritis Section of the American College of Rheumatology [7], with concomitant synovitis. ①hand pain, soreness, and stiffness most of the month; ②hard tissue hypertrophy in 2 or more of the 10 designated hand joints; ③swelling of less than 2 metacarpophalangeal joints; ④swelling of more than 1 distal interphalangeal joint; ⑤deformity in 2 or more of the 10 designated joints. Osteoarthritis is diagnosed when①+②+③+④, or①+②+③+⑤are satisfied. (Note: The 10 designated joints include the 2nd and 3rd interphalangeal and proximal interphalangeal joints and the 1st carpal joint bilaterally)

Exclusion criteria: (1) patients with severe systemic disease, such as severe cardiovascular or cerebrovascular disease; (2) patients with severe hand and joint deformities; (3) patients with short-term glucocorticosteroid therapy; (4) patients who did not agree to be enrolled.

Exclusion criteria: (1) self withdrawal midway through the study due to their own reasons and inability to persist; (2) serious adverse reactions during the study.

This study has been approved by the ethics committee of our hospital, and all included patients were introduced to the study process and signed an informed consent form.

2.3 Treatment protocol

Group P: Prednisolone 5 mg/mL/day, 2 ml, orally. Group C: Placebo 2 mL/day, orally, continued this regimen for 6 weeks. Patients in Group P changed to 5 mg/mL/day, continued the medication for 1 week, changed the dosage to 2.5 mg/day continued the medication for 1 week and then discontinued the medication. Group C changed the placebo dosage usage according to Group P, during treatment. When the patient's VAS score was>5, paracetamol 300 mg/time was applied for remedial analgesia, with a maximum allowable dose of 3 g/day. After discontinuation of the drug, follow-up was started at week 9 and continued until 14week.

2.4 Observations

Swollen joints are graded according to whether the patient's joints are swollen and the degree of swelling: no swelling (grade 0), fullness (grade 1), thickening of the joint (grade 2), significant swelling of the joint (grade 3).

Visual Analogue Score (VAS score) During treatment and follow-up, the patient's joint pain was assessed according to the VAS score: a 10 cm horizontal line was drawn on a piece of paper, with 0 at one end for no pain, 10 at the other end for severe pain, and different levels of pain in the middle. The patient is asked to indicate the level of pain by putting a level number on the line according to how he or she feels. A higher score indicates a higher level of pain.

Use of remedial analgesics the number of times remedial analgesics were administered at the time of treatment was recorded separately for all patients.

Joint function scores Joint range of motion decreased by ≤1/3 with mild limitation of motion (3 points); joint range of motion decreased by>1/3 and was≤2/3 with significant limitation of motion (6 points); joint range of motion decreased by>2/3 with severe limitation of motion (9 points).

Serum C-reactive protein (CRP) levels were measured by enzyme-linked immunosorbent assay (ELISA) in peripheral venous blood of patients before (T0), 6 weeks (T1), 8 weeks (T2) and 14 weeks (T3) of treatment, respectively.

2.5 Statistical analysis

The statistical software SPSS 22.0 was used to analyze and process the data. The mean plus or minus standard deviation (x ± s) was used for measurement data, and paired-sample t-test was used for intra-group comparisons; the percentage (%) was used for count data, and x2 test was used.

3. Results

The follow-up showed that the VAS score of the hand osteoarthritis in the two groups was reduced at 6 weeks of treatment (T1) and pain was relieved at 8 weeks of treatment (T2) compared with the pre-treatment (T0), and the difference was statistically significant (P<0.05).The patients in group P received prednisolone treatment and the swelling of the hand joints was reduced at T1 and T2, the joint function score was reduced at T1 and T2, the Serum CRP level was reduced at T1 and T2, and the difference was statistically significant (P<0.05).The pain level, reduction in joint swelling at T1 and T2, reduction in joint function score at T1 and T2, and reduction in serum CRP level at T1 and T2 in group P compared to group C were statistically significant (P<0.05), see Table 2 and Table 3.

