Traditional surgical techniques versus intraoperative methylene blue spraying for recurrent laryngeal nerve and parathyroid gland saving during total thyroidectomy

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Article History: Received: 26.06.2023 **Revised:** 29.07.2023 **Accepted:** 06.08.2023

Abstract
Background: In this research, we used a technique for the identification of recurrent laryngeal nerves (RLN) and the parathyroid gland intraoperatively, by spraying methylene blue dye in the tracheoesophageal groove area, following ligation of the superior pole during the thyroid dissection. This technique is supposed to be an adjuvant method for the RLN and parathyroid glands identification. In order to correctly detect and preserve the parathyroid glands and RLN during complete thyroidectomy, the goal of this research was to assess the usefulness of utilizing methylene blue spray throughout surgery to minimize post-operative complications. **Methods:** This was a Comparative prospective randomized controlled cohort study by simple randomization (envelope) that consisted of 30 Egyptian individuals of either gender, aged 18-60 years old presenting with benign thyroid disorders requiring total thyroidectomy. The participants were divided into two distinct categories: group 1 had 15 instances that required surgical intervention using intraoperative methylene blue spray and group 2 included 15 cases to be operated with the conventional technique. **Results:** There was a non-statistically substantial variation among the groups under study as regard total Ca, Ionized Ca 1 day and 1 month postoperative of the studied patients. Timing started after the skin incision to the end of the operation. The mean thyroidectomy duration in the non-MB group was 91.33±7.98 min, while it was 114.73±6.79min with MB application with a statistically substantial variation. Hospital stays among studied groups ranged from one to three days (1.43 ± 0.73), during which time patients underwent clinical assessments, calcium level monitoring, and treatment for hypocalcemia with the non-statistically substantial variation among the groups under study. **Conclusions:** Methylene blue spray could be used during thyroidectomy to correctly identify the parathyroid glands and RLN to reduce the incidence of complications. The use of intraoperative methylene blue spraying is thought to be a secure, affordable, and accessible technique that can lessen the anxiety associated with thyroidectomy dissection**.**

Keywords: methylene blue, thyroidectomy, parathyroid gland, recurrent laryngeal nerve

Introduction:

One of the procedures utilized most often in areas with an iodine deficit is a thyroidectomy. The parathyroid glands must be spared, the recurrent laryngeal nerves must not be injured, the hemostasis must be precise, and the cosmetic results must be good [1].

The major thyroidectomy postoperative consequences include RLN damage and hypoparathyroidism. Risk elements for the complications of thyroid surgery include the surgeon's lack of expertise, the amount of the resection, the volume of the thyroid gland, and the completion of the thyroidectomy. Effective

dissection is crucial in limiting the emergence of complications [2].

One of the most common consequences of thyroid surgery is hypoparathyroidism. PTH, which plays a crucial role in controlling blood calcium levels, is produced by the parathyroid glands. PTH causes bone resorption, leading to greater calcium absorption by the kidneys, raising blood calcium levels. PTH also stimulates phosphorus excretion from the kidneys. As a consequence, elevated serum phosphorus levels are caused by low PTH levels [3].

Hypocalcemia is brought on by insufficient PTH production. Hypocalcemia brought on by hypoparathyroidism may be temporary or chronic. 0.4-1.9% of people have persistent hypoparathyroidism. Direct damage to the parathyroid glands, glands devascularization, or removing the glands during surgery are all potential causes of the syndrome [4].

Recurrent laryngeal nerve palsy (RLNP) is the other significant side effect of thyroid surgeries. RLNP significantly reduces quality of life and has a negative impact on work performance. In 1.8% of case-reports, RLNP was seen [5].

The inferior thyroid artery, the tracheoesophageal groove, and the ligament of Berry serve as anatomic indications of nerve anatomy that help the majority of surgeons recognize the RLN intraoperatively. There are several anatomical changes of this neurovascular connection due to the pathologic circumstances of the gland. As a result, accurate detection and preservation of the RLN are not guaranteed by the detection of the inferior thyroid artery [2].

In this work, after ligating the superior pole throughout the thyroid dissection, we experimented with a technique for intraoperatively identifying the RLN and the parathyroid gland by spraying methylene blue dye in the region of the tracheoesophageal groove. This procedure is intended to be an adjunct to the identification of the parathyroid glands and RLN.

