

The Effect of Etoricoxib in Knee Osteoarthritis and its Impact on Immune Inflammatory Response

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We aim to investigate the value of family rehabilitation training with etoricoxib treatment in knee osteoarthritis and its impact on immune inflammatory response. We selected 100 knee osteoarthritis patients admitted to our hospital from October 2021 to October 2022 and divided them into an experimental group (50 cases) and a control group (50 cases) according to the envelope randomization method. Control group received etoricoxib treatment and experimental group received family rehabilitation training with etoricoxib treatment. Compared the therapeutic effect of both groups, as well as the Western Ontario and McMaster universities osteoarthritis index scale score, Lysholm score, arthritis impact measurement scale score and immunoinflammatory response before and after 3 mo of treatment. The effective aggregate rate of 94.00 % in experimental group after family rehabilitation training with etoricoxib treatment was higher than the effective aggregate rate of 80.00 % in control group after etoricoxib treatment ($p < 0.05$). After 3 mo of treatment, all Western Ontario and McMaster universities osteoarthritis index scale scores and arthritis impact measurement scale scores decreased in both groups and experimental group had lower Western Ontario and McMaster universities osteoarthritis index scale scores and arthritis impact measurement scale scores of joint function, stiffness and pain than control group; Lysholm scores increased in both groups, and experimental group had higher Lysholm scores than control group ($p < 0.05$). After 3 mo of treatment, all immune inflammatory response indicators decreased in both groups, and experimental group had lower interleukin-1, nuclear factor-kappa B and matrix metalloproteinase 3 indicators than control group ($p < 0.05$). In the treatment of knee osteoarthritis disease, family rehabilitation training with etoricoxib has a significant effect, which helps to reduce the level of immune inflammatory response and promote the recovery of their knee joint function.

Key words: Knee osteoarthritis, family rehabilitation, immune inflammatory response, etoricoxib

Knee Osteoarthritis (KOA), a degenerative joint disease in which the structure and function of the knee joint are compromised by a combination of factors, occurs mostly in the middle-aged and elderly population, if not managed promptly, can adversely affect the patient's quality of life^[1,2]. Appropriate use of medication is one of the most effective ways to treat KOA^[3,4]. Etoricoxib, a commonly used drug for KOA, is a highly selective cyclooxygenase-2 inhibitor that can have analgesic and anti-inflammatory effects and is effective in KOA. However, the use of this drug alone tends to lead to poor outcomes^[5,6]. In recent years, exercise therapy has gradually attracted the attention of the community. Family rehabilitation focuses on family training, by correcting the patient's motor training movements

during hospitalization and supervising the patient's training at home after discharge, it can improve the curative effect and improve the patient's joint function, while also reducing medical costs and the burden on the family. However, the mechanism of family rehabilitation with etoricoxib on the immune inflammatory response of KOA patients still needs to be further investigated. Based on this, 100 KOA patients were selected for this study to investigate the value of combining the two protocols. We selected 100 KOA patients admitted to our hospital from October 2021 to October 2022 and divided them into two groups according to the envelope randomization method. Control group consisted of 38 females and 12 males; age were from 44 y to 76 y old, mean (60.40 ± 6.56) y old; 26 cases in the right knee and 24

