Research Paper

The Impact of Intraarticular Injection of Ropivacaine into Knee Joint on the Postoperative Analgesia and Local Inflammatory Response after Patellar Fracture Fixation

CHAO LIU, LONGWEI LU[1*]

Neurosurgery of Chinese PLA, Hospital of the 80th Group Army, Weifang 261021,Shandong, [1]Department of Orthopedics, Xiuzhou District People's Hospital, Jiaxing,China

To explore the impact of intraarticular injection of ropivacaine into knee joint on the postoperative analgesia and local inflammatory response after patellar fracture fixation is the main objective. The subjects of this study are 136 patients with patellar fracture who received selective open reduction Kirschner wire tension band fixation of patellar fracture in our hospital from March 2018 to November 2020 were divided into two groups on the basis of random number table, each with 68 cases. After operation, both groups were given patient controlled intravenous analgesia for 48 h and the observation group was also administrated with intraarticular injection of ropivacaine into knee joint, while the control group with the same dosage of normal saline. Both groups were assessed with visual analogue scale at different time points and in both resting and active states after operation. The two groups were compared in the aspects of analgesic pump dosage and active knee flexion, 48 h after operation. The interleukin 6 and tumor necrosis factor alpha levels were tested using enzyme linked immunosorbent assay by drawing 2 ml of arthrohydrops, 48 h after operation. And statistical analysis was conducted on adverse reactions of the two groups. The observation group had much lower visual analogue scale scores at resting state 6 h, 12 h, 24 h and 48 h after operation ($p<0.05$) and remarkably lower visual analogue scale scores at active state 1 d, 2 d, 3 d and 4 d after operation ($p<0.05$), than the control group did at identical time points. 48 h after operation, the observation group used much less analgesic pump ($p<0.05$) and obtained more active knee flexion than the control group did ($p<0.05$). The concentration of interleukin 6 and tumor necrosis factor alpha of the observation group in arthrohydrops 48 h after operation was much lower than that of the control group over the same period ($p<0.05$). The observation group saw obviously lower incidence of nausea, vomiting and urinary retention as well than the control group did ($p<0.05$). The application of intraarticular injection of ropivacaine into knee joint can effectively relieve the pain patients suffer after patellar fracture fixation and alleviate local inflammatory response without significant adverse reactions.

Key words: Ropivacaine, intraarticular injection, patellar fracture, postoperative analgesia, local inflammatory response

Patellar fracture is mostly caused by direct or indirect violence, such as crashing, kicking and falling. The incidence of patellar fracture is about 0.7 %-1 % of systemic fractures, with a tendency to increase in recent years[1,2]. Patellar fracture is an intraarticular fracture. To maximize the recovery of knee joint function, it is clinically recommended to receive surgical internal fixation treatment to achieve anatomic reduction. However, the presence of severe postoperative pain after fracture may affect postoperative rehabilitation[3,4]. Early rehabilitation after patellar fracture fixation is very important to restore joint function, so it is of great value in the prevention and treatment of postoperative pain. Intraarticular injection of ropivacaine has been shown to provide good postoperative analgesia in patients undergoing knee surgery and to alleviate tissue inflammation by reducing the production of substance P (is an undecapeptide, member of the tachykinin neuropeptide family)[5]. In order to further investigate the effect of intraarticular injection of ropivacaine into

***Address for correspondence**
E-mail: bfmdx@126.com

knee joint in postoperative analgesia of patellar fracture fixation, this study was conducted to compare the effect of intraarticular injection of ropivacaine into knee joint and patient controlled intravenous analgesia (PCIA) in postoperative analgesia of patellar fracture patients who were admitted in our hospital in recent years.

MATERIALS AND METHODS

The subjects of this study, 136 patients with patellar fracture who received fixation of patellar fracture in our hospital from March 2018 to November 2020, were divided into two groups on the basis of random number table, each with 68 cases. In observation group, there were 43 males and 25 females; aged 25-65 y old, with an average age of (46.2±9.4) y old; 36 cases of left patellar fracture and 32 cases of right patellar fracture; for the fracture types, 30 cases were transverse fracture, 27 cases were longitudinal fracture and 11 cases were comminuted fracture; 35 cases were fall injury, 29 cases were car accident injury and 4 cases were other injuries; 16 cases of complicated hypertension and 4 cases of diabetes mellitus. In the control group, there were 40 males and 28 females; aged 22-64 y old, with an average age of (44.8±10.5) y old; 39 cases of left patellar fracture and 29 cases of right patellar fracture; for the fracture types, 34 cases were transverse fracture, 26 cases were longitudinal fracture and 8 cases were comminuted fracture; 39 cases were fall injury, 27 cases were car accident injury and 2 cases were other injuries; 14 cases of complicated hypertension and 2 cases of diabetes mellitus. There was no statistical difference in the data between the two groups ($p>0.05$), which was comparable.

