Effect of Dexmedetomidine Combined with Dezocine for Cervical Plexus Block in Thyroid Surgery

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This study mainly explores the clinical effects of dexmedetomidine and dezocine assisted ultrasound-guided nerve block in thyroid surgery. The data from a total of 72 patients who underwent thyroid surgery in our hospital were analyzed. All patients were given ultrasound-guided cervical plexus block anesthesia and divided into three groups. Group A (n=20) and group B (n=22) received dexmedetomidine and dezocine assisted anesthesia respectively, and group C (n=30) was given dexmedetomidine plus dezocine assisted anesthesia. Anesthesia time, operation time and other clinical indicators were compared among the three groups. The results showed that at 12 h and 24 h, group C had a lower degree of pain than groups A and B. The postoperative comfort score of group C was higher compared to groups A and B. The incidence of postoperative adverse reactions reported was lower in group C compared with the other two groups. The above outcomes shows that the combined use of dexmedetomidine and dezocine in ultrasound-guided assisted nerve block during thyroid surgery contributes to better clinical efficacy compared with their single use.

Key words: Dexmedetomidine, dezocine, cervical plexus block, thyroid surgery, sedation, analgesia

Epidemiological statistics has shown that prevalence of thyroid diseases remarkably rises globally, particularly among women^[1-3]. Surgical intervention is a well-established treatment for several thyroid diseases, including thyroid adenoma, retrosternal goiter and thyroid tumors^[4]. However, the degree of pain during thyroidectomy is relatively moderate, but there is still a risk of postoperative complications during thyroid surgery^[5]. Despite the great advancement in medical instrumentation that has refined surgical procedures, postoperative complications remain inevitable after thyroidectomy. The most common complication following thyroid surgery is recurrent laryngeal nerve injury^[6,7] which can be temporary or permanent. Although the incidence of permanent nerve injury is lower than temporary injury, the minimum recovery time of patients with minor temporary laryngeal nerve injury is around 4 w^[8,9]. However, in complex clinical scenarios which may involve neurovascular or peripheral soft tissue injury, it may require longer time for recovery^[10].

Cervical Plexus Block (CPB) anesthesia can be operated during thyroid surgery to improve analgesia

after thyroidectomy and cut the demand for opiates during and after anesthesia^[11]. CPB is an ideal method of anesthesia during thyroid surgery as it is easy to perform and cost-effective compared to general anesthesia^[12,13]. However, dense blood vessels and nerves in the neck can limit the probability of obtaining a complete nerve block resulting in tachycardia and hypertension^[14,15], particularly in patients with comorbidities such as hypertension^[16] and coronary heart disease^[17]. Therefore, Intravenous (IV) anesthesia is required while performing a CPB.

Dexmedetomidine is an alpha-2 (α_2) type adrenergic receptor agonist that offers cooperative sedation without highly selective complications^[18]. Dezocine is a new type of opioid receptor agonist-antagonist^[19]. This study compared the sedative and analgesic effects of ultrasound-guided nerve block anesthesia using dexmedetomidine or dezocine as single drugs or in combination during thyroid surgery.

Ourstudy hypothesis is that ultrasound-guided cervical plexus nerve block may improve postoperative analgesia when assisted with dexmedetomidine combining dezocine during thyroid surgery.

MATERIALS AND METHODS

Clinical data:

A total of 72 patients who underwent thyroid surgery at Hanchuan People's Hospital from March 2017 to March 2018 were retrospectively analyzed. All patients were given ultrasound-guided CPB anesthesia along with dexmedetomidine and/or dezocine sedative drug. The patients were divided into three groups according to the type of drugs administered. Group A (n=20) received dexmedetomidine assisted anesthesia, group B (n=22) received dezocine assisted anesthesia and group C (n=30) received dexmedetomidine combined with dezocine assisted anesthesia. No significant differences were observed in the general clinical baseline characteristics of the patient groups (p>0.05) (Table 1). All patients had American Society of Anesthesiologists (ASA) physical status range between grade I-II and no history of allergy to the drugs before the operation. There were no contraindications of CPB in all patients. This study was approved by the Ethics Committee of Hanchuan People's Hospital and all patients were recruited under written informed consent after the surgery, we paid attention to personal privacy and confidentiality when collecting the data and did not disclose the identity of the patients to anyone. Sample size was calculated using an "A Priori" power analysis of G-power 3.1 to analyze the difference between two-independent equal groups, with effect size 0.8 to achieve a power of 80 %, yielding a total sample size of 42 (21 patients in each group), with alpha error 0.05. Therefore, our sample size for each group is above 20.

