Influence of muscle relaxation on neuromonitoring of the recurrent laryngeal nerve during thyroid surgery

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Background. The influence of muscle relaxation on the intra-operative neuromonitoring of the recurrent laryngeal nerve during thyroid surgery is unclear.

Methods. In a prospective study involving 200 patients undergoing elective thyroid surgery, the influence of muscle relaxation on neuromonitoring of the recurrent laryngeal nerve was investigated. The patients received balanced anaesthesia with oxygen–nitrous oxide–isoflurane, and rocuronium bromide was used as the non-depolarizing neuromuscular blocking agent. The degree of relaxation was monitored continuously by accelerometry [twitch (% TW)]. Summed action potentials (SAcP) obtained from the vocalis muscle were characterized by the area under the electromyographic curve expressed in millivolt seconds.

Results. Evoked potentials were obtainable in all patients and at all time points. With decreasing neuromuscular blockade a significant increase in the potentials evoked at the vocalis muscle was observed. At 0% TW SAcP was 1.27 (SD 1.02) mV s. An increase in TW to 10% was accompanied by an increase in SAcP to 2.68 (2.01) mV s (P<0.01). At a TW of 25%, mean SAcPs of 5.08 mV s were recorded.

Conclusions. There was a significant difference in the degree of relaxation of the adductor pollicis muscle and the vocalis muscle. The laryngeal muscles exhibited a shorter response time than the adductor pollicis and recovered more quickly. These results confirm the feasibility of intra-operative neuromonitoring of the recurrent laryngeal nerve during neuromuscular blockade.

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One of the most serious complications of thyroid gland surgery is injury to the recurrent laryngeal nerve (RLN) resulting in temporary or permanent paresis. Bilateral loss of RLN function may be life-threatening. Although the reported incidence of permanent recurrent laryngeal nerve paresis following thyroid surgery varies between 0.5% and 2.7%, it may increase to 25% for certain conditions such as thyroid carcinoma or recurrent goitre.

The summed action potentials (SAcPs) of the vocalis muscle are often measured intra-operatively to minimize the risk of RLN damage during surgery. The absence of these potentials is a sign of permanent or temporary paralysis of the RLN. General anaesthesia and muscle paralysis have the potential to decrease or even abolish these potentials, suggesting nerve damage although the conduction system is actually intact. This raises the question of whether relaxant-free anaesthesia is mandatory for intra-operative neuromonitoring (IONM) of the RLN.

The aim of the present study was to analyse the influence of muscle relaxation on the SAcPs of the vocalis muscle.

Methods

The study was approved by the ethics committee of the medical faculty of the Otto-von-Guericke University, Magdeburg, and written informed consent was obtained from each patient. Two hundred adult patients scheduled for elective thyroidectomy were enrolled prospectively between September 2000 and May 2003. Inclusion criteria included ASA I–III and BMI between 20 and 40 kg m⁻².
Exclusion criteria were intolerance to the medications employed in the study, regular medication which may interfere with muscle relaxants, neurological or neuromuscular disease, and hepatic or renal insufficiency. All patients underwent laryngoscopy by an ENT specialist both before the operation and 2–4 days afterwards. In the event of a postoperative recurrent nerve paresis, ENT surveillance was provided for 4–9 months after the operation.

All patients received premedication with dipotassium chlorazepate 25–50 mg given orally at 20.00 on the day before the operation, and 25 mg given at 07.00 on the day of the operation. Following induction of anaesthesia with fentanyl 3 μg kg⁻¹ and etomidate 0.3 mg kg⁻¹, the patient’s lungs were ventilated with 100% oxygen via a mask to an end-expiratory carbon dioxide pressure of 4.5–5.0 kPa. Quantitative monitoring of the neuromuscular blockade with the TOF-GUARD system (Organon Teknika, Belgium) was established at this time. In order to exclude movement artifacts, the patient’s hand was immobilized on a foam rubber support. For the entire examination period, the peripheral skin temperature was kept constant at 36°C using appropriate heating pads. After a stabilization phase for the relaxometry of 60 s, all patients were given rocuronium bromide 0.9 mg kg⁻¹ i.v. When maximum neuromuscular blockade was achieved, orotracheal intubation was performed, and general anaesthesia maintained with a mixture of nitrous oxide (70%) and oxygen (30%), isoflurane at an end-expiratory concentration of 0.3–0.6 vol% and fentanyl as required. A control group of 10 patients (seven women and three men) underwent measurement of the SAcP of the unrelaxed vocalis muscle. In these patients, induction of general anaesthesia was accomplished with fentanyl 0.3 μg kg⁻¹ and propofol 3 mg kg⁻¹, and orotracheal intubation was performed without use of a muscle relaxant. Maintenance of general anaesthesia was achieved as in the study group with isoflurane in nitrous oxide and oxygen with supplemental doses of fentanyl. These 10 patients underwent bilateral subtotal thyroidectomy for a benign goitre. The operative procedure in terms of the IONM of the RLN went bilateral subtotal thyroidectomy for recurrent goitre (22 lobes) and 12 resections for cancer of the RLN (25% TW). The time point of the first SAcP measurement was determined by the time needed for the surgeon to expose the recurrent laryngeal nerve. If neuromuscular relaxation in the TOF was <100% at this time, further relaxation was given to enable measurement of the SAcP at the desired degrees of relaxation. Recording and evaluation of the SAcP (EWACS EMG Software System Inomed, GmbH Teningen) was performed by an anaesthesit. The magnitude of the SAcP obtained from the vocalis muscle was defined by the area under the entire biphasic EMG curve expressed in millivolt seconds. An SAcP of 0.05 mV s was defined as positive neuromonitoring. In the control group not receiving relaxants, four SAcPs were measured for each patient without neuromuscular blockade.

