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Efficacy of Intraoperative Single Dose Methylprednisolone on Recurrent Laryngeal Nerve Function After Thyroidectomy

Ali Ugur Emre[1], Guldeniz Karadeniz Cakmak[1], Dilek Karakaya Arpaci[2], Sevil Uygun Ilikhan[3], Murat Damar[4]

[1]*Faculty of Medicine, General Surgery Department, Bulent Ecevit University, Zonguldak, Turkey*

[2]*Faculty of Medicine, Endocrinology and Metabolic Diseases Department, Bulent Ecevit University, Zonguldak, Turkey*

[3]*Faculty of Medicine, Internal Medicine Department, Bulent Ecevit University, Zonguldak, Turkey*

[4]*Faculty of Medicine, Ear Nose and Throat Surgery Department, Bulent Ecevit University, Zonguldak, Turkey*

Recurrent laryngeal nerve (RLN) palsy is an important complication of thyroid surgery. Injuries can either be permanent or temporary. Prevention or shortening the recovery period of temporary palsies is an area of interest. Some surgeons prefer to use corticosteroids for this purpose as is used for facial nerve palsies although there are conflicting data in the literature. We aimed to investigate the efficacy of perioperative single dose methylprednisolone on recurrent laryngeal nerve function. A total of 438 nerves under risk in 237 surgeries are investigated in 2 groups. In Group 1, patients are administered a single intraoperative dose of methylprednisolone (1 mg/kg) intravenously for 220 nerves under risk. A total of 218 nerves under risk in Group 2 were operated and followed without methylprednisolone. The demographic data of the patients, operation time, the final pathology reports, incidence of recurrent laryngeal nerve palsy, and recovery time are documented and compared. No statistically significant difference was determined in terms of age, sex distribution, number of nerves under risk, and the operation time between groups. There were 3 unilateral RLNP in each group and the mean recovery time for Group 1 and 2 palsies were 20.4 and 19.8 days, respectively,

Corresponding author: Ali Ugur Emre, MD, Bulent Ecevit University Hospital, General Surgery Department. 67600 Kozlu, Zonguldak, Turkey.
Tel.: +90372 2612991 or +90532 7692798; Fax: +90372 2610155; E-mail: auemre@gmail.com

without statistical significance. The presented data indicates that a single intraoperative dose of steroid does not seem to affect the rate and recovery period of RLNP in thyroid surgery.

Key words: Thyroidectomy – Recurrent laryngeal nerve injuries – Methylprednisolone

Recurrent laryngeal nerve palsy (RLNP) is one of the most annoying and probable complications of thyroid surgery. Temporary or permanent loss of nerve function due to operative trauma leads to clinical situations ranging from hoarseness to glottic obstruction and asphyxia in case of bilateral fashion. The incidence of recurrent laryngeal nerve (RLN) injury varies in literature, with a reported range between 0.4% and 7.2% and 0% to 5.2% for temporary and permanent paralysis, respectively.[1,2] Gold standard technique to be recommended for the prevention of injury is to identify the nerve and follow its course under direct visualization to the muscle insertion.[3] Currently, novel inventions like nerve monitoring provided some kind of relief on the way to refrain from injury. However, either direct or continuous vagal stimulation is still controversial about the prevention of permanent nerve palsy. Vagal stimulation can be useful in prevention of traction injury that is most commonly temporary.[4,5] The mechanism of injury varies from neuropraxia to axonotmesis and neurotmesis. Nerve palsy due to neuropraxia and to some extent axonotmesis recovers within several days or weeks, dependent on the mechanism of injury. This period is troublesome for both surgeons and patients. Accordingly, researchers have a great enthusiasm to discover a remedy to avoid or at least reduce the recovery period. Intraoperative corticosteroid administration is an empirical method that has been in use for ages. Some surgeons prefer steroids to overcome the edema and prevent or shorten the temporary palsy of the nerve routinely.[6] The presented study aimed to evaluate the effect of a single intraoperative dose of systemic steroid on RLN function after thyroidectomy.