Treatment plan:

In the preparation room of central operating theater,

TABLE 1: GENERAL DATA OF THREE GROUPS

IV access was obtained and ringer lactate 10 ml/kg intravenously was administered. In the operating room, the subject received oxygen supplementation 2 l/min through a nasal cannula. Philips MP50 multi parameter monitor was used to monitor Electrocardiogram (ECG), Mean Arterial Pressure (MAP), Heart Rate (HR) and Saturation of peripheral Oxygen (SpO₂) of blood. The puncture sites of all patients were routinely disinfected and the CPB was performed under ultrasound guidance employing a one-point block. 5 ml of 0.4 % ropivacaine (10 ml:75 mg) for deep cervical plexus on one side and 10 ml of 0.4 % ropivacaine (10 ml:75 mg) for superficial cervical plexus on each side. To relieve intraoperative discomfort 10 min after the block, patients in group A were given IV dexmedetomidine (0.5 µg/kg)+IV of normal saline infusion (15 ml/h). Patients in group B were given IV dezocine (0.1 mg/kg)+IV pump of normal saline infusion (15 ml/h). Patients in group C were given IV dexmedetomidine (0.5 μ g/ kg)+dezocine (0.1 mg/kg)+IV infusion of normal saline (15 ml/h). The administration of all drugs was stopped 30 min before the end of the operation.

Anesthesia depth monitoring and indicators observation:

The anesthesia time, operation time and the recovery time after anesthesia were recorded in the Post-Anesthesia Care Unit (PACU) and compared amongst the three groups. Moreover, to monitor the indicators of anesthesia depth, including the hemodynamic marker changes (MAP, HR and SpO_2) and Ramsay sedation scores were recorded before anesthesia (T1), 10 min after anesthesia (T2), the beginning of the skin incision (T3), before dissecting the thyroid (T4) and at the end of the operation (T5).

| Variables | Group A (n=20) | Group B (n=22) | Group C (n=30) | χ²/t | р |
|----------------------------------|----------------|----------------|----------------|---------|--------|
| Gender (Male/Female) | 9/11 | 8/14 | 10/20 | 0.7143 | 0.6997 |
| Age (y) | 43.5±8.5 | 42.9±8.8 | 43.1±9.1 | 0.0007 | 0.9754 |
| ASA status | | | | 13.1 | 13.1 |
| I | 12 | 15 | 18 | 0 424 4 | 0.004 |
| II | 8 | 7 | 12 | 0.4364 | 0.804 |
| Approach of surgery | | | | 13.1 | 13.1 |
| Subtotal thyroidectomy | 8 | 11 | 14 | | |
| Unilateral thyroid lobectomy | 5 | 4 | 10 | 1.774 | 0.7767 |
| Bilateral subtotal thyroidectomy | 6 | 5 | 6 | | |

The Visual Analog Scale (VAS) scores were compared across the three groups at 2, 6, 12 and 24 h after operation according to the following system (0: Painless; <3: Excellent analgesia; 3-5: Satisfactory analgesia; >5: Unsatisfactory analgesia and 10: Severe pain). The Bruggemann Comfort Scale (BCS) ^[20] were evaluated according to the following scores (0: Continuous pain; 1: No pain when quiet but with pain in deep breathing and coughing; 2: No pain when lying in the supine position but slight pain while deep breathing and coughing; 3: No pain during deep breathing and 4: No pain while coughing). The postoperative adverse reactions and anesthesia satisfaction of the three groups were also recorded.

Statistical methods:

Statistical analysis was performed using Statistical Package for the Social Sciences (SPSS) 21.0 software (SPSS Inc.). Measurement data were expressed as the mean±standard deviation (x±s) while the counts data were expressed as percentages. T-test was used for the comparison between the two groups of quantitative data and Chi square test was used for the comparison between the two groups of qualitative data. Differences between the means were analyzed using single, two or three-factor Analysis of Variance (ANOVA), with or without repeated measures, followed by Bonferroni correction (Bonferroni post-mortem analysis). α =0.05 was used as the test standard and p<0.05 was considered as statistically significant difference.

