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The Effect of Nerve Monitoring Device Use on Hypocalcemia in Thyroid Surgery

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Abstract

Objective: Compare the effect of the use of Intraoperative Nerve Monitoring (IONM) device on postoperative hypocalcemia that may develop postoperatively in the patient groups with and without the use of IONM device.

Methods: Demographic data, radiologic imaging reports, serum biochemistry values, pathology reports, duration of surgery, IONM reports, and surgical records of the records of 612 patients who underwent total thyroidectomy by the same surgical team between January 2013 and January 2021 were reviewed.

Results: Of the 612 patients who underwent total thyroidectomy, 440 patients who met the criteria were included in the study. Total thyroidectomy was performed in 342 (78%) patients without IONM device and 98 (22%) patients with IONM device. Of the patients, 363 (82.5%) were female and 77 (17.5%) were male. The mean age was 49.2 years (20-87) and the mean length of hospitalization was 1.48 (1-5) days. Significant amplitude values were obtained at an average of 34.7 min after incision. The mean postoperative 24^{th}-h biochemical calcium value was 8.93 mg/dL (6.15-10.9), 9.05 mg/dL (6.15-10.9) in patients without IONM and 8.5 mg/dL (6.6-10.6) in patients with IONM.

Conclusion: The use of IONM in thyroid surgeries, calcium values may decrease and the risk of hypocalcemia may increase due to the prolongation of the time until amplitude acquisition from the nerve and the increase in manipulations in the surgical area until the nerve is detected.

Keywords: Thyroidectomy; Hypocalcemia; Intraoperative nerve monitoring; Recurrent laryngeal nerve

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Introduction

Thyroidectomy is the most commonly performed endocrine surgery worldwide for benign and malignant thyroid diseases. Despite the technical advances in thyroid surgery in recent years, Recurrent Laryngeal Nerve (RLN) injuries and associated permanent and transient nerve damage can impair the patient's quality of life, cause complications ranging from hoarseness to respiratory distress requiring tracheostomy, and impose medico-legal responsibilities on the surgeon. Temporary nerve damage is seen in 5% to 8% of cases, while permanent damage is seen in 0.3% to 3% of cases. Intraoperative RLN injuries develop due to nerve cutting, nerve suturing, nerve traction, aspiration, compression, contusion, applied pressure, ischemia during tissue skeletonization, and electrothermal injuries [1,2]. Receiving radiotherapy, recurrent surgeries, Graves' disease, thyroiditis, large thyroid size, and retrosternal extension increase the risk of nerve injury [3]. Intraoperative Nerve Monitoring (IONM) has found widespread use all over the world to reduce nerve injuries, visualize the nerve, and determine intraoperative and postoperative treatments with information about its function [4] (2-13). It has found widespread use among endocrine surgeons in the last two decades, especially in terms of revealing the nerve, reducing transient nerve paralysis, and eliminating the risk of bilateral paralysis, and has changed surgical strategies [1].

The most common early complication after thyroid surgery is hypocalcemia [5]. It develops due to disruption of the parathyroid gland blood supply, iatrogenic removal of the parathyroid gland, interruption of venous drainage, dilutional hypocalcemia, or hungry bone syndrome. In studies, transient hypocalcemia is observed with a rate of 19% to 38%, while permanent hypocalcemia is observed with a rate of up to 3% [6]. In the literature, female gender, recurrent operations, retrosternal location, advanced age, hyperthyroidism, malignant pathology, neck dissection, and large thyroid gland are blamed for the factors that increase the risk of hypocalcemia after thyroidectomy. Apart from all these, prolonged operation time and failure to protect the parathyroid glands during surgery are also blamed for the development of hypocalcemia [7]. At this point, it is likely that the use of the IONM device may predispose to postoperative hypocalcemia since parathyroid gland functions may be adversely affected due to the aforementioned reasons such as prolonged operation time and increased manipulations.

The aim of our retrospective study in terms of complications after thyroidectomy was to compare the effect of the use of IONM device on postoperative hypocalcemia that may develop postoperatively in the patient groups with and without the use of IONM device.

