Int J Clin Exp Med 2015;8(1):770-775
www.ijcem.com /ISSN:1940-5901/IJCEM0003878

Original Article

Safe distance between electrotome and recurrent laryngeal nerve: an experimental canine model

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Received November 15, 2014; Accepted January 8, 2015; Epub January 15, 2015; Published January 30, 2015

Abstract: Background: Various energy based surgical devices (ESD) like electrotome have been widely applied in thyroid surgery. This is the first canine model to determine the safety margin of using the electrotome near the recurrent laryngeal nerve (RLN) to prevent injury to this nerve during thyroid surgery. Methods: Eighteen healthy male dogs were divided equally into three groups according to the distance between electrotome application and the RLN: Group A (5 mm), Group B (3 mm), Group C (1 mm). The parameters of evoked electromyography (EEMG) of vocal muscles between right normal RLNs and left RLNs after electrotome application at a power of 30 W for 1 second in each group were recorded and compared. The acute microstructural morphological changes of the RLNs were observed immediately after the operation under electron microscope. Results: In Group B and Group C, after using the electrotome at a vertical distance of 3 mm or 1 mm from the left RLNs, the stimulating thresholds of left RLNs had a significant increase (P = 0.005; P = 0.002) compared with right normal RLNs, and there occurred obvious acute microstructural morphological changes under electron microscope for left RLNs. While there was no significant functional or histological changes for left RLNs after using the electrotome at a vertical distance of 5 mm from the RLN (P = 0.187) in Group A. Conclusions: When using the electrotome near the RLN at a power of 30W in thyroid surgery, a safety margin of more than 3 mm should be recommended.

Keywords: Thyroid surgery, electrotome, neuromonitoring, recurrent laryngeal nerve, safe distance

Introduction

Thyroid surgery is a commonly performed operation, and because the thyroid gland is highly vascularized, effective hemostasis is a crucial part of the procedure [1]. With advances in technology, over the last ten years, energy based surgical devices (ESD) like electrotome have been developed as welcome adjuncts to the thyroid surgeon's armamentarium [2], due to their easy application, significant blood-loss reduction, and commercial effort.

Intraoperative recurrent laryngeal nerve (RLN) injury causes are manifold and most are due to mistakes of technique: section of the nerve, ligature, traction, suction by aspiration near to the nerve, compression, contusion, pressure, ischemia by excessive skeletization, and finally electrical and thermal injury [3-5]. It is undeniable that ultrasonic scalpel has the potential for invisible and undesirable heat-related collateral/proximity iatrogenic injury to adjacent structures. But there is little published experimental evidence for heat-related injury of electrotome in thyroid surgery. The thermal spread needs to be studied to determine a clinically acceptable distance safety margin for the application of electrotome in the vicinity of RLN.

This study aims to develop an experimental canine model of neuromonitoring (NM) as an adjunct to visual identification of nerve injury during the use of electrotome. Electrophysiological and histological changes of the RLNs were recorded before and after electrotome application in order to determine the safety distance of the instrument from the RLN.

Materials and methods

Operative procedures

Eighteen healthy male dogs weighing 15-20 kg were divided equally into three groups accord-

Figure 1. The relationship between the RLN and the application point of electrotome (white arrow: RLN; yellow arrow: the application point of electrotome at a vertical distance of 5 mm from the RLN).

Table 1. The stimulating threshold changes of RLNs after HS application at different distances

Groups	RLNs	Mean ± SD (mA)	N	*t*	*P* value
Group A	Right	0.256 ± 0.101	6	1.406	0.187
	Left	0.308 ± 0.073			
Group B	Right	0.234 ± 0.122	6	3.310	0.005
	Left	0.425 ± 0.118			
Group C	Right	0.248 ± 0.099	6	4.109	0.002
	Left	0.513 ± 0.176			

ing to the distance between electrotome application and the RLN: Group A (5 mm), Group B (3 mm), Group C (1 mm). The animals were administered 3 to 5 mg/kg of intramuscular zolazepam as a premedication followed by 25 mg/kg of intramuscular cefazolin. The animals were then intubated and administered 1% to 3% isoflurane as a general anesthetic. A midline skin incision of approximately 10 cm was made in the neck, and the bilateral lobes of the thyroid and the bilateral RLNs were identified. Bilateral thyroidectomies were performed. The electrotome (DGD-300C-2 Medical Electronic High-Frequency Electrotome, Beilin, Beijing) was applied near the RLN at the assigned distance with a power of 30 W for 1 second. The wounds were closed in multiple layers. To limit variability, all procedures were performed by the same surgeon, who was experienced in thyroid surgery. An aseptic technique was used throughout all procedures. An intramuscular injection of 0.4 ml/kg meloxicam was administered for postoperative pain control.