RESULTS AND DISCUSSION

Anesthesia time, operation times and recovery room residence times were explained here. We have recorded all clinical information to investigate the effect of the sedative drugs on anesthesia time, operation time and postoperative recovery time and status. Our results showed no significant differences in the anesthesia time, operation time, PACU completion and the length of stay in the recovery room amongst the three groups (p>0.05) according to the recorded times. These data indicate that the use of dexmedetomidine and/or dezocine have no significant effect on the basic characteristics of anesthesia (Table 2).

Administration of dexmedetomidine and dezocine during CPB improves sedative effects is shown here. The anesthesia indicators information was recorded to monitor the anesthetic depth in dexmedetomidine and/or dezocine three groups. The changes in hemodynamic markers of the three groups were compared before CPB anesthesia, 10 min after CPB anesthesia, at the beginning of the operation, before dissecting the thyroid and at the end of the operation.

Our results have shown that the difference in SpO₂ percentage among groups wasn't significant, although it was significantly elevated at T5 in the dexmedetomidine-administered group (group A) and dexmedetomidine combined with dezocine (group C) compared to T4 (fig. 1A). On the other hand, we observed that the MAP and HR rates in dexmedetomidine administered group (group A) was significantly higher before dissecting the thyroid in comparison to dezocine administered group (group B) and dexmedetomidine combined with dezocine (group C) (p < 0.05) (fig. 1B and fig. 1C). While the Ramsay sedation scores in dezocine administered group (group B) at the beginning of skin incision, before dissecting the thyroid and at the end of operation was significantly lower compared to dexmedetomidine (groups A) and dexmedetomidine combined with dezocine (group C) (p<0.05) (fig. 1D). Overall, these data showed that the effect of dexmedetomidine combined with dezocine on hemodynamics is relatively stable and that the combination has a better sedative effect compared to the single drugs.

| Groups | Anesthesia completion time (min) | Time of operation (min) | PACU completion time (min) |
|----------------|-------------------------------------|-------------------------|----------------------------|
| Group A (n=20) | 14.5±1.3 | 68.7±13.2 | 28.2±3.9 |
| Group B (n=22) | 15.1±1.8 | 69.4±12.9 | 29.3±4.3 |
| Group C (n=30) | 14.2±1.7 | 67.3±13.5 | 28.8±4.0 |
| χ^2/t | 0.0533 | 0.0049 | 0.011 |
| р | 0.1506 | 0.8436 | 0.6829 |

TABLE 2: BASIC INFORMATION OF SURGICAL ANESTHESIA



Fig. 1: The hemodynamic changes and Ramsay sedation scores of three groups at different time points

Note: (A) The SpO₂ changes at different time points, (→) Group A; (→) Group B and (→) Group C; (B) The HR changes at different time points; (C) The MAP changes at different time points and (D) The Ramsay score changes at different time points, (→) Group A; (→) Group B and (→) Group C. Comparison among groups, *indicates comparison to group A, p<0.05; #indicates comparison to the previous time points, p<0.05, color corresponding to the same group

Administration of dexmedetomidine and dezocine during CPB reduces VAS scores postoperative pain. After thyroid surgery, the effects of Bilateral Superficial Cervical Plexus Block (BSCPB) are on cutaneous, subcutaneous and muscular layers which are under post-thyroidectomy analgesia but pain arises from areas that cannot be blocked by a simple approach^[21]. To investigate the postoperative pain in the patients who underwent thyroid surgery, we analyzed the VAS scores at different time points after surgery. No significant differences were observed in the VAS scores between administering dexmedetomidine and/or dezocine three groups at 2 h and 6 h after the operation (p>0.05) (fig. 2A and fig. 2B). Interestingly, at 12 h and 24 h after the operation, the VAS scores of groups administered with dexmedetomidine and dezocine (i.e., group C) was significantly lower (p < 0.05) than group administered with dexmedetomidine or dezocine (i.e., groups A and B, respectively) (fig. 2A and fig. 2B).

Thyroidectomy patient's postoperative voice and comfort significantly improved in CPB administered with dexmedetomidine and dezocine. Phonatory, comfort and swallowing symptoms are wellknown postoperative complications after early thyroidectomy, even without laryngeal nerve injuries^[22]. To monitor the patient's voice and comfort after thyroid surgery, we have recorded the BCS scores. Our results have shown that patients have no temporary or permanent recurrent laryngeal nerve injury in the three groups. The BCS scores showed that the comfort levels of patients administered with dexmedetomidine and dezocine (group C) were significantly higher compared to the patients administered with dexmedetomidine or dezocine (group A and B respectively) (p<0.05) (Table 3).

