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Analgesic effect of continuous femoral nerve block combined with infiltration anesthesia after total knee replacement

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ABSTRACT

Objective: To study the analgesic effect of continuous femoral nerve block combined with infiltration anesthesia after total knee replacement. **Methods:** Patients who received unilateral total knee replacement in our hospital from May 2012 to August 2015 were included for study and randomly divided into experimental group who received continuous femoral nerve block combined with infiltration anesthesia and control group who received continuous femoral nerve block, and then the contents of postoperative serum pain-promoting-related mediators, pain-suppressing-related mediators and pain-related signal molecules were detected. **Results:** Serum CGRP, PS, Hist, 5-HT, AM and BK contents of experimental group were significantly lower than those of control group, AEA, β-EP, RvE1, LXA4 and LXB4 contents were significantly higher than those of control group, and $P2X_2$, $P2X_7$, $P2X_3$, $P2X_4$, $P2Y_1$, $P2Y_2$, $P2Y_4$, $P2Y_6$, $P2Y_{13}$, $P2Y_{14}$, p38MAPK and PI3K contents were significantly lower than those of control group. **Conclusions:** Continuous femoral nerve block combined with infiltration anesthesia after total knee replacement can increase the generation of pain-suppressing mediators, decrease the generation of pain-promoting mediators and achieve more exact analgesic effect.

1. Introduction

Total knee replacement is commonly used surgery in the clinical treatment of knee joint disease, and the pain caused by surgical trauma will affect the exercise of the knee joint and the recovery of joint function. Continuous femoral nerve block is currently the main clinical way for postoperative analgesia, and can alleviate the pain to a certain extent[1,2]. However, because the nerve plexus around the knee joint is relatively rich, and is from the femoral nerve, sciatic nerve, the obturator nerve and other multiple neuves, continuous femoral nerve block for analgesia alone has the deficiency of incomplete analgesia[3,4]. Infiltration anesthesia is the analgesia method proposed in recent years, which relieves local pain through the mixed use of long-term amides local anesthetics, opioid receptor agonist and glucocorticoid[5,6]. In the following research, the analgesic effect of applying continuous femoral nerve block combined with infiltration anesthesia after total knee replacement was analyzed.

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2. Materilas and methods

2.1. Research subjects

Patients who received unilateral total knee replacement in our hospital from May 2012 to August 2015 were included for study, all patients met surgical indications and signed informed consent forms, ASA grades were I-III grades and there were a total of 76 cases. Random number table was used to divide included patients into experimental group (n=30) and control group (n=30). Experimental group received continuous femoral nerve block combined with infiltration anesthesia for analgesia and control group received continuous femoral nerve block for analgesia.

2.2. Analgesic methods

Both groups received femoral nerve block at first after entering into the operating room, the puncture point was in 1.5 cm outside of femoral artery and 1.0 cm below inguinal ligament, continuous nerve plexus block suite was used for operation, 1.0 mA galvanism was used to confirm the quadriceps contraction, then 20 mL of

0.5% ropivacaine was injected through mandrin, and then catheter was indwelled and mandarin was removed. After femoral nerve block worked, general anesthesia induction, general anesthesia and surgery operation were conducted. Before installation of prosthesis, experimental group received injection of 20 mL mixed solution of ropivacaine 2.5 mg/mL, fentanyl 2.5 g/mL and methylprednisolone sodium succinate 1 mg/mL in the back of the joint capsule; after the installation of prosthesis was complete, 20 mL of above mixed solution was injected again in left and right accessory ligament and the incision. The control group received injection of same value of normal saline with reference to the methods of experimental group.

2.3. Evaluating methods of pain degree

Three days after operation, 8-10 mL of fasting peripheral venous blood was collected from both groups, placed in EDTA anticoagulative tubes and let stand for 15-20 minutes, and enzyme-linked immunosorbent assay was used to detect pain-promoting-related mediators, pain-suppressing-related mediators and pain-related signal molecules contents. Pain-promoting-related mediators included calcitonin gene-related peptide (CGRP), P substance (PS), Histamine (Hist), 5-hydroxytryptamine (5-HT), adrenomedullin (AM) and bradykinin (BK); pain-suppressing-related mediators included anandamide (AEA), β-endorphin (β-EP), Resolvin E1 (RvE1), lipoxin A4 (LXA4) and lipoxin B4 (LXB4); pain-related signal molecules included $P2X_2$, $P2X_7$, $P2X_3$, $P2X_4$, $P2Y_1$, $P2Y_2$, $P2Y_4$, $P2Y_6$, $P2Y_{13}$, $P2Y_{14}$, p38MAPK and PI3K.