Intraoperative neuromonitoring

NIM-Response2.0 (Medtronic, USA) was applied to intraoperative neuromonitoring (IONM). A laryngeal surface electrode was applied and adhered to the concave surface of the endotracheal tube just proximal to the vocal cord. The RLN was identified at the tracheoesophageal groove early during dissection and was stimulated by the application of a bipolar probe to deliver an electric current that ranged from 0.1 to 3.0 mA at a frequency of 30 Hz. The identity of an intact RLN would be confirmed through a series of audible acoustic signals that were generated by the machine. The parameters of the nerve integrity monitor were set at: stimulating rate 4 times/sec; pulse width 100 μs; event threshold 100 μs.

Preparation of nerve electrical and thermal damage model

Group A: First we measured the average stimulating threshold and evoked EMG amplitude of six right RLNs under normal physiological conditions. Then, the HS was applied at a vertical distance of 5 mm from six left RLNs for 1 second. After 1 minute, we stimulated the left RLNs at the proximal end of injury point to record stimulating threshold and evoked EMG amplitude (**Figure 1**).

Group B: First we measured the average stimulating threshold and evoked EMG amplitude of six right RLNs under normal physiological con-

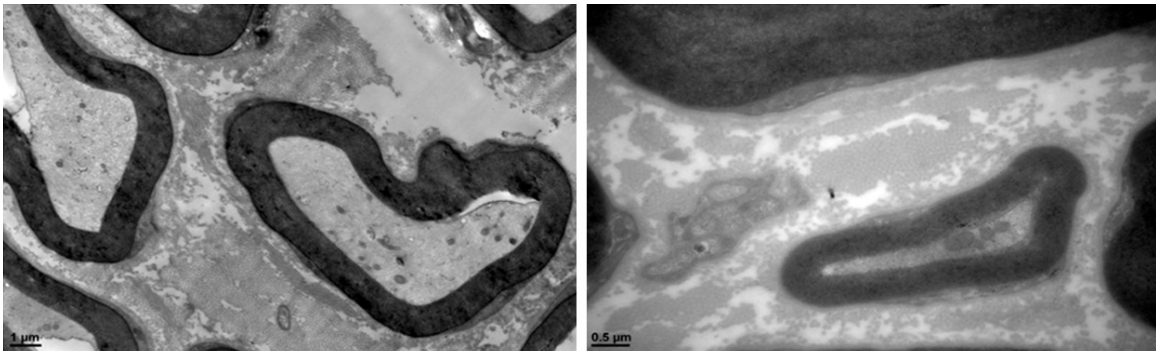

Figure 2. The microstructure of left RLN in Group A (no obvious microstructural changes).

ditions. Then, the HS was applied at a vertical distance of 3 mm from six left RLNs for 1 second. After 1 minute, we stimulated the left RLNs at the proximal end of injury point to record stimulating threshold and evoked EMG amplitude.

Group C: First we measured the average stimulating threshold and evoked EMG amplitude of six right RLNs under normal physiological conditions. Then, the HS was applied at a vertical distance of 1 mm from six left RLNs for 1 second. After 1 minute, we stimulated the left RLNs at the proximal end of injury point to record stimulating threshold and evoked EMG amplitude.

