Application of Ultrasound-guided Intercostal Nerve Block in Retroperitoneal Laparoscopic Nephrectomy

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Research Article

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Application of ultrasound-guided intercostal nerve block in retroperitoneal laparoscopic nephrectomy

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Abstract:

Purpose: Surgical stimulation causes many pathophysiological changes which are not conducive to the recovery of patients, this trail aims to investigate whether intercostal nerve block can reduce the perioperative stress response and postoperative pain in patients undergoing elective retroperitoneal laparoscopic nephrectomy.

Patients and methods:40 patients were recruited and randomly assigned to Test groupand Blank group.

Results: Our study found that the catecholamine and cortisol levels in two groups were higher than the baseline value after pneumoperitoneum, ($P<0.05$), while the catecholamine level was lower in Test groupthan in Blank group ($P<0.05$), and there is no differences of cortisol levels was observed in two groups. The catecholamines and cortisol levels of two groups were basically restored to the preoperative level after 24 hours surgery, The concentration of IL-6 and IL-10 in two groups increased at 24 hours after surgery, but there was no differences was observed between the two groups at the same point. And the usage of analgesic during operation was less in the Test group than Blank group ($P<0.05$).

Conclusion : Intercostal nerve block can reduce the stress response of patients undergoing retroperitoneal laparoscopic nephrectomy and reduce the usage of perioperative analgesics.

Key words: stress, catecholamine, cortisol, atelectasis

clinical trial (Registration No.: chictr2000041277)**,** date of registration：23/12/2021

Tial registration statement

This trial has been applied by the ethics Association of Chongqing cancer hospital.

Background

At present, laparoscopic surgery is more and more popular among surgical patients because of its advantages, including small tissue injury, small surgical incision, fast recovery and short hospital stay, which reduces the medical cost [1]. Although laparoscopic surgery is considered minimally invasive, this method may cause moderate stress response [2]. In addition, hemodynamic changes and local immune function injury may lead to strong stress response during CO_2 pneumoperitoneum, making the treatment of patients more complex[3]. Traditionally, this stress response can be alleviated by increasing the depth of anesthesia and the intensity of analgesia [4]. However, excessive use of opioids will lead to more adverse events, such as delayed awakening and postoperative nausea and vomiting.

In addition, studies have shown that systemic inflammation after surgery is very unfavorable to patients [5,6]. The degree of this inflammatory response varies from person to person, depending on the type, duration and degree of surgery and the type of anesthesia [7-9]. The study also confirmed the diagnostic value of IL-6 and IL-10 in predicting complications after abdominal surgery. For example, gene polymorphisms encoding IL-6 and IL-10 are related to the occurrence of complications after pneumonectomy [10,11].

Previous studies have shown that the immediate use of nerve block after operation can the use of opioids and inflammatory reaction [12,13], such as transverse abdominal muscle plane block after laparoscopic appendectomy, intercostal nerve block during thoracoscopic lobectomy and bilateral intercostal nerve block after subtotal gastrectomy. However, few studies have implemented nerve block before general anesthesia to observe the perioperative stress response, the total use of perioperative analgesic drugs and the perioperative inflammatory response. Therefore, the purpose of this study was to observe whether intercostal nerve block can reduce perioperative stress response and postoperative inflammation in patients undergoing elective

retroperitoneal laparoscopic nephrectomy.

Methods

Research design

The study was approved by the Ethics Committee of Affiliated Tumor Hospital of Chongqing University(Approval document of ethics committee: 2020 lunshen (028).) and registered with the Clinical Trial Registry of China(ChiCTR2000041277) before recruitment of participants . Our trail design complies with relevant guidelines and European directive 2010 / 63 / EU. Before first enrollment of study, informed consent was obtained from each individual patient or their Legal agent. Practicing physician qualificated with qualification certificate and GCP certificate.

Inclusion criteria: ages from 18 to 70 years; ASA I-II, retroperitoneal laparoscopic nephrectomy under general anesthesia and the operation time was less than 5 hours. The involved patients did not suffer from hypertension, heart disease, or diabetes or medication history which includes β blockers, ACEI, other cardiovascular drugs and steroids. The subject should not receive preoperative cell suppression, radiation or further pretreatment. If the subject has malignant tumors, hypertension, diabetes, heart disease, adrenal gland disease, severe kidney or liver disease, chronic pain, bradycardia, pregnancy, long-term use of corticosteroids, analgesics, and adrenergic receptor agonists and antagonists, or abuse of alcohol, nicotine, or opioids were excluded. If the subject is allergic to local anesthetics, or body mass index more than 35kg/m2, or converted to open surgery due to failure of laparoscopic, or has failed intercostal nerve block, it should also be excluded.

