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Original Article

Thyroidectomy facilitated with Harmonic Caliper and intraoperative neural monitoring in three horses

M. Al Naem[†,*]**, *L. F. Litzke***[†] ***and A. A. G. Mourad***[‡]

[†]*Equine Clinic (Surgery, Orthopaedics), Faculty of Veterinary Medicine, Justus-Liebig-University, Giessen, Germany; and* [‡]*Department of Surgery, Anaesthesiology and Radiology, Faculty of Veterinary Medicine, University of Sadat City, Sadat City, Egypt*

**Corresponding author email: Mohamad.Al-Naem@vetmed.uni-giessen.de*

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Summary

Background: Thyroidectomy in horses is performed conventionally; however, both iatrogenic and post-operative complications occur, mostly due to injury of the recurrent laryngeal nerve (RLN).

Objective: To facilitate sufficient understanding of the use of the Harmonic Focus® Shear (HFS) together with intraoperative neuromonitoring (IONM) of the RLN during thyroidectomy in horses.

Study design: Retrospective case series.

Methods: Three horses were presented with a thyroid mass, and a hemithyroidectomy was performed using the HFS together with IONM. Medical records were reviewed. Findings at short-term follow-up at 6 weeks after surgery and long-term follow-up obtained from the referring veterinarian or owner 3 years after surgery were evaluated.

Results: The horses were 9–17 years old. Thyroid enlargement was unilateral in all horses, with two on the left side and one on the right side. Histological findings were consistent with adenocarcinoma, C-cell adenocarcinoma and adenoma in each horse. Neither intraoperative- nor post-operative complications were encountered. Short- and long-term follow-up showed that all horses returned to previous activity.

Main limitations: The limitation of this study is the small sample size, reflecting the low prevalence of this disease and the rarity of this procedure in horses.

Conclusions: The use of the HFS and IONM enabled an easy, precise dissection, adequate haemostasis and direct visualisation of the RLN during thyroidectomy, avoiding its damage and allowing evaluation of its function intraoperatively.

Clinical relevance

- These procedures caused minimal/no iatrogenic or post-operative complications.
- The combined use of IONM of the RLN with the HFS was an effective method for localisation and evaluation of the function of the RLN during the operation, thus it prevented damage and improved the outcome.
- The procedures achieved good health outcomes for the patient group.

Results of this work were presented in part as a poster at the 4th International Equine Congress, DVG, Vet-Congress 17–18 October 2020, Berlin, Germany.

Introduction

Thyroidectomy due to enlargement of the thyroid gland has been reported rarely in horses, either under general anaesthesia (Elce et al., 2003; Troillet et al., 2016) or as a standing procedure (Marcatili et al., 2018). Adenocarcinomas (79%) and adenomas (21%) have the highest prevalence in thyroid cancers (Troillet et al., 2016) and C-cell tumours have also been reported (Elce et al., 2003; Marcatili et al., 2018). In human patients, thyroidectomy is a conventional world-wide endocrine intervention; however, changes in the voice can occur due to injury of the recurrent laryngeal nerve (RLN) (Miccoli et al., 2010).

A major concern during thyroidectomy is the direct intraoperative visualisation of the RLN to avoid iatrogenic damage, which has been reported to have a prevalence of 50% in horses (Elce et al., 2003). Intraoperative neuromonitoring (IONM) of the RLN is a superior method that allows identification and preservation of the nerve, reveals non-function of an apparently intact nerve during procedures, predicts vocal cord action postoperatively (Medas et al., 2019) and allows detection of anatomic variations of the RLN in human patients (Dralle et al., 2013; Eid et al., 2013). Its visualisation requires adequate haemostasis, thus avoiding inadvertent damage to important structures during thyroid surgery (Miccoli et al., 2010). Recently, a Harmonic Focus Shear (HFS) (Ethicon Endo-surgery, Inc.) was developed for thyroidectomy that enables haemostasis, dissection and division and has been used effectively in human patients (Hahn et al., 2015; Miccoli et al., 2010).

To the best of our knowledge, the use of the HFS with IONM of the RLN during hemithyroidectomy in horses has not been reported. The aims of presenting the three cases in this series were to describe the surgical procedures for thyroidectomy using the HFS and the role as well as the efficacy of RLN-IONM regarding post-operative nerve palsy.

