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The effect of percutaneous endoscopic lumbar discectomy under different anesthesia on pain and immunity of patients with prolapse of lumbar intervertebral disc

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Abstract. – OBJECTIVE: To explore the effect of percutaneous transforaminal endoscopic discectomy under different anesthesia on pain and immunity of patients with lumbar disc herniation.

PATIENTS AND METHODS: 92 cases of patients with lumbar disc herniation in the Affiliated Hospital of Qingdao University from February 2015 to January 2016 were collected. These patients were randomly divided into control group and observation group (n = 46). Patients in the control group underwent percutaneous transforaminal endoscopic discectomy with the use of local anesthesia, while patients in the observation group used continuous epidural anesthesia. Oswestry Disability Index (ODI) and Visual Analogue Scale of Pain (VAS) were used to compare the surgical effect and the degree of pain of patients in the two groups. Adverse reactions (nausea, vomiting, dizziness, drowsiness) of patients in two groups were compared. T lymphocytes subset level (CD4+, CD8+) and inflammatory cytokines (IL-2, TNF) in the immune system were compared on the 1st, 3rd, and 10th day post-operatively.

RESULTS: The pain degree of patients in the two groups had no significant difference before their operations ($p > 0.05$). The intraoperative pain rate of patients in the observation group was significantly lower than the control group ($p < 0.05$). Patients in both groups achieved a remarkable decrease of pain intensity on month 1 and month 3 post-operatively ($p < 0.05$). There is no significant difference between the two groups ($p > 0.05$). ODI scores of patients in the two groups had no significant difference pre-operatively ($p > 0.05$). Patients in both groups achieved a remarkable decrease of ODI scores after surgery ($p < 0.05$), and there is no significant difference between the two groups ($p > 0.05$). The occurrence of adverse reactions in the observation group was significantly lower than the control group ($p < 0.05$). On day 1 and 3 post-operatively, CD4+ and CD8+ levels of patients in both groups were lower than before operation, and data in the control group decreased more than the observation group ($p < 0.05$). IL-2 and TNF-α levels of patients in the two groups were significantly higher than pre-operatively, and data in the control group was higher than the observation group ($p < 0.05$). On day 10 post-operatively, all the indexes returned to the preoperative level.

CONCLUSIONS: Both continuous epidural anesthesia and local anesthesia can reduce or avoid perioperative pain, but continuous epidural anesthesia has more advantages than local anesthesia, and it can improve the immune function for patients undergoing PTED for LDH.

Key Words:
Percutaneous transforaminal endoscopic discectomy, Anesthesia, Lumbar disc herniation, Immune function.

Introduction

Lumbar disc herniation (LDH) is a common orthopedic disease and a worldwide health problem characterized by low-back and radiating pain[1]. In fact, pain has become the fifth vital sign and that caused by LDH has a serious impact on patients' daily lives[2]. LDH can be treated by conservative, interventional or surgical treatment. Continuous development of spinal surgical technology has developed percutaneous transforaminal endoscopic discectomy (PTED), which integrates endoscopy with radiofrequency. PTED has become one of the

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optimal clinical treatments for LDH due to the advantages of minimal invasion, less blood loss and rapid recovery[3]. PTED is undertaken with epidural anesthesia or local anesthesia[4]. Surgery and anesthesia are associated with a stress reaction, immunosuppression, and postoperative pain, which prolong hospital stays and increase the economic burden of patients[5]. Therefore, it is important to evaluate pain intensity and the immune function of patients as well as an appropriate anesthesia scheme to reduce adverse reactions, pain sensations and accelerate rehabilitation[6]. This work aimed to evaluate and compare the clinical outcomes of patients undergoing PTED for LDH under local anesthesia and continuous epidural anesthesia.