Methods

This study is performed with the approval of the Clinical Researches Ethical Committee of Bulent Ecevit University. We retrospectively analyzed the prospectively gathered data of patients who underwent total lobectomy or thyroidectomy in a tertiary referral center. The demographic data of the patients, operation time, and final pathology reports are documented. A total of 237 patients operated by the same surgeon are included in the study. All patients who had total or hemithyroidectomy are included in the research, excluding patients with ASA III and IV risk of anesthesia, recurrent goiter and completion thyroidectomies, and patients under any kind of steroid treatment. Patients have undergone either total thyroidectomy (n = 201) or lobectomy (n = 36) and the ratio of recurrent laryngeal nerve palsy is calculated for 438 nerves according to the total number of nerves under risk. The thyroidectomy techniques were the same and recurrent laryngeal nerves are visualized up to the entrance point to the larynx. A total number of 23 central compartment neck dissections are performed on patients, increasing the risk of nerve palsy (Group 1 = 12, Group 2 = 11 nerves at risk). Nerve monitorization is not used for any of the patients. All patients are examined with direct video laryngoscopy before and 48 hours after, and every week thereafter until 6 months after the operation, regardless of the presence or absence of hoarseness or other symptoms. Telephone call interviews are done between weekly hospital examinations, and patients are invited to ENT examinations for any observed change in voice quality. The functional assessments of nerves are done by visualizing the motion of the vocal cords by an ENT surgeon. Loss of motility is regarded as RLN palsy. Patients are divided into 2 groups. Groups are formed from the patients operated on before and after the initial administration of single-dose intraoperative methylprednisolone by the surgeon. In Group 1, patients are administered a single intraoperative dose of methylprednisolone (1 mg/kg) intravenously for 220 nerves under risk just at the beginning of RLN inquiry. Group 2 patients (n = 127) were devoid of intraoperative methylprednisolone administration. Patients treated with any other kind of steroid for various medical conditions were excluded from the study cohort.

Statistical Analysis

Results are statistically interpreted with Chi square and Mann-Whitney *U* tests using SPSS (Statistical

Table 1 Characteristics, operation data, and results of patients

	Group 1 Methylprednisolone 1 mg/kg (+) (n = 110)	Group 2 Methylprednisolone 1 mg/kg (−) (n = 127)
Age	49.8 (24–65)	49.4 (20–68)
Sex		
Woman	98	110
Man	12	17
No. of nerves under risk	220	218
Lobectomy	0	36
Total thyroidectomy	110	91
Operation time	82.2 (56–118)	79.6 (49–113)
RLN palsy		
Temporary	3 (1.36%)	3 (1.37%)
Permenant	0	0
Recovery period(days)	20.4 (8–23)	19.8 (10–24)

$P > 0.05$ for all comparisons

RLN, recurrent laryngeal palsy.

Package for Social Sciences) v.19 (IBM Corporation, Armonk, New York). $P < 0.05$ is assigned to be significant.

Results

Group 1 (n = 110) consists of 98 women and 12 men with a mean age of 49.8 (range, 24–65). All patients in this group had a total thyroidectomy, so there were a total number of 220 nerves at risk in this group. The mean operation time was 82.2 minutes (56–118 minutes). In group 2, 110 women and 17 men had undergone 91 total thyroidectomy and 36 lobectomy operations. Total number of nerves at risk was 218 in this group. The mean age of the group is 49.4 (range, 20–68) and the mean operation time is 79.6 minutes (49–113 minutes). The age, sex distribution, number of nerves at risk, and the operation time were not different statistically between the 2 groups (Table 1).

Histopathologic results of the groups in terms of benign and malignant diseases were similar as shown in Table 2. In Group 1 there were a total number of 23 malignant diseases, which consisted of 10 papillary and 13 micropapillary carcinomas. There were also 23 multinodular goiter associated with thyroiditis and 14 Graves' disease in Group 1. Histopathologic analysis determined 20 cases of papillary thyroid cancer (including 10 micropapillary cases), 42 multinodular goiter, 10 Graves' disease, and 19 thyroiditis in Group 2 (Table 2).

Both in Group 1 and Group 2, the number of recurrent laryngeal nerve palsy was 3 (Group 1: 1.36%, Group 2: 1.37%). All 6 palsies were unilateral and diagnosed by direct visualization of vocal cords. All patients had clinical loss of voice quality in varying degrees. In the first group the mean recovery time of recurrent laryngeal nerve palsies was 20.4 days (8–23 days). For Group 2 the mean recovery time was 19.8 days (10–24 days). None of the patients were treated with additional postoperative corticosteroids. Statistical analysis of the 2 groups revealed no difference about the number of RLNP and recovery time.

Table 2 Pathologic diagnoses of Group 1 and 2

Diagnoses of cases	GROUP 1 (n)	GROUP 2 (n)
Malignant disease	23	20
Papillary carcinoma	10	10
Micropapillary carcinoma	13	10
Multinodular goiter	50	42
Thyroiditis + MNG	23	19
Graves' disease	14	10
Nodular goiter	-	36

MNG, multinodular goiter.

