



# Effect of ropivacaine fascia iliaca compartment block combined with dezocine multimodal analgesia on the pain and stress response after hip replacement

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## ABSTRACT

**Objective:** To study the effect of ropivacaine fascia iliaca compartment block combined with dezocine multimodal analgesia on the pain and stress response after hip replacement.

**Methods:** A total of 74 cases of elderly patients who received hip replacement in Mianyang Central Hospital between December 2015 and June 2017 were selected and randomly divided into multimodal analgesia group (MMA group), and patient-controlled intravenous analgesia group (PCIA group), MMA received ropivacaine fascia iliaca compartment block, dezocine preemptive analgesia combined with patient-controlled intravenous analgesia, and PCIA group received patient-controlled intravenous analgesia. The levels of pain-related molecules and stress-related hormones in serum as well as the levels of stress-related immune molecules in peripheral blood were detected immediately after surgery and 12 h after surgery.

**Results:** 12 h after surgery, serum SP, PGE<sub>2</sub>, TNF- $\alpha$ , IL-1 $\beta$ , IL-10, FC, NE, E and GH levels and peripheral blood Foxp3+ cell fluorescence intensity of both groups of patients were significantly higher than those immediately after surgery, peripheral blood CD3+, CD4+, CD8+ cell fluorescence intensity were significantly lower than those immediately after surgery, serum SP, PGE<sub>2</sub>, TNF- $\alpha$ , IL-1 $\beta$ , IL-10, FC, NE, E and GH levels and peripheral blood Foxp3+ cell fluorescence intensity of MMA group 12 h after surgery were significantly lower than those of PCIA group, and peripheral blood CD3+, CD4+, CD8+ cell fluorescence intensity were significantly higher than those of PCIA group. **Conclusion:** Ropivacaine fascia iliaca compartment block combined with dezocine multimodal analgesia can reduce the pain and stress response after hip replacement.

## 1. Introduction

Hip replacement is the preferred treatment for hip fracture in the elderly and can effectively improve the function of the hip joint and ensure the quality of life after surgery. Postoperative pain is an important factor affecting function recovery and joint function exercise, and it is necessary to relieve the pain through effective analgesic scheme[1,2]. Patient-controlled intravenous analgesia (PCIA) is a common way of analgesia after hip replacement,

but the effect of single mode analgesia is not ideal. Multimodal Analgesia (MMA) is a concept of Analgesia that has arisen in recent years, which combines the analgesic drugs with different pharmacological mechanisms and the different ways of medication to achieve a better analgesic effect. Preemptive analgesia and local nerve block are both important components of the multimodal analgesia, dezocine is the analgesic drug that has agonistic effect on opioid kappa receptors and is used for preemptive analgesia[3], and the fascia iliaca compartment block (FICB) is that nerve block way able to block the lateral femoral cutaneous nerve and femoral nerve, and achieve analgesic effects[4,5]. In the following studies, we specifically analyzed the effect of ropivacaine fascia iliaca compartment block combined with dezocine multimodal analgesia on the pain and stress response after hip replacement.

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## 2. Research subjects and methods

### 2.1 Research subjects

A total of 74 cases of elderly patients who received hip replacement in Mianyang Central Hospital between December 2015 and June 2017 were selected, and all patients received artificial femoral head replacement for hip fracture, were 60-85 years old, and were with ASA II-III grade. The patients with severe local infection and those combined with diabetes as well as liver and kidney insufficiency were excluded. Random number table was used to divide the 74 patients into multimodal analgesia group (MMA group) and patient-controlled intravenous analgesia group (PCIA group), 37 cases in each group. MMA group included 22 men and 15 women that were 62-85 years old, and 23 cases were combined with osteoporosis; PCIA group included 21 men and 16 women that were 65-85 years old, and 21 cases were combined with osteoporosis. There was no statistically significant difference in general information between the two groups ( $P>0.05$ ).

