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Efecto de celecoxib combinado con mesilato de ropivacaína en el tratamiento de lesiones deportivas y analgesia

Effect of Celecoxib Combined with Ropivacaine Mesylate in the Treatment of Sports Injury and Analgesia

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Resumen
Los medicamentos antiinflamatorios no esteroideos, como la aspirina, el diclofenaco, el ibuprofeno y el celecoxib, son los antiinflamatorios y analgésicos más utilizados en humanos en la actualidad. Estos medicamentos tienen buenos efectos antiinflamatorios y analgésicos y se usan ampliamente en el tratamiento de la osteoartritis, la artritis reumatoide, el dolor agudo, las lesiones deportivas y las enfermedades de los tejidos blandos. Este artículo analiza los efectos de celecoxib combinado con mesilato de ropivacaína sobre las lesiones deportivas y la analgesia. Debido al dolor postoperatorio, la mayoría de los pacientes serán tratados con analgésicos temprano en el período postoperatorio, y el ejercicio funcional se iniciará lo antes posible sobre la base del control del dolor para evitar adherencias articulares postoperatorias. Aunque algunos estudios han demostrado que el efecto analgésico es satisfactorio, también han aparecido informes de sus reacciones adversas de vez en cuando. El ejercicio funcional temprano después de la cirugía de lesiones deportivas es una parte importante para lograr la función ideal, sin embargo, el ejercicio funcional suele ir acompañado de un dolor bastante intenso. El dolor causa actividades de rehabilitación retrasadas y conduce a la contractura, adhesión y rigidez de las articulaciones alrededor de las articulaciones, lo que afecta el efecto de reemplazo. El buen control del dolor desempeña un papel importante en el movimiento articular temprano de los pacientes y la recuperación del estado normal.

Palabras clave: Medicamentos antiinflamatorios no esteroideos; Mesilato de ropivacaína; Lesion deportiva; Efecto analgésico

Abstract
Non-steroidal anti-inflammatory drugs, including aspirin, diclofenac, ibuprofen, and celecoxib, are the most commonly used anti-inflammatory and analgesics in humans today. These drugs have good anti-inflammatory and analgesic effects and are widely used in the treatment of osteoarthritis, rheumatoid arthritis, acute pain, sports injuries and soft tissue diseases. This article analyzes the effects of celecoxib combined with ropivacaine mesylate on sports injury and analgesia. Due to postoperative pain, most patients will be treated with pain medication early in the postoperative period, and functional exercise will be started as soon as possible on the basis of controlling pain to avoid postoperative joint adhesions. Although some studies have proved that the analgesic effect is satisfactory, reports of its adverse reactions have also appeared from time to time. Early functional exercise after sports injury surgery is an important part of achieving ideal function, however, functional exercise is often accompanied by quite severe pain. Pain causes delayed rehabilitation activities and leads to contracture, adhesion, and stiffness of joints around the joints, which affects the replacement effect. Good pain control plays an important role in patients' early joint movement and normal state recovery.

Key words: Nonsteroidal anti-inflammatory drugs; Ropivacaine mesylate; Sports injury; Analgesic effect

1. Introduction

Non-steroidal anti-inflammatory drugs, including aspirin, diclofenac, ibuprofen, and celecoxib, are the most commonly used anti-inflammatory and analgesics in humans today [1]. These drugs have good anti-inflammatory and analgesic effects and are widely used in the treatment of osteoarthritis, rheumatoid arthritis, acute pain, sports injuries and soft tissue diseases [2]. For patients with full-thickness rotator cuff injury, arthroscopic repair can obtain a more definite treatment effect, and it has now become the international gold standard for treating this disease [3]. Due to postoperative pain, most patients will be treated with pain medication early in the postoperative period, and functional exercise will be started as soon as possible on the

basis of controlling pain to avoid postoperative joint adhesions. Although some studies have proved that the analgesic effect is satisfactory, reports of its adverse reactions have also appeared from time to time [4]. Early functional exercise after sports injury surgery is an important part of achieving ideal function, however, functional exercise is often accompanied by quite severe pain. Pain causes delayed rehabilitation activities and leads to contracture, adhesion, and stiffness of joints around the joints, which affects the replacement effect. Good pain control plays an important role in patients' early joint movement and normal state recovery [5].