Patients and Methods

Patients

A total of 92 patients with LDH who underwent PTED from February 2015 to January 2016 in the Department of Spinal Surgery at the Affiliated Hospital of Qingdao University, were selected as the research subjects and divided by computer-generated random allocations into an observation group and control group with 46 cases in each. This study was approved by the ethics committee of the Affiliated Hospital of Qingdao University. Signed written informed consents were obtained from the patients. Inclusion criteria were: 1- patients were diagnosed as LDH by discography and imaging examination; 2- patients have varying degrees of low-back pain and positive reaction to femoral or sciatic nerve stretch test; 3- patients have not been treated with steroids or non-steroidal drugs within a month. Exclusion criteria were: 1- contraindication to radiography; 2- malignant tumor; 3- severe cardiac-cerebral vascular disease (CCVD); 4- hepatic or renal insufficiency. As shown in Table I, there was no significant difference between the baselines of the two groups ($p < 0.05$).

Methods

Description of Surgery

PTED was carried out in the prone position under continuous epidural anesthesia with patients in the observation group, whereas the control group received injections of 1% lidocaine for local infiltration anesthesia. Discography was performed after X-ray guided positioning for the perspective puncture. A dilated cannula was used to fix the working channels, through which the endoscope was gently introduced to remove target tissues. The operative zone was washed with a mixed solution of 0.9% saline solution, gentamicin (16 million units) and epinephrine (1 mg) to keep the visual field clear. At the end of the procedure, the working zone was washed with 0.9% saline solution and followed by suture closure of the incision. The patients in control group were treated with intravenous infusion of sufentanil. The patients in observation group were given epidural analgesia with sufentanil and 0.12% ropivacaine. Epidural catheter was removed if the platelets density of the patients was > 100,000/mm^3, INR values < 1.5 and clotting time returned to normal.

Monitored Indicators and Experimental Procedures

5 ml of venous blood was collected from patients in the morning (fast for more than 8 h) before

Table I. Baseline data of patients in 2 groups.

Item	Observation Group No. = 46	Control Group No. = 46	t/χ^2	p
Sex (Male/Female)	27/19	24/23	0.282	0.595
Age (Years)	30-68	30~65		
Average age (Years)	43.56 ± 4.42	44.85 ± 3.53	1.547	0.125
Duration (Months)	17.63 ± 3.73	18.08 ± 2.68	0.665	0.508
Type (no., %)				
Central LDH	12 (26.08)	15 (32.61)	0.210	0.646
Paramedian LDH	19 (41.31)	21 (45.65)	0.043	0.834
ELLDH	15 (32.61)	10 (21.74)	0.879	0.348
Pain radiation in lower extremity	36 (78.26)	39 (84.78)	0.288	0.591
Neurological deficit in cauda equina	25 (54.34)	27 (58.69)	0.044	0.833
Motor weakness in back	16 (34.78)	12 (26.08)	0.463	0.496
Diminished achilles reflex	11 (23.91)	13 (28.26)	0.056	0.812

ELLDH is extreme lateral LDH.

Table II. Comparison of intraoperative pain rate between 2 groups.

Group	No.	Level I	Level II	Level III	Level IV
Observation Group	46	33 (71.74)	9 (19.56)	4 (8.69)	0 (0.00)
Control Group	46	17 (36.95)	13 (28.26)	11 (23.91)	5 (10.86)
χ^2		14.114			
p		0.002			

Table III. Comparison of VAS scores on lumbocrural pain between 2 groups.

Group	No.	Before Surgery	1 m after Surgery	3 m after Surgery	F	*p*
Observation Group	46	6.95±1.14	4.36±1.13	3.13±1.12	136.97	0.001
Control Group	46	7.16±1.23	4.73±1.25	3.26±1.17	120.45	0.001
t		0.849	1.489	0.544		
p		0.398	0. 139	0.587		

