



Effects of parecoxib sodium intervention before induction on inflammatory stress response and endocrine steady state after laparoscopic surgery

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ABSTRACT

Objective: To study the effects of parecoxib sodium intervention before induction on the inflammatory stress response and endocrine steady state after laparoscopic surgery. **Methods:** 120 cases of patients who accepted laparoscopic cholecystectomy in the Second Affiliated Hospital of Xi'an Medical University between March 2015 and December 2016 were selected and randomly divided into the parecoxib group who accepted parecoxib sodium combined with general anesthesia and the control group who accepted general anesthesia. Before anesthesia induction (T0), immediately after extubation of anesthesia (T1) and 6 hours after extubation (T2), serum levels of inflammatory cytokines and stress hormones as well as peripheral blood levels of immune cells were determined. **Results:** At T0, serum PGE2, TNF- α , IL-6, CRP, Cor, NE, Ins, C-P and AT-II levels as well as peripheral blood IFN γ +CD4+T cell and Perforin+CD8+T cell levels were not significantly different between two groups of patients; at T1 and T2, serum PGE2, TNF- α , IL-6, CRP, Cor, NE, Ins, C-P and AT-II levels of parecoxib group were significantly lower than those of control group while peripheral blood IFN γ +CD4+T cell and Perforin+CD8+T cell levels were significantly higher than those of control group. **Conclusion:** Parecoxib sodium intervention before induction can inhibit inflammatory stress response and improve endocrine steady state after laparoscopic surgery.

1. Introduction

Laparoscopic surgery is widely used in general surgery, surgical operation under laparoscope can achieve clear surgical field and reduce operation trauma, and thus also reduce the activation of inflammatory stress response caused by surgical trauma and the destruction of endocrine steady state[1]. However, laparoscopic surgery needs to establish pneumoperitoneum, and the elevated pneumoperitoneum pressure will affect cardiopulmonary function and cause the blood circulation state fluctuation, and can also

cause inflammatory stress response[2,3]. Parecoxib sodium is a selective inhibitor of cyclooxygenase 2 (COX-2) that can inhibit the expression of COX-2 and decrease the prostaglandins catalyzed by COX-2 at the same time so as to alleviate pain reaction and inflammatory response mediated by prostaglandins. In recent years, more and more clinical studies have confirmed that using parecoxib sodium before general anesthesia induction can significantly reduce vital signs fluctuations in the process of operation, and can also reduce the postoperative incision pain[4]. However, the parecoxib sodium effects on inflammatory stress response and endocrine steady state after general anesthesia operation were not clear. In the following study, the effects of parecoxib sodium intervention before induction on the inflammatory stress response and endocrine steady state after laparoscopic surgery were specifically analyzed.

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2. Enrolled patient information and clinical research methods

2.1 General information of enrolled patients

120 cases of patients who accepted laparoscopic cholecystectomy in the Second Affiliated Hospital of Xi'an Medical University between March 2015 and December 2016 were selected, all patients were in line with the indications of laparoscopic cholecystectomy and with ASA I-II grade, and patients with surgical contraindications and those combined with endocrine system disease and mental illness were ruled out. Random number table was used to divide the enrolled 120 patients into two groups, each with 60 cases. The parecoxib group received parecoxib sodium combined with regular anesthesia, including 38 men and 22 women that were 37-56 years old; the control group received general anesthesia, including 36 men and 24 women that were 35-53 years old. There was no significant difference in general information between the two groups of patients ($P>0.05$).

2.2 Anesthesia methods

After two groups of patients entered into the operating room, the vital signs were regularly monitored and the venous pathway was established, parecoxib group received intravenous injection of the solution of parecoxib sodium 1.5 mg/kg in 5 mL saline before induction, control group received intravenous injection of 5 mL saline before induction, and then the following methods were followed for anesthesia induction and maintenance: intravenous injection of midazolam 0.2 mg/kg, cis atracurium 0.2 mg/kg, remifentanyl 2.00 μ g/kg; after induction worked, endotracheal intubation was conducted, the ventilator parameters were adjusted, and propofol 4 mg/kg/h and remifentanyl 0.25 μ g /kg/min were infused through micropump for anesthesia maintenance.