Celecoxib is also called celecoxib. It is suitable for patients with osteoarthritis, rheumatoid arthritis, acute pain, and primary dysmenorrhea. At present, the drug has been approved for use in 120 countries and local doctors, including China. As a new generation of non-steroidal anti-inflammatory analgesics, celecoxib inhibits prostaglandin production by selectively inhibiting cyclooxygenase-2 (COX-2). COX-1, a physiological enzyme that protects the gastrointestinal tract, has a significantly lower risk of gastrointestinal adverse reactions than traditional non-steroidal anti-inflammatory analgesics [6]. Ropivacaine hydrochloride has been widely used in peripheral nerve blocks and has achieved good results. Ropivacaine mesylate is a new domestic amide-type local anesthetic, which is based on the chemical structure of ropivacaine hydrochloride to mesylate [7-8]. Only has changed its physical and chemical properties, has not changed its pharmacological effects and has more stability. Ropivacaine mesylate, as a long-acting amide-type local anesthetic, has been widely used in various nerve blocks and epidural blocks [9]. Compared with bupivacaine, it has low cardiovascular and central nervous system toxicity. Strong analgesic effect, long duration of action, low concentration of ropivacaine can produce sensory. Motor nerve block separation. This article uses celecoxib in combination with ropivacaine mesylate to analyze the effects of treating sports injury and analgesia, so as to explore new clinical uses [10].

2. Materials and Methods

2.1 Experimental Objects

This study selected from December 2018 to December 2019 in the Sports Injury Department of our hospital for rotator cuff full-thickness surgical repair, 63 patients received pain medication after surgery, 36 males and 27 females, with an average age of 44.5 (22 to 64) years old [11]. The specific admission criteria are as follows: (1) small-scale full-thickness rotator cuff injury; (2) the rotator cuff injury range only involves simple supramolecular tear; (3) arthroscopic single-row suture method for anatomical repair of rotator cuff; Consent to postoperative pain medication observation; (5) Patients who cooperated with postoperative rehabilitation exercises; (6) No other medical system diseases, a long history of taking medications; (7) Long-term follow-up [12\. Exclusion criteria were: (1) rotator cuff injury repaired with more than two anchors; (2) medium, large and huge rotator cuff injury; (3) microscopic findings of other tendon injuries or other diseases such as biceps tendon Inflammation, etc .; (4) some patients with rotator cuff injury who only undergo debridement treatment; (5) patients who are unwilling to conduct this study; (6) patients who cannot cooperate with rehabilitation training and long-term follow-up after surgery; (7) mergers such as digestion Medical system diseases such as canal ulcers are not suitable for non-steroidal drugs or a long-term medical history [13]. For all selected patients, an informed consent was signed before drug treatment, which was approved by the rationale committee of our hospital.

2.2 Method

2.2.1 Surgery

All surgeries were performed by the same group of doctors, and arthroscopic techniques were used to repair the torn rotator cuff. General anesthesia was used for the operation, and the patient was placed on a beach chair to establish the rear, posterolateral, anterolateral, and anterior superior pathways. First enter the glenohumeral joint to evaluate the rotator cuff articular surface [14]. Then enter the acromion space and decompress under the acromion. After that, the bursa surface of the rotator cuff was explored, and the rotator cuff tissue was pulled back to its anatomical end point without tension after releasing the adhesion with the surrounding tissue. Do a cortical treatment on the surface of the large nodule to obtain a better healing environment. Drill holes at the apex of the large nodule and screw in suture anchors [15]. The number of anchors depends on the anterior and posterior diameter of the injury. The tail line is passed through the tendon in a simple suture and tied to fix the rotator cuff.

2.2.2 Postoperative rehabilitation

The patient's neck and wrist straps were braked after the operation. On the first day after surgery, passive shoulder motion was performed, and there was no restriction on forward flexion and internal and external rotation. After 6 weeks, the sling was removed, active activities were started, and muscle training was started 3 months later.