surgery and on day 1, 3, 10 after surgery. The serum was separated with a centrifuge (provided by Changsha Xiangrui Centrifuge Co., Ltd, Hunan, China). Anti-CD4 and anti-CD8 antibodies were added in the serum, which incubated at 4°C for 30 min and was protected from exposure to light. Then, the levels of CD4+ and CD8+ were detected with flow cytometry (Thermo Fisher Scientific, Waltham, MA, USA). The levels of IL-2 and TNF-α were examined with ELISA (enzyme-linked immunosorbent assay) kit (Thermo Fisher Scientific, Waltham, MA, USA), and procedures were performed in strict accordance with instructions. A 50 μl/well of serum and 50 μl/well of standard with 100 μl/well of enzyme-tagged solution were placed into ELISA plate using a pipette, and incubated at 37°C for 1 h. These were washed 5 times with 15 s of standing time during each wash step, then color reagent A and B (50 μl of each) was added and mixed well. The solution was incubated at room temperature (20°C) for 15 min and exposure to direct sunlight was avoided, followed by the addition of 50-μl-stop solution. Then the OD value was detected with the ELISA reader at the wavelength of 450 nm within 15 min and the concentration of IL-2 and TNF-α was calculated.

Evaluation Criteria

Visual Analog Scale (VAS)

The pain experienced by patients was assessed by visual analog scale (VAS). VAS scores range from 0 to 10, where 0 represents no pain and 10 represents extremely excruciating pain. Criteria for pain intensity: Level I (0-2 points): no pain or barely noticeable pain; Level II (3-5 points): moderate but tolerable pain; Level III (6-8 points): distressing pain that affects daily activities; Level IV (more than 8 points): unbearable severe pain.

Adverse Reactions

The adverse reactions were recorded and compared to anesthesia including nausea, vomiting, dizziness and drowsiness within 24 h after surgery in both groups.

Oswestry Disability Index (ODI)

The ODI questionnaire was adopted for functional assessment of patients, where 0 represents the least disability and 5 the greatest disability on a scale of 0 to 5. It is divided into 3 sections to evaluate multiple aspects of disability: 1- pain: pain intensity and impact on sleeping; 2- single ability: sitting, standing, lifting and walking; 3- comprehensive ability: social life, personal care, traveling and sex life. The ODI is expressed as a percentage with the following formula: (total score/100 × 100%), where the total score is obtained by summing up the scores from all sections, and higher ODI indicating more severe symptoms.

Monitored Indicators

5 ml fasting venous blood was collected from each patient before surgery and on day 1, 3, and 10 after surgery for isolation of serum. Levels of T-Lymphocytes subsets (CD4+, CD8+) and serum concentrations of IL-18 and TNF-α were measured by flow cytometer and ELISA, respectively.

Table IV. Comparison of adverse reactions between 2 groups (no., %).

Group	No.	Nausea	Vomiting	Dizziness	Drowsiness
Observation Group	46	3 (6.52)	2 (4.34)	0 (0.00)	1 (2.17)
Control Group	46	6 (13.04)	5 (10.86)	5 (10.86)	4 (8.69)
χ^2				9.061	
p				0.002	

Table V. Comparison of ODI scores between 2 groups.

Group	No.	Before surgery	1 m after surgery	3 m after surgery	F	p
Observation Group	46	30.85±7.23	11.56±3.83	4.73±2.53	345.27	0.001
Control Group	46	31.26±7.16	13.13±4.35	5.56±2.47	315.51	0.001
t		0.273	1.873	1.590		
p		0.785	0.069	0.114		

Table VI. Comparison of ODI scores between 2 groups.