Study Group

After signing the informed consent form, the patients were randomly divided into the following groups according to the computer-generated random number table: Blank group (received 0.9% normal saline 20ml) and Test group(only received 0.375% ropivacaine + 10 mg digitalis + 2 mg morphine, the total volume was 20 ml, and the block range was T_8-T_{12} nerve in the posterior axillary line). Randomization was performed by the pharmacy department using the schedule provided by the statistician, which was not known to the anesthesia team, operation team, patients and clinical researchers. The drug was prepared by the pharmacist, labeled with the

study subject number, and personally delivered by the pharmacy staff to the anesthesiologist performing nerve block (trained in ultrasound and nerve block classes and more than 2 years of clinical practice experience).

Anesthesia protocol

Anesthesia was induced by intravenous injection of propofol (2 ~ 3 mg / kg) and sufentanil (0.2 ~ 0.4 μg/kg) and rocuronium (0.6 mg/kg) induced general anesthesia. After induction, the surgical position (folding knife position) was placed immediately, and intercostal nerve block was performed immediately under aseptic operation and ultrasound guidance. The block sites were the 8-10 intercostal space of the posterior axillary line and under the costal margin, and the block range wasT_8-T_{12}. Propofol was used to maintain the operation, and muscle relaxants were added in time according to the operation process. If the operation center rate increased by 10 times / min or the blood pressure increased by 10% compared with the basic value, analgesics were added immediately, and the total amount of sedatives and analgesics used during the operation were recorded; A unified formula was used for postoperative analgesia pump: 100ml of morphine 50mg + droperidol 4mg + 0.9% normal saline, the background measurement was 0, bolus was 0.02g/kg, and the interval was 5min; All patients underwent retroperitoneal laparoscopic approach. Rescue measures: if the patient's heart rate is less than 50 beats / min or systolic blood pressure is less than 80mmHg during anesthesia, use vasoactive drugs immediately and withdraw from the final data analysis.

Collection index

Venous blood was collected at different time point to analysis the concentration of epinephrine(E) and norepinephrine(NE), cortisol (COR), IL-6 and IL-10. The time points were expressed as T_0(the morning of the operation day),T_1(10min after pneumoperitoneum),T_2(Suturing the abdominal incision),T_4(24 hours after surgery).

Observation outcomes

Primary outcomes: The concentration of E,NE,COR,IL-6 and IL-10 at different time points. secondary outcomes: the dosage of analgesics used during operation, the times of postoperative analgesic pump presses, postoperative analgesia Drug dosage, postoperative pulmonary

complications, length of hospital stay.

Statistics analysis

The calculation of sample size depends on the expected experimental results. Based on the test efficiency of 80%, whether there is a statistical difference between the observation results of each group can be detected. Through calculation, the sample size of each group is 20 cases, which can meet the requirements of this experiment. Spss23.0 statistical software was used for statistical analysis. The counting data adopts the mean ± standard deviation（ χ± s）expression, multiple time points in the group were compared with repeated measurement analysis of variance, and single time point was compared with one-way analysis of variance. Measurement data adopted χ2 inspection. $P < 0.05$ was considered as statistically significant.

Results

During the experiment, 2 patients in the experimental group withdrew from the experiment due to conversion to laparotomy and 1 patient withdrew from the experiment due to severe arrhythmia during operation. Two patients in the blank group withdrew from the trial due to conversion to laparotomy and one patient withdrew from the trial due to excessive blood loss and severe hypotension. Finally, 20 subjects in both groups were included in the data analysis (Fig. 1). There was no significant difference in ASA grade, age, heart rate and blood pressure between the two groups ($P > 0.05$, table 1)

