Methylene Blue Injection in the Inferior Thyroid Artery for Identification of Parathyroid Glands during Thyroidectomy

Mohamed Aboul Naga, MD; Mostafa Omar Abdelrahman, MD; Mahmoud Talaat, MD
Department of General Surgery, Faculty of Medicine, Ain Shams University

Introduction: One typical delayed consequence following thyroidectomy is hypocalcemia. Numerous studies have done to identify risk factors and how to avoid hypocalcemia following thyroidectomy. Our study aims to assess the usefulness of an intraoperative methylene blue injection in the inferior thyroid artery during thyroidectomy for parathyroid gland identification.

Aim of work: To identify parathyroid gland intraoperatively by injection of sterile methylene blue.

Patients and methods: We have conducted a prospective non-randomized cohort study with 50 patients who underwent hemithyroidectomy or total thyroidectomy between June 2021 and sept 2022. During thyroidectomy, 1 ml (10 mg) of 1% methylene blue was injected in the inferior thyroid artery.

Results: Intraoperative injection of methylene blue has a significant effect in reduction of post operative hypocalcemia and hypoparathyroidism.

Conclusion: Use of methylene blue injection in the inferior thyroid artery is an effective method to identify parathyroid gland during thyroidectomy and so reduce the incidence of postoperative hypocalcemia.

Key words: Thyroidectomy, parathyroid gland, methylene blue spray, ypocalcemia.

Introduction

Ca2+ equilibrium is maintained by parathyroid glands. Following a thyroidectomy, damage to the parathyroid glands or their blood supply may cause 3.3% of patients to experience lifelong hypocalcaemia or 33.3% to experience transitory hypocalcaemia.[1]

Following surgery, calcium medication is necessary for more than six months in order to address hypocalcaemia. Regrettably, hypocalcemia not only impairs patients' emotional and physical well-being but also prolongs their hospital stay. Perioral or finger numbness, cramps, convulsions, muscular spasms, cardiac arrhythmia, and, in more severe situations, a positive Chvostek's sign can all be indicators of hypocalcaemia. First-line treatment for the illness might involve calcium supplements and vitamin D.[2]

Optical coherence tomography during thyroid surgery, parathyroid specific luminescence, fine needle aspiration cytology for parathyroid analysis, measurement of parathyroid hormone levels in blood or an intravenous methylene blue injection are some of the methods used to correctly identify the parathyroid thyroid glands and prevent affection during thyroid surgery.[3]

Heinrich Caro initially introduced methylene blue in 1876. This thiazine dye, also called methylthioninium chloride, changes hemoglobin's ferric iron into ferrous iron. Although it is no longer advised for these uses, methylene blue was primarily used to treat cyanide poisoning, urinary tract infections, and methemoglobinemia. Headache, dizziness, difficulty breathing, elevated blood pressure, serotonin syndrome, hemolysis, and allergic responses are some of the side effects. Urine, sweat, and feces can frequently become blue or green after receiving methylene blue injections.[4]

Although easily accessible, methylene blue dye might have some side effects, particularly when used intravenously. In order to prevent injuries and further difficulties, our goal was to assess the diagnostic utility of identifying parathyroid glands during thyroidectomy using a methylene blue spray.

Aim of work

We aimed to evaluate the safety and reliability of the methylene blue injection technique in the identification of parathyroid glands as a cheap modality which does not entail the use of costly equipment or require further training to decrease post-thyroidectomy hypocalcaemia

Pathients and methods

Study population: Type of Study: This is a retrospective study. An investigation was conducted on fifty individuals who had complete thyroidectomies at AS University Hospital between June 2021 and September 2022. 30% (N=15) were male and 70% (N=35) were female, with ages ranging from 20 to 48 34.20 ± 14.96.

Study setting: ASU hospitals, Airforce Specialized Hospital and Cairo Specialized Hospital.

Study period: Between June 2021 and sept 2022

DOI: 10.21608/ASJS.2024.351443

Study population

Inclusion criteria

All patient candidate for total thyroidectomy.

Exclusion criteria

1. Recurrent goiter.
2. All patient with goiter needs more then thyroidectomy such as malignant goiter need lymphadenectomy.
3. Patient refusal.
4. Previous neck surgery.

Sample size: The required sample size has been estimated to be 30 patients.

Ethical considerations

1. An approval was taken from all patients to perform this new technique.
2. All data were confidential and patients were not mentioned by name in any published paper.
3. Patients had the right to refuse joining the research or withdraw at any time without affecting their chance to receive the traditional therapy at any time.
4. Approval of the ethical committee and approval of participants were obtained.

Study procedures

All patients included in the study will be candidates for:

1-Clinical assessment:

- Detailed medical, surgical and family history.
- General examination.
- Local breast examination.

2-Investigations:

- Routine laboratory investigations.
- Neck US.
- Serum calcium level.