Material and Method

In our study, the records of 612 patients who underwent total thyroidectomy by the same surgical team between January 2013 and January 2021 in the General Surgery Clinic of Memorial Kayseri Hospital were reviewed. The IONM device has been used in our center since June 2018. Retrospective information was obtained from the patients' clinical files and hospital automation systems. Demographic data, radiologic imaging reports, serum biochemistry values, pathology reports, duration of surgery, IONM reports, and surgical records of the patients were analyzed. The approval of the study was obtained from the Ethics Committee of Memorial Hospital. All patients who underwent IONM were informed about the operation and informed consent was obtained. Patients with previous thyroid surgery, patients who underwent radical neck dissection, patients who underwent unilateral total thyroidectomy and total complementary thyroidectomy, and 172 patients with comorbidities that may affect calcium values were excluded from the study. The surgical indication was not considered to be benign or malignant. Of the 440 eligible patients, 342 underwent thyroidectomy before the introduction of the IONM and 98 after the introduction of the IONM. Thus, we grouped the patients as those who underwent thyroidectomy without IONM device and those who underwent thyroidectomy with IONM. Homogeneous distribution was achieved between the groups in terms of patient characteristics, type of surgery and diagnoses. All patients underwent vocal cord examination preoperatively and 24 h postoperatively. Postoperative 24th-h calcium values were recorded. A calcium value below 8 mg/dl in the first 48 h postoperatively, tingling in the perioral region and fingers, muscle cramps, and prolonged QT interval on ECG were considered hypocalcemia. Asymptomatic hypocalcemic patients received only oral calcium after discharge, while symptomatic hypocalcemic patients received oral calcium and active vitamin D. Patients who needed calcium and vitamin D supplementation for more than two years were considered to have permanent hypocalcemia and those who needed less than two years of medical support were considered to have transient hypocalcemia [8].

All patients were operated by the same surgeon experienced in endocrine surgery (performing more than 100 thyroidectomies per year) and his team, and surgical decisions were made according to the 2015 American Thyroid Associations Guidelines [9]. We did not estimate a learning period because the surgeon had been using the IONM device for two years in another center. Patients were operated in the supine position with shoulders elevated, head back, and neck tense. All patients received a combination of inhalation and intravenous anesthesia. Intubation was performed with a Nerve Integrity Monitor (NIM) Standard Reinforced Electromyography (EMG) Endotracheal Tube® (Medtronic, Xomed, Jacksonville, FL, USA) with surface electrodes. Intubation was performed by the same anesthesia team to ensure the correct placement of the electrodes. Electrode impedance was routinely checked.

Results

Of the 612 patients who underwent total thyroidectomy, 440 patients who met the criteria were included in the study. Total thyroidectomy was performed in 342 (78%) patients without IONM device and 98 (22%) patients with IONM device. Of the patients, 363 (82.5%) were female and 77 (17.5%) were male. The mean age was 49.2 years (20-87) and the mean length of hospitalization was 1.48 (1-5) days. While this period was 1.42 days before the use of IONM, this period increased to 1.7 days after the use of IONM. The mean operative time was 118 minutes, which increased to 147 min in surgeries using IONM and 109.6 min in surgeries without IONM. Significant amplitude values were obtained at an average of 34.7 min after incision. While 93 (21%) of our patients were operated for malignant pathology, the others were operated for benign reasons such as nodular colloidal goiter, follicular lesion, and thyroiditis. Among all our patients, only one patient (0.2%) in the non-IONM group developed permanent vocal cord paralysis. Thyroid tissue showed retrosternal extension in 32 (7%) of our patients, while 53 (12%) patients underwent central lymph node dissection. During the follow-up period, 22 (5%) of our patients developed transient hypocalcemia, which resolved after medical treatment. Demographic data of the patients are summarized in Table 1. The mean postoperative 24th-h biochemical calcium value was 8.93 mg/dL (6.15-10.9), 9.05 mg/dL (6.15-10.9) in patients without IONM and 8.5 mg/dL (6.6-10.6) in patients with IONM. A statistically significant difference was found between the groups in terms of calcium value, operation time, and age ($p<0.05$). Calcium values were also compared between groups according to whether the pathology was benign or malignant. In the group without IONM device, calcium values were 9.3 mg/dL (6.8-10.9) in patients operated for benign pathology and 8.7 mg/dL (6.1-10.6) in patients operated for malignant causes. Calcium values of 8.5 mg/dL (6.6-10.4) were observed in those operated for benign pathology and 8.4 mg/dL (7.0-10.6) in those operated for malignant

Table 1: Demographic and other characteristics of the patients.