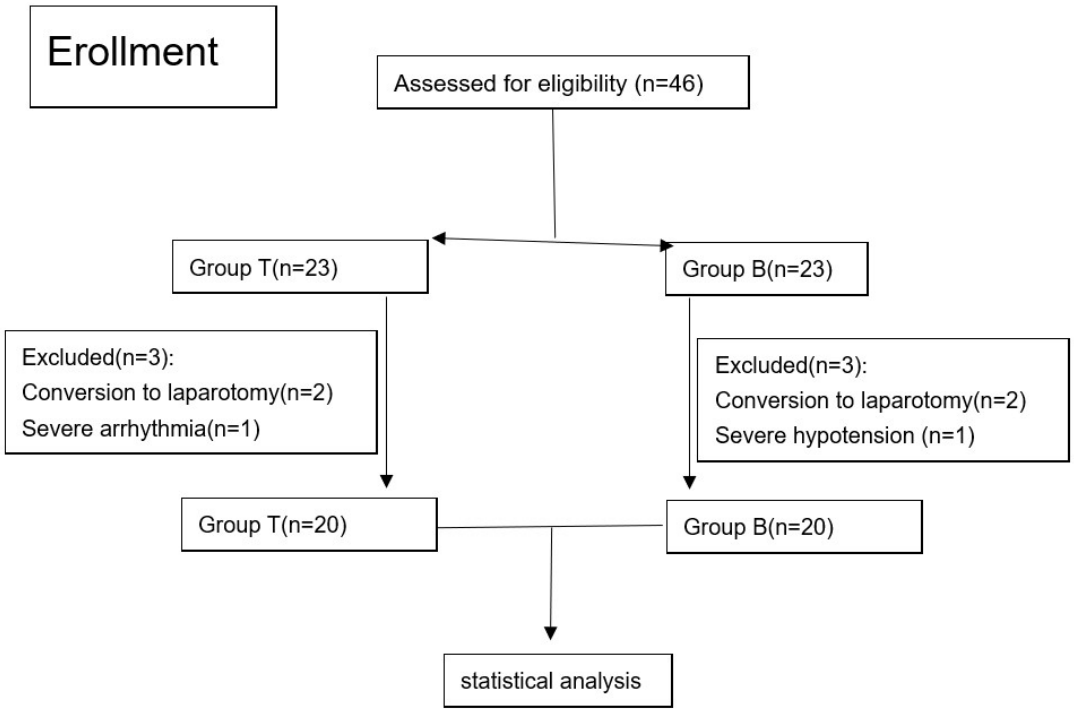

Fig.1 Consort flow diagram. Group T: Test group (received 0.375% ropivacaine + 10 mg digitalis + 2 mg morphine, the total volume was 20 ml). Group B: Blank group (received 0.9% normal saline 20ml)

Table1

Table1 General data

group	N	ASA(I/II)	age（Y）	F/M	BMI（kg/m^2）	HR (beats/min)	MAP (mmHg)
Test group	20	7/13	50.35±10.44	10/10	23.02±1.95	74.1±7.96	76.5±6.75
Blank group	20	9/11	53.15±10.50	9/11	23.12±1.17	75.3±9.72	76.4±7.78

Note: age、BMI、HR、MAP was expressed as mean $\bar{x}\pm s$

Catecholamines and cortisol

There was no difference in catecholamines and cortisol before surgery. We found that the catecholamine and cortisol levels of the two groups were higher than baseline after the establishment of pneumoperitoneum (P<0.05). During the pneumoperitoneum, the catecholamines in Test group were lower than those in Blank group (P<0.05). There was no

statistical difference in cortisol levels between two groups at any time points. 24 hours after operation, the catecholamines and cortisol levels of the two groups of recovered to preoperative levels, and the cortisol levels were even lower than operation before(Table 2).

IL-6 and IL-10

The IL-6 and IL-10 levels of the two groups increased to varying degrees at 24 hours after surgery, but there was no statistical difference between the groups at the same time point (Table 3).

Table3

Table 3 changes of IL-6 and IL-10 in two groups during perioperative period （$\bar{x}\pm s$）（pg/ml）

cell factor		T_0	T_1	T_3
IL-6	Test group	1.83±0.79	1.97±0.35	7.84±1.39$^{\#}$
	Blank group	1.79±0.94	1.85±1.23	6.96±2.83$^{\#}$
IL-10	Test group	3.83±2.51	4.33±1.52	8.97±3.53$^{\#}$
	Blank group	4.01±1.76	4.23±2.11	10.32±1.05$^{\#}$

Note: "#" indicates that each time in the group is compared with T_0, $^{\#}p < 0.05$

Analgesic usage

Table2

Table2 Changes of catecholamine and cortisol in two groups during perioperative period （$\bar{x}\pm s$）

		T_0	T_1	T_2	T_3
E	Test group	49.38±22.81	55.90±20.04$^{\#}$	68.44±22.46$^{\#}$	50.69±21.56
	Blank group	52.41±13.95	94.25±29.72$^{\#*}$	108.91±31.52$^{\#*}$	57.79±14.90
NE	Test group	45.61±15.31	52.56±25.48$^{\#}$	61.98±42.00$^{\#}$	46.9±30.93
	Blank group	45.06±10.97	68.47±25.19$^{\#*}$	79.09±27.81$^{\#*}$	47.37±20.41
COR	Test group	98.02±60.96	122.27±67.77$^{\#}$	145.75±97.00$^{\#}$	80.33±43.31$^{\#}$
	Blank group	100.44±46.51	142.35±44.21$^{\#*}$	174.89±64.48$^{\#*}$	74.27±39.90$^{\#}$

Note: "#" indicates that each time in the group is compared with T_0 time, $^{\#}p < 0.05$; "*" indicates the corresponding time of the Blank group compared with the Test group, $^{*}P < 0.05$

The use of analgesics usage during operation was significantly lower in Test group compared with Blank group (P<0.05, Table 4).

