

# Methylene Blue Spray versus Conventional Surgical Techniques for Identification of Recurrent Laryngeal Nerve and Parathyroid Glands during Thyroidectomy

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## ABSTRACT

**Background:** Thyroid surgeries are commonly operated head and neck surgeries. Significant morbidity is caused by thyroidectomy complications such as recurrent laryngeal nerve (RLN) and parathyroids injuries.

**Objective:** To reduce the risk of complications after thyroidectomy, we employed methylene blue spray to locate the RLNs and parathyroid glands.

**Patients and method:** This was a prospective, randomized, controlled trial of 80 patients with thyroid disease who were eligible for total thyroidectomy. Group 1: patients were managed by traditional thyroidectomy where the RNL and parathyroid glands were identified anatomically. Group 2: Diluted methylene blue spray was used to aid in the identification of the RLN and the parathyroid glands.

**Results:** Both groups had the RLN identified. In group 2 the nerve did not take the dye and remained white. At least one of the parathyroid glands could be identified in 35 patients in group 1, while it was identified in 37 patients in group 2. The parathyroid was stained with methylene blue then the dye was washed out in 3 minutes. Neither group had a statistically significant advantage over the other in identifying the parathyroid gland, p-value=0.356. The RLN was identified in all patients of both groups.

**Conclusion:** Methylene blue dye spraying is technically feasible, safe, and effective method for identifying and protecting the RLN and parathyroid glands during thyroidectomy. It can be used as adjunct for the identification of these structures in difficult cases. Minimizing postoperative hypocalcemia requires accurate identification of at least one of the parathyroid glands.

**Keywords:** Parathyroid gland, Recurrent laryngeal nerve, Thyroidectomy.

## INTRODUCTION

After diabetes, thyroid disorders are the most frequent endocrine disease [1]. Thyroid surgeries are commonly operated head and neck surgeries [2]. Thyroidectomy related complications are not uncommon. Extreme morbidity can result from thyroidectomy complications, including parathyroid glands and RLN injury [3].

The aim of the present study was to reduce the risk of complications after thyroidectomy, we employed methylene blue spray to locate the RLNs and parathyroid glands.

## PATIENTS AND METHODS

Eighty patients who had complete thyroidectomy surgeries at Zagazig University Hospitals in Egypt participated in this randomized control research, between January 2020 and January 2022. Using a random number generator, 80 patients were split evenly between two groups.

We included eighteen years old patients or older in this study. All patients were euthyroid. We excluded patients with hypo- or hyper-thyroid status, patients with vocal cord palsy either unilateral or bilateral diagnosed by preoperative indirect laryngoscopy, patients with thyroid cancer diagnosed by preoperative fine-needle aspiration cytology (FNAC), patients who were unfit for surgery, and patients with hypersensitivity to methylene blue. Serum Ca was

measured 24 hours preoperatively; patients with serum Ca less than 8.5 mg /dl were excluded.

All patients were clinically evaluated by history taking and clinically examined. Also, were preoperatively investigated by complete blood count (CBC), T3, T4, TSH, PT, PTT, INR, serum calcium, hepatitis B and C viral indicators, HIV antibodies, and kidney and liver function tests. The patients all underwent a neck ultrasound. Ultrasound-guided FNAC was performed to patients with solitary thyroid nodule or the presence of suspicious nodule on ultrasonic examination. Dermal sensitivity test using diluted methylene blue 1:100[4] to detect patients with hypersensitivity to methylene blue.

## The technique:

Kocher's neck incision was used for the procedure, and it was done under general anesthesia.

Group 1: the identification of the RLN and parathyroid glands depended on their anatomical location.

Group 2: The medial aspect of the thyroid lobe was retracted, and a diluted methylene blue solution was applied after the middle thyroid vein and the upper pole had been ligated (0.5 ml methylene blue 2% diluted by 5 ml 0.9 saline). After spraying the dye, features such as the reticuloendothelial system (RLN), parathyroid glands, and arteries could be seen in the lobe and perilobar region.

The serum calcium was measured 24 h postoperatively. There was no routine use of postoperative calcium supplementation. Calcium was prescribed for patients with hypocalcemia. Hypocalcemia was considered if serum Ca was less than 8 mg/dl.