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cases in the left knee. Experimental group consisted of 37 females and 13 males; ages were from 45 y to 77 y old, mean (66.48 ± 6.41) y old; 27 cases in the right knee and 23 cases in the left knee. The baseline data of the two groups were compared ($p > 0.05$), so it had comparability. Inclusion criteria including the KOA diagnosis was in accordance with the osteoarthritis treatment guidelines (2018 version)^[7]; all patients could communicate normally; no history of knee surgery. Exclusion criteria those who withdrew on their own midway; secondary KOA; accompanied by concomitant patellofemoral osteoarthritis and hip osteoarthritis; receiving intra-articular treatment within 1 mo. The trial design of this study was reviewed and approved by the ethics committee of our hospital. Control group received etoricoxib (H20193303, 60 mg, Chengdu Yuandong Biopharmaceutical Co., Ltd.) orally twice a day, 60 mg/time, for a course of 3 mo. Experimental group received family rehabilitation training with etoricoxib treatment. In supine position training, place a soft pad of approximately 10 cm in diameter under the popliteal fossa, in the process to straighten the knee joint and extend the ankle forcefully dorsally, then press the soft pad downward forcefully, alternate legs, hold for approximately 10 s, repeat 5-10 times; flex one knee joint as close to the chest as possible, hold the thigh with both hands and slowly straighten the knee, followed by a slow flattening. Alternate legs and repeat 5-10 times, taking care to descend slowly when extending the knee; straighten the knee as far as possible and extend the ankle back hard, then slowly lift the straight leg up 30° and hold for about 10 s, allowing the knee to flex slowly, repeat 5-10 times. In seated training, bend your knees 90° , place your feet flat on the floor, straighten one knee as much as possible and slowly lower it, alternate legs, repeat 5-10 times; bend your knees 90° , place your heels on the floor and press your toes forward against the wall, making sure your feet don't shift, or repeat the braking motion, paying attention to the power, you need to let the muscles of your legs tense up and then relax. In prone training, bend one knee as close to the hip as possible, keep it in the bent position until it becomes sore, then slowly straighten the knee and do this with both feet alternately, repeat 5-10 times. Bedside knee flexion exercise; step on the head of the bed with both feet, straighten both knees and move the body back. In one-legged balance training, train to stand on one foot with the back against a wall, using no hands for balance if possible,

taking care not to lift the foot too high, alternating legs, for about 5 min each time, for a course of 3 mo. The KOA patient was instructed to adhere to the training after discharge and to standardize the patient's rehabilitation movements on the next admission. The efficacy was evaluated according to the relevant criteria^[8], after treatment, patients whose knee pain and swelling disappeared, joint function basically returned to normal indicated markedly effective, those whose knee pain and swelling were significantly relieved and whose joint function improved indicated effective and those who did not meet the above criteria indicated ineffective. The Western Ontario and McMaster Universities Osteoarthritis Index Scale (WOMAC)^[9] score scale was applied to assess the knee joint function before and after 3 mo of treatment in both groups, including joint function (17 items in total), stiffness (2 items in total) and pain (5 items in total), etc. Each item was scored 0 to 4 points, with a total score of 96 points, the lower the score, the better the joint function. In Lysholm scoring criteria^[10] and Arthritis Impact Measurement Scale (AIMS)^[11]; the Lysholm scoring criteria was used to assess the degree of knee ligament damage in both groups before and after 3 mo of treatment, with a score of 11 points, the higher the score, the better the knee function. The AIMS scale was used to assess joint function in both groups, with a total score of 46 points, the higher the score, the more severe the effect of arthritis on them. In immune inflammatory response, 3 ml of peripheral blood was drawn from both groups before and after 3 mo of treatment, centrifuged and serum was extracted for the determination of Interleukin (IL)-1 index by cellular immunohistochemistry, and Nuclear Factor-Kappa B (NF- κ B) and Matrix Metalloproteinase-3 (MMP-3) indexes were also measured. The measurement data were expressed as ($\bar{x} \pm s$), with independent samples t-test for comparison between groups and paired t-test for comparison within groups; the count data were expressed as n (%), with Chi-square (χ^2) test for comparison between groups. Data were analyzed with Statistical Package for the Social Sciences (SPSS) 23.0 software, and $p < 0.05$ indicating a statistical difference. The effective aggregate rate of 94.00 % in experimental group after family rehabilitation training with etoricoxib treatment was higher than the effective aggregate rate of 80.00 % in control group after etoricoxib treatment ($p < 0.05$) as shown in Table 1. After 3 mo of treatment, WOMAC scores decreased in both

