

The effect of sodium hyaluronate treating knee osteoarthritis on synovial fluid interleukin -1 β and clinical treatment mechanism

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Abstract: in order to explore the influence of sodium hyaluronate on knee osteoarthritis (KOA) patients synovial fluid interleukin -1 β (IL-1 β) and analyze its clinical mechanism, this study analyzed 40 cases of KOA patients in our hospital's orthopaedic department, randomly divided them into two groups: Sodium hyaluronate group (group A) and normal saline group (group B), each consists 20 patients. Besides, we selected another 20 patients as normal control group. Group A treated knee joint cavity by injecting sodium hyaluronate, and group B injected knee joint cavity in equal amount of normal saline, once a week for five weeks. Collect respectively knee joint synovial fluid in patients of group A and group B before treatment and after five weeks of treatment, detect the content of knee joint synovial fluid IL-1 β in of all the three groups by using enzyme linked immunosorbent assay (ELISA). We can conclude that (1) IL-1 β content of knee joint synovial fluid in KOA patients before treatment was significantly higher than healthy people; (2) IL-1 β content of group A knee joint synovial fluid after treatment was significantly reduced than before treatment, there was no significant difference for group B IL-1 β content before and after treatment; (3) there was no significant difference between group A knee joint synovial fluid IL-1 β content after treatment and healthy people. Thus it can be proved that content of IL-1 β in knee joint synovial fluid KOA patients is higher than healthy people; sodium hyaluronate can reduce the content of IL-1 β in synovial joints and can be effective in the treatment of knee osteoarthritis.

Keywords: sodium hyaluronate, KOA, content of IL - 1 β

INTRODUCTION

Knee osteoarthritis is a kind of the most common degenerative joint diseases in human peripheral power joints, which belongs to osteoarthritis and occurs mostly in the elderly group. It can lead to severe damage of patients late cartilage, thus affect the joint functions. Its etiology and pathogenesis has not yet fully illuminated, but the treatment methods in recent years have constantly updated with the deepening of the research (Ming *et al.*, 2013). Liu Yuan *et al.*, in Survey on Using Acupuncture and Moxibustion in the Treatment of Knee Osteoarthritis (Yuan *et al.*, 2011), analyzed the methods, mechanism of action, curative effect and curative effect evaluation criterion of acupuncture and moxibustion treating Knee Osteoarthritis in the latest decade. The method was verified to be definite effective, simple and convenient, economical and practical and with mild untoward effect, and it is worthy of clinical popularization. Gao Mingli, Wang Yao and Zhu Yingqi, in Evaluation of the Efficacy of Pricking-cupping Bloodletting Method plus Glucosamine Hydrochloride in Treating Knee Osteoarthritis (Mingli *et al.*, 2014) applied contrast experiment and proved Pricking-cupping Bloodletting Method could promote the absorption and utilization of glucosamine hydrochloride and was an effective way to improve the symptoms of knee osteoarthritis by comparing the recovery situation of two groups of patients who received different therapies. Pricking-

cupping Bloodletting Method provides a new method for Knee Osteoarthritis treatment.

In recent years, a lot of evidences have indicated that cytokine interleukin -1 β (IL-1 β) plays an important role in KOA articular cartilage matrix recession and cartilage destruction, as one of the judge standard of the KOA clinical curative effect (Juanjun *et al.*, 2010; Wei *et al.*, 2010). And articular cavity injection of sodium hyaluronate (hyaluronic acid, HA) to prevent and treat KOA is also a currently widely used clinical treatment, but the relationship research about the HA and knee joint synovial cavity (IL-1 β) is still not so much. Therefore, this paper compared the IL-1 β content of KOA patients knee joint synovial fluid with healthy people by examining the HA before and after the treatment, which provides experimental and theoretical basis for clinical evaluation on HA effect.

MATERIALS AND METHOD

General materials

This study selected 40 KOA patients in our hospital orthopaedic clinic from April 2012 to April 2013 upon the approval of the hospital ethics committee and the informed consent of all patient's signature, in which men and women were respectively 20 cases, ranging in age from (65.94 \pm 8.54) years. All of the patients did not have knee joint cavity puncture, injection treatment for half a year and no application of cortical hormone drugs. Rheumatoid disease, infectious arthritis, systemic

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infection, metabolic arthritis, intra-articular tumor were excluded (Hui *et al.*, 2010). Through the completely random design method, 40 cases of KOA patients were randomly divided into two groups (male and female are equal): sodium hyaluronate group (group A) and normal saline group (group B), 20 cases in each group. And we also selected 20 healthy volunteers as normal control group (group C), in which men and women were respectively 10 cases, ranging in age from (64.97 \pm 7.59) years.

Inclusion criteria and exclusion criteria

Excluded: (1) those who have received knee joint cavity paracentesis during 6 months before grouped; (2) those with concurrent rheumatic arthritis and infectious arthritis; (3) those with concurrent metabolic disease or tumor in arthrosis.

Included: (1) those who have not received treatment, such as knee joint cavity paracentesis and injection, and have not taken corticoid medicine. Those with rheumatic disease, infectious arthritis, systemic infection, metabolic arthropathy or tumor in joint were excluded (Hui *et al.*, 2010).

Method

Inject 2.5mL HA into knee joint cavity in Group A; inject the same amount of 0.9% saline solution into knee joint cavity in Group B. Treatment time of two groups was once a week, and lasted for five weeks. Two groups of KOA patients was respectively extracted 1mL knee joint fluid before the first injection (before treatment) and during the first week after the fifth injection (after treatment) to evaluate clinical efficacy; and extract group C healthy volunteers knee joint fluid 1mL. Get all joint fluid from recumbent patients, do knee joint puncture under aseptic condition, extract 1mL joint fluid to inject into pollution-free plastic centrifuge tube, centrifuge for 5min at 3,000 r/min, store it in -70 $^{\circ}$ C refrigerator for test.