2.4. Statistical methods

SPSS20.0 software was used to input and process data, data between two groups was analyzed by t test and $P<0.05$ was the standard of statistical significant differences between two groups.

3. Results

3.1. Pain-promoting-related mediators

Serum CGRP, PS, Hist, 5-HT, AM and BK contents of experimental group were significantly lower than those of control group (Table 1).

3.2. Pain-suppressing-related mediators

Serum AEA, β-EP, RvE1, LXA4 and LXB4 contents of experimental group were significantly higher than those of control group (Table 2).

3.3. P2X receptors and related signal molecule

Serum $P2X_2$, $P2X_3$, $P2X_4$, $P2X_7$ and p38MAPK contents of experimental group were significantly lower than those of control group (Table 3).

3.4. P2Y receptors and related signal molecule

Serum $P2Y_1$, $P2Y_2$, $P2Y_4$, $P2Y_6$, $P2Y_{13}$, $P2Y_{14}$, p38MAPK and PI3K contents of experimental group were significantly lower than those of control group (Table 4).

Table 1

Contents of serum pain-promoting-related mediators of two groups after operation.

Groups	PS(pg/mL)	Hist(pg/mL)	5-HT(nmol/L)	CGRP(pg/mL)	AM(ng/mL)	BK(pg/mL)
Experimental group	37.1±4.7	76.5±8.2	183.5±21.7	65.6±7.1	15.8±1.7	135.2±17.8
Control group	76.3±8.1	123.9±15.7	256.3±29.3	114.8±13.2	46.3±5.8	279.5±31.4
t	11.039	8.769	7.127	9.374	19.138	12.158
P	<0.05	<0.05	<0.05	<0.05	<0.05	<0.05

Table 2

Contents of serum pain-suppressing-related mediators of two groups after operation.

Groups	AEA (pg/mL)	β-EP (pg/mL)	RvE1 (pg/mL)	LXA4 (pg/mL)	LXB4 (ng/mL)
Experimental group	134.4±16.9	223.5±26.3	176.7±17.8	25.8±2.7	19.3±2.3
Control group	78.4±9.2	104.7±11.4	103.4±12.6	14.6±1.8	8.6±1.0
t	8.833	11.337	7.968	7.117	10.393
P	<0.05	<0.05	<0.05	<0.05	<0.05

Table 3

Contents of serum P2X receptors and related signal molecule of two groups after operation.

Groups	P2X receptors				p38MAPK(pg/mL)
	$P2X_2$ (pg/mL)	$P2X_3$ (ng/mL)	$P2X_4$ (pg/mL)	$P2X_7$ (ng/mL)	
Experimental group	83.5±10.2	13.9±1.8	47.9±5.5	9.3±1.0	135.2±15.8
Control group	145.7±16.8	32.4±3.8	88.3±9.2	15.9±1.7	336.5±42.3
t	8.393	13.955	9.182	7.698	16.855
P	<0.05	<0.05	<0.05	<0.05	<0.05

Table 4

Contents of serum P2Y receptors and related signal molecule of two groups after operation.

Groups	P2Y receptors						PI3K(pg/mL)
	P2Y1 (pg/mL)	P2Y2 (ng/mL)	P2Y4 (pg/mL)	P2Y6 (ng/mL)	P2Y13 (pg/mL)	P2Y14 (pg/mL)	
Experimental group	156.4±17.8	7.8±0.9	113.8±12.5	4.2±0.6	92.6±10.5	203.2±22.6	331.2±36.8
Control group	331.7±37.9	12.4±1.5	189.3±21.4	8.9±0.9	144.3±16.7	551.6±62.6	502.2±57.5
t	11.395	8.183	7.778	10.833	6.283	15.484	8.038
P	<0.05	<0.05	<0.05	<0.05	<0.05	<0.05	<0.05