Demographic and Other Characteristics	n=440 (%)
Age	49.2 (87-20)
Gender	
Female	363 (82.5%)
Male	77 (17.5%)
Thyroid Pathology	
Benign	347 (79%)
Malignant	93 (21%)
Retrosternal Extension	
Yes	32 (7%)
No	408 (93%)
IONM	
Yes	98 (22%)
No	342 (78%)
Central Lymph Node Dissection	
Yes	53 (12%)
No	387 (88%)

Table 2: Patient characteristics between groups.

	Total	IONM	IONM-free	*p*-value
Count	440	98	342	
Mean age	49.2	43.05	51	<0.001
Length of hospitalization (days)	1.48	1.7	1.42	<0.05
Operation time (minutes)	118	147	109.6	<0.001
Calcium values 24. h (mg/dL)	8.93	8.5	9.05	<0.001

pathology. Similarly, when calcium values were evaluated according to whether the thyroid gland was located retrosternally between the groups before and after IONM use, 9.2 mg/dL (6.1-10.2) was found in patients with retrosternal extension of thyroid tissue in the group without IONM and 9.2 mg/dL (6.3-10.9) in patients without retrosternal extension. In the group using IONM device, calcium values of 7.9 mg/dL (6.6-9.9) in patients with retrosternal extension and 8.6 mg/dL (6.6-10.6) in patients without retrosternal extension were reported. Statistically significant results were found when calcium values were compared with benign or malignant pathology in the group without IONM device (p<0.001). There was no significant difference between the retrosternal extension of thyroid tissue and calcium values between the groups with and without IONM device. Similarly, no significant difference was found between the calcium values of patients who underwent central lymph node dissection and the groups with and without IONM device. A significant difference was found between the groups in terms of length of hospitalization (p<0.05). Comparative results of the groups are shown in Table 2.

Discussion

Total thyroidectomy is currently the standard surgical procedure for many thyroid diseases. Although it is accepted as a safe method, RLN injury that develops during thyroid surgery is considered as a major complication of thyroidectomy because it negatively affects the patient's postoperative quality of life and leads to medico-legal problems [3]. Intraoperative RLN injuries develop due to transection of the nerve, suturing of the nerve, nerve traction, aspiration, compression, contusion, applied pressure, ischemia during tissue skeletonization, and electrothermal injuries [1,2]. The largest multicenter study was conducted in Germany on 16,000 patients and it was reported that the use of IONM reduced the risk of nerve injury [10-12]. Today, there is no doubt about the importance of knowing the anatomy of RLN in thyroid surgery and its protection during surgery. Despite all these advances, transient nerve injury is seen in 5% to 8% of patients, while permanent damage is seen in 0.3% to 3% of patients [1,2]. IONM has been widely used all over the world in recent decades to reduce nerve injuries, visualize the nerve, and determine intraoperative and postoperative strategies with information about its function [4]. Despite all these, the role and benefits of IONM use in thyroid surgery remain controversial. There is no consensus on the reduction in nerve injury rates in studies and meta-analyses conducted after the introduction of the IONM device [13,14]. However, a meta-analysis conducted in 2014 showed a decrease in nerve injury rates [15]. In our study, permanent nerve injury developed in only one patient in the control group, and no permanent nerve injury was observed in the group using the IONM device.