### 2.2 Anesthesia and analgesia methods

Both groups of patients underwent routine intravenous inhalational anesthesia, the inhalation anesthetic for anesthesia maintenance was 1%-3% sevoflurane, and the intravenous anesthetic drugs were 2-5 mg/(kg·h) propofol and 0.05-0.20 µg/(kg·h) remifentanyl micropump injection. After anesthesia was effective, MMA group received 30 mL of 0.25% ropivacaine injection into the iliopsoas surface under the fascia iliaca under the guidance of ultrasound; at the end of the operation, MMA group received intravenous injection of the mixture of 5 mg of dezocine injection and 5 mL of saline, and PCIA group received intravenous injection of 5 mL of saline. Both groups of patients received PCIA analgesia after operation, the drug was configured with 2 µg/kg sufentanil and 100 mL of normal saline, the background dose was 2 mL/h, the additional dose was 2 mL/time, and the locking time was 30 min.

**Table 1.**

Changes in serum pain-related molecule levels (pg/mL).

Groups	n	Time	SP	PGE2	TNF-α	IL-1β	IL-10
MMA group	37	Immediately after surgery	93.5±11.2	39.5±5.2	11.5±1.8	7.5±0.9	8.3±1.1
		12 h after surgery	125.2±15.2 <sup>⊗*</sup>	50.4±7.7 <sup>⊗*</sup>	15.6±2.2 <sup>⊗*</sup>	11.3±1.5 <sup>⊗*</sup>	14.4±1.8 <sup>⊗*</sup>
PCIA group	37	Immediately after surgery	94.2±9.8	39.1±4.8	11.8±1.5	7.7±0.8	8.5±1.0
		12 h after surgery	168.3±20.1 <sup>†</sup>	64.8±8.1 <sup>†</sup>	24.9±3.5 <sup>†</sup>	18.6±2.2 <sup>†</sup>	27.5±3.3 <sup>†</sup>

<sup>†</sup>: comparison between immediately after surgery and 12 h after surgery, differences in indexes were significant; <sup>⊗</sup>: comparison between MMA group PCIA group, differences in indexes were significant.

### 2.3 Serum index detection

Immediately after surgery and 12 h after surgery, 3 mL of cubital venous blood was collected from two groups of patients and centrifuged in centrifuge to separate serum, and enzyme-linked immunosorbent assay kit was used to detect SP, PGE2, TNF-α, IL-1β, IL-10, FC, NE, E and GH levels; another 1-2 mL of cubital venous blood was collected to incubate the monoclonal antibody of CD3, CD4, CD8 and Foxp3, and then the fluorescence intensity of CD3+, CD4+, CD8+ and Foxp3+ cells were determined in the flow cytometer.

### 2.4 Statistical methods

SPSS 19.0 software was used to input data, the differences in data between two groups were by t test, and  $P<0.05$  indicated statistical significance in differences.

## 3. Results

### 3.1 Pain-related molecule levels

Immediately after surgery and 12 h after surgery, analysis of serum pain-related molecules SP, PGE2, TNF-α, IL-1β and IL-10 levels between two groups of patients was as follows: immediately after surgery, serum SP, PGE2, TNF-α, IL-1β and IL-10 levels were not significantly different between two groups of patients ( $P>0.05$ ); 12 hours after surgery, serum SP, PGE2, TNF-α, IL-1β and IL-10 levels of both groups of patients were significantly higher than those immediately after surgery ( $P<0.05$ ), and serum SP, PGE2, TNF-α, IL-1β and IL-10 levels of MMA group 12 h after surgery were significantly lower than those of PCIA group ( $P<0.05$ ).

### 3.2 Stress-related hormone levels

Immediately after surgery and 12 h after surgery, analysis of serum stress-related hormones FC (nmol/L), NE (pg/mL), E (pg/mL) and GH (ng/mL) levels between two groups of patients was as follows: immediately after surgery, serum FC, NE, E and GH levels were not significantly different between two groups of patients ( $P>0.05$ ); 12 h after surgery, serum FC, NE, E and GH levels of both groups

**Table 2.**

Changes in serum stress-related hormone levels.