Table 2 VAS score, joint function score and serum CRP levels in the two groups of patients (n=40, x±s)

group	Time	VAS(score)	Joint Function Score(score)	CRP(mg/l)
Group P	T_0	6.43±0.21	6.52±0.11	25.12±1.31
	T_1	4.12±0.11*#	3.52±0.12*#	15.32 ± 1.25*#
	T_2	3.28± 0.09*#	3.28±0.05*#	12.51 ± 1.13*#

Group C	T_3	5.31±0.07	5.21±0.12	22.14±1.23
	T_0	6.36±0.19	6.76±0.15	25.31±1.42
	T_1	5.13±0.12*	4.13±0.11*	19.32±1.23*
	T_2	4.11±0.11*	3.81±0.06*	17.28±1.21*
	T_3	5.32±0.09	5.22±0.07	23.24±1.13

Note: compared to T0 *P<0.05; compared to Group C #P<0.05

Table 3 Swelling of hand joints in both groups (n=40)

Time	Level	Group P	Group C
T_0	Level 0	5	4
	Level 1	14	10
	Level 2	11	15
	Level 3	10	11
T_1	Level 0	6	5
	Level 1	15*#	12
	Level 2	12*#	13
	Level 3	7*#	10
T_2	Level 0	7	6
	Level 1	16*#	14
	Level 2	13*#	12
	Level 3	4*#	8
T_3	Level 0	4	4
	Level 1	13	12
	Level 2	15	13
	Level 3	8	11

Note: compared to T0 *P<0.05; compared to Group C #P<0.05

The remedial analgesic medication use in group P was 1 case and 2 cases at T1 and T2, respectively, and the remedial analgesic medication use in group C was 7 cases and 12 cases at T1 and T2, respectively, and the difference between the two groups was statistically significant (P<0.05), see Table 4.

Table 4 Remedial analgesia in both groups (n=40)

Group	T_1	T_2
Group P	1(2.5%)#	2(5.0)#
Group C	7(17.5%)	12(30.0%)

Note: compared to Group C #P<0.05

Group C had one case of gastrointestinal discomfort with an incidence of 2.50%; group P had one case of gastrointestinal discomfort with an incidence of 2.50%, two cases of elevated blood glucose with an incidence of 5.00%, and one case of rash with an incidence of 2.50%. The difference in the occurrence of adverse reactions between the two groups was not statistically significant (P>0.05), see Table 5.

Table 5 Incidence of adverse events in both groups (n=40)

adverse events（case（%））	Group P	Group C
Gastrointestinal discomfort	1（2.50%）	1（2.50%）
elevated blood sugar	2（5.00%）	0
skin rash	1（2.50%）	0

4. Discussions

Osteoarthritis of the hand, a degenerative pathology, due to age, trauma, strain, inflammation and other factors caused by degenerative damage to articular cartilage, joint edges and subchondral bone reactive hyperplasia, the main clinical manifestations: joint pain, joint swelling, morning stiffness, joint deformity and limited joint movement, accompanied by synovitis, the symptoms are prone to recurrence, in severe cases may eventually lead to severe joint deformity or even disability [8-10]. At present, as the pathogenesis is not yet clear, there is no effective standard of treatment measures for hand osteoarthritis in clinical practice, mainly through drugs (anti-inflammatory drugs, analgesics) to alleviate pain, and in the advanced stage of the disease can only perform joint replacement surgery, which will eventually seriously affect the quality of life of patients [11-13]. Therefore, it is very important to intervene in patients with osteoarthritis associated with synovitis.