Indicator	Group	Before surgery	1 d after surgery	3 d after surgery	10 d after surgery
CD4+ (cells/μL)	Observation Group	684.53±89.54	414.36±67.42	378.56±56.45	630.74±35.66
	Control Group	685.86±89.35	375.45±57.57	267.86±46.37	617.47±45.73
CD8+ (cells/μL)	Observation Group	397.56±63.45	318.76±51.34	302.36±47.38	384.48±43.87
	Control Group	396.61±64.32	248.36±42.26	207.42±36.45	364.25±38.65
TNF-α (pg /mL)	Observation Group	3.74±1.06	4.32±1.27	5.46±1.35	3.56±1.14
	Control Group	3.92±1.12	6.86±1.33	7.83±1.47	4.24±1.18
IL-2 (pg/mL)	Observation Group	1.54±0.36	3.16±0.33	4.23±0.47	1.76±0.34
	Control Group	1.52±0.32	4.72±0.47	5.86±0.45	2.74±0.28

Statistical Analysis

Statistical software SPSS version 19.0 (Version X; IBM, Armonk, NY, USA) was used for data analysis. Measurement data was expressed as mean and standard deviation, and compared with the *t*-test, while enumeration data was expressed as percentage, and compared by the χ^2-test. There was a significant difference if the *p*-value was less than 0.05.

Results

Comparison of Intraoperative Pain

Table II indicates that the rate of intraoperative pain in the observation group was lower than the control group with statistical significance ($p < 0.05$).

As described in Figure 1, there were 33, 9, 4, and 0 cases of level I, II, III, and IV pain in the observation group, and 4, 11, 0 and 5 cases of level I, II, III, and IV pain in the control group, respectively.

Comparison of VAS Scores before and After Surgery

Table III demonstrates that patients in both groups achieved a remarkable decrease of VAS scores after treatment ($p < 0.05$), and there was no significant difference between two groups ($p > 0.05$).

Comparison of Adverse Reactions to Anesthetic

Table V suggests that in comparison with the observation group 13.04% (6 cases), the rate of adverse reactions, including nausea, vomiting, dizziness and drowsiness in control group, was evidently higher and achieved 43.47% (20 cases).

Comparison of ODI Scores Before and After Surgery

As shown in Table IV, postoperative ODI scores were obviously reduced in comparison with preoperative scores for both groups ($p < 0.05$), and

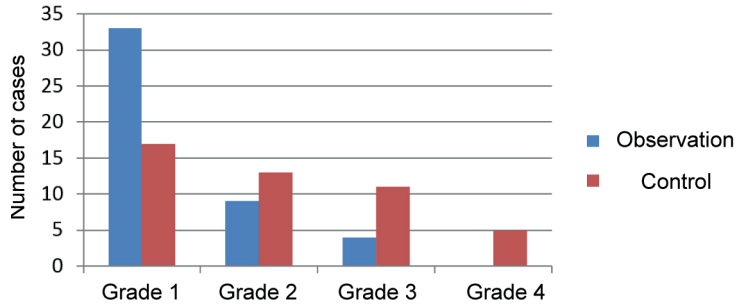

Figure 1. Number of cases suffering different grades of pain in the two groups.

no significant difference was found between the two groups ($p > 0.05$).

Comparison of Indicators at Different Time Points

Table V indicates a declining trend on the level of CD4+ and CD8+ in both groups on day 1 and 3 after surgery, and data in the control group decreased more remarkably than the observation group ($p < 0.05$). There was advancement on the level of IL-2 and TNF-α of patients in the observation group, but evidently to a lesser extent when compared with the control group ($p < 0.05$). All indicators restored to normal values on day 10 after surgery.

Discussion

Treatments for LDH

LDH can be treated by conservative, interventional or surgical treatment, where surgical treatment is commonly used and includes traditional discectomy, microendoscopy discectomy (MED) and PTED[7]. Traditional discectomy has the shortcomings of extensive operative trauma and a high risk of complications caused by postoperative long-term bed rest[8]. MED offers a better operational field as well as less damage to surrounding tissues because of accurate surgical manipulation. On the other hand, it is a more difficult operation due to the technological limitations of bi-dimensional images, electric surgical instruments, injuries and adhesions caused by stretching and exposure of the nerve root during the surgical process, which increases the suffering of the patients. These limit the popularization of MED in tertiary hospitals[9,10]. By precise location of the puncture site, PTED has a direct focus from outside to inside, and it can reach any desired target, which transcends the limitations of far lateral, posterolateral and interlaminar approaches. Under endoscopic observation, bipolar radiofrequency is applied for coagulation in collagen fibrils and inactivation of pain-sensitive nerve endings to effectively relieve the pain of patients[11,12].

