

ORIGINAL ARTICLE

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The effect of intraoperative neuromonitoring on complications of hypocalcemia following thyroid surgery **Mehmet Turan Cicek**,  **Mehmet Aslan***Inonu University, Faculty of Medicine, Department of ENT Surgery, Malatya, Turkey*

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**Abstract**

Hypocalcemia is a common and significant complication that may develop after a total thyroidectomy operation. In our study, the effects of neuromonitoring on the development of hypocalcemia in total thyroidectomy operations were retrospectively investigated. Patients who underwent only total thyroidectomy in our clinic between 2013 and 2020 and had no history of operation or radiation treatment in their neck region were retrospectively evaluated and divided into two groups. A total of 96 patients, 42 patients in Group 1 on whom neuromonitoring was used and 54 patients in Group 2 without neuromonitoring, were examined. Transient hypocalcemia was manifest in 12 (28.5%) of the 42 patients in Group 1 and 16 (29.6%) of the 54 patients in Group 2, while the difference between the two groups was not statistically significant ($p=0.910$). In total thyroidectomy operations, the proven benefits of using intraoperative neuromonitoring are still controversial. In our study, it was observed that intraoperative neuromonitoring did not make a significant difference in transient hypocalcemia development after total thyroidectomy operations.

Keywords: Hypocalcemia, intraoperative neuromonitoring, thyroidectomy**Introduction**

Hypocalcemia is the most common complication following thyroidectomy [1,2]. In the literature, the incidence of hypocalcemia has been reported to vary between 30% and 60%, possibly due to the adoption of different diagnostic criteria [3,4]. While the risk of hypocalcemia is increased in proportion to the size of the surgical field (e.g., total thyroidectomy instead of subtotal, or application of concomitant central neck dissection), it is reduced in proportion to recognizing and preserving at least three of the parathyroid glands during the operation [5].

A sudden drop in parathyroid hormone (PTH) levels is thought to be the main cause of hypocalcemia after total thyroidectomy. Despite the few cases of hypocalcemia caused by hyperthyroidism,

hypercalcitoninemia or hungry bone syndrome caused by vitamin D deficiency, recent studies have shown that the most significant factor causing postoperative hypocalcemia is a decrease in serum PTH concentrations [6].

There are reports that intraoperative neuromonitoring (IONM) shortens the duration of operation and reduces the rates of hypocalcemia. However, the evidence on its effect on Recurrent Laryngeal Nerve (RLN) paralysis is still controversial [7]. It is also believed that the use of IONM reduces the degree of surgical exploration required to identify RLN, and therefore, the parathyroid glands are better protected during surgery. The aim of this retrospective clinical study was to evaluate the effects of the use of IONM in total thyroidectomy operations on the development of postoperative hypocalcemia.

Materials and Methods**Design**

This study was planned to be carried out retrospectively in a tertiary university hospital. The data of patients who underwent total thyroidectomy surgery due to thyroid pathology in our clinic between 2013 and 2020 were collected retrospectively. The data

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were grouped as patients using intraoperative neuromonitoring and those not using intraoperative neuromonitoring and based on the determined inclusion and exclusion criteria before the statistical analyses.

Sample selection

Our patient group included patients who had total thyroidectomy surgery due to thyroid pathology in our clinic between 2013 and 2020, separated into two groups as those on whom IONM was used and those on whom it was not. All patients who were treated in our clinic within the specified 7-year period and met the inclusion criteria were included in the study. While forming the groups, attention was paid to achieve a statistically similar distribution in terms of age and sex.

Inclusion criteria

The study included patients who underwent surgical treatment in our clinic due to thyroid pathologies in the period of 2013-2020, whose physical examinations, laboratory tests and pathological examinations were performed in our clinic, including all examinations at the stages of diagnosis and treatment, and whose data were available. Male and female patients between the ages of 18 and 80 were included in our study.

Exclusion criteria

Patients with missing data, patients with hematological disorders affecting calcium metabolism, cardiac disorders, systemic autoimmune diseases, systemic inflammatory or infectious diseases, endocrinological diseases, other malignancies except thyroid gland malignancies, liver and kidney diseases, pregnant patients, patients younger than 18 years of age, patients with a history of preoperative neck surgery or radiation treatment in the neck area, and patients who had neck dissection in addition to total thyroidectomy were excluded from the study.

Standardization

It was ensured that the analyzed data of both patient and control groups included in the study belonged to our hospital records. It was made sure that the patients included in the study were operated by the same surgeon. The postoperative calcium levels of all patients were evaluated, and calcium levels below 8.5 mg/dl were considered as hypocalcemia. Patients with clinical signs of acute hypocalcemia (numbness and tingling sensation in the perioral region or fingers, carpopedal spasm, tetany) were treated with oral calcium+vitamin D preperates and intravenous calcium gluconate. Patients who needed calcium replacement therapy for more than 6 months were considered to have permanent hypocalcemia, while others were considered to have transient hypocalcemia.