Inclusion criteria: Clear history of trauma, knee joint swelling and pain, patellar fracture diagnosed by computed tomography (CT) or X-ray; simple transverse or longitudinal patellar fracture (both fresh and closed fractures), comminuted patellar fracture and unilateral fracture; no surgical contraindication in preoperative examination and planned open reduction Kirschner wire tension band fixation; age 18-65 y old, either gender; time from fracture to admission <7 d.

Exclusion criteria: Old fracture, pathological fracture, open fracture, comminuted fracture with burst; anterior cruciate ligament fracture or injury; fracture in other sites of the same side; obvious skin injury or infection around knee joint; complicated with history of joint dysfunction; complicated with other serious medical diseases and malignant tumors; complicated with organic diseases such as cardiopulmonary and renal diseases; complicated with unconsciousness and mental disorder.

Methods

Surgery methods

Both groups were treated with open reduction Kirschner wire tension band fixation of patellar fracture. The patients were placed in supine position and underwent general anesthesia, conventional disinfection and draping and pneumatic tourniquet on the affected limb. Take the midline incision in front of the knee joint to expose the fracture site, rinse and clean the fracture end and reduce it. Use the reduction forceps to maintain the reduction. After the articular surface of patella is examined under the fluoroscopy of C-arm machine, place two 2 mm Kirschner wires in the longitudinal direction of patella, fix the fracture end. Use a steel wire to make an 8 character tension band to bundle the fracture site on the patellar surface through the two ends of Kirschner wire, cut the Kirschner wire and bend the two ends and place them in the patellar ligament. The surgical area was irrigated and the incision was closed layer by layer.

Postoperative analgesia method

The patients in both groups were given PCIA. PCIA formula: sufentanil 100 μg+granisetron 3 mg+tramadol 0.6 g, diluted with 0.9 % normal saline to 100 ml. Set the single press dose to 0.5 ml with a background rate of 1.5 ml/h and lock for 15 min for 48 h. In the observation group, except PCIA for analgesia, 0.45 % ropivacaine 20 ml was injected intraarticularly at the time of operation, while in the control group, normal saline was used to repeat the above mentioned intraarticular injection.

Observation indicators

Pain degree: The visual analogue scale (VAS) of pain was performed in both groups at resting state 6 h, 12 h, 24 h and 48 h after operation and at active state 1 d, 2 d, 3 d and 4 d after operation. A 10 cm long roving scale was used, with 0-10 graduations engraved on the scale. Both ends were scored as 0 and 10 points respectively, 0 point was scored as no pain and 10 points were scored as intolerable severe pain. With the increase of scores, the pain gradually aggravated. The dosage of analgesic pump: The dosage of analgesic pump within 48 h after operation was compared between the two groups. Active knee flexion range of the affected knee: The patients with active knee flexion range of the affected knee 48 h

after operation was compared between the two groups. Local inflammatory response: 2 ml of arthrohydrops was collected from two groups at 48 h after operation and the levels of interleukin 6 (IL-6) and tumor necrosis factor alpha (TNF-α) were measured by enzyme linked immunosorbent assay (ELISA). The operation shall be carried out in strict accordance with the requirements of kit.

Adverse reaction

Compare the occurrence of adverse reactions between the two groups, including nausea, vomiting, urinary retention and skin pruritus, etc.

Statistical analysis

SPSS 20.0 statistical software was used to process the data, in which $\chi 2$ test was used for counting data and t test was used for measuring data. $p<0.05$ was considered statistically significant.

RESULTS AND DISCUSSION

VAS scores comparison of the two groups at resting state 6 h, 12 h, 24 h and 48 h was done after operation. The VAS scores in the observation group were significantly lower than those in the control group at resting state 6 h, 12 h, 24 h and 48 h after operation ($p<0.05$) (Table 1).