Groups	n	Time	FC	NE	E	GH
MMA group	37	Immediately after surgery	146.3±20.1	45.6±6.1	55.6±7.7	6.52±0.89
		12 h after surgery	194.4±23.6 <sup>&amp;*</sup>	64.5±7.8 <sup>&amp;*</sup>	72.1±8.9 <sup>&amp;*</sup>	8.94±1.02 <sup>&amp;*</sup>
PCIA group	37	Immediately after surgery	145.8±18.9	44.7±5.7	56.2±7.2	6.48±0.76
		12 h after surgery	277.6±31.5 <sup>*</sup>	89.5±10.5 <sup>*</sup>	102.5±11.5 <sup>*</sup>	14.41±1.89 <sup>*</sup>

\*: comparison between immediately after surgery and 12 h after surgery, differences in indexes were significant; &: comparison between MMA group PCIA group, differences in indexes were significant.

**Table 3.**

Changes in peripheral blood stress-related immune molecule levels.

Groups	n	Time	CD3+	CD4+	CD8+	Foxp3+
MMA group	37	Immediately after surgery	42.18±5.82	29.42±3.42	23.12±2.98	3.48±0.44
		12 h after surgery	37.62±4.96 <sup>&amp;*</sup>	25.63±3.14 <sup>&amp;*</sup>	20.34±2.46 <sup>&amp;*</sup>	4.66±0.51 <sup>&amp;*</sup>
PCIA group	37	Immediately after surgery	42.41±5.77	29.64±3.61	23.30±2.85	3.52±0.39
		12 h after surgery	31.35±4.52 <sup>*</sup>	20.26±3.51 <sup>*</sup>	17.03±1.84 <sup>*</sup>	5.96±0.77 <sup>*</sup>

\*: comparison between immediately after surgery and 12 h after surgery, differences in indexes were significant; &: comparison between MMA group PCIA group, differences in indexes were significant.

of patients were significantly higher than those immediately after surgery ( $P<0.05$ ), and serum FC, NE, E and GH levels of MMA group 12 h after surgery were significantly lower than those of PCIA group ( $P<0.05$ ).

### 3.3 Stress-related immune molecule levels

Immediately after surgery and 12 h after surgery, analysis of peripheral blood stress-related immune molecules CD3+, CD4+, CD8+ and Foxp3+ cell fluorescence intensity between two groups of patients was as follows: immediately after surgery, peripheral blood CD3+, CD4+, CD8+ and Foxp3+ cell fluorescence intensity were not significantly different between two groups of patients ( $P>0.05$ ); 12 h after surgery, peripheral blood CD3+, CD4+, CD8+ cell fluorescence intensity of both groups of patients were significantly lower than those immediately after surgery, Foxp3+ cell fluorescence intensity were significantly higher than those immediately after surgery ( $P<0.05$ ), and peripheral blood CD3+, CD4+, CD8+ cell fluorescence intensity of MMA group 12 h after surgery were significantly higher than those of PCIA group, Foxp3+ cell fluorescence intensity were significantly lower than those of PCIA group ( $P<0.05$ ).

## 4. Discussion

The pain after hip replacement can affect the rehabilitation exercise of the joint function, and it is necessary to relieve postoperative pain by analgesic drugs. PCIA is commonly used for postoperative analgesia, but the analgesic effect of single-mode analgesia is not ideal. Multimodal analgesia is the concept of analgesia which has arisen in recent years, which uses nerve block, preemptive

analgesia and ways to improve the analgesic effect[6,7]. Preemptive analgesia applies analgesic drugs in perioperative period to suppress the hyperpathia induced by the afferent noxious stimulation, and dezocine is a common drug for preemptive analgesia. It is a new opioid receptor agonist-antagonist, which has a strong agonistic effect on opioid  $\kappa$  receptor and can relieve the pain[8]. Fascia iliaca compartment block is a way of regional nerve block analgesia, and local ropivacaine injection can block the branched lateral femoral cutaneous nerve and femoral nerve of lumbar plexus end within iliac fascia space, and then realize the effect of analgesia[9]. In recent years, studies have reported the positive value of the ropivacaine fascia iliaca compartment block and dezocine preemptive analgesia for multimodal analgesia after hip replacement[10,11], but it is not yet clear about the analgesic effect of combined use of the two ways.