Table 1.

Serum inflammatory cytokine levels in two groups of patients at T0-T2.

Groups	n	Time	PGE2	TNF- α	IL-6	CRP
Parecoxib group	60	T0	35.2 \pm 4.6	10.3 \pm 1.6	147.3 \pm 22.1	4.29 \pm 0.66
		T1	47.1 \pm 6.8 ^{*&}	15.2 \pm 1.9 ^{*&}	194.5 \pm 26.4 ^{*&}	6.04 \pm 0.79 ^{*&}
		T2	53.4 \pm 8.2 ^{*&}	18.4 \pm 2.2 ^{*&}	236.4 \pm 33.1 ^{*&}	6.98 \pm 0.93 ^{*&}
Control group	60	T0	35.9 \pm 5.1	10.6 \pm 1.4	149.1 \pm 24.2	4.35 \pm 0.69
		T1	60.2 \pm 7.8 [*]	21.3 \pm 3.5 [*]	263.3 \pm 36.7 [*]	8.51 \pm 0.93 [*]
		T2	74.6 \pm 9.3 [*]	27.9 \pm 3.9 [*]	301.5 \pm 45.8 [*]	11.25 \pm 1.85 [*]

Note: "*" indicated that comparison of two groups at T1 and T2 with those at T0, $P<0.05$; "&" indicated that comparison between parecoxib group and control group at the same point in time, $P<0.05$.

2.3 Observation indexes and detection methods

Before anesthesia induction (T0), immediately after extubation of anesthesia (T1) and 6 h after extubation (T2), 10 mL cubital venous blood was collected respectively and divided into two, one was centrifuged to separate serum and detect PGE2, TNF- α , IL-6, CRP, Cor, NE, Ins, C-P and AT-II levels by enzyme-linked immunosorbent assay kits, and the other was used to incubate fluorescent antibody and detect IFN γ +CD4+T cell and Perforin+CD8+T cell levels by flow cytometer.

2.4 Statistical methods

SPSS 22.0 software was used to input and analyze data, analysis of serum indexes and peripheral blood indexes between the two groups at different points in time was by t test, and $P<0.05$ indicated statistical significance in differences.

3. Results

3.1 Serum inflammatory cytokine levels

At T0-T2, analysis of serum inflammatory cytokines PGE2 (μ g/L), TNF- α (μ g/L), IL-6 (pg/L) and CRP (mg/L) levels between two groups of patients was as follows: at T0, serum PGE2, TNF- α , IL-6 and CRP levels were not significantly different between two groups of patients ($P>0.05$); compared with those at T0, serum PGE2, TNF- α , IL-6 and CRP levels of both groups increased significantly at T1 and T2 ($P<0.05$); serum PGE2, TNF- α , IL-6 and CRP levels of parecoxib group were significantly lower than those of control group at T1 and T2 ($P<0.05$).

Table 2.

Serum stress hormone levels in two groups of patients at T0-T2.

Groups	n	Time	Cor	NE	Ins	C-P	AT-II
Parecoxib group	60	T0	172.3±22.3	39.5±5.1	5.8±0.8	1.58±0.22	15.2±2.2
		T1	223.5±31.6 ^{*&}	50.3±7.7 ^{*&}	7.3±0.9 ^{*&}	2.03±0.36 ^{*&}	22.5±3.1 ^{*&}
		T2	246.7±36.2 ^{*&}	56.2±7.9 ^{*&}	8.2±1.0 ^{*&}	2.42±0.41 ^{*&}	25.3±4.2 ^{*&}
Control group	60	T0	175.3±19.4	40.1±4.8	5.9±0.7	1.61±0.27	15.5±2.6
		T1	302.4±41.7 [*]	68.6±8.1 [*]	10.5±1.1 [*]	2.98±0.42 [*]	31.4±4.9 [*]
		T2	367.3±48.9 [*]	81.3±10.3 [*]	13.5±1.8 [*]	4.12±0.57 [*]	38.6±6.1 [*]