Hypocalcemia is the most common complication after thyroid surgery and usually occurs in the first 24 h after surgery and may be symptomatic or asymptomatic. If hypocalcemia develops, patient satisfaction decreases, the length of hospitalization increases, hospital costs increase and health resources are consumed. The definition of postoperative hypocalcemia varies from study to study. In some studies, parathormone serum levels, tetany, and clinical symptoms are taken into consideration, while in others serum calcium levels are based on laboratory reference ranges. Mathur et al. have also shown that PTH levels are not safe in the evaluation of postoperative hypocalcemia [16,17]. In the most recent studies, transient hypocalcemia is observed in 19% to 38%, while permanent hypocalcemia is observed in up to 3% [6]. In the study by Mahenna et al., the incidence of hypocalcemia in the same group was found between 0% to 46% due to inconsistencies in these definitions [18]. Hallgrimsen et al. also reported an increase in transient hypocalcemia due to prolonged operation time and enlargement of the dissection area, especially in patients undergoing thyroidectomy for Graves' disease [19]. In our study, transient hypocalcemia was observed in only 22 (5%) patients with lower rates than those reported in the literature. To date, there have been many studies investigating the causes of hypocalcemia after thyroidectomy, but they have not been fully clarified because of inconsistent definitions and heterogeneity of the studies [20]. In our study, total thyroidectomy was performed in all patients with the same technique by the same experienced surgeon and anesthesia team to ensure homogeneity. At the same time, conditions that may affect calcium levels such as retrosternal extension, central lymph node dissection, and malignant pathology were homogeneously distributed among the groups. In our comparison between the groups, a significant decrease in postoperative calcium values was observed in patients using the IONM device, possibly due to prolonged operation time. The mean calcium value of 8.93 mg/dL was 9.05 mg/dL in the group without IONM device and 8.5 mg/dL in the group with IONM device. Dissection around the parathyroid glands, dissections performed while identifying RLN, venous stasis, and edema caused by ligation of thyroid veins may disrupt parathyroid functions and cause hypocalcemia [21]. The hypothesis we formed based on this, especially the time until the RLN is detected with the IONM device (the time until significant amplitude occurs) prolongs the total duration of the operation and increases the risk of transient hypocalcemia because it will cause more tissue trauma, tissue edema, and increased inflammation while trying to detect the nerve. In our study, a significant difference was observed between prolonged operation time and calcium values (p<0.001). Female gender, recurrent operations, retrosternal localization, advanced age, hyperthyroidism, malignant pathology, neck dissection, prolonged operation time, failure to protect the parathyroid glands during surgery, and large thyroid gland have been accused among the factors that increase the risk of hypocalcemia after thyroidectomy [7]. Many studies have searched for an answer to the predisposition to hypocalcemia after thyroidectomy in women, but although no clear conclusion could be obtained, it was thought that the effect of sex steroids on PTH secretion and genetic and anatomical differences in cellular signal transduction pathways may be the cause [22]. The importance of the surgeon's experience has also been emphasized. Although female gender and advanced age have been reported as risk factors in the development of hypocalcemia in meta-analyses, no significant difference was found between advanced age and female gender and the development of hypocalcemia in our study [23-25]. Malignant thyroid pathology has also been found to be effective in the development of hypocalcemia [21]. In our study, when the patients were divided into patients operated for benign pathology and patients operated for malignant pathology, no statistically significant result was found when calcium values were compared between patients with and without IONM device (p>0.05). When retrosternal extension, which was also evaluated among the risk factors, was compared with calcium values, no statistically significant result was found between the group using IONM device and the control group. However, statistically significant results were found when the length of hospitalization and calcium values were compared between the groups (p<0.05).

In light of this information, it is possible that the introduction of IONM for the protection of the RLN may have an effect on hypocalcemia due to the reasons mentioned above, such as prolongation in the total duration of surgery and increased manipulations in the period until the nerve fixation. Hallgrimsen et al. reported that the risk of symptomatic transient hypocalcemia increased in patients operated for Graves' disease and in patients with prolonged operation time [19]. In other studies, on this subject, no connection between the duration of surgery and hypocalcemia has been shown [26-29]. In our study, we found that the mean time to obtain amplitude after incision was 34.7 min. In terms of the time to obtain amplitude, we divided our patients into groups with a mean time to obtain the amplitude of less than 30 min (Group 1), between 30 min to 60 min (Group 2), and more than 60 min (Group 3). While the calcium values of 24 patients in Group 1 and 36 patients in Group 2 were close to each other (8.55 and 8.58, respectively), the mean calcium value of 38 patients in Group 3 was 8.3. In our study, a significant difference was observed between amplitude acquisition time and calcium values in the 3rd Group (p<0.001). In light of our knowledge to date, since there is no study examining the effect of the use of IONM device on postoperative hypocalcemia in terms of complications after thyroidectomy, we retrospectively evaluated the factors that may cause a decrease in calcium values in patients with and without the use of IONM device in line with our hypothesis. We found that the use of IONM may have an increasing effect on hypocalcemia, as the prolongation in the total duration of surgery as well as the prolongation in the time until the nerve is detected will bring increased manipulations.