Postoperative pain is associated with abnormal secretion of various pain-related molecules caused by surgical operation. SP and PGE2 are the neurotransmitters closely related to pain, the former is a kind of tachykinin and can reduce the pain threshold of surrounding tissues[12,13], and the latter is the proinflammatory mediator generated after cyclooxygenase catalyzes arachidonic acid, and has pain sensitization effect[14]. TNF- $\alpha$ , IL-1 $\beta$  and IL-10 are the inflammatory cytokines closely related to pain, TNF- $\alpha$  and IL-1 $\beta$  can mediate the cascade activation of the inflammatory response and increase the degree of pain, IL-10 has anti-inflammatory activity and its compensatory secretion increases in the process of pain generation[15]. In order to define the analgesic effect of ropivacaine fascia iliaca compartment block combined with dezocine preemptive analgesia for hip replacement, the changes of postoperative pain related molecules in serum were analyzed in the study, and the results showed that serum SP, PGE2, TNF- $\alpha$ , IL-1 $\beta$  and IL-10 levels of both groups of patients 12 h after surgery were significantly higher than those immediately after surgery, and serum SP, PGE2,

TNF- $\alpha$ , IL-1 $\beta$  and IL-10 levels of MMA group 12 h after surgery were significantly lower than those of PCIA group. This means that the secretion of pain-related molecules increases after total hip replacement and it mediates the body's pain perception, and ropivacaine fascia iliaca compartment block combined with dezocine multimodal analgesia is more effective than PCIA alone to reduce pain-related molecular secretion and relieve postoperative pain.

Surgical operation and postoperative pain are both intense stressors that will activate the body's stress response and increase the secretion of many stress hormones. FC as well as NE and E is the hormones secreted by the adrenal cortex and medulla respectively, the former participates in material metabolism and sodium-water metabolism in the process of stress reaction, and also exerts permissive action on catecholamine hormones, and the latter two are involved in the regulation of vasoconstriction and myocardial work, and can affect hemodynamics[16,17]. GH is a kind of glucose-elevating endocrine hormone secreted by the pituitary gland, and the enhancement of the pituitary gland secretion in the stress state will promote the secretion of GH. To clarify the effect of ropivacaine fascia iliaca compartment block combined with dezocine preemptive analgesia on the stress response caused by pain after hip replacement, the changes of postoperative serum stress-related molecules were analyzed in the study, and the results showed that serum FC, NE, E and GH levels of both groups of patients 12 h after surgery were significantly higher than those immediately after surgery, and serum FC, NE, E and GH levels of MMA group 12 h after surgery were significantly lower than those of PCIA group. This means that the secretion of stress-related molecules increases after hip replacement, and the pain caused by the stress response is activated, and ropivacaine fascia iliaca compartment block combined with dezocine multimodal analgesia is more effective than PCIA alone to reduce the secretion of stress-related molecules, and reduce the degree of stress response caused by postoperative pain.

The activation of stress response not only affects the synthesis and secretion of various endocrine hormones, but also inhibits the immune response. T lymphocyte is an important immune cell subgroup in the body, CD3 is the marker on the surface of T cells, and it is differentiated into mature T cells of CD3+CD4+ and CD3+CD8+ after positive selection and negative selection[18]. Treg is a type of T cell subgroup with immunosuppressive activity, and Foxp3 is its surface molecule, which exerts negative immune regulation by intercellular contact inhibition and secreting inhibitory cytokines[19]. In order to further clarify the effect of ropivacaine fascia iliaca compartment block combined with dezocine preemptive analgesia on stress reaction after hip replacement, the postoperative stress-related immune molecule levels in the peripheral blood were analyzed in the study, and the results showed that peripheral blood CD3+, CD4+ and CD8+ cell fluorescence intensity of both groups

of patients significantly decreased while Foxp3+ cell fluorescence intensity increased significantly 12 h after surgery, and peripheral blood CD3+, CD4+ and CD8+ cell fluorescence intensity of MMA group 12 h after surgery were significantly higher than those of PCIA group while Foxp3+ cell fluorescence intensity was significantly lower than that of PCIA group. This means that the T cell differentiation and maturation are in disorder, and the proportion of inhibitory T cells increases relatively after hip replacement, and ropivacaine fascia iliaca compartment block combined with dezocine multimodal analgesia is more effective than PCIA alone to reduce the immunosuppression caused by stress.

The conclusion of this study is as follows: ropivacaine fascia iliaca compartment block combined with dezocine multimodal analgesia is more effective than PCIA alone to relieve pain and stress reaction after hip replacement, and also improve postoperative immune response.

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