groups, and experimental group had lower WOMAC scores of joint function, stiffness and pain than control group, as shown in Table 2. After 3 mo of care, Lysholm scores increased and AIMS scores decreased in both groups and experimental group had higher Lysholm scores but lower AIMS scores than control group ($p < 0.05$), as shown in Table 3. After 3 mo of treatment, all immune inflammatory response indicators decreased in both groups and experimental group had lower IL-1, NF- κ B and MMP-3 indicators than control group ($p < 0.05$), as shown in Table 4. According to data, there are approximately 250 million KOA patients worldwide, with more than 1/3rd of the elderly suffering from this disease and the prevalence of this disease is on the rise with age^[12]. The main symptoms of KOA are recurrent joint swelling, morning stiffness, joint pain and impaired movement, which in severe cases can cause deformities of the knee joint and have an impact on the patient's normal life. Therefore, intensive treatment of KOA is essential^[13]. Etoricoxib, a new generation of specific cyclooxygenase-2 inhibitors, can inhibit the production of prostacyclin from arachidonic acid by inhibiting the activity of cyclooxygenase, thus achieving analgesic and anti-inflammatory effects and the drug has low gastrointestinal adverse effects, helping to improve the patient's knee pain symptoms. However, etoricoxib treatment alone is not effective in rapidly improving the level of immune inflammatory response in patients^[14]. Exercise therapy, a safe and inexpensive treatment for KOA, has been shown to reduce pain, slow the progression of the disease and improve knee function. Exercise therapy is usually carried out under the guidance of a hospital doctor, but some patients choose to forego exercise therapy in hospital for financial and time reasons, so it is necessary to move the rehabilitation training venue from hospital to out-of-hospital. Family rehabilitation training uses hospital instruction as an adjunct and the home as the main treatment venue, instructing patients to perform supine training, seated training, prone training, bedside knee flexion training and one-legged balance training at home, by correcting patients' motor training movements during hospitalization and supervising them to train at home after discharge, it helps to alleviate their pain symptoms and promote functional recovery of the knee joint^[15]. The results of this study showed that the effective aggregate rate of 94.00 % in experimental group after family rehabilitation training with

etoricoxib treatment was higher than the effective aggregate rate of 80.00 % in control group after etoricoxib treatment ($p < 0.05$). After 3 mo of treatment, all WOMAC scores and AIMS scores decreased in both groups and experimental group had lower WOMAC scores and AIMS scores of joint function, stiffness and pain than control group; Lysholm scores increased in both groups and experimental group had higher Lysholm scores than control group ($p < 0.05$). It is suggested that family rehabilitation training with etoricoxib treatment can reduce knee ligament damage and improve knee function in KOA patients with significant efficacy, which is consistent with the results of previous studies^[16]. The reasons for this are, on the one hand, family rehabilitation can provide rapid pain relief and reduce the impact of arthritis on patients, thus improving knee function. In addition, family rehabilitation can help to compensate for, and support the motor function of the knee joint by providing continuous strength exercises for the periarticular muscle groups, which can contribute to knee ligament injuries and improve the treatment efficacy. KOA patients tend to develop various inflammatory responses during the disease progression, among which IL-1 can stimulate the secretion of tissue interstitial cells, thus enhancing the body's pain perception; NF- κ B can inhibit the expression of type I collagen and promote chemokine, inflammatory and MMP expression, aggravating joint damage; MMP-3 destroys joint bone, thus making the degree of joint damage more severe and the condition worse. In this study, it was found that after 3 mo of treatment, all immune inflammatory response indicators decreased in both groups, and experimental group had lower IL-1, NF- κ B and MMP-3 indicators than control group ($p < 0.05$). It is suggested that family rehabilitation training with etoricoxib treatment can reduce the immune inflammatory response in KOA. The contributing factors may be that family rehabilitation training is based on active non-weight-bearing exercise, which promotes muscle strength, improves and maintains joint range of motion, helps to improve the muscular endurance of joint tissues, and stabilizes the balance of the joint. The use of family rehabilitation training with etoricoxib accelerates the metabolism of diseased tissues, which helps to regulate the expression of IL-1, NF- κ B and MMP-3 indicators in patients and promotes a lower inflammatory response. However, there are still shortcomings in this study, such as the short duration