Materials and methods

Medical records of horses that underwent hemithyroidectomy due to enlargement of the thyroid gland between 2013 and 2016 were reviewed. The horses' characteristics are described in **Table 1**. Inclusion criteria were horses that had been treated with hemithyroidectomy using the HFS (Ethicon, Johnson & Johnson Medical GmbH) and IONM of the RLN. Case data included history, breed, age, sex, ultrasonographic finding, blood analysis, current medication therapy, triiodothyronine (T3) and thyroxine (T4) assessment, pre- and post-operative upper respiratory tract endoscopy, intra- and post-operative complications and histological examination. Follow-up information was obtained at 6 weeks after hospital discharge and 3 years later by telephone contact with the referring veterinarian or owner. They were asked: 'Are there any long-term complications such as laryngeal hemiplegia (poor performance or respiratory sound) or metastases?'.

Standardisation of IONM

The IONM was standardised according to the six-stages standard of thyroid surgery defined by the International Neural Monitoring Study Group in 2011, which included measurements in the following sequence: (1) preoperative laryngoscopy (L1); (2) intraoperative stimulation of the vagus nerve before thyroidectomy (V1); (3) RLN stimulation upon initial identification intraoperatively (R1); (4) RLN stimulation at the end of thyroid dissection and complete haemostasis (R2); (5) vagus nerve stimulation after complete thyroidectomy and haemostasis (V2) and (6) post-operative laryngoscopy (L2).

We used the intermittent-intraoperative neuromonitoring (I-IONM) system (Inomed Medizintechnik GmbH) after employing electromyography (EMG), adhering a surface/laryngeal electrode to the endotracheal tube and employing a C2 NerveMonitor. IONM combines two electrical circuits (stimulation and recording sides) with four probes: (1) one stimulation probe, (2) two ground electrodes and (3) one surface electrode; both stimulation and recording sides were connected to the monitor through an interconnection box (Medas et al., 2019).

We set the electrodes as follows: an excitation electrode was set at 0.5–3 mA (0.5 mA for RLN sub-branching confirmation, 1 mA for RLN confirmation and 2–3 mA for both vagal nerve and RLN identification), the stimulation frequency was set to 4 s with a stimulation period of 100 μs and the electrode threshold was set to be less than 5 kΩ, with less than a 1 kΩ difference between both positive and negative electrodes. Any increase in these thresholds meant contact inadequacy between the endotracheal tube (ET) and vocal cords.

First, the surface electrode was adhered to the ET at the site where the vocal cords contacted the ET after intubation (determined by measuring the distance from the nostril to the vocal cords during the preoperative laryngoscopy), then a twisted-pair of needle grounding electrodes for both the recording and stimulation sides were placed at the neck muscles, which filled the roles of control and stimulus return, and then an excitation probe was used for neural stimulation. With intact nerve function, the surface electrode estimated the adductor function of the vocal cord, thus the EMG recording of the target muscle (*M. vocalis*) was mediated via the *N. vagus* and *N. recurrens*, and this was then transformed into an acoustic signal. The EMG signals of the *M. vocalis* were recorded using the lead electrodes and displayed on the monitor.

TABLE 1: Descriptive details of the three understudy clinical cases

Number of horses	Age (years)	Breed	Sex	Affected lobe
1	9	Warmblood	Gelding	Left
2	15	Warmblood	Mare	Right
3	17	Quarter Horse	Gelding	Left

Surgical technique

Preoperatively, each horse received amoxicillin (10 mg/kg bwt, IV, b.i.d., Belamox® 20%; bela-pharm GmbH), gentamicin (6.6 mg/kg bwt IV, q.d. vetagent®; MSD Animal Health GmbH) and flunixin meglumine (1.1 mg/kg bwt, IV, b.i.d.; Finadyne® paste 5%; Intervet GmbH). In all cases, pre- and postsurgical endoscopic examinations of the larynx were performed. The distance between the nostril and vocal cords was measured during presurgical endoscopy and the laryngeal electrode was adhered to the ET so that a direct contact between the electrode and vocal cords was achieved.

Cases were sedated with detomidine hydrochloride (10 μg/kg bwt IV, Cepesedan® 1%; CP-Pharma Handelsges GmbH) and butorphanol tartrate (10 μg/kg bwt IV; Butorgesic® 1%; Cp-Pharma). Then, anaesthesia was induced with ketamine hydrochloride (2.5 mg/kg bwt, IV, Ursotamin®; Serumwerk Bernburg AG) and midazolam (0.05 mg/kg bwt, IV, Dormazolam®; Dechra Veterinary Products Limited) and maintained with isoflurane (Baxter Inhal Lös; Baxter AG) in 100% oxygen. Horses were placed with the affected thyroid lobe uppermost and head and neck in slight extension (**Fig 1**). The surgical site extending from the middle third of the neck to the middle third of the mandible was clipped, aseptically prepared and covered with a self-adhering-incision drape (Ioban™ 2).

