Application of inflation fluid containing ropivacaine hydrochloride in endoscopic thyroidectomy on stress response and pain mediators

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Objective: To study the effect of the application of inflation fluid containing ropivacaine hydrochloride in endoscopic thyroidectomy on stress response and pain mediators. Methods: 128 patients receiving endoscopic thyroidectomy in our hospital between November 2015 and November 2016 were selected and randomly divided into two groups (n=64), observation group of patients received the inflation fluid containing ropivacaine hydrochloride as the inflating medium during endoscopic thyroidectomy and control group of patients received saline inflation fluid as the inflating medium during endoscopic thyroidectomy. Serum was collected before and after operation respectively to determine the levels of stress response-related hormones and pain-related mediators. Results: Serum adrenocorticotropic hormone (ACTH), cortisol (Cor), norepinephrine (NE), epinephrine (E), renin (PRA), angiotensin-2 (ANG-2), aldosterone (ALD), dynorphin (DYN), β-endorphin (β-EP), nitric oxide (NO) and substance P (SP) levels of both groups after operation were significantly higher than those before operation (P<0.05), and serum ACTH, Cor, NE, E, PRA, ANG-2, ALD, DYN, β-EP, NO and SP levels of observation group after operation were significantly lower than those of control group (P<0.05). Conclusions: The application of inflation fluid containing ropivacaine hydrochloride in endoscopic thyroidectomy can reduce the postoperative stress response and suppress pain mediator secretion.

1. Introduction

Thyroidectomy is a common operation method for clinical treatment of benign and malignant thyroid nodules, and traditional open thyroidectomy makes an incision in the neck, leaves behind the surgery scar and affects the appearance. In recent years, with the continuous development of endoscopic technique, endoscopic thyroidectomy has also been increasingly used in the surgical treatment of benign and malignant thyroid nodules[1,2]. During the operation of endoscopic thyroidectomy, inflating medium is needed to achieve good operation space and avoid damage to adjacent blood vessels and nerves. Normal saline is the common inflating medium used in endoscopic thyroidectomy, the use of inflating medium can achieve good operation space, but it can stretch the soft tissue and cause postoperative pain[3]. The inflation fluid containing ropivacaine hydrochloride not only has the function of inflating medium, but also has the function of local anesthetics, and it can relieve the pain caused by soft tissue stretch. In the following study, the effect of the application of inflation fluid containing ropivacaine hydrochloride in endoscopic thyroidectomy on stress response and pain mediators was analyzed.

2. Materials and methods

2.1. Research subjects

128 patients receiving endoscopic thyroidectomy in our hospital between November 2015 and November 2016 were selected as the research subjects, all the patients were in line with the indications...
for endoscopic thyroidectomy, and patients requiring lymph node dissection were excluded. Random number table was used to divide the included patients into two groups, 64 cases in each group. Observation group of patients received the inflation fluid containing ropivacaine hydrochloride as the inflating medium in endoscopic thyroidectomy, 42 cases were male and 22 cases were female, they were 42–58 years old, 39 cases were with benign tumor and 25 cases were with malignant tumor; control group of patients received saline injection fluid as the inflating medium in endoscopic thyroidectomy, 39 cases were male and 25 cases were female, they were 41–60 years old, 37 cases were with benign tumor and 27 cases were with malignant tumor. Two groups of patients were not statistically different in general data (P>0.05).

2.2. Surgical operation methods

After anesthesia, the patients were put in supine position with two legs apart, and the operator stood between the two legs of the patients, made an arc incision in about 1.0 cm to the right of the cleavage, separated the tissue until deep fascia, used a special needle to inject 100 mL of inflation fluid in the subcutaneous tissue that was to be separated (observation group received saline injection fluid containing 20 mL of 0.75% ropivacaine hydrochloride, and control group received 100 mL of saline injection fluid), then used nondestructive puncture rod for subcutaneous tissue separation, established a cathetering channel, put in the sleeve and endoscope, and injected CO₂ to maintain pressure; the operator made arc incisions of 5 mm in the outer edge of the right and left areola, put in the sleeve, separated to the superior plane of the thyroid gland, exposed the surgical field, then performed the operation of thyroidectomy and placed drainage tube after operation.