Histological evaluation

Thirty-six RLNs (including eighteen right normal RLNs and eighteen left RLNs after electrotome application) from Group A, Group B and Group C were evaluated for the presence of acute microstructural morphological changes under electron microscope. All the specimens were prepared as the following steps: 1) fixed in 3% glutaraldehyde immediately; 2) washed with phosphate buffet solution for 20 minutes by 3 times; 3) fixed in osmic acid for 1.5-2 hours; 4) washed with distilled water for twice; 5) immersed in uranium for half an hour; 6) washed with distilled water for twice; 7) dehydrated with graded ethanol: 50%, 70%, 90%, 100% for 15 minutes each; 8) embedded in 1:1 100% acetone: embedding medium under vacuum for 2-3 hours; 9) embedded in 1:3 100% acetone: embedding medium under vacuum for 2-3 hours; 10) embedded and immersed at 37°C for 16-20 hours; 11) polymerized at 60°C for 48 hours; 12) dried for 24 hours. Finally we mainly focused on these nerve microstructures under electron microscope: myelin sheath, neuraxon and Schwann cell.

Statistical analysis

The data from this study were analyzed using SPSS 17.0 statistics software (SPSS Inc., USA). Comparison of the average stimulating thresholds between normal RLNs and the RLNs after electrotome application in each group was made using paired t tests. A P value less than 0.05 was considered statistically significant.

Results

Neuromonitoring outcome

Under normal physiological conditions, the average stimulating thresholds of right RLNs in Group A, Group B and Group C were 0.256 ± 0.101 mA, 0.234 ± 0.122 mA and 0.248 ± 0.099 mA, separately. The average stimulating thresholds of left RLNs after electrotome application in Group A, Group B and Group C were 0.308 ± 0.073 mA, 0.425 ± 0.118 mA and 0.513 ± 0.176 mA, separately. Compared with right normal RLNs, the average stimulating thresholds of left RLNs in Group B and Group C both had a significant increase ($P = 0.005$; $P = 0.002$), while there was no significant difference in Group A ($P = 0.187$) (**Table 1**).

Histological outcome

Group A: Under electron microscope, the nerve fibers were arranged regularly with well-organized myelin sheaths. Aligned microfilaments, evenly-distributed matrix and normal organelles were clearly observed without degeneration or proliferation of Schwann cells (**Figure 2**).

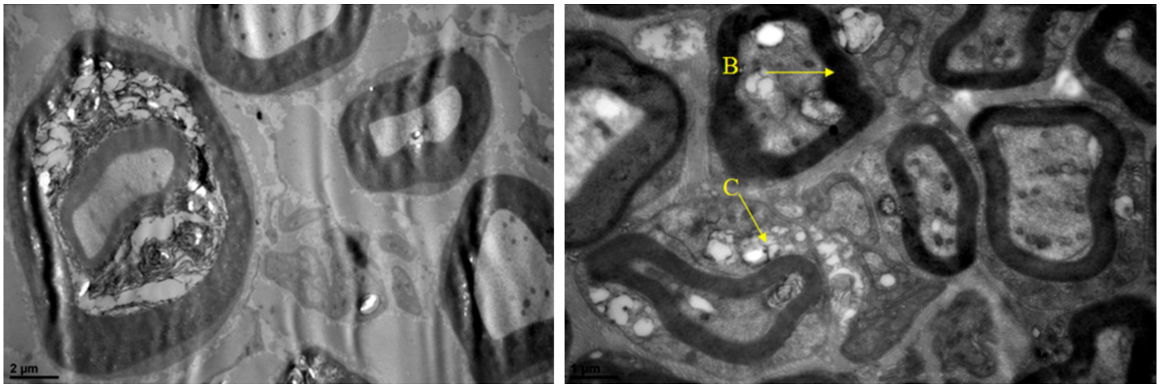

Figure 3. The microstructure of left RLN in Group B (A: Released myelin sheath; B: Axon degeneration; C: Schwann cell degeneration).