In order to reduce postoperative problems, this research evaluated the effectiveness of utilizing methylene blue spray during complete thyroidectomy to accurately detect and maintain parathyroid glands and RLN.

Patients and Methods:

This was a Comparative prospective randomized controlled cohort work that included 30 Egyptian individuals of either gender, aged 18-60 years old presenting with benign thyroid disorders requiring total thyroidectomy at Helwan university Hospital. The study period was six months, and the duration was from February 2022 to August 2022.

The Helwan University school of Medicine's research ethics committee granted its clearance. After being told of the study's goal and potential negative effects, each participant signed a permission form.

Criteria of exclusion were individuals who declined to be involved in the study, had previously undergone thyroid surgery, were allergic to methylene blue, had a deficiency of G6PD, were

pregnant, had taken monoamine oxidase inhibitors (MAOIs), were receiving antidepressants, had preoperative vocal cord malfunction and abnormalities, and had a huge goiter with extension retrosternally, patients with a history of radiation therapy, patients with hypersensitivity to methylene blue, and patients unfit for surgery such as poor general condition, ejection fraction <40%, uncontrolled kidney.

The participants were divided into two distinct categories, with group 1 including 15 cases for surgery with the usage of intraoperative methylene blue spray and group 2 included 15 cases to be operated with the conventional technique.

Study Tools:

Methylene blue spray (sterile methylene blue 1%).

Study Procedures:

Both group's pre-operative workup:

The following procedures were applied to all participants:

Full medical history and clinical examination (general & local) which include:

Complete history taking: A detailed history was taken including: personal history, complaint, analysis of the complaint, swelling, pressure symptoms, hyperthyroidism symptoms (toxic symptoms), cardinal toxic symptoms, hypothyroidism symptoms, malignant and metastatic symptoms, past History, medication for hyper or hypothyroidism, medication for hyper or hypocalcemia, and family History:

B- comprehensive physical examination including:

a) General examination:

A full general examination was done, to evaluate the overall functioning of the organism, thyroid function, and the presence of metastasis: head, eye signs, buccal examination, hands, chest and heart examination, abdominal examination, and lower limb examination.

b)Local examination full neck examination was done: inspection, palpation, percussion, and auscultation.

Full pre-operative investigations were done for both groups:

Laboratory: thyroid function tests, complete Blood count (CBC), liver function tests, renal function test, coagulation profile, fasting blood sugar, serum calcium level, virology (Hepatitis C, Hepatitis B, HIV)

Radiological: neck ultrasound (US) with TIRADS score, neck computerized tomography (CT) (when indicated), and examination of vocal cords by indirect laryngoscopy and:

using cytology to evaluate the flexibility of the two vocal cords: Fine needle aspiration cytology (FNAC) with Bethesda scoring.

Surgical technique (Intraoperative)

Total thyroidectomies were performed by experienced endocrine surgeons from our general surgery department at Helwan University hospitals under general anesthesia.

Operative workup for Group 1 (Controlled Group)

Fifteen cases established thyroidectomy with the Conventional Technique: All patients received general anesthesia with endotracheal intubation. Prophylactic antibiotic (amoxicillin-

clavulanic acid) was taken with induction of anesthesia.

Fifteen cases established thyroidectomy with Methylene Blue Spraying Technique:

General anesthesia, patient positioning, skin preparation, skin incision, and dissection, Exposing the thyroid gland, and dissection of the upper pole are all the same as the conventional technique. After the superior pole of the gland was ligated and dissected, we were able to rotate it medially and anteriorly mobilise the gland due to the superior vessels' division, so the thyroid lobe was deviated medially, which resulted in best possible accessibility of the crucial structures and helped us to expose the field where parathyroids and RLN suspected to be at. In this field, we could apply the Methylene Blue spray. Methylene blue was sprayed [in a spray of methylene blue 1% concentrated in 100ml alcohol 70%] over the lobe of the thyroid and perilobar area which included the parathyroids, inferior thyroid veins, artery, RLN, and peri thyroidal muscles, in addition to structures that are lipoid and tendinous, and at this area, the parathyroid glands and RLN could be injured. We sprayed one or two sprinkles according to the size of the field to make the area getting blue dye. We observed post-spraying that after 4 to 7 minutes the dye washed out over the region where the parathyroid gland may be located and the normal yellowish-brown color of the parathyroid appeared in the blue field. So, the parathyroid absorbed the dye and got back to its original color after 4 to 7 minutes while the remaining thyroid and peri thyroidal area were still in blue dye. We noted that the RLN almost completely not take the stain as the washing out of the dye timing was 0.1 min. that time was the time taking to wash out the dye from Schwann sheath covered the nerve as it didn't take the stain. So after 5 to 7 mins, we could identify the parathyroid gland and the RLN. That helped us to avoid their injury and handling them easily. We also observed that after 15 to 25 minutes of spraying the Methylene Blue, the dye washed out from the thyroid, peri thyroidal area and all the field which got back to its normal color. After identification and preserving the RLN and the parathyroid glands, dissection of the lower thyroid pole, removal of the lobe, dissection of the pyramidal lobe when present, and closure in this group were done the same way as the conventional technique.