2.3. Serum index detection methods

Before operation and 24 h after operation, 5–8 mL of peripheral venous blood was collected from two groups of patients and centrifuged to get serum, and enzyme-linked immunosorbent assay kits were used to detect renin (PRA), angiotensin-2 (ANG-2), aldosterone (ALD), adrenocorticotropic hormone (ACTH), cortisol (Cor), norepinephrine (NE), epinephrine (E), dynorphin (DYN), β-endorphin (β-EP), substance P (SP) and nitric oxide (NO) levels.

2.4. Statistical analysis

SPSS20.0 software was used to input and statistically process data, measurement data analysis between two groups was by t test and P<0.05 meant statistical significance in differences.

3. Results

3.1. Serum adrenal gland–related hormone levels of two groups of patients before and after operation

Before operation and 24 h after operation, analysis of serum adrenal gland–related hormones ACTH, Cor, NE and E between two groups of patients is as follows: before operation, differences in serum ACTH, Cor, NE and E levels were not statistically significant between two groups of patients (P>0.05). After operation, serum ACTH, Cor, NE and E levels of both groups were significantly higher than those before operation (P<0.05). After operation, serum ACTH, Cor, NE and E levels of observation group were significantly lower than those of control group (P<0.05) (Table 1).

3.2. Serum RAAS system–related hormone levels of two groups of patients before and after operation

Before operation and 24 h after operation, analysis of serum RAAS system–related hormones PRA, ANG-2 and ALD between two groups of patients is as follows: before operation, differences in serum PRA, ANG-2 and ALD levels of both groups were statistically significantly higher than those before operation (P<0.05). After operation, serum PRA, ANG-2 and ALD levels of both groups were significantly higher than those of control group (P<0.05) (Table 2).

### Table 1

Comparison of serum adrenal gland-related hormone levels before and after operation (n=64, ±x).

<table>
<thead>
<tr>
<th>Groups</th>
<th>Operation</th>
<th>ACTH (pg/mL)</th>
<th>Cor (pg/mL)</th>
<th>NE (ng/mL)</th>
<th>E (ng/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observation</td>
<td>Before operation</td>
<td>7.95±0.93</td>
<td>68.75±8.93</td>
<td>52.31±7.63</td>
<td>44.57±5.78</td>
</tr>
<tr>
<td></td>
<td>After operation</td>
<td>12.31±1.67&lt;sup&gt;a&lt;/sup&gt;</td>
<td>102.14±12.57&lt;sup&gt;a&lt;/sup&gt;</td>
<td>67.66±8.13&lt;sup&gt;a&lt;/sup&gt;</td>
<td>59.68±7.03&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Control</td>
<td>Before operation</td>
<td>7.88±0.95</td>
<td>69.14±9.24</td>
<td>53.34±6.94</td>
<td>45.12±5.47</td>
</tr>
<tr>
<td></td>
<td>After operation</td>
<td>17.24±2.03&lt;sup&gt;b&lt;/sup&gt;</td>
<td>176.87±22.15&lt;sup&gt;b&lt;/sup&gt;</td>
<td>93.68±10.24&lt;sup&gt;b&lt;/sup&gt;</td>
<td>82.35±9.58&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

<sup>a</sup>: comparison within same group before and after operation, P<0.05; <sup>b</sup>: comparison between groups at same operation time point, P<0.05.

### Table 2

Comparison of serum RAAS system-related hormone levels before and after operation (n=64, ±x).