A linear incision was made with a No. 10 scalpel blade over the affected thyroid lobe ventral to the linguofacial vein and sternomandibularis muscle. A combination of blunt and sharp dissection was performed through the subcutaneous tissue, the omohyoideus muscle was transected along its fibres to expose the thyroid gland and then a stay suture was placed through the thyroid capsule using 1 USP Ethibond to pull out and displace the affected thyroid lobe ventrally.

We tested the IONM system by stimulating the sternothyroid muscle (Medas et al., 2019) after we ensured the presence of normal muscle twitching. Then the vagus nerve and the RLN were identified by stimulating the tissue close to their expected sites as during dissection. We did not visualise the RLN, we identified it by careful dissection (stepwise) combined with use of the neuromonitoring probe at the expected site of the nerve to localise the nerve. Then, after localising the nerve, we repeated the neuromonitoring in the proximal and distal direction (along the operation field) to identify the course of the nerve (**Figs 2 and 3**). In this manner, the course of the RLN near the affected thyroid gland was identified, thus we avoided its damage during dissection. A Volkmann retractor was applied and held by an assistant to facilitate dissection and visualisation of the vessels to avoid damage to the RLN. We assumed that the combination of retracting the tissue and using neuromonitoring would provide the best results and would be the safest method to perform the thyroidectomy.

Dissection and haemostasis were continued along the cranial and caudal poles of the affected thyroid lobe using the HFS (**Fig 4**). The cranial thyroid artery was sealed in a stepwise fashion (Parker et al., 2009), starting with the sub-branches and ending with the main trunk. The IONM was repeated at this stage to ensure preservation of the RLN. Thereafter, the affected lobe was clearly identified, elevated and dissected off the trachea, freed by dividing the isthmus with the HFS and then was removed.

After ensuring complete haemostasis, a final testing of the RLN and vagus nerve was performed. The transected omohyoideus muscle and subcutaneous tissues were sutured in a continuous pattern using 2-0 USP glycomer 630 (Biosyn; Covidien). In all cases, the skin was closed in an interrupted vertical mattress pattern using 0 USP Ethibond (Johnson & Johnson Medical GmbH). Thereafter, a stent bandage was applied.

Fig 1: Rostral is left. Right thyroid lobe (yellow arrow). Linguofacial vein (black arrow).

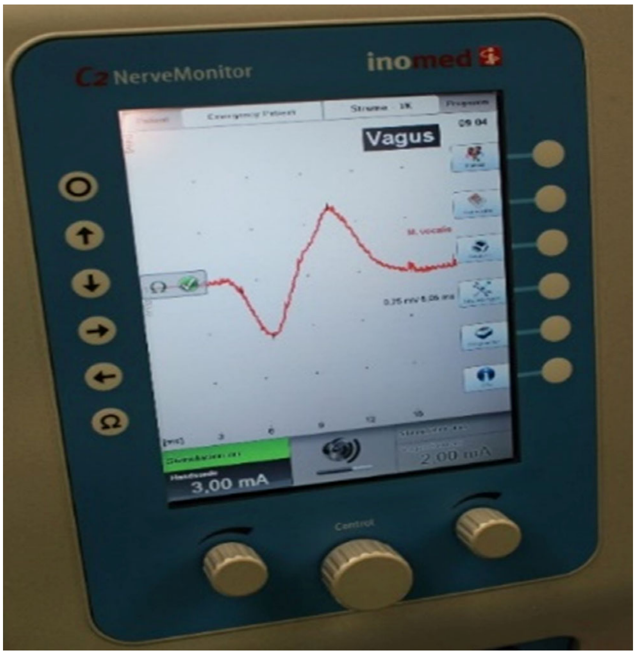

Fig 3: Electromyography signal of the muscle vocalis after stimulation of the vagus nerve using a C2 Nerve Monitor.

Fig 2: Stimulation of the vagus nerve using an excitation electrode.

Fig 4: Haemostasis and dissection of the cranial thyroid artery along the thyroid capsule (yellow arrow) using a Harmonic Focus Shear (black arrow).

Short-term follow-up and post-operative endoscopic examination were performed at 6 weeks after surgery, including upper respiratory tract endoscopy. Long-term follow-up (3 years) data were obtained from the referring veterinarian or owner.

Results

Three horses: a 9-year-old Warmblood gelding (Case 1), a 15-year-old Warmblood mare (Case 2) and a 17-year-old Quarter Horse gelding (Case 3), came to the clinic with a history of a rapidly expanding thyroid mass, with accompanying oesophageal obstruction (choking) in one case (Case 1).