When evaluated in terms of postoperative complications, many publications have reported a decrease in complication rates with the use of IONM. Barczyński et al. found a 2.9% decrease in early paralysis rates in the high-risk group and a 0.9% decrease in the low-risk group with the use of IONM [30]. Previous studies have also shown that the use of IONM increased the visibility and identification of RLN [31,32]. In our study, no permanent paralysis was observed in any of our patients after IONM use, but permanent paralysis was observed in one patient in the IONM-free group.

This study also has some limitations. Firstly, the number of patients in the study group was less than the control group and not all patient data could be accessed in a computerized environment due to the retrospective nature of the study. In addition, the approach to vocal cord examinations performed preoperatively and postoperatively may be subjective. Because Gianlorenzo et al. emphasized in their study that fiberoptic laryngoscopy is necessary for the detection of postoperative vocal cord paralysis [33]. On the other hand, our study is a single-center study, all patients were operated by the same surgeon, anesthesia technique was applied by the same anesthesia team and intubated by the same anesthesia team. Patients with previous thyroid surgery, radical neck dissection, unilateral total thyroidectomy, total complementary thyroidectomy, and 172 patients with comorbidities that may affect calcium values were excluded from the study to ensure homogeneous distribution. Since calcium values may be affected by malignant pathology, retrosternal extension, and central lymph node dissection, homogeneous distribution of these patients in the groups was ensured. In addition, the fact that the endocrine surgeon had been performing operations with IONM in another center for more than two years prevented any effect on the results that may occur due to the learning curve. The fact that the blood values of the patients were checked only on the first morning after surgery may have caused early hypocalcemia that may develop in the first 48 h to be overlooked. Therefore, it would be useful to check the electrolyte values in the following days. Since magnesium values and thus chronic proton pump inhibitors use may also have an effect on calcium values, these should also be taken into consideration in further studies [34,35]. There have also been reports suggesting that preoperative calcium values of patients may also affect postoperative hypocalcemia, but we did not look at preoperative calcium values in our study [36].

Conclusion

The risk of hypocalcemia after thyroidectomy increases due to prolonged operation time, retrosternal extension of thyroid tissue, and thyroidectomy indication. In addition, the development of hypocalcemia leads to prolonged hospitalization. Identification of known risk factors before surgery may provide early diagnosis and treatment for the development of postoperative hypocalcemia, especially when there are conditions such as IONM use and surgical technique that may prolong the duration of surgery. Loss of signal or inability to receive the signal during IONM use is also a technical issue that needs to be addressed. In our study, it was shown that with the use of IONM in thyroid surgeries, calcium values may decrease and the risk of hypocalcemia may increase due to the prolongation of the time until amplitude acquisition from the nerve and the increase in manipulations in the surgical area until the nerve is detected.

Further studies should be performed to establish standards on the effects of IONM device use on hypocalcemia.