VAS scores comparison of the two groups were performed at active state 1 d, 2 d, 3 d and 4 d after operation. The VAS scores in the observation group were significantly lower than those in the control group at active state 1 d, 2 d, 3 d and 4 d after operation ($p<0.05$) (Table 2).

Comparison was done between the dosage of analgesic pump and the active flexion range of the affected knee in the two groups, 48 h after operation. 48 h after operation, the observation group used much less analgesic pump and obtained more active knee flexion than the control group did ($p<0.05$) (Table 3).

Comparison of levels of IL-6 and TNF-α in arthrohydrops were performed 48 h after operation. The levels of IL-6 and TNF-α of the observation group in arthrohydrops 48 h after operation were much lower than that of the control group ($p<0.05$) (Table 4).

Comparison of adverse effects between the two groups was seen. The incidences of nausea, vomiting and urinary retention in the observation group were 22.06 % and 0 %, respectively and were significantly lower than those in the control group (55.88 % and 8.82 %, respectively) ($p<0.05$). There was no statistical difference in the incidence of skin pruritus between the two groups ($p>0.05$) (Table 5).

The patella is the largest sesamoid bone in the human body and is an important component of the knee joint. It can not only conduct and enhance the quadriceps strength, but also directly protect the femoral condyle, so as to protect it from violent trauma and maintain the stability of the knee joint. The principles of treatment for patellar fractures are restoration of the articular surface, anatomic reduction of the fracture, maintenance of extension mechanism continuity, early knee motion to promote restoration of knee function and reduction of complications such as traumatic arthritis[6]. In the surgical method of patellar fracture, Kirschner wire tension band internal fixation is a classical surgical method, which has the advantages of reliable fixation and compliance with biomechanical principles. However, this surgical method requires open reduction with severe postoperative pain, which is not conducive to early functional training[7,8].

Postoperative pain is a complex physiological reaction of the body to the tissue injury caused by surgery and the disease itself, which can have a wide impact on the body, including various systems such as endocrinology, immunity, nerves, respiration, circulation, urology and digestion, so as to increase the risk of occurrence of various complications and adversely affect

TABLE 1: THE COMPARISON OF VAS SCORES AT RESTING STATE 6 h, 12 h, 24 h AND 48 h AFTER OPERATION BETWEEN THE TWO GROUPS ($\bar{x}\pm s$, POINTS)

Group	Number of cases	6 h	12 h	24 h	48 h
Observation group	68	3.35±0.48#	3.03±0.42#	2.48±0.37#	1.95±0.24#
Control group	68	5.12±0.73	4.35±0.58	3.92±0.54	3.35±0.47
t		16.706	15.200	18.140	21.876
p		0.000	0.000	0.000	0.000

Note: Compared with the control group, #p<0.05

TABLE 2: THE COMPARISON OF VAS SCORES AT ACTIVE STATE 1 d, 2 d, 3 d AND 4 d AFTER OPERATION BETWEEN THE TWO GROUPS (x̄±s, POINTS)

Group	Number of cases	1 d	2 d	3 d	4 d
Observation group	68	3.75±0.46#	3.17±0.37#	2.66±0.37#	2.28±0.26#
Control group	68	5.28±0.69	4.85±0.55	4.34±0.62	3.72±0.43
t		15.214	20.899	19.187	23.631
p		0.000	0.000	0.000	0.000

Note: Compared with the control group, #p<0.05

TABLE 3: THE COMPARISON OF ANALGESIC PUMP DOSAGE AND ACTIVE KNEE FLEXION 48 h AFTER OPERATION BETWEEN THE TWO GROUPS (x̄±s)

Group	Number of cases	The dosage of analgesic pump 48 h after operation (ml)	Active flexion range of the affected knee 48 h after operation (degrees)
Observation group	68	78.21±6.74#	86.12±11.42#
Control group	68	90.27±10.25	73.05±14.28
t		8.107	5.894
p		0.000	0.000

Note: Compared with the control group, #p<0.05

TABLE 4: THE COMPARISON OF IL-6 AND TNF-α LEVELS IN ARTHROHYDROPS 48 h AFTER OPERATION BETWEEN THE TWO GROUPS (x̄±s, pg/ml)

Group	Number of cases	IL-6	TNF-α
Observation group	68	972.85±286.34#	58.27±11.36#
Control group	68	1575.44±470.92	72.36±16.24
t		9.015	5.863
p		0.000	0.000