Numerous recent studies have confirmed that inflammatory pain and radiographic changes in osteoarthritis are not only caused by mechanical injury, but also by local inflammatory responses [14,15]. Glucocorticoids, as a multi-targeted anti-inflammatory agent, are effective in suppressing the inflammatory response [16]. Prednisolone, a glucocorticoid, has anti-inflammatory properties that inhibit the development of connective tissue hyperplasia, reduce capillary permeability and decrease cell membrane permeability, thereby reducing inflammatory leakage. The results of this study showed that in patients with osteoarthritis of the hand associated with inflammatory symptoms, a 6-week regimen of applying prednisolone 10 mg significantly improved pain levels and hand osteoarthritis function. The VAS score of hand osteoarthritis was lower and pain was relieved at T1 and T2, the difference was statistically significant ($P<0.05$), and it was higher at T3, the difference was not statistically significant ($P>0.05$).Patients in group P, after receiving prednisolone treatment, had less swelling of hand joints at T1 and T2 and lower joint function score at T1 and T2, the difference was not statistically significant ($P>0.05$). Serum CRP levels were reduced at T1 and T2, and the difference was statistically significant ($P<0.05$), joint swelling degree was increased at T3, joint function score was increased at T3, and serum CRP level was increased at T3, and the difference was not statistically significant ($P>0.05$). Pain degree was reduced at T1 and T2 in group P compared to group C, joint swelling degree was reduced at T1 and T2, joint function Scores decreased at T1 and T2, serum CRP levels decreased at T1 and T2, the difference was statistically significant ($P<0.05$), joint swelling decreased at T3, joint function scores decreased at T3, and serum CRP levels decreased at T3, the difference was not statistically significant ($p>0.05$). Remedial analgesic medication use at T1 and T2 in group P patients were 1 In group C, the use of remedial analgesics at T1 and T2 was 7 and 12 cases, respectively, and the difference between the two groups

was statistically significant (P<0.05). These results fully demonstrate the effectiveness of prednisolone during the 6-week treatment period, which works mainly by reducing the level of inflammation [17-19]. In group C, there was one case of gastrointestinal discomfort with an incidence of 2.50%, and in group P, there was one case of gastrointestinal discomfort with an incidence of 2.50%, two cases of elevated blood glucose with an incidence of 5.00%, and one case of rash with an incidence of 2.50%. There was no statistically significant difference in the occurrence of adverse events between the two groups (P>0.05). Long-term application of glucocorticoids may lead to serious complications such as osteoporosis [20-22]. The results of the present study found no serious adverse events with the prednisolone short-term treatment regimen, and these amply demonstrate that prednisolone short-term therapy is a safe treatment option. Although this study was conducted only in the special population of patients with osteoarthritis of the hand with synovitis, and whether the results can be extrapolated to other symptomatic patients remains to be investigated, it is useful for the targeted treatment of patients with osteoarthritis of the hand with synovitis.

In summary, the prednisolone 10 mg, 6-week regimen is safe and effective in patients with osteoarthritis of the hand associated with inflammatory symptoms. Short-term treatment with prednisolone can significantly improve the pain symptoms and reduce the synovitis reaction in patients with synovitis hand osteoarthritis, and there are no significant adverse events, effectively improving hand joint function.

References

[1] *Bijlsma JW, Berenbaum F, Lafeber FP, et al. (2011) Osteoarthritis: an update with relevance for clinical practice. Lancet, 377(9783), 2115-2126.*

[2] *Branco JC, Rodrigues AM, Gouveia N, et al. (2016) Prevalence of rheumatic and musculoskeletal diseases and their impact on health-related quality of life, physical function and mental health in Portugal: results from Epi Reuma Ptanational health survey. RMD Open, 2(1), 166-168.*

[3] *RLiu, WDamman, M Reijnierse, et al. (2017) Bone marrow lesions on magnetic resonance imaging in hand osteoarthritis are associated with pain and interact with synovitis. Osteoarthritis and cartilage, 25(7): 1093-1099.*

[4] *Qin J, Barbour KE, Murphy LB, et al. (2017) Lifetime risk of symptomatic hand osteoarthritis: the Johnston County osteoarthritis project. Arthritis Rheumatol, 69(6): 1204-1212.*

[5] *Pham T, van der Heijde D, Altman RD, et al. (2004) OMERACT-OARSI initiative: Osteoarthritis Research Society International set of responder criteria for osteoarthritis clinical trials revisited. Osteoarthritis Cartilage, 12(5), 389-399.*