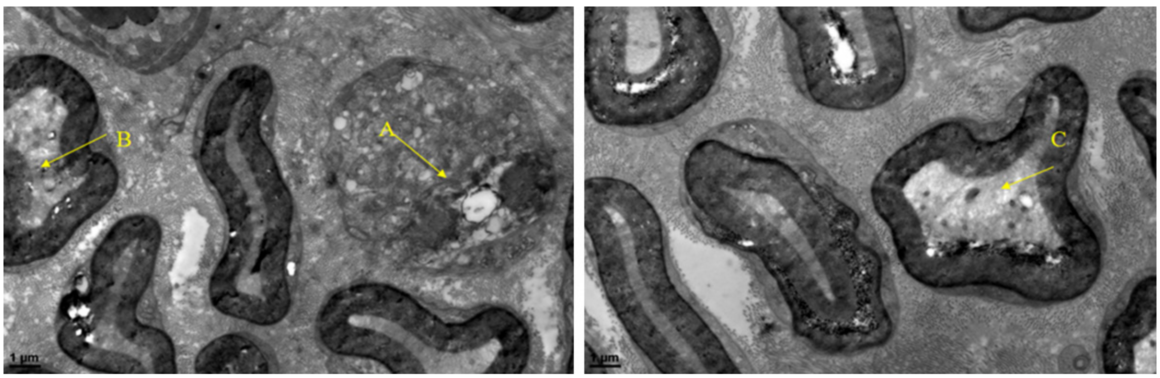

Figure 4. The microstructure of left RLN in Group C (A: Demyelination; B: Axonal degeneration; C: Axonal degeneration).

Group B: Under electron microscope, perineuriums were damaged along with a lot of phagocytes. Released and distorted lamellar myelin and even demyelination were observed with degeneration of Schwann cells. Degeneration of neuraxons was obviously seen with filament condensation and vacuolar changes. Phagocytes and fibroblasts were occasionally seen in looser intercellular substance (**Figure 3**).

Group C: Under electron microscope, perineuriums were damaged along with a lot of phagocytes. Released and distorted lamellar myelin and even demyelination were observed with degeneration of Schwann cells. Degeneration of neuraxons was obviously seen with filament condensation and vacuolar changes. Phagocytes and fibroblasts were occasionally seen in looser intercellular substance (**Figure 4**).

Discussion

With advances in surgical technology, using new energy based surgical devices such as electrotome for cutting and hemostasis during thyroid surgery has become a common practice. However, despite the overwhelming evidence supporting their advantages compared with traditional surgery, the presence of objective data exploring the safe distance for the application of electrotome in the vicinity of the RLN is still limited. Iatrogenic RLN injury is still a significant problem in thyroid surgery, and this study aimed to develop an animal model to determine the clinically acceptable distance safety margin for the application of electrotome in the vicinity of the RLN.

Kyu-Eun Lee et al [6] reported a study by using a canine model for RLN injury by harmonic scalpel (HS). Nine dogs were divided into 3 groups according to the distance between HS application and RLN, and vocal cord function was assessed pre- and postoperatively using video laryngoscopy. After application of HS, RLNs were evaluated for subacute and acute morphologic changes. Despite of the small sample, from both histological and functional outcomes, a safety margin of 3 mm could be postulated. Defechereux et al [7] has proposed an experimental model of neuromonitoring (NM) as an adjunct to visual identification of nerve injury during bipolar scalpel dissection. Electromyographic (EMG) potential with electrophysiologic and pathology of rat sciatic nerves was recorded before and after each experiment. With quantitative correlation of EMG, comparing changes of EMG signal, NM may reflect varying degrees of nerve dysfunction during thermal spread. Jiang H et al [8] published a study by comparing the parameters of evoked EMG of vocal muscles before and after application of HS at a power level of 3 in a rabbit model, and concluded that the activated HS tip should be more than 2 mm from the nerve and the duration of incision should less than 3 sec. The downside of this study was, of course, no nerve structure measurements were correlated with functional outcomes. To our knowledge, the present study is the first large animal experiment to have examined the effect of electrotome application in the vicinity of the RLN in thyroid surgery from both functional and histological outcomes.

In this study, we used eighteen dogs for evaluation of both functional and histological outcomes. For each dog, bilateral thyroid lobectomies were performed, and bilateral RLNs were monitored by evoked EMG and biopsied. As depicted in the results, there occurred functional abnormalities in Group B (3 mm) and Group C (1 mm), which manifested as the stimulating thresholds of the left RLNs had a significant increase compared with the right normal RLNs. In contrast, Group A with electrotome application with safety margin of 5 mm, there were no adverse outcomes.