For intra-operative neuromonitoring of the RLN, the bipolar needle electrode was inserted into the ipsilateral vocalis muscle. The neutral electrode was placed in platysma and the two electrodes were led out of the surgical field through a sterile lead to a pre-amplifier connected to a Neurosign 100 nerve monitor (Magstim Ltd, Carmarthenshire, UK). Bipolar stimulation of the RLN or vagus nerve was done using a sterile stimulation probe at a frequency of 3 Hz and a current strength of 3 mA in the form of a rectangular pulse (200 μs). The nerve was carefully dissected and stimulated directly under visual control. In addition, the evoked potentials from the vocalis muscle were represented graphically using an integrated EWACS IOM Software System (Inomed, GmbH Teningen, Germany). The RLN or vagus nerve was identified intra-operatively and its functional integrity demonstrated in all the patients. At each time point, SAcPs were recorded from the vocalis muscle as evidence of conduction system function.

Measurements during neuromonitoring were compared statistically using the GLM (General Linear Model) with repeated measurements. The repeat factor is defined by the time points. A difference with P≤0.05 was taken as significant.

Results

Two hundred patients (47 men and 163 women) with mean age 53 (14–80) yr and BMI 28 (SD 4.4) kg m⁻² were included in the study. In terms of age, height and weight, the patient population showed a normal Kolmogorov–Smirnov distribution (Table 1). The surgical procedures included 174 primary operations for benign goitre (334 lobes), 14 operations for recurrent goitre (22 lobes) and 12 resections for cancer.

<table>
<thead>
<tr>
<th>n</th>
<th>Sex (M/F)</th>
<th>Age (yr)</th>
<th>Height (cm)</th>
<th>Weight (kg)</th>
<th>BMI (kg m⁻²)</th>
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<tbody>
<tr>
<td>200</td>
<td>44/156</td>
<td>53 (14–80)</td>
<td>166.8 (8.3)</td>
<td>78 (13.9)</td>
<td>28 (4.4)</td>
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A total of 145 patients (72.5%) were euthyroid, while 55 patients (27.5%) had received treatment for hyperthyroidism. Of the 200 resections, 177 were bilateral and 23 were unilateral.

Twelve unilateral pareses of the recurrent laryngeal nerve were diagnosed postoperatively by an ENT specialist. Seven cases of paresis occurred after operation for a benign goitre (2.1%), three after reoperation for recurrent goitre (13.6%) and two after cancer procedures (9.5%). At the 6-month follow-up examination, a permanent side-related paresis of the RLN (‘nerve at risk’) was observed in two patients (0.59%) after benign goitre, one (4.5%) following recurrent disease and one (4.76%) after thyroid malignancy. Thus the overall side-related RLN paresis rate was 1.06%. All 12 postoperative RLN pareses were identified intra-operatively by neuromonitoring after resection of the corresponding lobe, and thus the postoperative outcome of vocal cord function testing was predicted. Prior to resection of the lobe, successful neuromonitoring was always possible. The 12 pareses occurred after the SAcP of the vocal muscle had returned to a level of relaxation of 70% (TW 30%), and at the end of the operation no SAcP was recordable on the damaged side. In all patients, the initial dose of Rocuronium bromide (0.9 mg kg−1) produced complete neuromuscular blockade with suppression of the accelerometry twitch amplitude to 0%. As the neuromuscular blockade wore off, the SAcP increased. The SAcP at time point 0% TW was 1.27 (1.02) mV s, and increased to 2.68 (2.09) mV s (P<0.01) at 10% TW, and to 5.08 (3.78) mV s (P<0.01) at 25% TW (Fig. 1). In the control group receiving no relaxant, an average SAcP of 8.45 (2.95) mV s was recorded (Fig. 2).