3-Intervention:

Patients were subjected to low neck incision of skin, subcutaneous fat and platysma muscle. Followed by midline incision in the deep cervical fascia, one or both lobes were dissected from strap muscles to see the anterolateral surface clearly. Sterile methylene blue was injected in the inferior and/or superior thyroid artery(s). hot towel was placed over the thyroid gland. We waited for 3 minutes till complete discoloration of the thyroid gland by blue color. At this point PTG did not take the dye and seen clearly. Carful dissection of the superior and inferior poles preserving all PTGs was done. Then we was completed all steps of thyroidectomy.

4-Follow-up:

Serum Ca was applied weekly for a month from Day 0.

Patients were monitored for hypocalcemia symptoms, such as perioral paraesthesia, cramps, numb fingers, delirium, convulsions, signs of confusion, disorientation, and delirium, as well as Chvostek's and Trousseau's signs.

We measured serum PTH if there was a decrease in serum Ca levels at any time.

Results

The mean age of all patients was 34 years, with SD 14. Of all patients in this study there were 35 female and 15 male.

In this study, 14 of our patients (28%) were diabetic, 11 patients (22%) were hypertensive and 1 patient (2%) was having ischemic heart disease.

According to TIRADS score no patient with TIRADS score 1 and 6 were included in this study. 30 patient (60%) with TIRADS score 2, 14 patients (28%), 4 patients (8%) and 2 patients (2%) were included in this study.

As shown in the last table only 3 patients out of 50 suffered from Tingling and circumoral numbness (6%). Only one patient suffered from Neurological symptoms in the form of confusion and delirium (2%).

In this study 3 patients from total 50 suffered from D0 had hypocalcemia. In patients of D1 there were 2 out of 50. Then from week 1 till week 3 only one suffered from delayed hypocalcemia. By w4 there were no patient with hypocalcemia.

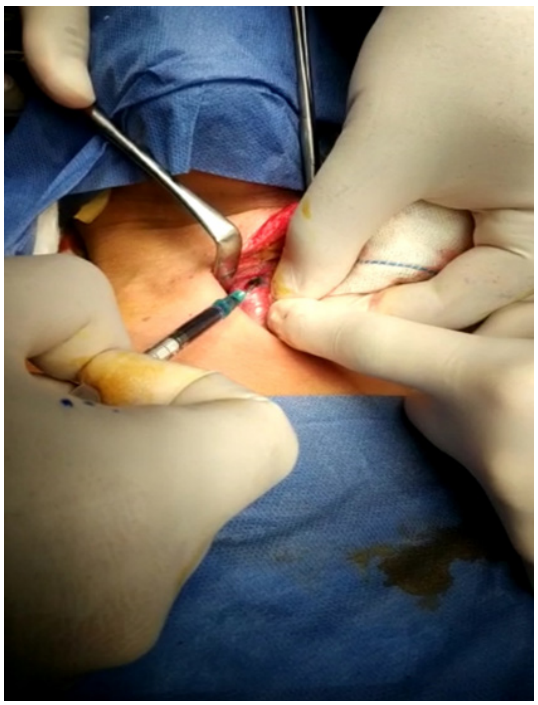
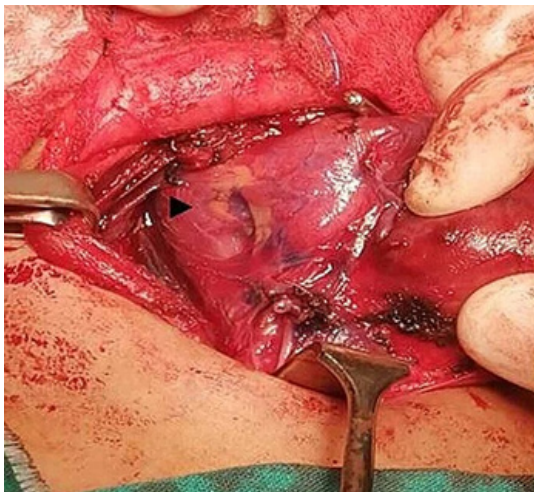


Fig 1: Injection of methylene blue in the Inferior thyroid artery.



Figs 2,3: Before and after injection of methylene blue.

Table 1: Shows age and gender of our patients

		No. = 15
Age	Mean±SD	34.20 ± 14.96
	Range	20 – 48
Gender	Female	35
	Male	15

Table 2: Shows medical history of our patients

		No.	%
Diabetic	No	36	72.0%
	Yes	14	28.0%
Hypertensive	No	39	78%
	Yes	11	22%
IHD	No	49	98 %
	Yes	1	2%

Table 3: Show the pathology according to TIRADS score

		No.	%
Location of tumour	1	0	0%
	2	30	60.0%
	3	14	28%
	4	4	8%
	5	2	4%
	6	0	0%

Table 4: Intraoperative identification of PTG after 5 mins from injection of methylene blue

	No.	%
Identified	47	94.0%
Not Identified	3	6.0%

Table 5: Postoperative Symptoms of hypocalcemia

		No.	%
Tingling and circumoral numbness	No	47	94.0%
	Yes	3	6.0%
Neurological symptoms (confusion or delirium)	No	49	98.0%
	Yes	1	2.0%
Chvostek's sign, Trousseau's sign	No	49	98%
	Yes	1	2%
		1	