2.2.3 Grouping

In the trial, patients were randomly divided into oral celecoxib, oral celecoxib, ropivacaine mesylate, and intravenous mesosulfone according to the envelope method before receiving medication after arthroscopic

rotator cuff repair. Ropivacaine 3 groups, 21 cases in each group [16]. The celecoxib group was administered at a dose of 400 mg orally every 131 times. The dose of ropivacaine mesylate group was 0.250% and the dose of ropivacaine mesylate was 50 mg, which was administered intravenously once daily. All three groups were treated continuously for 5 days.

2.3 Evaluation Method

All patients' age, sex, height, weight, course of disease, smoking, and visual analogue scale (VAS) of pain before, on the same day and 5 days after operation were recorded, including stationary phase and active phase. The patients' pain scores on the 5th day after surgery were compared with the pain scores on the day after surgery and compared between groups [17]. While assessing pain, patients were recorded for early postoperative adverse reactions (nausea and vomiting, urine retention, skin allergies, edema) and compared with each other. Shoulder joint function was assessed by simple shoulder joint score (SST), UCLA score (UCLA), and Constant-Murley score. Previous flexion and lift (FE), lateral external rotation (ER), and internal rotation reached spinal height (IR) Assess joint range of motion. Patients' pain, function scores, and activity were recorded before and 12 months after surgery, and compared between groups.

2.4 Statistical Processing

All count data were expressed by $\bar{x} \pm S$, using SPSS17.0 software, and the significance test was performed by one-way analysis of variance (ANOVA). All measurement data were tested by X^2. P <0.05 was considered statistically significant.

3. Result

3.1 Comparison of Basic Conditions of the Three Groups of Patients

There were no statistically significant differences in weight, age, gender, duration of disease, proportion of smokers, and BMI among the three groups of patients (Table 1).

Table 1: Comparison of Basic Conditions of the Three Groups of Patients ($\bar{x} \pm S$)

Project	Celecoxib Formation	Joint group	Ropivacaine mesylate group	P
Number of cases	21	21	21	
Age	42.01±16.46	47.11 ±16.84	39. 79±16. 56	0. 051
Gender (eg, male / female)	13/8	11/10	12/9	0. 351
Course of disease (year)	16.5±70.2	20.1±47.2	12.3±10.7	0. 106
Smoking rate (example)	5/16	8/13	4/17	0. 121
BMI (kg / m2)	23. 32±9. OS	25. 24±12. 40	20. 01±14. 29	0. 458
VAS score (points)	7. 7±1.9	6. 9±2. 2	7.2±2.4	0. 322
Constant (minutes)	68. 3±18. 6	64.9±10.9	71. 4±14. 3	0. 418
UCLA (points)	17.9±9.4	15. 4±6. 6	18. 1 ±19. 2	0. 662
SST (points)	5. 9±2. 1	6. 9±3. 6	6.6±2.3	0. 741
IR (segment)	L1	L1	L 3	0. 121
FE(°)	122.1±31. 9	143. 5 ±24. 5	133. 8 ±29. 9	0. 195
ER(°)	42. 1±12. 0	37. 5±19. 4	33.5±12.9	0. 089

3.2 VAS Score

The pain in the three groups was significantly reduced with the postoperative time. From the first day after the operation, the pain was significantly different in the three drug groups compared with the postoperative day, but within the first three days after the operation, there were differences between the three drug groups. There was no statistical significance; starting from the 4th day after surgery, the combination group had higher pain relief than the ropivacaine mesylate and celecoxib groups (Tables 2, 3).

Table 2: VAS Scores at Different Times after Operation in the Three Groups (points, $\bar{x} \pm S$)

Time	Celecoxib group (21)	Joint Group (21)	Ropivacaine mesylate group (21)
Postoperative day			
Stationary phase	7.3±0. 7	7.1±0. 9	6. 9±0. 7