**Ethical consent:**

Research Ethics Council at Zagazig University approved the study (ZU-IRB6694/15-1-2020). All participants provided informed consent forms. Ethics guidelines for human by the World Medical Association's, Helsinki Declaration, were adhered to.

**Statistical analysis**

To analyze the data acquired, Statistical Package for the Social Sciences (SPSS), version 25 was used to execute it on a computer. The quantitative data were presented in the form of the mean and standard deviation. The qualitative data were presented as frequency and percentage.

Mann-Whitney test and Wilcoxon signed ranks test were used to assess the data while dealing with quantitative independent and paired variables respectively. Pearson Chi-Square ( $X^2$ ) and Fisher's

exact test were used to assess qualitatively independent data. P value of 0.05 or less was considered significant.

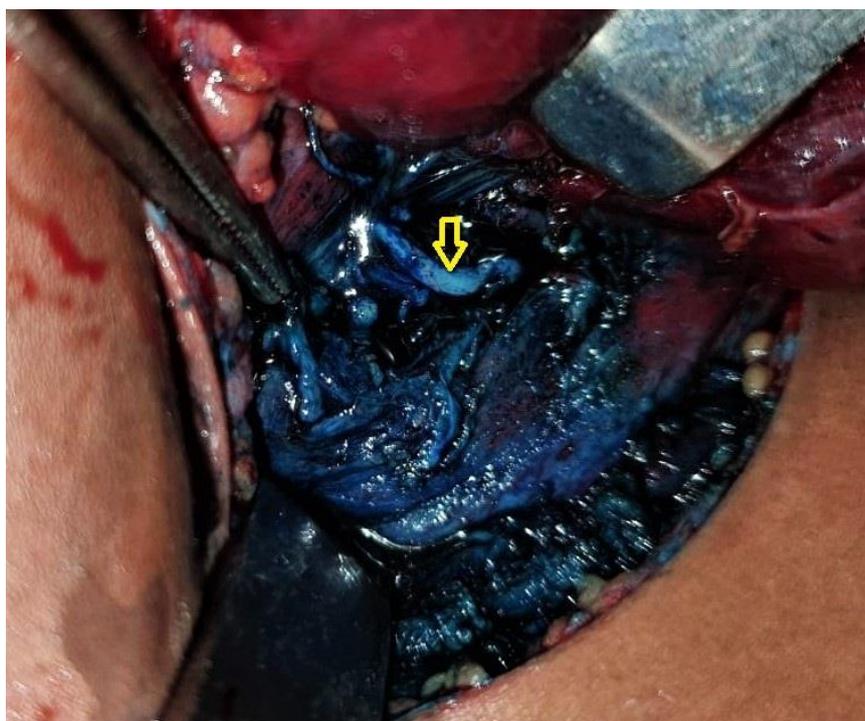
**RESULTS**

There was no significant difference between both groups as regard age and sex (Table 1).

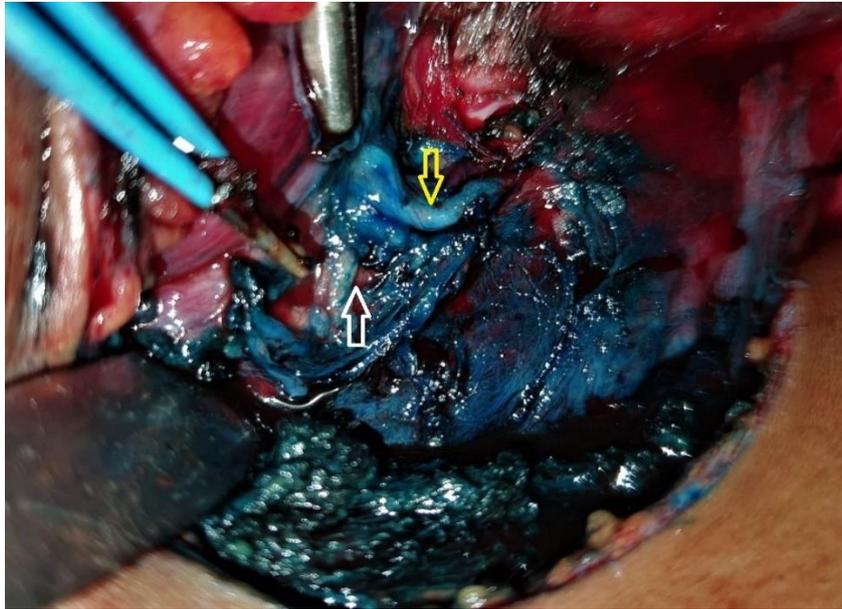
**Table (1):** The demographic data of both groups