Histological changes were evaluated using the RLNs harvested immediately after the operation. Acute microstructural morphological changes of left RLNs under electron microscope were observed in Group B and Group C, which were the groups of dogs with electrotome application in vicinity of 3 mm or 1 mm, while Group A with safety margin of 5 mm, there were no adverse acute morphologic changes for left RLNs. We could conclude from these results that the histological outcomes could be matched with the functional outcomes. The anatomical and functional correlation of this canine model might provide a rationale to evaluate the safety margin of HS during thyroid surgery. In a further study of rat sciatic nerves, Owaki et al [10] concluded similarly that usage of the ultrasonic shears at a distance of 3 mm from the RLN for less than 10 seconds at level 3 was safe. According to our results, we could postulate a safety margin of more than 3 mm should be recommended.

The canine model was selected since the anatomy of the thyroid gland is similar in dogs and humans, which facilitates the surgeons to mimic the real thyroid surgery as in human. In both species it is a dark red, elongated structure that is attached to fascia along the ventrolateral surfaces of the proximal trachea. The right thyroid lobe extends between the cricoid cartilage and the 5th tracheal ring, and the left thyroid lobe extends from the 3rd to the 8th tracheal ring. The gland is covered by the sternocephalicus and the sternohyoideus muscles ventrally and by the sternothyroideus muscle laterally. The common carotid artery, the internal jugular vein, and the vagosympathetic trunk are situated on the dorsolateral surface of the right thyroid lobe, and the esophagus lies over the dorsolateral surface of the left thyroid lobe. The caudal laryngeal nerves, termed the RLNs in humans, are dorsal to the thyroid lobes [9].

This study still has some limitations including: (1) did not analyze other influencing factors, such as the blade temperature of the instruments and duration, (2) did not evaluate other energy sources, such as harmonic scalpel and so on, (3) have other ways to evaluate the function, such as observing vocal cord movement by video laryngoscopy, and (4) a larger sample size should be further investigated. However, this study would warrant further study to determine the clinically acceptable distance safety margin for the application of an energy device in the vicinity of the RLN.

Disclosure of conflict of interest

None.

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References

[1] The Surgical Outcomes Monitoring & Improvement Program (SOMIP) report volume 2 (July 2009-June 2010). Coordinated by the Quality and Safety Division of the Hong Kong Hospital Authority. Accessed on 22nd June 2012.

[2] Manouras A, Markogiannakis HE, Kekis PB, Lagoudianakis EE, Fleming B. Novel hemostatic devices in thyroid surgery: electrothermal bipolar vessel sealing system and harmonic scalpel. Expert Rev Med Devices 2008; 5: 447-466.

[3] Bergenfelz A, Jansson S, Kristoffersson A, Mårtensson H, Reihnér E, Wallin G, Lausen I. Complications to thyroid surgery: results as reported in a database from a multicenter audit comprising 3,660 patients. Langenbecks Arch Surg 2008; 393: 667-673.

[4] Chiang FY, Lu IC, Kuo WR, Lee KW, Chang NC, Wu CW. The mechanism of recurrent laryngeal nerve injury during thyroid surgery: the application of intraoperative neuromonitoring. Surgery 2008; 143: 743-749.

[5] Snyder SK, Lairmore TC, Hendricks JC, Roberts JW. Elucidating mechanisms of recurrent laryngeal nerve injury during thyroidectomy and parathyroidectomy. J Am Coll Surg 2008; 206: 123-130.

[6] Lee KE, Jee HG, Kim HY, Park WS, Park SH, Youn YK. Development of a canine model for recurrent laryngeal injury by harmonic scalpel. Lab Anim Res 2012; 28: 223-228.

[7] Defechereux T, Carlender J, Johanson K, Meurisse M. How safe is the new harmonic scalpel close to a nerve. A comparative animal study with bipolar cautery. European Society of Endocrine Surgeons ESES-Abstract Book O31-3rd Biennial Congress Barcelona. European Society of Endocrine Surgeons, Barcelona 2008.

[8] Jiang H, Shen H, Jiang D, Zheng X, Zhang W, Lu L, Jiang Z, Qiu M. Evaluating the safety of the Harmonic Scalpel around the recurrent laryngeal nerve. ANZ J Surg 2010; 80: 822-826.

[9] Hullinger R. The endocrine system. In: Evans H, Christensen G, editors. Miller's Anatomy of the Dog. Philadelphia, PA: W. B. Saunders Company; 1979.

[10] Owaki T, Nakano S, Arimura K, Aikou T. The ultrasonic coagulating and cutting system injures nerve function. Endoscopy 2002; 34: 575-579.