Active phase	8.2±1.2	8.0±1.2	7. 2±1. 0
1st day after surgery			
Stationary phase	6. 8±0. 8	6.5±1.3	5.9±0. 9
Active phase	7.6±1.4	7.7±1.2	6.2±0.9
Day 2 after surgery			
Stationary phase	5.4±1.9	5.8±1.0	4. 6±0. 8
Active phase	6.3±0.4	6.8±1.2	5. 0±1.5
3rd day after surgery			
Stationary phase	4. 1±1.2	3. 7±1.5	3. 0±0. 2
Active phase	5. 1±1.2	5. 4±2. 5	4. 1±1.0
4th day after operation			
Stationary phase	4.0±1.0	3.4±1.4	2. 0±1. 3
Active phase	4. 6±1. 3	5.0±1. 1	2. 4±0. 8
5th day after operation			
Stationary phase	3. 4±1.2	3.0±0.2	1.7±1.7
Active phase	4. 0±1.4	4.2±1.0	2. 1±1. 0

Table 3: VAS Difference in Pain Relief between the 3 Groups (Points, $\bar{x} \pm S$)

Time	Celecoxib group (21)	Joint Group (21)	Ropivacaine mesylate group (21)	P
The day after surgery ~ the first day after surgery				
Stationary phase	0.5± 0.7	0.6±0.2	1.0±0. 7	0.12
Active phase	0. 6±0.8	0.4±1.2	1.1±1.0	0. 25
The day after surgery ~ the second day after surgery				
Stationary phase	1.9±1.0	1.3±1.0	2. 3 ±0. 7	0. 24
Active phase	1.9±0. 4	1.2±1.0	2. 2±1. 2	0.23
Postoperative day ~ 3rd postoperative day				
Stationary phase	3.3±1.1	3.4±1.2	4.0±0.7	0. 45
Active phase	3. 2±1.3	2. 7±2. 0	3.1±1.3	0. 43
Postoperative day ~ 4th postoperative day				
Stationary phase	3.3±1.0	3. 7±1. 3	4. 9±1. 7	0. 03
Active phase	3.5±1.9	3.0±1.0	4.8±1.0	0. 04
The day after surgery ~ the 5th day after surgery				
Stationary phase	3.9±1.3	4.2±0.8	5. 2±2. 0	0. 03
Active phase	4. 1±2.5	3.8±1.4	5.1±1. 9	0. 03

3.3 Adverse Reactions

The ropivacaine mesylate group and the combined group had a lower adverse reaction rate than the celecoxib group, but the differences were not statistically significant (Table 4).

Table 4: Postoperative Adverse Reactions in the Three Groups of Patients (Cases)

Group	Number of cases	feel sick and vomit	Urine retention	Skin allergies	Edema
Celecoxib Formation	21	6	1	0	1
Joint group	21	1	0	1	1
Ropivacaine mesylate group	21	2	0	0	0

3.4 Postoperative Situation

At 1-year follow-up, patients had significantly improved VAS, Constant, UCLA, SST, forward flexion, external rotation, and internal rotation compared with those before surgery (P <0.05). There was no significant difference in the indicators (Table 5).

Table 5: Comparison of Pain, Function Score, and Activity at 1 Year after Operation in the 3 Groups

Project	Celecoxib group (21)	Joint Group (21)	Ropivacaine mesylate group (21)	P
VAS (minutes)	2. 0±1. 3	2. 1±0. 9	1. 9±0. 5	0. 741
Constant (minutes)	82. 7±12. 3	91. 2±23. 2	90.51±14.9	0. 123
UCLA (points)	29. 9±7. 2	33.2±11.9	30. 3±2. 5	0. 631
SST (points)	9.2±1.5	8.8±2.6	10.5±1.5	0. 210

1R (minutes)	T12	T12	T8	0. 781
FE(°)	151.2±19.2	150. 0±29. 7	160. 3±14. 4	0. 126
ER(°)	49. 2±25. 6	50. 7±11.0	56. 7±12. 4	0. 069

Figure 1. Sports Injury

4. Discussion

Non-steroidal anti-inflammatory drugs (NSAIDs) are the most widely used class of prescription drugs worldwide. They are taken by more than 30 million people every day. They are a class of drugs with antipyretic, analgesic, anti-inflammatory and anti-rheumatic effects. The main mechanism for this is to inhibit cyclooxygenase (COX) in the body, thereby reducing the synthesis of prostaglandins that cause fever, swelling and hypersensitivity to pain. British physiologist JohnVane et al. Found that NSAIDs inhibit COX and reduce prostaglandin production (JohnVane was awarded the Nobel Prize for Medicine in 1982).