4. Discussion

In this study, continuous femoral nerve block combined with infiltration anesthesia was used after total knee replacement, aiming at exerting the analgesic effect of infiltration anesthesia. Surgical operation damage to local tissue will increase the synthesis of a variety of pain mediators, resulting in the body's pain perception. PS is an important pain transmitter in the body that can transmit pain signals into the center and increase the release of histamine, 5-HT and other mediators, resulting in pain[7,8]; CGRP and its receptor are mainly distributed in the trigeminovascular system, and external trauma can increase the expression of CGRP and transmit pain signals into the center vascular system through the vascular nervous system, and cause the corresponding pain perception[9]; AM is a newly discovered member of the CGRP family, main acts on spinal cord tissue and causes the release of substance P, bradykinin and other pain-promoting mediators, and has the effect of inducing pain and morphine tolerance[10]. In the research, analysis of the contents of above serum pain-promoting molecules showed that serum CGRP, PS, Hist, 5-HT, AM and BK contents of experimental group were significantly lower than those of control group.

There are a series of pain-suppressing molecules inside body, which can inhibit the pain perception caused by the external trauma to a certain extent, and is the body's way of self protection. β -EP mainly exerts analgesic effect by inhibiting the synthesis and release of substance P[11]; AEA can be combined with corresponding receptors CB1 and CB2 to exert analgesic effect, CB1 and CB2 are mainly distributed in the central nervous system, and AEA combination with receptors can inhibit the transmission of pain signals in the central nervous network and ease pain[12]; Rvs is the metabolite of ω -3 polyunsaturated fatty acids, the RvE1 from Rvs-E series is from eicosapentaenoic acid metabolism, its receptor ChemR23 is mainly distributed in the spinal cord tissue, and RvE1 combination with receptor can antagonize the pain effect mediated by leucotriene B4[13]; LXs are the metabolites of arachidonic acid, and can be divided into LXA4, LXB4, 15-epi-LXA4 and 15-epi-LXB4 according to different space conformation, and LXA4 and LXB4 can suppress pain through the JAK2-STAT3, SOCS1/3 and other signaling pathways[14]. In the research, analysis of the contents of above serum pain-suppressing molecules showed that serum AEA, β -EP, RvE1, LXA4 and LXB4 contents of experimental group were significantly higher than those of control group.

Purinoceptors in the nervous tissue can participate in the transduction of pain signals, purinoceptors specifically include P1 and P2 receptors, and P2 receptors include seven ligand-gated P2X receptors ($P2X_{1-7}$) and nine kinds of G protein-coupling P2Y receptors ($P2Y_1$, $P2Y_2$, $P2Y_4$, $P2Y_6$, $P2Y_{11}$, $P2Y_{12}$, $P2Y_{13}$, $P2Y_{14}$ and $P2Y_{15}$)[15]. $P2X_2$ and $P2X_7$ are widely distributed in the central nervous system and peripheral nerve system, $P2X_3$ and $P2X_4$ are distributed in the spinal dorsal horn, and after activation, the above four P2X receptors can promote the depolarization of neurons through downstream p38-MAPK phosphorylation, causing increased pain sensitivity[16]; $P2Y_1$, $P2Y_2$, $P2Y_4$, $P2Y_6$, $P2Y_{13}$ and $P2Y_{14}$ are expressed in the spinal nerve roots and spinal dorsal horn, and after activation, the above P2Y receptors can activate PKB and Rap1b through phosphorylation of the downstream PI3K, thus promoting calcium inflow and TRPV1 sensitization, and enhancing the pain response. In the research, the contents of serum P2X receptors, P2Y receptors and related downstream signal molecules were analyzed, and results showed that serum $P2X_2$, $P2X_7$, $P2X_3$, $P2X_4$, $P2Y_1$, $P2Y_2$, $P2Y_4$, $P2Y_6$, $P2Y_{13}$, $P2Y_{14}$, p38MAPK and PI3K contents of experimental group were significantly lower than those of control group.

Based on above analysis, it is believed that applying continuous femoral nerve block combined with infiltration anesthesia after total knee replacement can achieve more exact analgesic effect, specifically manifested as increasing the generation of pain-suppressing mediators and decreasing the generation of pain-promoting mediators.

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