Note: "^{*}" indicated that comparison of two groups at T1 and T2 with those at T0, $P < 0.05$; "[&]" indicated that comparison between parecoxib group and control group at the same point in time, $P < 0.05$.

Table 3.

Peripheral blood immune cell levels in two groups of patients at T0-T2.

Groups	n	Time	IFN γ +CD4+T cell	Perforin+CD8+T cell
Parecoxib group	60	T0	47.9±7.2	27.4±3.7
		T1	42.1±5.2 ^{*&}	23.1±3.5 ^{*&}
		T2	40.4±5.9 ^{*&}	21.8±3.1 ^{*&}
Control group	60	T0	48.3±7.8	28.0±4.1
		T1	33.2±4.9 [*]	20.1±2.8 [*]
		T2	30.2±4.1 [*]	17.5±2.3 [*]

Note: "^{*}" indicated that comparison of two groups at T1 and T2 with those at T0, $P < 0.05$; "[&]" indicated that comparison between parecoxib group and control group at the same point in time, $P < 0.05$.

3.2 Serum stress hormone levels

At T0-T2, analysis of serum stress hormones Cor (nmol/L), NE (ng/mL), Ins (U/mL), C-P (ng/mL) and AT-II (ng/mL) levels between two groups of patients was as follows: at T0, serum Cor, NE, Ins, C-P and AT-II levels were not significantly different between two groups of patients ($P > 0.05$); compared with those at T0, serum Cor, NE, Ins, C-P and AT-II levels of both groups increased significantly at T1 and T2 ($P < 0.05$); serum Cor, NE, Ins, C-P and AT-II levels of parecoxib group were significantly lower than those of control group at T1 and T2 ($P < 0.05$).

3.3 Peripheral blood immune cell levels

At T0-T2, analysis of peripheral blood immune cells IFN γ +CD4+T cell and Perforin+CD8+T cell levels between two groups of patients was as follows: at T0, peripheral blood IFN γ +CD4+T cell and Perforin+CD8+T cell levels were not significantly different between two groups of patients ($P > 0.05$); compared with those at T0, peripheral blood IFN γ +CD4+T cell and Perforin+CD8+T cell levels of both groups decreased significantly at T1 and T2 ($P < 0.05$); peripheral blood IFN γ +CD4+T cell and Perforin+CD8+T cell levels of parecoxib group were significantly higher than those of control group at T1 and T2 ($P < 0.05$).

4. Discussion

Laparoscopic surgery is a common way of minimally invasive surgery in general surgery department, it has the advantages of clear vision and small trauma, but intraoperative establishment of pneumoperitoneum can affect the cardio-pulmonary function and cause vital sign fluctuations, and also cause inflammation and oxidative stress and affect the recovery after anesthesia. COX-2 plays an important role in perioperative inflammatory stress response and pain response, COX-2-catalyzed arachidonic acid metabolite PGE2

is an important pain mediator in the body, it can reduce the pain threshold and increase sensibility to pain, and it is also an important inflammatory mediator that plays a promoting role in cascade amplification of the inflammatory response. Parecoxib sodium is a highly selective COX-2 inhibitor that not only inhibits the expression of COX-2, but also antagonizes the catalytic function of COX-2[5,6]. In recent years, more and more clinical studies have confirmed that providing parecoxib sodium before general anesthesia induction helps to stabilize the vital signs during operation and awakening period[7,8], but there is no clear report about the effect of parecoxib sodium application before induction on the surgical trauma-induced inflammatory stress response and endocrine steady state. In the study, the value of parecoxib sodium application before induction was specifically analyzed from the aspects of inflammatory stress response and endocrine steady state.