References

1. Calo PG, Pisano G, Medas F, Pittau MR, Gordini L, Demontis R, et al. Identification alone versus intraoperative neuromonitoring of the recurrent laryngeal nerve during thyroid surgery: experience of 2034 consecutive patients. J Otolaryngol Head Neck Surg. 2014;43:16.
2. Jiang K, Zhu Y, Zhou G, Ye Y, Xie Q, Yang X, et al. Safe distance between electrotome and recurrent laryngeal nerve: an experimental canine model. Int J Clin Exp Med. 2015;8:770-75.
3. Calo PG, Medas F, Erdas E, Pittau MR, Demontis R, Pisano G, et al. Role of intraoperative neuromonitoring of recurrent laryngeal nerves in the outcomes of surgery for thyroid cancer, Int J Surg. 2014;12(Suppl 1):S213-7.
4. Liu XL, Wu CW, Zhao YS, Wang T, Chen P, Xin JW, et al. Exclusive real-time monitoring during recurrent laryngeal nerve dissection in conventional monitored thyroidectomy. Kaohsiung J Med Sci. 2016;32:135-41.
5. Christou N, Mathonnet M. Complications after total thyroidectomy. J Visc Surg. 2013;150:249-56.
6. Edafe O, Antakia R, Laskar N, Uttley L, Balasubramanian SP. Systematic review and meta-analysis of predictors of post-thyroidectomy hypocalcaemia. Br J Surg. 2014;101(4):307-20.
7. Sonne-Holm E, Hahn CH. Prolonged duration of surgery predicts postoperative hypoparathyroidism among patients undergoing total

thyroidectomy in a tertiary referral centre. Eur Thyroid J. 2017;6(5):255-62.