of the study, which does not allow for evaluation of the long-term effects of family rehabilitation training with etoricoxib treatment, so a longer case analysis could be conducted to improve the accuracy of the results. In summary, family rehabilitation with

etoricoxib is effective in the treatment of KOA disease, helping to reduce the level of immune inflammatory response and promoting the recovery of their knee function, and can be promoted.

TABLE 1: COMPARISON OF THE CLINICAL EFFICACY OF BOTH GROUPS [n (%)]

Group	Cases	Markedly effective	Effective	Ineffective	Effective rate
Experimental	50	26 (52.00)	21 (42.00)	3 (6.00)	47 (94.00)
Control	50	22 (44.00)	18 (36.00)	10 (20.00)	40 (80.00)
χ^2					4.332
p					0.037

TABLE 2: COMPARISON OF WOMAC SCORES BETWEEN BOTH GROUPS ($\bar{x} \pm s$, POINTS)

Group	Cases	Joint function			Stiffness			Pain					
		Before treatment	After treatment	t	p	Before treatment	After treatment	t	p	Before treatment	After treatment	t	p
Experimental	50	17.72±2.43	8.53±0.09	15.73	0.001	4.55±0.80	1.48±0.20	8.325	0.001	6.86±1.26	2.54±0.48	8.254	0.001
Control	50	17.65±2.40	13.18±0.16	13.43	0.001	4.51±0.78	2.53±0.45	7.832	0.001	6.82±1.22	3.06±0.65	6.242	0.001
t	-	0.324	7.062	-	-	0.145	5.423	-	-	0.162	4.472	-	-
p	-	0.740	0.001	-	-	0.848	0.001	-	-	0.857	0.001	-	-

TABLE 3: COMPARISON OF LYSHOLM SCORES AND AIMS SCORES BETWEEN BOTH GROUPS ($\bar{x} \pm s$, POINTS)

Group	Cases	Lysholm scores		t	p	AIMS score		t	p
		Before treatment	After treatment			Before treatment	After treatment		
Experimental	50	49.45±5.54	73.92±7.58	23.33	0.001	20.32±5.22	4.56±0.60	25.73	0.001
Control	50	49.49±5.41	66.82±6.18	18.43	0.001	20.31±5.20	7.30±1.23	22.24	0.001
t	-	0.985	8.825	-	-	0.295	9.471	-	-
p	-	0.328	0.001	-	-	0.769	0.001	-	-

TABLE 4: COMPARISON OF IMMUNE INFLAMMATORY RESPONSES BETWEEN BOTH GROUPS ($\bar{x} \pm s$)

Group	Cases	IL-1 (pg/ml)			t	p	NF-κB (ng/l)			t	p	MMP-3 (μg/l)			t	p
		Before treatment	After treatment				Before treatment	After treatment				Before treatment	After treatment			
Experimental	50	82.42±8.08	34.72±3.40	28.43	0.001		46.73±4.05	30.07±3.03	17.75	0.001		205.33±22.96	126.36±15.65	25.33	0.001	
Control	50	82.33±8.09	45.65±4.49	24.95	0.001		46.50±4.06	38.42±3.54	14.25	0.001		204.61±22.37	173.95±16.54	20.95	0.001	
t	-	1.493	16.870	-	-		0.315	7.573	-	-		1.151	16.824	-	-	
p	-	0.139	0.001	-	-		0.729	0.001	-	-		0.253	0.001	-	-	

Conflict of interests:

The authors declared no conflict of interests.

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