Post-operative care in both groups

Vocal cord assessment, clinical assessment of postoperative complications, histopathological examination of the excised specimen of thyroid with reporting if any tissues of parathyroid was existed in a similar samples as thyroid in both groups, level of serum Ca (Total serum Ca & Ionized Ca) was measured at 24 hours postoperative then followed up every 24 hours till patient discharge with normal ranges. Then, 1 month after discharge, any signs and symptoms of hypocalcemia in the form of facial paresthesia (perioral paresthesia), finger numbness, muscle cramps, confusion, delirium, Seizure, positive Chvostek or Trousseau signs, and muscular spasm were noted in the immediate post-operative period and on follow-up, any signs and symptoms of

RLN injury in the form of Voice changes, difficulty breathing, Dyspnea, and needed tracheostomy or not in cases with severe O2 drop and choking. Any patient-induced signs of RLN were kept under observation till improvement. If patient-induced voice changed it was treated by I.V dexamethasone and oral steroids (traditional dose: Oral, IM, and IV: between 4 and 20 mg/day administered as a single dosage or in two to four split dosages; while Large dose: 0.4 to 0.8 mg/kg/day and typically not exceeding 40 mg/day). If improvement happened it was considered neuropraxia. If no improvement, the patient was referred to phoniatrics.

Patients who developed asymptomatic hypocalcemia were treated with oral Ca carbonate (3-6 g/d) our regimen started with 4g/d for one week and then re-measured serum Ca every week. The dose decreased 1g per week and stopped Ca carbonate at the end of the month if serum calcium level was above 8.5mg/dl. Symptomatic hypocalcemia was treated by oral calcitriol supplementation 1.0 μg/d and parenteral Ca gluconate 4 gm per day (1 amp contains 500 mg, which was done by giving 2-amp Ca gluconate slowly in 500 cc glucose 5% over 2-4 hours the 4 times per day for 3 days and everyday total calcium serum level was also measured. In group 2 we took care of any intra or post-operative signs or symptoms of Methylene Blue Dye side effects like; urine color changes, local reaction (redness/ hotness/ swelling), GIT symptoms and increase creatinine levels post-operative. If any patient induced signs of dye reaction, the dye stopped and washed out manually then we gave ampule of avil and dexamethasone once to stop reaction. At the outpatient clinic, the participants received routine follow-up care. at 1, 2 and 3 months. We calculated the number of days post-operative which the patient stayed at hospital in both groups to compare the hospital stay range.

Statistical analysis

Version 24.0 of the IBM SPSS software suite was used to analyze the data. Numbers and percentages were used to describe the qualitative parameters. Mean, standard deviation, median, minimum, and maximum were all used to describe quantitative parameters. The Chi-square test (2) was used to compare categorical data between several groups. The Monte Carlo correction test or Fisher's exact test were used to compensate for chi-square when over twenty percent of the cells had an anticipated count of fewer than five. Significance level (p-value): $p > 0.05$ Insignificant, $p \leq 0.05$ Significant (95% level of confidence).