<table>
<thead>
<tr>
<th>Groups</th>
<th>Operation</th>
<th>PRA (pg/mL)</th>
<th>ANG-2 (pg/mL)</th>
<th>ALD (pg/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observation</td>
<td>Before operation</td>
<td>0.93±0.11</td>
<td>297.65±36.61</td>
<td>105.67±13.26</td>
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<td></td>
<td>After operation</td>
<td>1.52±0.18&lt;sup&gt;a&lt;/sup&gt;</td>
<td>373.16±42.58&lt;sup&gt;a&lt;/sup&gt;</td>
<td>142.21±17.84&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Control</td>
<td>Before operation</td>
<td>0.96±0.10</td>
<td>301.24±38.42</td>
<td>106.12±12.92</td>
</tr>
<tr>
<td></td>
<td>After operation</td>
<td>2.45±0.31&lt;sup&gt;b&lt;/sup&gt;</td>
<td>588.71±71.36&lt;sup&gt;b&lt;/sup&gt;</td>
<td>194.67±24.51&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

<sup>a</sup>: comparison within same group before and after operation, P<0.05; <sup>b</sup>: comparison between groups at same operation time point, P<0.05.
3.3. Serum pain mediator levels of two groups of patients before and after operation

Before operation and 24 h after operation, analysis of serum pain mediators DYN, β-EP, NO and SP between two groups of patients is as follows: before operation, differences in serum DYN, β-EP, NO and SP levels were not statistically significant between two groups of patients (P>0.05). After operation, serum DYN, β-EP, NO and SP levels of both groups were significantly higher than those before operation (P<0.05). After operation, serum DYN, β-EP, NO and SP levels of observation group were significantly lower than those of control group (P<0.05) (Table 3).

4. Discussion

Endoscopic thyroidectomy is a method of minimally invasive thyroidectomy gradually developed in recent years, which, on the one hand, avoids the incision in the neck and is with more ideal postoperative aesthetic effect, and on the other hand, uses the endoscope to magnify the surgery image and is helpful to identify nerves, blood vessels and parathyroid gland. During endoscopic thyroidectomy, inflating medium is required to get good operation space, the normal saline inflation fluid, as inflating medium, can quickly increase the tension between tissues and set up the operating space, but inflation fluid stretch to soft tissue can cause tissue injury and lead to postoperative pain[4,5]. The inflation fluid containing ropivacaine hydrochloride has the effects of both inflating medium and local anesthetics, and it can not only establish operation space, but also lighten the pain caused by tissue stretch. Study has shown that the application of inflation fluid containing ropivacaine hydrochloride in endoscopic thyroidectomy can effectively decrease the intraoperative fluctuations in blood, heart rate and other vital signs, and can also reduce the VAS score and Ramsay score and relieve postoperative pain[6]. In spite of this, there is no report about the effect of inflation fluid containing ropivacaine hydrochloride on the stress response and pain mediator secretion caused by the pain after endoscopic thyroidectomy.

Stress response is a type of non-specific defense response when the body suffers from damaging stimuli, and the postoperative pain caused by inflating medium, as damaging stimuli, can activate the postoperative stress reaction and lead to the abnormal secretion of a variety of stress hormones[7,8]. Activated HPA axis and increased sympathetic nerve excitability damage are the important characteristics of stress response caused by damaging stimuli, which are characterized by the enhanced adrenal endocrine function, massive synthesis of adrenal cortex and medulla as well as the secretion of a variety of endocrine hormones. The activation of HPA axis can stimulate the adrenal cortex to synthesize and secrete cortisol, and the enhancement of sympathetic excitability can stimulate the adrenal medulla to synthesize and secrete epinephrine and norepinephrine[9,10]. In the study, analysis of serum levels of above adrenal gland-related hormones between of two groups of patients before and after operation showed that serum ACTH, Cor, NE and E levels of both groups after operation were significantly higher than those before operation (P<0.05), and serum ACTH, Cor, NE and E levels of observation group after operation were significantly lower than those of control group (P<0.05). It illustrates that the surgical trauma will activate the adrenal endocrine function to a certain extent, intraoperative application of the inflation fluid containing ropivacaine hydrochloride can reduce the activation of the postoperative adrenal endocrine function, and it may be associated with the analgesic effect of ropivacaine hydrochloride.