All vital signs were unremarkable. Two horses showed a left unilateral thyroid enlargement (Cases 1 and 3) and one horse (Case 2) had a right unilateral thyroid enlargement. None of the three cases showed signs of hormonal disturbances nor were administrated phenylbutazone in the previous few months. The routine complete blood count analysis and measurements of triiodothyronine (T3), and thyroxine (T4) were within the normal range in all three cases.

Ultrasonographic examination revealed an enlargement of the affected thyroid lobe, which were 5.2 × 7.9 cm in Case 1, 7.1 × 4.7 cm in Case 2 and 7.6 × 5.3 cm in Case 3. The ultrasonographic examination revealed a rounded mixed texture of hypoechoic to hyperechoic areas that were inhomogeneous to slightly homogenous appearance in Cases 1 and 3, and an encapsulated, homogenous texture surrounded by an anechoic area in Case 2 (**Fig 5**).

Histological findings were consistent with an adenocarcinoma (Case 1), a C-cell adenocarcinoma (Case 2) and an adenoma (Case 3).

***Fig 5:** Ultrasound imaging shows parenchyma with homogenous echogenicity of the tumour (T) in Case 2; black arrow = capsule.*

Surgical outcome

We did not encounter any intraoperative complications; bleeding was almost negligible during the use of the HFS and the operative field allowed direct visualisation of the RLN. The normal stimulation response was present in all horses during the procedures and no post-operative complications were encountered. The hospitalisation period ranged between 7 and 9 days. Antimicrobial agents and anti-inflammatory therapy were administered in total for 5 days. Horses were restricted to box rest for 14 days. Suture removal was performed at 10 days postoperatively. Short-term follow-up and a post-operative endoscopic examination were performed at 6 weeks after surgery and did not reveal any abnormalities (normal movement of the vocal cord and laryngeal cartilage at the corresponding side). Long-term follow-up (3 years) reported no complications and no evidence of metastasis and all horses returned to their previous level of performance.

Discussion

This study is the first that describes the use of Harmonic Focus® Shears and IONM of the RLN in hemithyroidectomy in horses and reports their efficacy in avoiding iatrogenic injury of the RLN and eliminating bleeding and seroma formation.

One of the major concerns in thyroidectomy is to preserve the RLN anatomically and physiologically. As in human patients, the average incidence of temporary recurrent laryngeal nerve paralysis (RLNP) after thyroidectomy is 9.8%, but the incidence of permanent RLNP is 2.3% (Jeannon et al., 2009). In horses, post-operative laryngeal hemiplegia has been described in 50% of cases that underwent hemithyroidectomy (Elce et al., 2003). In our study, none of the horses developed laryngeal hemiplegia postoperatively or other complications.

Two mechanisms for RLNP have been described; that is, transection and non-transection injuries (Chiang et al., 2008). In most of the cases, RLN is visually intact but not physiologically. Therefore, the assessment of its physiological function by IONM is an important aspect that must be considered during hemithyroidectomy. IONM allows both pre-visual identification and safe dissection around the RLN, thus preserving its physiological function via avoiding an iatrogenic injury. This is clinically advantageous, especially in horses with regionally anatomical distortion due to the enlarged mass of the thyroid tumour causing difficulty in nerve location (Zhou et al., 2019). The use of IONM during thyroid surgery in human patients has gained widespread acceptance as an adjunct to the standard of visually identifying the RLN (Dralle et al., 2013) and proved to be a safe and effective method for RLN identification (Lu et al., 2018) that enables an objective evaluation of its function during the entire dissection (Dralle et al., 2013).

In our study, the IONM technique was used. It was a safe and reliable method for identifying the RLN and assessing its function, thereby avoiding damage. Standardisation of IONM is crucial for successful surgical outcomes through factual assessment of RLN morbidity with preoperative and post-operative laryngoscopy (L1 and L2) (Zhou et al., 2019). In addition, early identification of the vagus nerve is important to confirm that the IONM system is working properly and to obtain the pathway of the RLN (Medas et al., 2019).

In horses, various techniques have been described to preserve the RLN (Troillet et al., 2016). An improvement of the visual field has been achieved after ventral displacement of the thyroid lobe, and a close dissection along the affected thyroid lobe led to preservation of the RLN (Marcatili et al., 2018; Troillet et al., 2016). In the case of bilateral thyroidectomy performed in the standing horse, a combination of skin displacement and tilting of the head is advocated to improve visualisation, thus preservation of the neurovascular structures (Marcatili et al., 2018). However, all these approaches aimed to improve the visibility of the RLN but not assess its physiological function during the surgery.