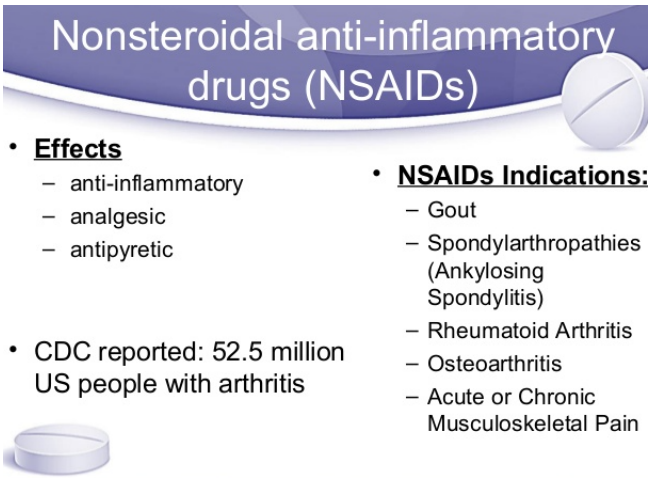

Figure 2. Non-steroidal Anti-inflammatory Drugs

NSAIDs fall into two broad categories, non-selective NSAIDs and selective COX-2 inhibitors. Non-selective NSAIDs, also known as traditional NSAIDs (such as ibuprofen, diclofenac, meloxicam, etc.), have inhibitory effects on both COX-1 and COX-2. Its inhibition of COX-1 leads to a reduction in gastrointestinal protection and a higher incidence of gastrointestinal adverse reactions (ulcers, bleeding, etc.). The new generation of NSAID, which is a selective COX-2 inhibitor, specifically inhibits COX-2, has anti-inflammatory and analgesic effects while greatly reducing adverse reactions in the digestive tract, and has successfully solved the century-old problem of traditional NSAID gastrointestinal injury. "Milestone Breakthrough".

Investigations have shown that patients taking traditional NSAIDs can't help digestive tract events occur earlier, with a higher incidence, strong concealment and serious consequences. The data showed that after taking some traditional non-steroidal anti-inflammatory analgesics in healthy people, 19% of patients developed microscopic gastric ulcers after one week. Among people taking this class of drugs, the average incidence of indigestion can reach up to 50%; if taken for more than 2 months, the average incidence of gastric ulcer under microscope is as high as 21%. In addition, a 1997 study from the United States Shows that: 81% of patients admitted to the hospital due to adverse reactions have no symptoms before severe attacks; approximately 16,500

people in the United States die each year from complications associated with traditional non-steroidal anti-inflammatory analgesics; taking traditional non-steroidal anti-inflammatory anti-inflammatory drugs Patients with pain medicines have an annual mortality rate related to gastrointestinal events: osteoarthritis is 0.1%; rheumatoid arthritis is 0.2%. Therefore, comprehensive evaluation of gastrointestinal risk factors in patients should be conducted before clinical treatment, especially those that may cause serious gastrointestinal adverse reactions (such as ulcers, bleeding, perforation), to minimize the patient's stomach after taking non-selective NSAIDs. Intestinal events, which in turn alleviate patients' illness, reduce medical expenses, and reduce the burden of national medical expenses.

Siloxan is the first selective COX-2 inhibitor approved by the FDA, and it is currently the largest non-steroidal anti-inflammatory analgesic in the world. According to 2008 statistics, Xylo's monthly prescription volume exceeds 1 million. Xilepan is also a non-steroidal anti-inflammatory drug with the most clinical research data, and has the best evidence-based medical evidence for its efficacy and safety.

In the "Arthritis Treatment Guideline" developed by the American Rheumatological Society in 2000, selenium was recommended as the first choice for the treatment of arthritis. In the American Pain Society's "Guidelines for the Treatment of Arthritis Pain" in 2002, celecoxib was listed as the drug of choice for moderate and severe arthritis pain and inflammation. Since the introduction of Xilepan in China in 2001, the number of prescriptions has also increased rapidly year by year, and has now become the largest non-steroidal anti-inflammatory analgesic in China.