Thyroidectomy patients administered with dexmedetomidine and dezocine have lower postoperative adverse reactions and higher anesthesia satisfaction. Postoperative Nausea and Vomiting (PONV), respiratory depression, headache and other adverse reactions are common in patients subjected to thyroidectomy treatment^[23]. We analyzed the adverse reactions in the patients who underwent thyroidectomy employing CPB and administered dexmedetomidine and/or dezocine. Our results showed that the incidence of postoperative adverse reactions were 35 % in group A, 31.8 % in group B and 10 % in group C (p<0.05) (Table 4).

However, no significant difference in anesthesia satisfaction was observed amongst the three groups (p<0.05). These data suggested that the three modes of anesthesia administration had minimal impact on patient satisfaction (Table 5). From the above, the incidence of postoperative adverse reactions in patients administered with dexmedetomidine and dezocine was significantly lower than in patients administered with dexmedetomidine or dezocine, and it has minimal impact on anesthesia satisfaction.

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Fig. 2: The postoperative VAS scores in the three groups

Note: The VAS score, (A) 2 h after the operation; (B) 6 h after the operation; (C) 12 h after the operation and (D) 24 h after the operation, where *p<0.05; *p<0.01 and *p<0.001 compared to group A and group B

TABLE 3: POSTOPERATIVE VOICES AND COMFORT LEVEL

| Groups | Temporary or permanent recurrent BCS score laryngeal nerve injury | |
|----------------|---|-------------|
| Group A (n=20) | 0 | 2.64±0.37 |
| Group B (n=22) | 0 | 2.77±0.49 |
| Group C (n=30) | 0 | 3.14±0.45*# |

Note: *Compared to group A, p<0.05 and *compared to group B, p<0.05

TABLE 4: POSTOPERATIVE ADVERSE REACTIONS

| Groups | Nausea | Emesis | Respiratory depression | Headache | Exudation | Total incidence (%) |
|----------------|--------|--------|------------------------|----------|-----------|---------------------|
| Group A (n=20) | 2 | 1 | 1 | 2 | 1 | 7 (35.0) |
| Group B (n=22) | 3 | 1 | 1 | 2 | 0 | 7 (31.8) |
| Group C (n=30) | 1 | 1 | 0 | 1 | 0 | 3 (10.0)*# |

Note: *Compared to group A, p<0.05 and #compared to group B, p<0.05

TABLE 5: ANESTHESIA SATISFACTION AMONG THREE GROUPS

| Groups | Great satisfaction | Quite satisfaction | Dissatisfaction | Total satisfaction rate |
|----------------|--------------------|--------------------|-----------------|-------------------------|
| Group A (n=20) | 10 | 4 | 6 | 14 (70.0) |
| Group B (n=22) | 12 | 5 | 5 | 17 (77.3) |
| Group C (n=30) | 16 | 9 | 5 | 25 (83.3) |

Currently, thyroid diseases that include lesions and cancers are mainly treated by surgery, which is considered an effective and safe treatment. However, patients who undergo thyroid surgery treatment often experience relatively high levels of postoperative pain and postoperative recurrent laryngeal nerve injury^[21,24]. The effective reduction of thyroidectomy postoperative complications and postoperative analgesia remain as urgent clinical needs. In this study, we used CPB anesthesia under ultrasound guidance for thyroid surgery. This surgery procedure was accompanied by administering dexmedetomidine and/or dezocine anesthesia to determine the sedative and analgesic effects of the different drugs on thyroidectomy patients during and after surgery.

According to our observations, there were no significant differences in anesthesia response time, operation time and the length of anesthesia recovery duration in all three patient groups. These data suggest that auxiliary anesthesia with dexmedetomidine and/ or dezocine has minimal impact on the anesthesia basic clinical indicators during the operation. On the other hand, the changes in the hemodynamics markers (MAP, HR and SpO₂) and the Ramsay sedation scores in the thyroid surgery patient groups who administered with dexmedetomidine and/or dezocine showed that the MAP and HR rates in the patients groups who were given dexmedetomidine alone were higher compared to those who were given dezocine alone or in combination with dexmedetomidine. These results suggest that dexmedetomidine elevated the MAP and HR compared to dezocine and both combinations. On the other hand, Ramsay sedation scores of the dezocine administered patient's group was significantly lower at the beginning of the operation, before dissection of the thyroid and at the end of operation compared to the patient's groups given dexmedetomidine and combination. In accordance with previously reported results that dexmedetomidine administered with ropivacaine or different doses of only dexmedetomidine and the Ramsay sedation score was higher and improved the duration of the analgesia^[25,26]. These results were suggesting that dexmedetomidine combined with dezocine had a stronger sedative effect.