Another critical concern in visualising the RLN is bleeding, as it prevents proper identification of the nerve. The equine thyroid gland is highly vascularised and has a blood flow rate of 4–6 ml/min/g, which is greater than other highly vascular organs (Ueki et al., 2004) and it is close to the RLN. Therefore, exhaustive haemostasis should be applied to avoid bleeding, provide a clear view of the surgical field and prevent injury to vital structures (Cannizzaro et al., 2016). In horses, manual ligation, an electrocautery vessel sealing devices system, or Enseal G2 Super Jaw have been used during thyroidectomy for haemostasis (Marcatili et al., 2018; Troillet et al., 2016). However, an excessive intraoperative haemorrhage was reported in a horse with a massively enlarged thyroid lobe (Troillet et al., 2016). In our cases, the HFS proved to be an easy and safe method that achieved exhaustive haemostasis, which allowed dissection without the need for other surgical instruments and haemostasis without collateral heat damage.

The harmonic devices use focused ultrasound energy to cut and coagulate soft tissue and vessels at much lower temperatures (50°–100°) than electrocoagulation devices (150°–400°), with both providing minimal thermal damage to the surrounding tissue (Cannizzaro et al., 2016; Dionigi et al., 2013) and less time in human patients undergoing thyroidectomy compared with electrocautery vessel sealing devices (Dionigi et al., 2013) or conventional ligation (Arslan et al., 2018). Other reports have demonstrated that post-operative pain, intra- and post-operative haemorrhage and length of hospital stay were less with the high frequency ultrasound scalpel when compared with other surgical techniques (Hahn et al., 2015; Miccoli et al., 2010; Parker et al., 2009).

Another prospective multicentre study investigated the impact of the HFS on complications in thyroid surgery in human patients. In this study, a significant advantage in operative time, need of haemostatic agents and the decision to leave a suction drainage at the end of surgery, as well as a lower rate of post-operative hypocalcaemia due to the limited trauma and ischaemic effect induced by the Harmonic Focus, was demonstrated (Materazzi et al., 2013). The excellent outcome of the surgical use of the HFS in thyroidectomy was achieved by the ultrasonic coagulation mechanism. Denaturation of proteins and successive coaptation contribute to closing the vessels without leaving any eschar, thus avoiding delayed bleeding (Materazzi et al., 2013). In equine practice, the HFS has been successfully used for laparoscopic bilateral ovariectomy in standing horses (Düsterdieck et al., 2003).

Seroma formation has been reported in 29%–33% of the cases in horses undergoing thyroidectomy under general anaesthesia (Elce et al., 2003; Troillet et al., 2016). In the three reported cases, no intra- or post-operative complications occurred. Use of the HFS provided a dry operative field, appropriate haemostasis of the vessels and good visualisation of the surgical field at all times during the surgical procedure. Long-term prognoses in our cases appear to be excellent as none of the operated horses developed clinical signs related to metastasis and could return to their previous activity. These findings are similar to the outcomes in other studies (Marcatili et al., 2018; Troillet et al., 2016).

The limitation of this study is the small sample size, reflecting the low prevalence of this disease and the rarity of this procedure in horses.

We recommend the combined use of the HFS and IONM in equine thyroidectomy, as it helps in detection of the RLN before its visual inspection, even in anatomically distorted regions; assesses the neurophysiological integrity of the RLN; makes the procedures safe; predicts the post-operative RLN function (Dralle et al., 2013); and diminishes post-operative complications. Future studies should evaluate the use of continuous intraoperative neuromonitoring in horses, although continuous intraoperative neuromonitoring has been reported to be superior to I-IONM in human patients (Jonas & Boskovic, 2014; Sedlmaier et al., 2019; Yu et al., 2019).

This study demonstrated that the use of the HFS in combination with IONM in equine thyroidectomy is excellent in terms of ease of use, safety and post-operative complications and could be recommended as an alternative to electrosurgery. The IONM was a reliable method for identification of the RLN, thus avoiding damage and allowing evaluation of its function during and at the end of the operation and it could be considered as a promising procedure in the future of equine surgery. Additionally, the HFS enabled easy, precise dissection and adequate haemostasis during thyroidectomy that facilitated direct visualisation of the RLN without intra- or post-operative complications.

Authors' declaration of interests

No conflicts of interest have been declared.

Ethical animal research

These cases do not require any ethical review or approval from local or national bodies that relate to the study.

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Authorship

All authors made substantial contributions to the conception and design of the study, acquisition of data and analysis and interpretation of data. All authors contributed to drafting the article or revising it critically for important intellectual content, and all approved of the submitted version of the manuscript.

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