Data analysis

The data collected in the study were analyzed using the SPSS "Statistical Package for the Social Sciences (SPSS22.0, version 22.0)" software. Percentages, mean, median, standard deviation, minimum and maximum values were calculated. Since the variables were not normally distributed according to the Kolmogorov-Smirnov test results ($p < 0.05$), non-parametric test statistics were used. Kruskal Wallis Test was used to compare more than two

groups, and Mann Whitney U test was used to compare two groups. Chi-squared test was used to compare the qualitative variables. In the statistical analyses, the level of statistical significance was accepted as $p < 0.05$.

Ethical approval

Ethics committee approval of the study was obtained from XXX Scientific Research and Publication Ethics Committee (Decision No: 2021/1773).

Surgical technique

The patients were operated in the head extension position with under-shoulder support, a horizontal incision was made approximately 2 cm above the sternal notch, and the subcutaneous tissue and platysma muscle were dissected. The strep muscles were pulled laterally. When the thyroid tissue plane was reached, firstly the lateral vein and then the superior thyroid artery were exposed and ligated. The recurrent laryngeal nerve (RLN) was identified in all patients. The parathyroid glands were accessed and preserved. Finally, the tracheal ligamentous connections were resected, and the hemithyroidectomy procedure was completed. The same procedures were performed on the other side, and the total thyroidectomy procedure was completed. Negative-pressure hemovac drains were used in all patients.

The operations in both groups were performed under general anesthesia. In Group 1, the patients were operated using IONM (NeuroSign 400; Inomed, Germany). During intubation, an endotracheal tube with a surface electrode was inserted between the vocal cords by an anesthesiologist under direct vision. After the tachyphylaxis of muscle relaxants, neuromonitoring began. The repeated 1-mA-2-mA stimulation of RLN was performed with a standard monopolar probe.

In the patients in Group 2, all RLNs were identified by the surgeon.

Results

A total of 96 patients were included in the study and divided into two groups. Group 1 included the patients who underwent total thyroidectomy using IONM ($n_1=42$), and Group 2 included the patients who underwent total thyroidectomy without IONM ($n_2=54$). According to the results of the analysis on the data,

- Group 1 consisted of 42 (28 F + 14 M) patients in total, and Group 2 consisted of 54 (36 F+18 M) patients. There was no statistically significant difference between the groups in terms of age and sex (Table-1).
- The mean age of the patients was 45.14 ± 13.52 in Group 1 and 49.14 ± 12.782 in Group 2. There was no significant difference between the groups regarding this parameter (Table-1).
- In our study, the number of female patients was significantly higher in both patient groups, and this was consistent with the literature.
- The thyroid pathologies of the patient groups examined in our study were nodular hyperplasia, hurtle cell adenoma, Hashimoto's thyroid, papillary thyroid cancer, papillary

microcarcinoma, and follicular thyroid carcinoma (Table-2).

- In our study, hypocalcemia was detected in 12 patients (28.5%) in Group 1 and 16 patients (29.6%) in Group 2. The difference between the two groups was not statistically significant ($p=0.910$). Two patients in Group 1 and 3 patients in Group 2 were considered to have permanent hypocalcemia.
- In our study, we observed that hypocalcemia development

was more common in the patients operated due to nodular hyperplasia and thyroid papillary carcinoma (Table-2). This finding was consistent with the literature. We concluded the explanations of this situation as the fact that total thyroidectomy operations are performed frequently due to nodular hyperplasia, frequent total thyroidectomy due to thyroid papillary carcinoma being the most frequently differentiated thyroid malignancy, and wider surgical field resection due to oncological concerns.

Table 1. Demographic data and hypocalcemia data of the study

	Gender		Age	Hypocalcemia				P value	Chi-square
	Male n(%)	Female n(%)	Mean±S.Deviation	Hypocalcemia (+)		Hypocalcemia (-)		0.910	0.013
				Female	Male	Female	Male		
Neuromonitoring group (n1)	14	28							
	%33.33	%67.77	45.14±13.52	8(%19.04))	4(%9.52)	20(%47.61)	10(%23.80)		
	Total:42(%100)			Total: 12(%28.5)		Total:30(%71.5)			
Neuromonitor-free group (n2)	18	36		11(%20.37)	5(%9.25)	25(%46.29)	13(%24.07)		
	%33.33	%67.77	49.14±12.78	Total:16(%29.6)		Total: 38(%70.4)			
	Total:54(%100)								
p<0.05** was considered statistically significant									

$p<0.05^{**}$ was considered statistically significant

Table 2. Distribution of histologic types of benign and malignant thyroid gland pathology

Benign	Patient(n)				Malign	Patient(n)			
	Hypocalcemia(+)		Hypocalcemia(-)			Hypocalcemia (+)		Hypocalcemia (-)	
	Group-1	Group-2	Group-1	Group-2		Group-1	Group-2	Group-1	Group-2
Nodular hyperplasia	6	8	13	17	Papiller thyroid cancer	4	6	9	13
Hurtle cell adenoma	0	0	2	0	Papiller microcarsinoma	1	1	5	7
Hashimoto's thyroid	1	0	1	0	Follicular thyroid carsinoma	0	2	0	0
	7	8	16	17		5	9	14	20
Total	48					48			

Discussion

Hypocalcemia is by far the most common complication following thyroid surgery, with significant short- and long-term effects on patients. The effectiveness of preventive measures to reduce the risk of hypocalcemia has been evaluated in many previous studies.