	Groups	Mean ± Standard Deviation		P-value
		Age (years)	Group 1	
	Group 2	40.1000 ± 9.01224		
		Male	Female	P-value
sex	Group 1	3 (7.5 %)	37 (92.5%)	
	Group 2	2 (5%)	38 (95%)	

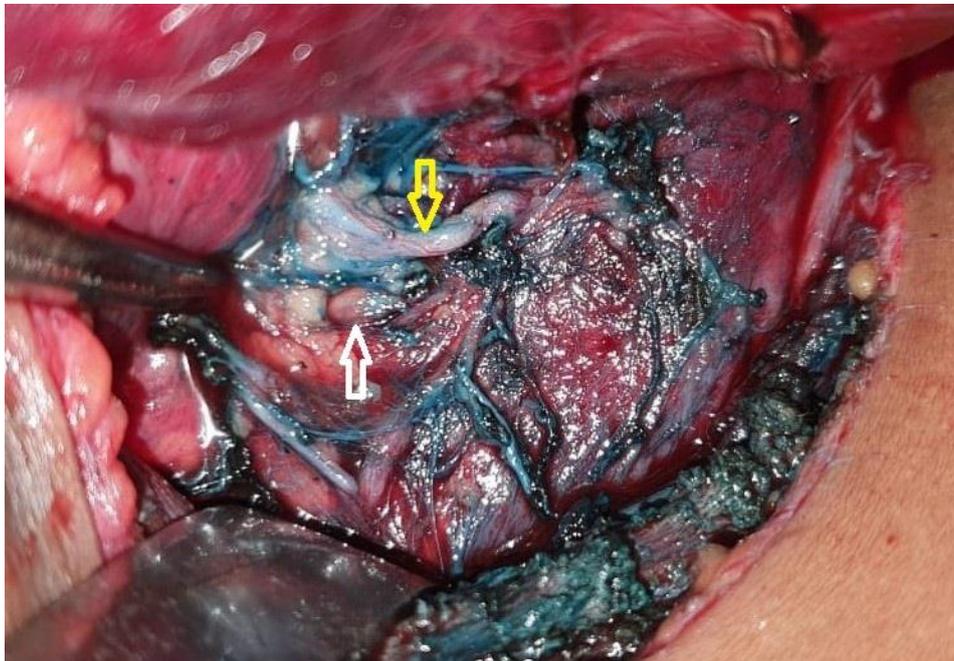
The recurrent laryngeal nerve did not stain with methylene blue in all cases in group 1, the parathyroid gland was stained initially, and the dye was washed out in 3 minutes from the parathyroid gland (Figs 1 and 2). Dye washout from the operative field was noticed after 7 minutes (Fig. 3). After the identification of the parathyroid gland all efforts to preserve the parathyroid and its blood supply were done.



**Fig. (1):** picture taken immediately after methylene blue spray. Notice the recurrent laryngeal nerve (marked by the yellow arrow) that appeared whitish in comparison to the bluish background. The parathyroid gland did not appear.



**Fig. (2):** Picture taken 3 minutes after methylene blue spray. Notice the recurrent laryngeal (marked by the yellow arrow) and parathyroid gland (marked by the white arrow).



**Fig. (3):** Picture taken 7 minutes after methylene blue spray. Notice the recurrent laryngeal (marked by the yellow arrow) and parathyroid gland (marked by the white arrow).

The preoperative serum Ca was not significantly different between both groups. Postoperative serum Ca was significantly decreased in both groups, but there was no significant difference between both groups regarding postoperative serum Ca level (Table 2).