In addition to causing the enhancement of adrenal endocrine function, the stress response caused by pain will also significantly activate the activity of RAAS system. The activation of RAAS system is also an important feature of the stress response caused by damaging stimuli. Surgical trauma and postoperative pain stimulation can increase the synthesis and secretion of PRA, PRA hydrolyzes the angiotensinogen into angiotensin 1, and the latter generates ANG2 under the action of angiotensin converting enzyme, which shrinks system small vessels and affects hemodynamic characteristics[11,12]. At the same time, ANG2 can also stimulate the zona glomerulosa of adrenal cortex to synthesize and secrete aldosterone, and lead to sodium water retention and sympathetic excitability increase[13]. In the study, analysis of serum RAAS system-related hormone levels before and after operation showed that serum PRA, ANG-2 and ALD levels of both groups after operation were significantly

Table 3

Comparison of serum pain mediator levels before and after operation (n=64, ±s).

<table>
<thead>
<tr>
<th>Groups</th>
<th>Operation</th>
<th>DYN (μg/mL)</th>
<th>β-EP (pg/mL)</th>
<th>SP (pg/mL)</th>
<th>NO (μmol/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observation group</td>
<td>Before operation</td>
<td>0.72±0.09</td>
<td>126.55±15.25</td>
<td>67.86±9.24</td>
<td>7.43±0.93</td>
</tr>
<tr>
<td></td>
<td>After operation</td>
<td>1.05±0.12&lt;sup&gt;a&lt;/sup&gt;</td>
<td>149.58±17.03&lt;sup&gt;a&lt;/sup&gt;</td>
<td>89.45±10.65&lt;sup&gt;a&lt;/sup&gt;</td>
<td>9.48±1.04&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Control group</td>
<td>Before operation</td>
<td>0.75±0.08</td>
<td>127.11±13.89</td>
<td>68.11±7.76</td>
<td>7.55±0.89</td>
</tr>
<tr>
<td></td>
<td>After operation</td>
<td>1.56±0.18&lt;sup&gt;a&lt;/sup&gt;</td>
<td>194.54±20.35&lt;sup&gt;a&lt;/sup&gt;</td>
<td>113.25±13.48&lt;sup&gt;a&lt;/sup&gt;</td>
<td>14.42±1.78&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

<sup>a</sup>: comparison within same group before and after operation, P<0.05; <sup>b</sup>: comparison between groups at same operation time point, P<0.05.
higher than those before operation ($P<0.05$), and serum PRA, ANG-2 and ALD levels of observation group after operation were significantly lower than those of control group ($P<0.05$). It shows that intraoperative application of the inflation fluid containing ropivacaine hydrochloride can reduce the activation of RAAS system and the activation of stress reaction after endoscopic thyroidectomy. The role of inflation fluid containing ropivacaine hydrochloride in reducing the stress response after endoscopic thyroidectomy is closely related to the intraoperative analgesia effect of ropivacaine, and lightening the pain perception caused by inflating medium can improve the stress response caused by pain. In order to further clarify the level of pain after endoscopic thyroidectomy, serum levels of corresponding pain mediators were analyzed in the study. DYN, β-EP, NO, SP and other pain mediators have played a vital role in the generation of pain perception. DYN is the neurotransmitter with opioids activity, and it increases in compensation during the pain response[14]; NO is a kind of gas signal molecule that can adjust the pain receptor sensitivity to nociceptive stimulation in peripheral tissue[15]; β-EP and SP are the neuropeptides that transmit pain signals, the former can increase the sensitivity of the peripheral nerve endings to pain stimulation, and the latter can mediate the transmission of pain signals from the nerve endings to the central nervous[16]. In the study, analysis of serum levels of above pain mediators showed that serum DYN, β-EP, NO and SP levels of both groups after operation were significantly higher than those before operation ($P<0.05$), and serum DYN, β-EP, NO and SP levels of observation group after operation were significantly lower than those of control group ($P<0.05$). It means that intraoperative application of the inflation fluid containing ropivacaine hydrochloride can inhibit the secretion of a variety of pain mediators after endoscopic thyroidectomy, and relieve the pain perception mediated by pain mediators.

To sum up, it is believed that the application of inflation fluid containing ropivacaine hydrochloride in endoscopic thyroidectomy can inhibit the postoperative activation of RAAS system and adrenal endocrine function, also reduce the secretion of pain mediators and relieve the pain perception mediated by pain mediators.

References