Discussion

RLN injury has been the most undesirable complication of thyroid surgery from a historical and current standpoint. This consequence is not totally avoidable even in the hands of the most experienced surgeons. Voice changes like dysphonia or hoarseness are the first issues that arise when informing patients about the risks. This can cause much anxiety and discomfort for both the surgeon and the patient. Reported rates of transient and permanent RLNP vary, with a median of 3% to 4% and 1% to 2%, respectively.[5,7] However, these rates are likely to be underestimated due to the fact that postoperative laryngeal examination is not standard in most clinics and is conducted only in case of significant and persistent symptoms. Another possible reason is that surgeons usually do not detect intraoperative injuries.[8] Another factor might be drawbacks regarding unfavorable data, since a tendency towards ignoring failure and identifying success exists as a basic instinct in humankind.[8] Accordingly, preoperative and postoperative laryngeal inspection should be a routine practice in all cases without exceptions to reach the accurate rates of RLN injuries. Moreover, medicolegal issues became catastrophic for surgeons. A recent article reported that RLN injuries comprised nearly half of the all kinds of thyroid surgery malpractice litigations.[9] As the physiopathology of RLNP is not very well

understood, the proposed mechanisms responsible for injury are mechanical surgical trauma of the nerve during dissection, local inflammatory processes, surgical devascularization, excessive retraction and traction, cautery injury, and partial or complete transection of the nerve. Surgical technique is one of the most crucial factors determining the outcome. The major principle is to identify, expose, and preserve the nerve throughout its course. This is the only confirmed maneuver to prevent injury. However, this approach requires full dissection with the possibility to harm RLN. Macroscopically the nerve might be intact at the end of the dissection; however, direct mechanical damage or manipulations may lead to edema and dysfunction causing reversible or irreversible function loss from neuropraxia to axonotmesis.[6,10] In this context, agents with the potential to exert positive effect on nerve function merit consideration. Empirically, steroids have long been admitted in an attempt to reduce neural edema due to inevitable manipulations during identification of RLN intraoperatively, as well as to promote recovery in the presence of paralysis postoperatively. However, there has been minimal published data concerning the efficacy of intraoperative steroids in the management or prevention of nerve dysfunction resulting from operation. Conventionally, patients have been treated systemically with corticosteroids in the presence of nerve injury after extubation. Nevertheless, there has been minimal published data in the category of level 1evidence to support this approach. Steroids are the agents with anti-inflammatory, analgesic, antiemetic, and immune-modulating effects. The exact mechanism by which steroids exert their action to reverse nerve damage is yet to be identified, but there is data supporting the hypothesis that steroid administration might prevent or reduce neural edema and promote recovery of nerve function when nerve paralysis occurs.[6,10] Furthermore, patients taking dexamethasone have decreased postoperative nausea and vomiting in some trials.[11] Lore *et al* have mentioned that both the rate and duration of temporary RLNP can decrease when perioperative steroids have employed.[12] In their prospective study, Wang *et al* concluded that steroids did not have any effect on temporary or permanent RLNP rates, but decrease recovery period for temporary RLNP.[6] On the contrary, Schietroma *et al* reported reduced rates of temporary RLNP and recovery time in patients who received a single dose of dexamethasone versus placebo.[10] Recently, Lachanas *et al* reported that a single dose of perioperative dexamethasone did not seem to add any benefit on voice-related quality of life after thyroid surgery.[13] According to the literature, the impact of steroids on postoperative RLNP in terms of recovery rate and period is still controversial. Our institution's routine surgical policy is to identify RLN and follow its course from thoracic outlet up to laryngeal entry point in every thyroidectomy case. In this study, the integrity of all RLNs was ensured at the end of the operation. However, temporary RLNP occurred in 3 patients of each group. The presented data demonstrated no significant difference in terms of RLNP rates and recovery periods with an intraoperative single dose of steroid therapy. Moreover, no association was determined in terms of histopathologic results and other thyroidectomy related complications overall. This finding asserts the hypothesis that even though inflammation and edema are 2 of the prevalent factors for the development of RLNP, other pathophysiologic pathways should be investigated to determine the exact reason and prevent this consequence. Nevertheless, there are some limitations of the study. In the retrospective review of prospectively collected data, lacking randomization is the first issue to be addressed. The other is the concern of steroid use on wound healing, infection, and blood glucose levels. Our patients experienced no adverse events due to steroid application.

Conclusion

The presented data indicates that a single intraoperative dose of steroid does not seem to affect the rate and recovery period of RLNP in thyroid surgery. In literature, the data about the topic of steroid impact on nerve function and recovery is still limited and controversial. Accordingly, the mechanisms responsible for RLNP, even if the nerve is intact at the end of the operation, need to be illuminated.

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