Note: Compared with the control group, #p<0.05

TABLE 5: THE COMPARISON OF ADVERSE REACTIONS BETWEEN THE TWO GROUPS [n (%)]

Group	Number of cases	Nausea and vomiting	Urinary retention	Skin pruritus
Observation group	68	15 (22.06)	0 (0)	0 (0)
Control group	68	38 (55.88)	6 (8.82)	1 (1.47)
x2		16.355	6.277	1.007
p		0.000	0.012	0.316

the recovery of the body after operation[9]. Early postoperative functional training plays an important role in postoperative rehabilitation of patellar fracture. If postoperative pain cannot be effectively controlled, increased muscle tension or muscle spasm caused by pain may seriously affect functional rehabilitation and may cause complications such as knee joint dysfunction, traumatic arthritis and bone nonunion. Therefore, it is necessary to prevent and treat the postoperative pain of patellar fracture fixation. At present, the clinical application method for relieving postoperative pain of patellar fracture fixation is mainly PCIA, but the analgesic effect of PCIA is positively correlated with the dose used. For example, the increased dose may cause adverse reactions such as nausea, vomiting, skin pruritus and urinary retention.

In this study, patients in the observation group were simultaneously given intraarticular ropivacaine in addition to conventional PCIA and the results showed satisfactory analgesia. Since the local analgesia method

for knee joint is simple in operation, definite in analgesic effect, without obvious adverse reaction and convenient in nursing, it has been gradually paid attention to by orthopedic surgeons in recent years. The study by Vendittoli *et al.*[10] showed that the mixed solution of ropivacaine+epinephrine+ketorolac injection injected around the joint significantly reduced the pain score at resting state 48 h and the dose of analgesic drugs used within 48 h after operation. Ropivacaine is a long acting amide agent. The separation effect between motor block and sensory block is obvious, with strong controllability. Ropivacaine has slight side effects on cardiovascular system and central nervous system. Ropivacaine can contract blood vessels, reduce plasma absorption and prolong drug effect[11]. Intraarticular injection of ropivacaine blocks noxious stimulus conduction due to surgical trauma or fracture itself, which can effectively inhibit pain signals triggered by nerve endings at the site of injury. The results of this study showed that compared with PCIA alone, patients treated with intraarticular injection of ropivacaine into knee joint had significantly lower pain VAS scores at resting state 6 h, 12 h, 24 h and 48 h after operation and lower pain VAS scores at active state 1 d, 2 d, 3 d and 4 d after operation than those treated with PCIA alone at the same time after operation. It is suggested that intraarticular injection of ropivacaine was more effective in reducing postoperative pain after patellar fracture fixation. In this study, intraarticular injection of ropivacaine significantly reduced the dose of PCIA drugs, resulting in a lower incidence of nausea, vomiting and urinary retention.

The patellar fracture can be anatomically reduced through surgical treatment but the fracture is often accompanied by damage of joint capsule, synovium and cartilage, etc. After the damage to the tissues around the knee joint, it will not only cause bleeding, exudation, muscle adhesion and tissue spasm, etc., but also cause the release of a large amount of local inflammatory mediators. After entering the arthrohydrops, inflammatory mediators are phagocytosed by synovial cells and develop into chronic inflammatory process. The diffusion of inflammatory factors through the arthrohydrops can further damage the tissues around the joint and affect the postoperative rehabilitation. A number of studies have demonstrated, that inflammatory cytokines such as TNF-α and IL-6 are involved in the development and progression of osteoarthritis[12,13]. TNF-α is one of the mediators that activate the inflammatory cascade and its expression is significantly higher in patients with joint diseases or trauma than in healthy individuals. IL-6 is an important pro inflammatory factor that promotes macrophage differentiation and infiltration, up-regulates adhesion molecule expression and promotes enhanced inflammatory response. IL-6 has been shown to stimulate the accumulation and activation of inflammatory cells, promote the release of inflammatory mediators and cause local pain and joint stiffness formation after knee joint trauma[14]. The results showed that the levels of IL-6 and TNF-α in arthrohydrops, 48 h after intraarticular injection of ropivacaine in the observation group were significantly lower than those in the control group. It is suggested that intraarticular injection of ropivacaine is beneficial to relieve the inflammatory reaction of the tissues around the knee joint after patellar fracture fixation. The main reason is that intraarticular injection of ropivacaine can infiltrate the nerve endings in the knee joint cavity and block the transmission of nociceptive stimulation, thus reducing the hyperalgesia, increasing the pain threshold and reducing the postoperative pain level significantly[15]. Intraarticular injection of ropivacaine also reduces the postoperative local stress response and inhibits the chemotaxis of inflammatory cells, thereby relieving the inflammatory response.