In a meta-analysis in which 76 studies including 39 randomized-controlled and 37 observational studies were evaluated, it was reported that the use of Harmonic™ or Ligasure™ was not superior to traditional methods in the prevention of hypocalcemia. In the same study, it was stated that the risk of hypocalcemia increased in cases of total thyroidectomy with increased scope of surgery, compared to near total or bilateral subtotal thyroidectomy. It is thought that routinely performed central neck dissection increases the risk similarly [8]. Total thyroidectomy was performed in all cases in our study, and central neck dissection was not performed

in any of the operations.

Some other measures, such as video-assisted thyroidectomy, preoperative magnesium infusion and use of a magnifying glass, have not been proven to be effective preventive measures [8]. Such methods were not used in our case series.

It has been reported in the literature that the use of IONM in thyroidectomy cases provides a significant reduction in operation time and hypocalcemia rates [7]. In a study on 11,350 cases examining recurrent nerve injuries, it was emphasized that RLN injury rates significantly decreased with the use of IONM [9]. In the same study, it was reported that hypocalcemia events were significantly more frequent in the presence of RLN injury. In explaining this finding, the authors emphasized the close relationship between RLN and the parathyroid glands and proposed RLN injury and possible parathyroid gland injury as the causes [9].

Likewise, in another study with a large case series, it was revealed that the rates of complications like hematoma and hypocalcemia were higher in the presence of RLN injury [10]. In the same study, it was stated that RLN injury was reduced with the use of IONM, and the rates of hypocalcemia and other complications also decreased indirectly. This result was explained with the conclusion that “hypocalcemia would be an expected morbidity associated with RLN damage, because RLN has a close anatomical relationship with not only the parathyroid glands but also the inferior thyroid artery. The injuries of any of these structures in addition to RLN injury would lead to transient or permanent hypocalcemia” [10]. There are studies in the literature that have reported that the use of IONM does not have a statistically significant superiority in terms of the identification and preservation of RLN or postoperative vocal cord paralysis [11-14]. In this context, it is clear that hypocalcemia development is linked with RLN injury. However, the effectiveness of IONM in preventing RLN injury is debatable. It was reported in the literature that the probability of developing hypocalcemia increased in female patients and young patients [15]. Our study reached similar results. The fact that the population from which the sample was selected consisted predominantly of female patients was naturally reflected on the rates of complications observed in this study.

In this study, it was revealed that hypocalcemia rates were lower in the group in which IONM was used. The author interpreted this to be coincidental or due to increased attention paid to the surrounding tissue. In our study, the use of IONM did not have a significant effect on the development of hypocalcemia. We believe that there was no significant difference between hypocalcemia rates because the surgical technique was the same in both groups, the nerve was only confirmed by IONM after being identified by the surgeon, and IONM did not contribute to the identification of the parathyroid glands. In the literature, the most significant factors affecting the development of postoperative hypocalcemia have been reported as intraoperative trauma to the parathyroid gland or vascular system, failure to identify the parathyroid gland during the operation, accidental parathyroidectomy, central neck dissection, bilateral total thyroidectomy, and insufficient experience of the surgeon [16,17]. We do not think that IONM has a direct effect on these factors.

Conclusion

In our case series in which the surgical method was determined as total thyroidectomy,

- Most of the patients who underwent total thyroidectomy were female patients, and this was also consistent with the literature.
- The risk of hypocalcemia increased in the patients who underwent total thyroidectomy due to very frequently encountered pathologies. Since benign pathologies are more common, wider resection is the main reason for malignant pathologies due to oncological concerns.
- It was observed that the use of IONM does not reduce the risk of postoperative hypocalcemia. As the reason for this, IONM was thought to be effective in confirming RLNs rather than reducing the degrees of surgical dissection.

- Larger prospective studies and series may be helpful in understanding the impact of IONM on hypocalcemia and other complications.

Conflict of interests

The authors declare that they have no competing interests.

Financial Disclosure

All authors declare no financial support.

Ethical approval

Ethics committee approval was received for the study from the Inonu University Scientific Research and Publication Ethics Committee Health Sciences Non-Interventional Clinical Research Ethics Committee. (Decision No: 2021/1773).

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