Results:

Comparison between No MB and MB groups revealed that there was a non-statistically substantial variation among the groups under the study as regard to anthropometric measures, demographic data, and co-morbidities of the studied patients. Table (1)

Table (1): Comparison between No MB and MB group regarding demographic data, anthropometric measures and co-morbidities of the studied patients

		No MB Group	MB Group	P-value
		No. = 15	No. = 15	
Age	Mean ± SD	42.33 ± 11.93	41.80 ± 10.58	0.898
	Range	27 – 59	26 – 60	
Gender	Female	13 (86.7%)	11 (73.3%)	0.361
	Male	2 (13.3%)	4 (26.7%)	
Weight	Mean ± SD	84.27 ± 16.62	84.87 ± 13.95	0.915
	Range	58 – 110	61 – 110	
Height	Mean ± SD	164.00 ± 7.42	165.27 ± 8.79	0.673
	Range	152 – 179	150 – 183	
DM	No	12 (80.0%)	10 (66.7%)	0.409
	Yes	3 (20.0%)	5 (33.3%)	
Hypertension	No	12 (80.0%)	11 (73.3%)	0.666
	Yes	3 (20.0%)	4 (26.7%)	

P-value > 0.05: Nonsignificant; P-value < 0.05: Significant; P-value < 0.01: Highly significant

non-statistically substantial variation was existed among the examined groups in terms of the type of thyroid pathology and thyroid profile when the No MB and MB groups were compared. (Table 2)

Table (2): Comparison between No MB and MB group regarding the type of thyroid pathology and thyroid profile

		No MB group	MB group	P-value
		No. = 15	No. = 15	
Type of thyroid pathology	MNG	11 (73.3%)	11 (73.3%)	1.000
	Graves	4 (26.7%)	4 (26.7%)	
Free T3	Mean ± SD	2.83 ± 0.60	2.82 ± 0.57	0.953
	Range	2.04 – 3.97	2.09 – 3.95	
Free T4	Mean ± SD	1.51 ± 0.49	1.55 ± 0.53	0.810
	Range	1.09 – 2.87	1.13 – 2.85	
TSH	Mean ± SD	1.76 ± 0.81	1.68 ± 0.65	0.770
	Range	0.92 – 3.95	0.95 – 3.42	

P-value > 0.05: Nonsignificant; P-value < 0.05: Significant; P-value < 0.01: Highly significant

No reports of long-term postoperative vocal cord palsy among the groups under study, Six months of follow-up revealed no more issues. Only four cases (13%) had biochemical hypocalcemia without signs of hypocalcemia in both groups following surgery, and it became better after four weeks. There was a non-statistically substantial variation among the groups under the study as regard total Ca, Ionized Ca 1 day and 1 month postoperative of the studied patients. Table (3)

Table (3): Comparison between No MB and MB group as regard total Ca, Ionized Ca 1 day and 1 month postoperative

		No MB group No. = 15	MB group No. = 15	P-value
1 day postoperative				
Total Ca	Mean ± SD	9.01 ± 0.47	8.91 ± 0.42	0.556
	Range	8.1 – 9.78	8.2 – 9.72	
Ionized Ca	Mean ± SD	4.67 ± 0.21	4.70 ± 0.15	0.706
	Range	4.1 – 5	4.41 – 4.95	
1 month postoperative				
Total Ca	Mean ± SD	9.16 ± 0.41	9.09 ± 0.38	0.647
	Range	8.4 – 9.8	8.5 – 9.8	
Ionized Ca	Mean ± SD	4.77 ± 0.12	4.80 ± 0.13	0.620
	Range	4.6 – 5	4.6 – 5	

P-value > 0.05: Non-significant; P-value < 0.05: Significant; P-value < 0.01: Highly significant

It was determined how long each thyroidectomy took for the groups under study. Timing began following the incision of the skin and continued till the finish of the procedure. The mean thyroidectomy time was 91.33±7.98 min in the non-MB group and 114.73±6.79 min in the MB administration group, with a substantial variation. Participants had clinical evaluations, calcium level monitoring, and therapy for hypocalcemia throughout their one- to three-day hospital stays in the analyzed groups (1.43 ± 0.73), with the non-statistically substantial variation among the groups under the study. Table (4)

Table (4): Time of surgery and hospital stay among both groups

		No MB group No. = 15	MB group No. = 15	P-value
Time of surgery (min.)	Mean ± SD	91.33 ± 7.98	114.73 ± 6.79	0.000
	Range	79 – 106	103 – 125	
Hospital stays (days)	Mean ± SD	1.40 ± 0.74	1.47 ± 0.74	0.807
	Range	1 – 3	1 – 3	

P-value > 0.05: Nonsignificant; P-value < 0.05: Significant; P-value < 0.01: Highly significant