Table4

Table 4 Analgesic usage（$\bar{x}\pm s$）

	sufentanil（ug)	First pression time	Pression times	Morphine usage（mg）
Test group	33.75±7.34	425.08±42.36	24.38±6.47	16.25±4.33
Blank group	42.54±6.45#	164.27±23.64#	48.27±3.79#	32.18±2.53#

Note:"#" means the corresponding time in the Test group compare with Blank group,#P＜0.05；

Others

Pulmonary ultrasound after surgery showed that there were 5 patients suffered from atelectasis in Test group compared with 12 patients in the Blank group (P<0.05), but neither of the two groups required respiratory treatment. No pneumothorax was observed in two groups. There was no difference in postoperative hospital stay between the two groups (P>0.05).

Discussion

Some degree of stress response is beneficial to surgical patients, but excessive stress response will lead to a series of pathophysiological changes such as tachycardia and hypertension, which will not only increase oxygen consumption, but also conducive to reducing the postoperative inflammatory reaction and hindering the postoperative recovery of the patient[14]. In the past few years, cytokines and many other widely accepted stress factors such as catecholamines and cortisol have been reported to be involved in the perioperative response of surgery[15-18]. IL-6 is considered to be a sensitive marker of early tissue damage, while interleukin-10 shows anti-tumor and anti-metastatic activity[19].

Recent studies indicate that effective analgesia can reduce surgical stress response[20], and our research confirms this view. our study found that the levels of catecholamines and cortisol in two groups increased to a varying degree after surgery beginning, indicating that surgical trauma and surgical stress response can trigger systemic inflammation and inhibit postoperative immune defense mechanisms. However, the catecholamine and cortisol concentrations in Test group at T_1

and T_2 were significantly lower than those in Blank group, which indicate that intercostal nerve block can alleviate stress response of patients undergoing retroperitoneal laparoscopic nephrectomy, which is also beneficial to the hemodynamic stability and postoperative recovery. At the same time, our study observed that the catecholamine concentrations of two groups returned to baseline level at 24 hours after surgery while the cortisol concentration was lower than baseline level. We think it may be due to the circadian rhythm of cortisol secretion and the different collection time points.

Our study also found that the levels of IL-6 and IL-10 in two groups were higher at 24 hours after surgery compared with baseline, but we did not observe significant differences between the two groups. We thought that the reason was intercostal nerve block cannot effectively block visceral pain, meanwhile, the reasons for the increase of postoperative inflammatory factors are various. the difference between T_0 and T_1 may be associated with antibiotics which was used 30 minutes before skin incision. or because the observation time was too short, studies have found that IL-6 and IL-10 can be detected in the blood at least 4 hours after tissue injury [21-23].

In addition, we observed that perioperative usage of sufentanil and morphine in patients with intercostal nerve block was significantly reduced. The first press time of analgesic pump was significantly delayed, the reason was the T_7-T_{12} intercostal nerve was blocked, and those nerves basically assumed the pain transmission of the abdominal.

We also observed that there was a significant difference in the number of pressions of the analgesic pump between the two groups after 8 hours of surgery. The effective number of pression in Test group was still lower than that of Blank group, and at this time the analgesia effect of intercostal nerve block has basically disappeared, we speculate that if the pain generated during the operation is suppressed at the beginning of the operation, will the patient's subjective pain cycle change, and the intensity and duration of pain will be reduced? So even after the analgesia effect of intercostal nerve block has disappeared, the patient still does not feel pain.

Previous studies have confirmed that patients with general anesthesia and mechanical ventilation were found to have varying degrees of atelectasis after surgery[24,25], but we found that

the incidence of atelectasis in Test group was significantly reduced. It is possibility because nerve block reduces the postoperative pain of patients, which is conducive to the effective sputum excretion and early activity after the operation.