Observation Index

(1) IL-1 β content of synovial fluid Rewarm the synovial fluid on ice when detecting; detect the contents of each IL-1 β by using ELISA (Enzyme-linked Immunosorbent Assay). (2) KOA condition: evaluate two groups KOA patients condition respectively before the first injection (before treatment) and after one week of the fifth injection (after treatment). Score assessment according to Michel Lequesne KOA severity index (index of severity for knee joint osteoarthritis, ISOA) (Yingjie *et al.*, 2014). Maximum score is 24 points, minimum is 0. The higher the score is, the more serious the condition will be. According to the ISOA score, it can be divided into five grades: (1) slight < 5 points; (2) moderate: 5-7 points; (3) serious: 8-10 points; (4) very serious: 11-13 points; (5) extreme serious: \geq 14 points.

STATISTICAL METHOD

Data analysis was performed using SPSS 19.0 software. Normal distribution measurement data was represented by mean \pm standard deviation. Measurement data between groups was compared by using one-way variance analysis. Pearson correlation analysis was used to analyze the relationship between before treatment KOA patient's knee ISOA scores and IL - 1 β content in synovial joints.

RESULTS

General situation comparisons of three groups

There were no significant differences in age, weight, gender of three groups comparison. Group A and group B had no differences in preoperative average duration, specific data as shown in table 1.

The severity comparison of the two groups KOA patients before and after treatment

(1) Comparison among groups: There was no significant difference in the comparison of two groups before treatment knee joint ISOA score: Group A knee joint ISOA score after treatment was significantly lower than group B. (2) Comparison among groups: Group A knee joint ISOA score after treatment was significantly lower than before treatment; there was no significant difference in group B knee joint ISOA score before and after treatment, specific data as shown in table 2.

IL-1 β content comparison in synovial fluid of three groups

(1) Comparison among groups: IL-1 β content in group A before treatment and group B after treatment in synovial fluid had significantly increased compared with group C; there was no significant difference in group A and group B before treatment; group A IL-1 β content in synovial fluid after treatment had significantly dropped compared with group B. (2) Comparison among groups: Group A knee joint synovial fluid IL-1 β content after treatment was significantly lower than before treatment; There was no obvious difference in group B knee joint synovial fluid IL-1 β content before and after treatment, specific data as shown in table 3.

DISCUSSION

KOA pathology is based on the retrogression of joint hyaline cartilage and corresponding synovial membrane inflammatory change, which is one of the most common disease in middle-aged and old people caused by many factors of increasing age, multiple trauma, obesity, and internal secretion change (Raman *et al.*, 2012; Angelique *et al.*, 2010). Patients always have joint support structure damage of different degrees and may even trigger meniscus injury, joint surface hardening in later period, which have high disability rate and make a serious influence on patient's quality of life.

Table 1: Each group patient's general comparison

Group	Age(years)	Weight(kg)	Gender(male/female)	Preoperative average duration(month)
A	64.54±7.22	59.74±6.55	10/10	15
B	65.33±8.01	60.46±6.83	10/10	16
C	64.97±7.59	59.15±7.02	10/10	Void

Table 2: Knee joint ISOA score comparison of two groups KOA patient's before and after treatment

Group	N	Before treatment(score)	After treatment(score)
A	20	8.15±1.13	3.13±1.01
B	20	8.35±1.20	8.23±1.13

Table 3: Each group knee joint synovial fluid IL - 1 β content comparison

Group	N	Before treatment (pg/ml)	After treatment (pg/ml)
A	20	76.08±8.35	45.31±7.39
B	20	78.17±8.11	77.58±9.14
C	20	43.01±6.25	

Notes: when compare with group C, $p < 0.05$; when compare with group B after the treatment, $p < 0.05$; when compare with group A before the treatment, $p < 0.05$.

In recent years, studies have shown that (Jinhui *et al.*, 2012) some cytokines play an important role in the pathological process of KOA, especially IL-1 β in osteoarthritis pathological process can obviously enhance cartilage matrix degradation and destruction of articular cartilage. IL-1 β can inhibit collagen synthesis of hyaline cartilage characteristic of type II, change and destroy surrounding environment of cartilage cells, occur variation in the structure of cartilage protein. This function is more destructive than promote the degradation of cartilage matrix. This research results show that IL-1 β content in IL-1 β patient's knee joint synovial fluid is higher than healthy people and IL-1 β content is significantly positive correlated with patient's knee joint ISOA score. These results suggest that IL-1 β content in knee joint synovial fluid not only can be used as a reference index in the diagnosis of KOA, but also can be used as important reference indicator of KOA disease severity evaluation.

At present, most domestic and overseas scholars think that KOA illness severity is mainly related to the degeneration degree of joint cartilage (Yi *et al.*, 2010). Thus, how to effectively prevent degeneration of joint cartilage is particularly important in the treatment and prevention of KOA. Study confirms that exogenous HA can adhere in joint surface or synovial surface by combining glycoprotein, form indeterminate structure layer in cartilage surface to protect the cartilage and HA on the surface of joints or synovial plays an important role in maintaining integrity of cartilage, nourishing cartilage and protecting it from the spread of bacteria, toxins, etc. However, at present there is no exact index can evaluate the effect of HA. This study found that KOA patients IL-1 β content in synovial fluid decreased significantly after HA treatment, which suggested that IL-1 β content in knee

joint synovial fluid also can be used as one of the reference indicator in judging HA curative effect.

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