The Effect of Different Anesthesia on Pain of Patients

The loss of water and annular fissures under external forces with the degeneration of intervertebral discs is responsible for LDH[13]. Low-back pain and radiating pain in the lower extremity occur when a herniated nucleus pulposus compresses the nerve root or cauda equine[14]. The sources of pain fall into two categories: 1- Cell kinase in intervertebral disc tissue can lead to the easy-to-be-activated state of lead nerve. Sustained high excitement state will produce a large number of signals, which will convey the spinal cord pain to damage neurons and affect central nervous system, so the pain relief is delayed[15]; 2- Bare nerve fibers can be found in articular, intervertebral disc, subcutaneous tissue, ligament, joint capsule and nerve. Nerve endings are widely distributed in low back area, so pain can becaused by the pressure from prominent nucleus pulposus[16]. Also, 1- emitted signals related to excited nerve states (activated by cellular kinase in intervertebral disc) transmit to the spinal cord and make synapses on neurons as well as on central nervous system, which provoke persistent pain[15]; 2- pain caused by compression of nerve fibers and nerve endings due to a herniated nucleus pulposus, and exposed nerve fibers distribute in the facet joint, intervertebral disc, subcutaneous tissue, ligament, capsula articularis and nerve, while nerve endings spread throughout the back and lower back area[16]. For patients with LDH undergoing surgery with spinal anesthesia

or general anesthesia, it is hard to detect the accidental injury of the cauda equina nerve and nerve root due to sensory blockade. Therefore, local anesthesia or continuous epidural anesthesia is most commonly applied to PTED. In this study, patients in the observation group have a significantly higher rate of level-I pain and a lower rate of level II-IV pain than the control group with statistical significance ($p < 0.05$). This indicates the shortcoming of local anesthesia, which is a non-perfect anesthetic effect, more frequent intraoperative pain and stress reaction (rise in blood pressure, heart rate or shock, etc.). Continuous epidural anesthesia is a good alternative with minimal risk of inadvertent injury to nerve root and more reduction in pain owing to unblocking tactile sensation and the motor nerve, so patients can remain fully conscious and keep timely communication with operators[17,18].

The Effect of Different Anesthesia on Immune Function

A stress reaction is induced by preoperative anxiety, surgical trauma and anesthetic, which give rise to immune suppression and an inflammatory reaction[19]. Furthermore, stress reaction can lead to the recruitment of adrenaline and catechol as well as inhibition of T-Lymphocyte immune function. CD4+ is induced T-cell subset that has a positive immunoregulatory activity while CD8+ is an inhibitory T-cell subset that leads to immune dysfunction[20]. Stress reaction during perioperative period can activate IL-2 and TNF-α in serum and induce inflammatory reactions. Results of this study demonstrate a declining trend on the level of CD4+ and CD8+ in both groups on day 1 and 3 after surgery, while data in the control group decreased more remarkably than the observation group ($p < 0.05$). An increase in level of IL-2 and TNF-α of patients occurred in the control group on day 1 and day 3, but evidently to a lesser extent when compared with the observation group ($p < 0.05$). The temporal aggravated inflammatory reaction and immune dysfunction in patients in the postoperative period is associated with surgical trauma and anesthetic. The ODI scores indicate effective rehabilitations in both groups, while patients under continuous epidural anesthesia have reduced adverse psychological effects like postoperative anxiety due to painless surgery, and the indicators restored effectively with postoperative nutritional support and vigilant post-operative care.

Conclusions

Continuous epidural anesthesia reduces intraoperative pain intensity more than local anesthesia and can improve the immune function for patients undergoing PTED for LDH.

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Conflict of interest

The authors declare no conflicts of interest.

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