Discussion

Nowadays, thyroid surgeries-related complications are noticeably less common. Throughout the past few decades, there has been a dramatic decline in overall morbidity and mortality due to the standardization of thyroidectomy techniques and improvements in perioperative management [7]

The two most serious consequences of thyroidectomy surgery are hypoparathyroidism and recurrent laryngeal nerve (RLN) damage, both of which result in catastrophic, permanent impairment. [8]

To protect the RLN and the parathyroid glands during total thyroidectomy, many anatomical landmarks and boundaries needs to be recognized. The potential for RLN harm and subsequent hypocalcemia occurs occasionally when surgeons have trouble spotting them. The easy method of

methylene blue spraying aids in avoiding all such issues and lowers morbidity [9].

Dralle et al. came to the conclusion that visual nerve identification emerged as the gold standard of care for RLN therapy in a recent multicenter evaluation of 16,448 thyroidectomies [10].

Recent years have seen an increase in the usage of methylene blue, a heterocyclic aromatic chemical molecule, in sentinel lymph node biopsies. Staining of the parathyroid glands is not a novel method for preventing hypoparathyroidism; Klopper et al. initially reported it in 1966 [11]. Trypan blue, a toluidine derivative isomer, and toluidine blue were the first dyes utilized by writers. They started to be substituted with methylene blue as soon as their possible teratogenic effects were identified [2].

Reoperation, cancer, retrosternal goiter, Graves' disease, and inexperienced surgeons are a few of the risk factors that might lead to harm to these tissues [12].

Our study's goal was to determine if the methylene blue spraying approach would make it possible to safely detect the RLN and parathyroid glands during complete thyroidectomy.

The RLN hadn't been stained by MB staining in any patient group instance. All other tissues are dyed blue, whereas RLN stays white. The tracheoesophageal groove provided an easy location to locate the nerve. The blue stain washed off and the parathyroid glands returned to their natural yellow hue four to seven minutes later. In every instance, the thyroid tissue needed over 15 minutes to completely remove the stain. Postoperatively, no palsy of the vocal cords was seen.

In thyroidectomy, intra-operative RLN detection with MB is almost free. It provides reduced stress and a clearer area that aids in the identification and protection of the RLN without increasing danger, giving the surgeons better verification of the anatomically suspected nerve. The use of MB staining may be supplemented with other approaches, such as identifying anatomical landmarks or using nerve detection tools, and is not intended to be used as a stand-alone procedure.

In a 2012 study, Sari S et al. examined how methylene blue spraying helped 56 thyroidectomy patients identify their parathyroid glands. They discovered that whereas other tissues took longer, the parathyroid gland had the capability to absorb the blue staining and return to its natural yellow hue in only 3 minutes. They hypothesized that parathyroid glands absorb methylene blue more quickly compared to other tissues due to their dense lymphovascular architecture [2].

In order to evaluate RLN recognition and preservation after total thyroidectomy, Nofal and El-Anwar [13] evaluated the application of MB in 46 patients. They compared intra-operative RLN staining with MB on one side with ocular recognition solely on the other side in the same individual. According to our findings, there are substantial variations in the mean lobectomy time (measured from the beginning of the lobectomy following the midline strap muscles had been separated).

Similar outcomes were seen in our research as well. The RLN was clearly distinguishable in all 15 individuals as an unstained white structure against a blue backdrop. The parathyroid glands werehed out the blue stain and returned to their natural yellow hue three to five minutes later. In every instance, the thyroid tissue needed over 15 minutes to completely remove the stain.

The surgeon must first locate the location where the parathyroid gland is thought to be located before using methylene blue spray to verify it. It was highly advised against using methylene blue spray on its own without surgical training and expertise [14].

In the present investigation, there were no documented clinical or long-term occurrences of temporary biochemical hypocalcemia, however it was found in four instances (13%) in the two groups in the early postoperative period. This incidence is close to the lowest rates seen in the literature for both temporary and persistent hypoparathyroidism (6.9–46% and 0.4–3.3%). No further problems were recorded over a follow-up period of 6 months among the examined groups, and no persistent postoperative vocal cord palsy was found [15].

The safety of MB staining was confirmed by the fact that no side effects from its usage were identified in the present investigation.

Identification of the RLNs as well as the parathyroid glands is part of the present work. Our goal was to identify the parathyroid and RLN and then validate it using methylene blue staining. Only the parathyroid gland is visible thanks to intravascular methods.