Limitation

First, the reasons for the increase of postoperative inflammatory factors were not analyzed. Second, only a small sample is selected in this experiment. Therefore, a multicenter study with strong statistical ability is needed to determine whether this analgesic technique can be applied to upper abdominal surgery as a conventional method.

Conclusion

Ultrasound-guided intercostal nerve block can effectively reduce the intraoperative stress response and perioperative analgesic usage of patients undergoing retroperitoneal laparoscopic nephrectomy, and it can also reduce the occurrence of postoperative atelectasis.

Abbreviations:

E: epinephrine; NE: norepinephrine; COR: cortisol.

Ethics approval and consent to participate

Approval document of Chongqing Cancer Hospital Ethics Committee: 2020 lunshen (028). Ethical reviewing committees of all participating centers have additionally reviewed and approved the protocol. A written informed consent form for publication will be available for every study participant.

Consent for publication

Written informed consent has been obtained from all study participants.

Competing interests

All authors disclosed no relevant relationships.

Funding

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Authors' contributions

Chuang Wei and Lamei Zheng participated in the design, collection, statistical analysis and

writing of the experiment. Rong Lv participated in the early collection of test data. Tongxuan Wang participated in the translation of the article.

Acknowledge

The author is grateful to the Statistics Department of the Research Institute of Chongqing University for the statistical analysis of the data and to the Department of laboratory for the inspection of samples.. Article registration number：ChiCTR2000041277. Approval document of ethics committee: 2020 lunshen (028).

Trial status

Open for inclusion since June 2020

Authors' information

Chuang Wei is a chief physician and doctoral student in the Department of Anesthesiology of Chongqing Cancer Hospital, China. Lamei Zheng, Rong Lv and Tongxuan Wang are residents and postgraduates in the Department of Anesthesiology of Chongqing cancer hospital.

Availability of data and materials

In the Availability of data and materials section please contact Dr Lamei Zheng(Emai:1006469645@qq.com)

Declarations section

I can confirm that all methods were performed in accordance with the relevant guidelines and European directive 2010 / 63 / EU.

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Section/Topic	Item No	Checklist item	Reported on page No
Title and abstract			
	1a	Identification as a randomised trial in the title	1
	1b	Structured summary of trial design, methods, results, and conclusions (for specific guidance see CONSORT for abstracts)	1-2
Introduction			
Background and objectives	2a	Scientific background and explanation of rationale	2
	2b	Specific objectives or hypotheses	2
Methods			
Trial design	3a	Description of trial design (such as parallel, factorial) including allocation ratio	3
	3b	Important changes to methods after trial commencement (such as eligibility criteria), with reasons	3
Participants	4a	Eligibility criteria for participants	3
	4b	Settings and locations where the data were collected	
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	5
Outcomes	6a	Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed	5
	6b	Any changes to trial outcomes after the trial commenced, with reasons	5
Sample size	7a	How sample size was determined	4
	7b	When applicable, explanation of any interim analyses and stopping guidelines	4
Randomisation:			
Sequence generation	8a	Method used to generate the random allocation sequence	3
	8b	Type of randomisation; details of any restriction (such as blocking and block size)	3
Allocation concealment mechanism	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	3

Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions	3
Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those assessing outcomes) and how	3
	11b	If relevant, description of the similarity of interventions	3-4
Statistical methods	12a	Statistical methods used to compare groups for primary and secondary outcomes	5
	12b	Methods for additional analyses, such as subgroup analyses and adjusted analyses	5
Results			
Participant flow (a diagram is strongly recommended)	13a	For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analysed for the primary outcome	5-6
	13b	For each group, losses and exclusions after randomisation, together with reasons	5-6
Recruitment	14a	Dates defining the periods of recruitment and follow-up	5
	14b	Why the trial ended or was stopped	5
Baseline data	15	A table showing baseline demographic and clinical characteristics for each group	5-6
Numbers analysed	16	For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups	5-6
Outcomes and estimation	17a	For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval)	6-8
	17b	For binary outcomes, presentation of both absolute and relative effect sizes is recommended	6-8
Ancillary analyses	18	Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory	6-8
Harms	19	All important harms or unintended effects in each group (for specific guidance see CONSORT for harms)	NO
Discussion			
Limitations	20	Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses	10
Generalisability	21	Generalisability (external validity, applicability) of the trial findings	8-10
Interpretation	22	Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence	8-10
Other information			
Registration	23	Registration number and name of trial registry	1
Protocol	24	Where the full trial protocol can be accessed, if available	1,4
Funding	25	Sources of funding and other support (such as supply of drugs), role of funders	10

Supplementary Files

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- CONSORT2010Checklist1.doc