Figure 3. Celebrex

Ropivaca mesylate is mainly used for surgical anesthesia because of amide-type local anesthetics: epidural anesthesia (including epidural anesthesia for cesarean section); local infiltration anesthesia. Acute pain control: used for postoperative or childbirth analgesia, continuous epidural infusion, or intermittent medication; local infiltration anesthesia.

According to literature data, the pKa of ropivacaine is 8.1 and the distribution rate is 141 (n-octanol / phosphate buffer pH 7.4 at 25 °C). The plasma concentration of ropivacaine depends on the dose, route of administration, and vascular distribution at the site of injection. Ropivacaine conforms to linear algebra, and the maximum plasma concentration is proportional to the dose. The absorption of ropivacaine from the epidural is complete and biphasic, and its half-life order is 14 minutes and 4 hours, respectively. Slow absorption is the rate-limiting factor for ropivacaine clearance, which may explain why epidural medications have a longer half-life than intravenous medications. The total plasma clearance of ropivacaine was 440 ml / min. Free plasma clearance was 8 L / min. The renal clearance is 1ml / min, the steady-state distribution volume is 47L, and the final half-life is 1.8hr. The intermediate metabolic rate of ropivacaine through the liver is 0.4. Ropivacaine mainly binds to α1-acid glycoprotein in plasma, and the non-protein binding rate is 6%. When continuous epidural injection, an increase in the total plasma concentration of ropivacaine was observed to be associated with an increase in the α1-acid glycoprotein concentration after surgery. The change in unbound (pharmacologically active) concentration was greater than that in the total plasma concentration. Change is small. Ropivacaine easily penetrates the placenta and quickly reaches equilibrium relative to unbound concentrations. Compared with the mother, the degree of binding of ropivacaine to plasma proteins is lower, so that the total fetal plasma concentration is lower than that of the mother. Ropivacaine is fully metabolized mainly by aromatic hydroxylation. 86% of the total dose after intravenous injection is excreted through the urine, of which only 1% is related to unmetabolized drugs. The main metabolite is 3-hydroxyropivacaine, about 37% of which is excreted from urine as a conjugate, 4-hydroxyropivacaine excreted in urine, N-dealkyl metabolites and 4 -Hydroxydealkyl metabolites are about 1-3%. Bound and unbound 3-hydroxyropivacaine showed only measurable concentrations in plasma. 3-hydroxyropivacaine and 4-hydroxyropivacaine have local anesthetic effects, but the anesthetic effect is weaker than ropivacaine. Ropivacaine has no evidence of racemization in the body.

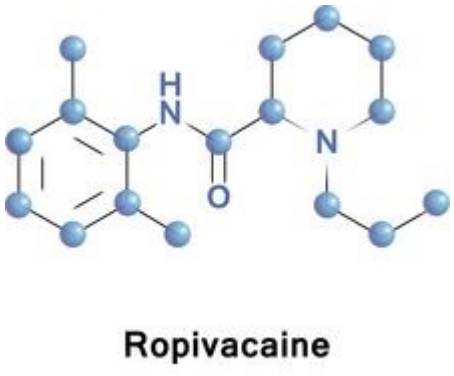

Figure 4. Structure Diagram of Ropivacaine

This study still has the following limitations and deficiencies: ① Because patients with huge rotator cuff tears, combined with scapula fractures, and labral avulsion injuries cannot be evaluated, it is impossible to evaluate whether the patients can obtain the same clinical efficacy; ② This study did not evaluate The effect of different surgical methods on rotator cuff tears can serve as the direction for our further research.

5. Conclusion

In short, celecoxib combined with ropivacaine mesylate as an analgesic drug can be used for early pain control after rotator cuff repair. The pain relief in the combination group was significantly better than ibuprofen and celecoxib from day 4 after surgery. Although celecoxib had a higher incidence of adverse reactions, the three drugs did not show statistical differences. Early postoperative use of celecoxib or ropivacaine mesylate did not affect the healing of the rotator cuff tendon.

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