[6] *Kvien TK, Fjeld E, Slatkowsky-Christensen B, et al. (2008) Efficacy and safety of a novel synergistic drug candidate, CRx-102, in hand osteoarthritis. Ann Rheum Dis, 67(7), 942-948.*

[7] *Altman R，Alarcon G，Appelrouth D，et al. (1990) The American College of Rheumatology criteria for the classification and reporting of osteoarthritis of the hand. Arthritis Rheum, 33(2), 1601-1610.*

[8] *Marshall M, Watt FE, Vincent TL, et al. (2018) Hand osteoarthritis: clinical phenotypes, molecular mechanisms and disease management. Nat Rev Rheumatol, 14(11), 641-656.*

[9] *Kroon FPB, Carmona L, Schoones JW, et al. (2018) Efficacy and safety of non-pharmacological, pharmacological and surgical treatment for hand osteoarthritis: a systematic literature review*

informing the 2018 update of the EULAR recommendations for the management of handosteoarthritis. RMD Open, 4(2), 734-736.

[10] Claire Y J, Elizabeth MA, Andrew J, et al. (2012) A randomized, double-blind, placebo-controlled trial of low-dose oral prednisolone for treating painful hand osteoarthritis. Rheumatology (Oxford, England), 51(12), 2286-2294.

[11] Kloppenburg M, Kroon FP, Blanco FJ, et al. (2019) 2018 update of the EULAR recommendations for the management of hand osteoarthritis. Ann Rheum Dis, 78(1), 16-24.

[12] Smith TO, Zou K, Abdullah N, et al. (2016) Does flare trial design affect the effect size of non-steroidal anti-inflammatory drugs in symptomatic osteoarthritis? Asystematic review and meta-analysis. Ann Rheum Dis, 75(11), 1971-1978.

[13] Haugen IK, Østergaard M, Eshed I, et al. (2014) Iterative development and reliability of the OMERACT hand osteoarthritis MRI scoring system. J Rheumatol, 41(2), 386-391.

[14] Spolidoro NO, Natour J, Machado FS, et al. (2015) Effectiveness of triamcinolone hexacetonide intraarticular injection in interphalangeal joints: a 12-week randomized controlledtrialin patients with handosteoarthritis. J Rheumatol, 42(10), 1869-1877.

[15] Kloppenburg M, vanBeest S, Kroon FPB. Thumbbaseosteoarthritis: ahandosteoarthritissubsetrequiringadistinct approach. Best Pract Res Clin Rheumatol, 31(4), 649-760.

[16] Duru N, van der Goes MC, Jacobs JW, et al. (2013) EULAR evidence-based and consensus-based recommendations on the management of medium to high-doseglucocorticoid therapy inrheumatic diseases. Ann Rheum Dis, 72(12), 1905-1913.

[17] Bhala N, Emberson J, Merhi A, et al. (2013) Vascular and upper gastrointestinal effects of non-steroidal anti-inflammatory drugs: meta-analyses of individual participant data from randomised trials. Lancet, 382(9894), 769-779.

[18] Zhang Y, Niu J, Kelly-Hayes M, et al. (2002) Prevalence of symptomatic hand osteoarthritis and its impact on functional status among the elderly: the Framingham Study. Am J Epidemiol, 156(11), 1021-1027.

[19] Zhang W, Doherty M, Leeb BF, et al. (2009) EULAR evidence-based recommendations for the diagnosis of hand osteoarthritis: report of a task force of ESCISIT. Ann Rheum Dis, 68(1), 8-17.

[20] Altman R, Alarcón G, Appelrouth D, et al. (1990) The American College of Rheumatology criteria for the classification and reporting of osteoarthritis of the hand. Arthritis Rheum, 33(5), 1601-1610.

[21] Keen HI, Lavie F, Wakefield RJ, et al. (2008) The development of a preliminary ultrasonographic scoring system for features of hand osteoarthritis. Ann Rheum Dis, 67(2), 651-655.