However, no significant difference in SpO_2 percentage was observed in all groups of patients at any time point. Previously, it has been shown that dexmedetomidine didn't affect SpO_2 compared to propofol in patients with obstructive sleep apnea undergoing drug-induced sleep endoscopy^[27].

As patients undergoing CPB anesthesia may experience fear or anxiety during the perioperative period, the body produces corresponding stress response hormones^[28]. After the CPB, there is an interaction between the arterial sinus and the vagus nerve, resulting in increased plasma catecholamine levels through sympathetic nerve excitation^[29]. Consequently, this causes physiological reactions that result in tachycardia and hypertension during the operation. Dexmedetomidine has a low-level inhibitory effect on respiration and can effectively release histamine to offset the hemodynamic effects of the nerve block to a certain extent.

Postoperative pain was commonly observed in the cohort of patients. No significant differences were observed in the pain scores amongst the three groups at 2 h and 6 h after the operation. However, at 12 h and 24 h after the operation, the pain score of the dexmedetomidine and dezocine combination group was significantly lower than the dexmedetomidine or dezocine only groups. These data suggest that dexmedetomidine combined with dezocine can effectively relieve postoperative pain.

Acute pain is one of the most common complaints after surgery, which seriously impacts adverse cardiovascular, pulmonary, metabolic and psychological outcomes^[30,31]. Thyroid surgery can be very painful in the early postoperative period. According to the results reported in previous studies, the VAS scores after thyroid surgery can reach 6.9±1.7 points and up to 90 % of patients require morphine for pain relief^[12]. Dexmedetomidine combined with dezocine can effectively relieve acute postoperative pain. These effects occur because dexmedetomidine can effectively reduce the concentration of catecholamines in the plasma to play an anti-sympathetic role and reduce the stress response caused by surgery^[32].

Dezocine is an opioid receptor agonist and antagonist that is more effective in relieving pain than morphine, to which patients fail to develop dependence^[33]. We found that dexmedetomidine combined with dezocine in assisted CPB greatly reduced the incidence of adverse reactions in patients after operation. Similarly, Tan et al. have suggested a sedative effect of dexmedetomidine with patients who experience no temporary or permanent recurrent laryngeal nerve injury^[34]. Moreover, our results have shown that dexmedetomidine and dezocine improved postoperative thyroid surgery adverse reactions such as voice and comfort. Similarly, dexmedetomidine could minimize polypharmacy by providing adequate sedative, analgesic and anxiolytic effects with no accompanying respiratory depression^[35]. Henceforth, our observations suggest that dexmedetomidine and dezocine can be used as sedative drugs after thyroid surgery to reduce the adverse effects and reduces polypharmacy.

In conclusion, administering the dexmedetomidine combined with dezocine in ultrasound-guided nerve block for thyroid surgery has improved the hemodynamic indicators like MAP and HR compared to a single drug. Moreover, dexmedetomidine combined with dezocine has remarkably improved Ramsay sedation scores, which means these drugs combination has a sedative effect during thyroid surgery. The combination of drugs also produce a strong postoperative analgesic effect and can reduce the incidence of postoperative complications and is a safe form of anesthesia auxiliary drugs. Furthermore, our results suggest that dexmedetomidine and dezocine sedative drugs have minimal impact on the anesthesia process during the operation and recovery.

But still, due to the design of this study, it is not without several limitations. The retrospective nature of analysis does not allow randomization of patients in each group, so that the similarity of patients in groups is jeopardized. A well-designed, randomized and controlled trial with prospective data collection and sample size calculation is needed to further confirm the findings in our study in the future.

Author's contributions:

Yongjun Zeng and Biwei Zhan: Methodology, investigation, data curation, original draft; Biwei Zhan: Writing, review and editing; Yongjun Zeng: Review and editing and Jingjing Liu: Idea, supervision, review and editing.

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Conflict of interests:

The authors declare that there is no conflict of interest regarding the publication of this paper.

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