Perioperative inflammatory response activation is closely related to the secretion of various inflammatory cytokines. PGE2 is the product after COX-2 catalyzes arachidonic acid metabolism, which activates inflammatory, promotes inflammatory cell activation and increases the expression of different inflammatory mediators[9]; TNF- α an important molecule that starts inflammatory response, which is secreted by mononuclear macrophages, increases in the early stages of the inflammatory response and can mediate inflammation cascade activation[10]; IL-6 is a cytokine with a variety of biological activities, which participates in the regulation of inflammatory response and immune response in the body[11]; CRP is the acute phase protein synthesized by liver cells in under the action of cytokines such as TNF- α and IL-6, which is massively secreted in the process of inflammatory response and has good consistency with inflammation degree. In the study, the analysis of the contents of these inflammatory cytokines showed that serum PGE2, TNF- α , IL-6 and CRP contents of both groups of patients at T0 were significantly higher than those at T1 and T2, and serum PGE2, TNF- α , IL-6 and CRP contents of parecoxib group at T1 and T2 were significantly lower than those of control group. This means that surgical operation will cause different degree of inflammatory reaction, and parecoxib

sodium application before induction could reduce the degree of inflammatory response activation caused by operation.

Surgical trauma will not only cause inflammatory response activation, but can also cause stress response and lead to the changes in secretion of a variety of endocrine hormones[12]. Adrenal gland is the endocrine gland that plays an important role in the process of stress reaction, adrenal medulla will synthesize NE under the influence of increased sympathetic nerve excitability, which can cause vasoconstriction and hemodynamic fluctuations after secreted into the blood circulation; adrenal cortex will synthesize Cor under the action of hypothalamus - pituitary axis, which can on the one hand, enhance the ability of the body to tolerate trauma, and on the other hand, lead to elevated blood sugar and cause compensatory secretion of Ins and C-P[13,14]. AT-II is a product activated by RAS system, which has strong vasoconstrictive activity and can affect the stability of vital signs. In the study, analysis of the contents of these stress hormones showed that serum Cor, NE, Ins, C-P and AT-II contents of both groups of patients at T0 were significantly higher than those at T1 and T2, and serum Cor, NE, Ins, C-P and AT-II contents of parecoxib group at T1 and T2 were significantly lower than those of control group. This means that surgical operation will cause different degree of stress reaction, and parecoxib sodium application before induction could reduce the degree of stress reaction activation caused by operation.

The activation of inflammatory stress response and the destruction of endocrine steady state will not only affect the hemodynamics and vital signs, but will also affect the immune response process and inhibit the differentiation and maturation of a variety of immune cells to a certain extent[15,16]. CD4+T lymphocytes and CD8+T lymphocytes are the important T lymphocytes in the body that mediate cellular immune response process, and in order to further clarify the parecoxib sodium effects on the perioperative inflammatory stress response and endocrine steady state, the contents of these immune cells in peripheral blood were analyzed in the study, and the results showed that peripheral blood IFN γ +CD4+T cell and Perforin+CD8+T cell levels of both groups at T0 were significantly lower than those at T1 and T2, and peripheral blood IFN γ +CD4+T cell and Perforin+CD8+T cell levels of parecoxib group at T1 and T2 were significantly higher than those of control group. This means that surgical operation can inhibit the immune response and affect the immune cell differentiation and maturation to different extent, and parecoxib sodium application before induction can reduce the immunosuppression caused by surgical operation, and promote the immune cell differentiation and maturation.

Parecoxib sodium intervention before anesthesia induction of laparoscopic surgery can effectively inhibit inflammatory stress reaction and improve endocrine steady state, and it can also reduce immunosuppression, and promote immune cell differentiation and maturation.

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