In conclusion, the intraarticular injection of ropivacaine into knee joint after patellar fracture fixation can effectively reduce the postoperative pain of patients, reduce the dosage of intravenous anesthetic drugs and significantly relieve local inflammatory reactions without obvious adverse reactions. With high safety, it is worthy of being widely popularized in the clinical application.

Funding:

The work was supported by Jiaxing Science and Technology Plan Project No 2019AD32211: Clinical application of endoscopic transforaminal lumbar body fusion (Endo-TLIF).

Conflict of Interests:

The authors declared no conflict of interest.

REFERENCES

1. Larsen P, Vedel JO, Vistrup S, Elsoe R. Incidence and epidemiology of patellar fractures. Orthopedics 2016;39:e1154-8.
2. Song L, Wei C, Wei W, Yueju L, Ran S, Tao S, *et al.* Epidemiological investigation of adult patellar fractures in the Third Affiliated Hospital to Hebei Medical University from 2003 through 2012. Chin J Orthop Trauma 2014;16:973-7.
3. Weishan W, Jianhua S, Kuanxin L. Clinical efficacy comparison and treatment strategy analysis of different treatment methods

for patellar fractures. J Pract Med 2013; 28: 3044-6.
4. Larangeira JA, Bellenzier L, da Silva Rigo V, Neto EJ, Krum FF, Ribeiro TA. Vertical open patella fracture, treatment, rehabilitation and the moment to fixation. J Clin Med Res 2015;7(2):129.
5. Rabinow B, Werling J, Bendele A, Gass J, Bogseth R, Balla K, *et al.* Intra articular (IA) ropivacaine microparticle suspensions reduce pain, inflammation, cytokine and substance p levels significantly more than oral or IA celecoxib in a rat model of arthritis. Inflammation 2015;38:40-60.
6. Shixin G, Jian S. Analysis of advantages and disadvantages in the treatment of patellar fractures. Med Recapitulate 2017;23: 2202-5.
7. Fei C, Jinzhu F, Tao S. Comparison of the efficacy of open reduction Kirschner wire tension band and closed reduction percutaneous hollow nail fixation in the treatment of patellar fractures. Chin J Bone Jt Inj 2017;32: 259-61.
8. Dongbin L. Modified Kirschner wire tension band internal fixation of patellar fracture. Chin J Orthop Trauma 2012;14:1101-2.
9. Kemin Z, Baoguo S, Wei L. Analysis of risk factors for chronic postoperative pain in patients undergoing orthotics for limb fractures. Chin J Public Health 2016;32:1415-7.
10. Vendittoli PA, Makinen P, Drolet P, Lavigne M, Fallaha M, Guertin MC, *et al.* A multimodal analgesia protocol for total knee arthroplasty: a randomized, controlled study. J Bone Joint Surg Am 2006;88:282-9.
11. Liu T, Feng H, Zhang Q, Wang X. Influence of different concentration of ropivacaine on heart rate variability following intersalene brachial plexus block. J Clin Anesthesiol 2016;32:853-6.
12. Nasi S, So A, Combes C, Daudon M, Busso N. Interleukin-6 and chondrocyte mineralisation act in tandem to promote experimental osteoarthritis. Ann Rheum Dis 2016;75:1372-9.
13. Shuting H, Jianhua X, Changhai D. Role of inflammatory cytokines and mechanical factors in pathogenesis and structural changes of knee osteoarthritis. Anhui Med J 2013;34:1417-9.
14. Cuellar JM, Scuderi GJ, Cuellar VG, Golish SR, Yeomans DC. Diagnostic utility of cytokine biomarkers in the evaluation of acute knee pain. J Bone Joint Surg Am 2009;91:2313-20.
15. Xiaochen H, Haitao F, Dan H. Analgesic effects of continuous and single intraarticular administration after total knee arthroplasty. J Clin Anesthesiol 2016;32:1131-2.

This article was originally published in a special issue, "Clinical Research in Pharmaceutical and Biomedical Sciences" Indian J Pharm Sci 2021:83(1)spl issue "148-153"