In contrast to the intraoperative nerve tracking method, the present research does not incur any extra costs for the patient. We didn't use any pricey equipment. We just utilized the colour and our vision.

Due to the small number of instances, many surgeons undertake thyroidectomies without doing a trial in order to detect the RLN and parathyroid in advance of their harm. The reliability and efficacy of this procedure need to be confirmed by further trials including greater numbers of patients and the use of the technique by other surgeons.

Conclusions:

Methylene blue spray could be used during thyroidectomy to properly identify the parathyroid glands and RLN to reduce the incidence of complications. The use of intraoperative methylene blue spraying is thought to be a secure, affordable, and accessible technique that can lessen the anxiety associated with thyroidectomy dissection. It is necessary to do more prospective controlled randomised multi-central research with a bigger sample size to verify the efficacy, dependability, and safety of this method and to provide evidence-based recommendations. Despite not experiencing any adverse responses, we nonetheless advise a skin test prior to surgery to rule out any potential allergic reactions.

Financial support and sponsorship: Nil
Conflict of Interest: Nil

References:

1. Miccoli P, Berti P, Raffaelli M, Materazzi G, Conte M, Galleri D. Impact of harmonic scalpel on operative time during video-assisted thyroidectomy. Surg Endosc. 2002;16:663-6.
2. Sari S, Aysan E, Muslumanoglu M, Ersoy YE, Bektasoglu H, Yardimci E. Safe thyroidectomy with intraoperative methylene blue spraying. Thyroid Res. 2012;5:15.
3. Melikyan AA, Menkov AV. Postoperative Hypoparathyroidism: Prognosis, Prevention, and Treatment (Review). Sovrem Tekhnologii Med. 2020;12:101-8.
4. Daskalaki A, Xenaki S, Lasithiotakis K, Chrysos A, Kampa M, Notas G, et al.

Early Postoperative Parathormone and Calcium as Prognostic Factors for Postoperative Hypocalcemia. J Clin Med. 2022;11.
5. Zakaria HM, Al Awad NA, Al Kreedes AS, Al-Mulhim AM, Al-Sharway MA, Hadi MA, et al. Recurrent laryngeal nerve injury in thyroid surgery. Oman Med J. 2011;26:34-8.
6. Randolph GW, Kobler JB, Wilkins J. Recurrent laryngeal nerve identification and assessment during thyroid surgery: laryngeal palpation. World J Surg. 2004;28:755-60.
7. Padur AA, Kumar N, Guru A, Badagabettu SN, Shanthakumar SR, Virupakshamurthy MB, et al. Safety and Effectiveness of Total Thyroidectomy and Its Comparison with Subtotal Thyroidectomy and Other Thyroid Surgeries: A Systematic Review. J Thyroid Res. 2016;2016:7594615.
8. Joliat GR, Guarnero V, Demartines N, Schweizer V, Matter M. Recurrent laryngeal nerve injury after thyroid and parathyroid surgery: Incidence and postoperative evolution assessment. Medicine (Baltimore). 2017;96:e6674.
9. Vural V, Comcali B, Saylam B, Coskun F. Identification of the recurrent laryngeal nerve during thyroidectomy can affect the complication rate. Ann Ital Chir. 2021;92:217-26.
10. 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.
11. Klopper PJ, Moe RE. Demonstration of the parathyroids during surgery in dogs, with preliminary report of results in some clinical cases. Surgery. 1966;59 6:1101-7.
12. Li W, Li H, Zhang S, Tao Y, Wang X, Cheng J. To explore the risk factors and preventive measures affecting the treatment of retrosternal goiter: An observational study. Medicine (Baltimore). 2020;99:e23003.
13. Nofal AA, El-Anwar MW. Recurrent laryngeal nerve identification in thyroidectomy by intra-operative staining with methylene blue in forty-six patients. Clin Otolaryngol. 2016;41:296-9.
14. Piromchai P, Juengtrakool T, Laohasiriwong S, Kasemsiri P, Ungarereevittaya P. The sensitivity and specificity of methylene blue spray to identify the parathyroid gland during thyroidectomy. PeerJ. 2019;7:e6376.
15. Beldi G, Kinsbergen T, Schlumpf R. Evaluation of intraoperative recurrent nerve monitoring in thyroid surgery. World J Surg. 2004;28:589-91.