**Table (2):** Preoperative and 24 hours postoperative Ca level in both groups

Ca (mg/dl)		Mean ± Standard Deviation	P-value
Preoperative Ca	Group 1	9.1925 ± 0.32612	0.242
Preoperative Ca	Group 2	9.1025 ± 0.27872	
Preoperative Ca	Group 1	9.1925 ± 0.32612	>0.001
Postoperative Ca		8.4225 ± 0.59290	
Preoperative Ca	Group 2	9.1025 ± 0.27872	>0.001
Postoperative Ca		8.2950 ± 0.51984	
Postoperative Ca	Group 1	8.4225±0.59290	0.304
Postoperative Ca	Group 2	8.2950±0.51984	

The RLN was identified for all patients of both groups without recorded nerve palsy. Identification of the parathyroid glands was considered when one of the parathyroid glands, at least, was identified and preserved. In group 1, parathyroid glands could not be identified in 5 patients versus 3 patients in group 2 which was considered insignificant (Table 3).

**Table (3):** Intraoperative identification of the RLN and parathyroid glands in both groups

		Parathyroids identification		P-value
		Identified	Non-identified	
Groups	Group 1	35 (87.5%)	5 (12.5%)	0.712
	Group 2	37 (92.5%)	3 (7.5%)	
		RLN identification		
		Identified		
Groups	Group 1	40 (100%)		
	Group 2	40 (100%)		

Among the studied patients, there was a significant relationship between the unidentified parathyroid gland and the occurrence of postoperative hypocalcemia (Table 4).

**Table (4):** The relation between early postoperative hypocalcemia and intraoperative identification of the parathyroid gland among the studied patients

Both Groups 1 and 2		Parathyroids identification		Total	P-value
		Identified	Non-identified		
Post-operative hypocalcemia	No hypocalcemia	60	2	62 (77.5%)	0.0001 8
	Hypocalcemia	12	6	18 (22.5%)	
Total		72	8	80	

The histopathological findings of the removed thyroid glands in this study were multinodular goiter, follicular adenoma, and colloid goiter with no significant differences between both groups (Table 5).

**Table (5):** The distribution of the excised histopathological gland among patients of both groups

		Postoperative histopathology			Total	P-value
		Multinodular goiter	Follicular adenoma	Colloid goiter		
Groups	Group 1	29	2	9	40	0.795
	Group 2	31	1	8		
Total		60	3	17	80	

## DISCUSSION

The occurrence complications has been decreased due to the advances in thyroid surgeries, but when occurred, they may cause lifelong handicaps. RLN and parathyroids injuries are commonly encountered complications. Meticulous dissection is the cornerstone factor for minimizing the occurrence these injuries [5-7]. Careful dissection may prevent parathyroid glands and RLN injuries. Various techniques are used including capsular dissection, attention to protect the blood supply to parathyroid glands and avoiding undue manipulation in the area of RLN [8].

Smith *et al.* [9] reported permanent and temporary RLN palsy rates of 1.7% and 6.1% respectively. Even with the use of intraoperative nerve monitoring, subsequent dissection did not determine the fate of RLN. There was no clear evidence that nerve monitoring has led to minimizing its injury [10]. Visual RLN identification remains essential factor for nerve preservation [11]. This is considered the gold standard of care and was supported by a multicenter study by Dralle *et al.* [12].

In this study, we compared two methods for the identification of the RLN and parathyroid glands, the first method depends on the anatomical localization of these structures, while the second method uses diluted methylene blue spray to help their identification.

Patient identification of the RLN and parathyroid glands did not differ significantly between the two groups. Group 2 patients were more likely than group 1 individuals to have at least one parathyroid gland identified. Postoperative hypocalcemia also did not differ significantly between groups.

Hypocalcemic patients in both groups received oral calcium therapy. Hypocalcemia was transient and no patient needed supplementation more than two months.

In a study by Monib and his colleagues [13], parathyroid glands, were identified intraoperatively in 82% of cases (N=41/50) by using methylene blue spray. Farghaly *et al.* [14] reported that the methylene blue spraying technique was effective in RLN identification without recorded injury in 50/50 (100%) versus one case (1/50) suffered from bilateral vocal cord affection in anatomical identification technique.

In this study, the development of postoperative hypocalcemia in patients (of both groups) with unidentified parathyroid glands was 6/8 (75%). This signifies the importance of the identification of the parathyroid gland during thyroidectomy.

## CONCLUSION

Methylene blue dye spraying is technically feasible, safe, and effective method for identifying and protecting the RLN and parathyroid glands during thyroidectomy. It can be used as adjunct for the identification of these structures in difficult cases. Minimizing postoperative hypocalcemia requires accurate identification of at least one of the parathyroid glands.

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**Author contribution:** Authors contributed equally in the study.

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