8. Sitges-Serra A, Ruiz S, Girvent M, Manjón H, Dueñas JP, Sancho JJ. Outcome of protracted hypoparathyroidism after total thyroidectomy. Br J Surg. 2010;97(11):1687-95.
9. Haugen BR, Alexander EK, Bible KC, Doherty GM, Mandel SJ, Nikiforov YE, et al. 2015 American thyroid association management guidelines for adult patients with thyroid nodules and differentiated thyroid cancer: the American thyroid association guidelines task force on thyroid nodules and differentiated thyroid cancer. Thyroid. 2016;26:1-133.
10. Thomusch O, Sekulla C, Walls G, Machens A, Dralle H. Intraoperative neuromonitoring of surgery for benign goiter. Am J Surg. 2002;183:673-8.
11. Thomusch O, Sekulla C, Machens A, Neumann HJ, Timmermann W, Dralle H. Validity of intra-operative neuromonitoring signals in thyroid surgery. Langenbecks Arch Surg. 2004;389:499-503.
12. Sanabria A, Ramirez A, Kowalski LP, Silver CE, Shaha AR, Owen RP, et al. Neuromonitoring in thyroidectomy: A meta-analysis of effectiveness from randomized controlled trials. Eur Arch Otorhinolaryngol. 2013;270:2175-89.
13. Pisanu A, Porceddu G, Podda M, Cois A, Uccheddu A. Systematic review with meta-analysis of studies comparing intraoperative neuromonitoring of recurrent laryngeal nerves versus visualization alone during thyroidectomy. J Surg Res. 2014;188:152-61.
14. Dralle H, Sekulla C, Haerting J, Timmermann W, Neumann HJ, Kruse E, et al. Risk factors of paralysis and functional outcome after recurrent laryngeal nerve monitoring in thyroid surgery. Surgery. 2004;136:1310-22.
15. Rulli F, Ambrogi V, Dionigi G, Amirhassankhani S, Mineo TC, Ottaviani F, et al. Meta-analysis of recurrent laryngeal nerve injury in thyroid surgery with or without intraoperative nerve monitoring. Acta Otorhinolaryngol Ital. 2014;34(4):223-9.
16. Mathur A, Nagarajan N, Kahan S, Schneider EB, Zeiger MA. Association of parathyroid hormone level with postthyroidectomy hypocalcemia: A systematic review. JAMA Surg. 2018;153(1):69-76.
17. Karefilakis CM, Mazokopakis EE. Re: management of post-thyroidectomy hypocalcaemia: Current trends. ANZ J Surg. 2009;79(7-8):574.
18. Mehanna HM, Jain A, Randeva H, Watkinson J, Shaha A. Postoperative hypocalcemia–the difference a definition makes. Head Neck. 2010;32(3):279-83.
19. Hallgrimsson P, Nordenstrom E, Bergenfelz A, Almquist M. Hypocalcaemia after total thyroidectomy for Graves' disease and for benign atoxic multinodular goitre. Langenbeck's Arch Surg. 2012;397(7):1133-7.
20. Lale A, Öz B, Akcan AC, Sözüer EM, Arıkan TB, Gök M. Determination of risk factors causing hypocalcaemia after thyroid surgery. Asian J Surg. 2019;42(9):883-9.
21. Kalyoncu D, Gonullu D, Gedik ML, Muzaffer E, Kuroğlu E, İğdem AA, et al. Analysis of the factors that have effect on hypocalcemia following thyroidectomy. Ulusal Cer Derg. 2013;29:171-6.
22. Sands NB, Payne RJ, Côté V, Hier MP, Black MJ, Tamilia M. Female gender as a risk factor for transient post-thyroidectomy hypocalcemia. Otolaryngol Head Neck Surg. 2011;145(4):561-4.
23. Yamashita H, Noguchi S, Tahara K, Watanabe S, Uchino S, Kawamoto H, et al. Postoperative tetany in patients with graves' disease: A risk factor analysis. Clin Endocrinol. 1997;47:71-7.
24. Erbil Y, Bozbora A, Ozbey N, Issever H, Aral F, Ozarmagan S, et al. Predictive value of age and serum parathormone and vitamin D3 levels for postoperative hypocalcemia after total thyroidectomy for nontoxic multinodular goiter. Arch Surg. 2007;142:1182-7.
25. Bergamaschi R, Becouarn G, Ronceray J, Arnaud JP. Morbidity and complication of total thyroidectomy. Am J Surg. 1998;176:71-5.
26. Lecerf P, Orry D, Perrodeau E, Lhommet C, Charretier C, Mor C, et al. Parathyroid hormone decline 4 hours after total thyroidectomy accurately predicts hypocalcemia. Surgery. 2012;152(5):863-8.
27. Lindblom P, Westerdahl J, Bergenfelz A. Low parathyroid hormone levels after thyroid surgery: A feasible predictor of hypocalcemia. Surgery. 2002;131(5):515-20.
28. Moriyama T, Yamashita H, Noguchi S, Takamatsu Y, Ogawa T, Watanabe S, et al. Intraoperative parathyroid hormone assay in patients with Graves' disease for prediction of postoperative tetany. World J Surg. 2005;29(10):1282-7.
29. Lombardi CP, Raffaelli M, Princi P, Dobrinja C, Carrozza C, Stasio ED, et al. Parathyroid hormone levels 4 hours after surgery do not accurately predict post-thyroidectomy hypocalcemia. Surgery. 2006;140(6):1016-23 discussion 1023-25.
30. Barczyński M, Konturek A, Cichoń S. Randomized clinical trial of visualisation versus neuromonitoring of recurrent laryngeal nerves during thyroidectomy. Br J Surg. 2009;96:240-46.
31. Wojtczak B, Sutkowski K, Kaliszewski K, Głód M, Barczyński M. Experience with intraoperative neuromonitoring of the recurrent laryngeal nerve improves surgical skills and outcomes of non-monitored thyroidectomy. Langenbecks Arch Surg. 2017;402:709-17.
32. Wojtczak B, Kaliszewski K, Sutkowski K, Głód M, Barczyński M. The learning curve for intraoperative neuromonitoring of the recurrent laryngeal nerve in thyroid surgery. Langenbecks Arch. Surg. 2017;402:701-8.
33. Makay O, Icoz G, Yilmaz M, Akyildiz M, Yetkin E. The recurrent laryngeal nerve and the inferior thyroid artery–anatomical variations during surgery. Langenbecks Arch Surg. 2008;393:681-5.
34. Famularo G, Gasbarrone L, Minisola G. Hypomagnesemia and proton-pump inhibitors. Expert Opin Drug Saf. 2013;12:709-16.
35. Koulouridis I, Alfayez M, Tighiouart H, Madias NE, Kent DM, Paulus JK, et al. Out-of-hospital use of proton pump inhibitors and hypomagnesemia at hospital admission: A nested case-control study. Am J Kidney Dis. 2013;62:730-7.
36. Hallgrimsson P, Nordenström E, Almquist M, Bergenfelz AOJ. Risk factors for medically treated hypocalcemia after surgery for graves' disease: a Swedish multicenter study of 1,157 patients. World J Surg. 2012;36:1933-42.