### Discussion

Preventing nerve damage is currently standard practice in operations on the thyroid gland. In addition to the atraumatic dissection of the RLN, intra-operative neuromonitoring has become accepted practice during surgery in this area.2–6 This procedure does not interfere with surgery, and only prolongs the operating time by ~5 min. This form of RLN monitoring is superior to surgical exposure of the nerve, as not only its morphological integrity but also its functional integrity can be demonstrated.

However, complete avoidance of damage to the RLN is not possible even with intra-operative neuromonitoring. The nerve is highly sensitive and even a little tension on it can result in temporary paresis. If, in addition, the nerve is adherent to surrounding tissue following a previous operation, the danger of a paresis occurring despite monitoring is higher. In our study, neuromonitoring failed to prevent paresis in 3.6% of patients (12 pareses out of 337 operated lobes). However, five of the 12 were in operations for recurrent goitre, and two in procedures carried out to treat cancer of the thyroid gland.
The main findings of the present study were that SAcP was recordable from the vocalis muscle at relaxation degrees of >90% in all patients, and that the laryngeal muscles exhibited a shorter response time than the adductor pollicis and recovered more quickly.

A quantitative neurophysiological evaluation of the RLN is based on the recording of evoked potential at the vocalis muscle. Thus neuromuscular blockade may interfere with intra-operative neuromonitoring of the RLN. It is generally accepted that the presence of the fourth evoked potential (T4) in the TOF corresponds to a 25% recovery (25% TW) of the first evoked potential (T1). A 25% recovery of the neuromuscular blockade is considered to represent the acceptable limit of surgical relaxation. For this reason, it was of interest to record the SAcP up to 30% TW, and thus to demonstrate the possibility of IONM under adequate surgical relaxation. There were clear differences between the magnitude and course of the EMG curve during neuromuscular blockade. Thus SAcP was greatly diminished at 100% relaxation (0% TW) and was often minimal. However, SAcP at the vocal muscle was reliably recordable at 90% relaxation (10% TW). Our data indicate that functional monitoring and recording of RLN activity during regression of neuromuscular blockade is effectively possible below 10% TW. At 30% TW, SAcP was >0.35 mV s (mean >5.55 mV s, corresponding to an SAcP of 60% with no relaxation). For the validity of intra-operative monitoring, confirmation of a functionally intact conduction system at the vocalis muscle is of critical importance. An attenuated SAcP is an expression of neuromuscular blockade, since paresis of the recurrent laryngeal nerve would always lead to the complete absence of SAcP. Consequently, neuromonitoring of the RLN is applicable despite muscle relaxation ≤90%. In comparison with the group not receiving relaxants, the SAcP at 30% TW corresponded to 65% SAcP at 100% TW.

The results of the present study can be explained by the physiology of the motor endplate and by differences in the action profiles of non-depolarizing neuromuscular blocking agents on various muscle groups. Neuromuscular transmission measured with the aid of TOF at the adductor pollicis muscle does not reflect the relaxation of other muscles. This applies in particular to muscles involved in specific organ functions. In this respect, muscle groups responsible for voice production and patency of the airways are of particular importance. The time course of neuromuscular blockade of the laryngeal musculature is comparable to that of the diaphragm. The geniohyoid and the masseter muscles also exhibit a shorter response time, but the neuromuscular recovery of the masseter is similar to that of the adductor pollicis. However, the masseter appears to be the only muscle of the upper respiratory tract that reacts with greater sensitivity to non-depolarizing muscle relaxants than the adductor pollicis. Possibly, greater perfusion of the laryngeal musculature enables more rapid transport of the active agent from the plasma to the receptor. In addition, the uneven density of acetylcholine receptors is thought to be

![Graph showing SAcP mV/s vs Patients](image-url)
a major factor.\textsuperscript{8–10} Meistelman\textsuperscript{9} found response times of 1.4 min and 2.4 min, respectively, for the laryngeal adductors and the adductor pollicis after application of rocuronium 500 $\mu$g kg\textsuperscript{-1} with a maximum blockade of 77(5)% and 98(1)%, respectively.

In conclusion, the results of the present study demonstrate the feasibility of intra-operative neuromonitoring during operations on the thyroid in the presence of neuromuscular blockade. It should be noted that the magnitude of the evoked potentials at the vocalis muscle exhibited considerable intra-individual variation. An increase in TW from 0% to 10% was accompanied by an increase in SAcP from 1.27 to 2.68 (2.09) mV s, which is sufficient for detection of RLN function. However, caution should be used regarding repeated doses of non-depolarizing muscle relaxants during the operation. Immediately after administration of the drug, evoked potentials at the vocalis muscle were hardly detectable. Even small evoked potentials must be considered a positive response of the vocalis muscle, and consequently adequate proof of the integrity of the recurrent laryngeal nerve as part of the nerve conduction system.

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