Table 6: Postoperative follow up of serum Ca level (Hypocalcemia)

			%
D0	No	47	94%
	Yes	3	6%
D1	No	48	96%
	Yes	2	4%
W1	No	49	98%
	Yes	1	2%
W2	No	49	98%
	Yes	1	2%
	No	49	98%
W3	Yes	1	2%
W4	No	50	100%
	Yes	0	0%

Table 7: Show the level of PTH in the 3 patents with hypocalcemia in the previous table

		No from total 50
Hypoparathyroidism	Do	3
	D1	3
	W1	2
	W2	2
	W3	1
	W4	1

Discussion

To reduce the frequency of post-operative hypocalcemia, a number of techniques have been done to identify the parathyroid gland.

The United States Food and Drug Administration has approved methylene blue. Numerous medical conditions can benefit from its application, such as acute acquired methemoglobinemia, hereditary methemoglobinemia, geriatric urinary tract infection prevention, and the localization of neurons and endocrine organs. Methylene blue has a limited number of adverse effects. However, if more than five mg/kg is administered, toxicity may develop. Toxic symptoms include headaches, nausea, vomiting, disorientation, headaches, stomach discomfort, and confusion.[5]

In sentinel lymph node biopsies, methylene blue, an aromatic heterocyclic chemical molecule, has been employed extensively in recent years. Staining the parathyroid glands is not a novel method for preventing hypoparathyroidism; Klopper et al. initially reported it in 1966. The initial dyes that the authors utilized were trypan blue, which is a derivative of toluidine, and toluidine blue. Methylene blue started to replace them as their possible teratogenic consequences were identified. The majority of writers discussed the intravenous infusion (IVI) of methylene blue during thyroid surgery. It is safe for IVI, though, as the injection in ITA is more accurate and requires a smaller dosage.[6]

Spray is an alternative way but need time for absorption and lower accuracy then injection in the ITA

In a prior study, the parathyroid gland was located using methylene blue spray on 56 individuals who had thyroidectomies. It took three minutes for the parathyroid gland to absorb the blue dye and return to its natural yellow hue, whereas other tissues required more time. It took them 15 minutes to find the thyroid, and almost 25 minutes to find the fat, tendon, and muscle. They postulated that parathyroid glands' rich lymphovascular architecture allows them to absorb methylene blue more quickly than other tissues.[7]

There were fifty patients in this trial. We also assessed the methylene blue injection's **(Fig. 1)** diagnostic utility in the inferior thyroid artery. Methylene blue injection has a 94% sensitivity and a 95% specificity. According to our findings, methylene blue injection in the ITA was a very sensitive screening method that could be used to detect the parathyroid gland without injuring it **(Figs. 2,3)**.

To achieve this high sensitivity, the surgeon needs to identify the area suspected to be parathyroid gland first and confirms by methylene blue injection. The solely use of methylene blue injection without surgical skills and knowledge was highly not recommended.

In contrast to previous studies using other tools of PTG identification, injection of methylene blue delivers the dye only to thyroid gland faster and more precise **(Table 4)**.

In a research conducted by Monib et al., fifty patients (aged 43.0±9.7) ranging in age from 18 to 80 years were included. With no major surgical problems, we were able to identify the parathyroid glands in 82% of instances using the intraoperative methylene blue spray. In 2020.[8]

In this investigation, the methylene blue injection's sensitivity was 94%, while its specificity was 95%.

In our study **(Table 6)** only 6 patient developed

very mild symptoms of hypocalcemia and only one patient developed hypoparathyroidism (2%). That resolved spontaneously after one month **(Table 7)**.

Research in the literature indicates that there are no appreciable variations in the incidence of complications between patients receiving a complete or partial thyroidectomy without the use of the methylene blue spraying technique and their study cohorts. However, our research reveals significant variances.

It was noted that the parathyroid glands had a wash-out period of less than three minutes, but the thyroid glands required more than fifteen minutes. We speculate that the tissues' lympho-vascular patterns account for the variations in time. The lymphovascular system of parathyroid glands is very thick histologically. This tissue feature is essential for the quick removal of methylene blue stains. Veins instantly become blue due to the transportation of methylene dye from tissues.

Conclusion

During total thyroidectomy most surgeons aim to preserve the parathyroid glands from potential risks and thus hypocalcemia. The sooner the parathyroid glands are identified, the lower the surgeon's level of stress.

Our new technique for safe thyroidectomy is based on visualization of the parathyroid glands. We demonstrated the effectiveness of the injection technique plus the lack of necessity of postoperative intravascular cannulation, along with its potential risks. This new technique ensures identification of parathyroid glands within three minutes.

References

1. Reeve T, Thompson NW: Complications of thyroid surgery: How to avoid them, how to manage them, and observations on their possible effect on the whole patient. ***World J Surg.*** 2000; 24: 971–975.
2. Falk SA, Birken EA, Baran DT: Temporary postthyroidectomy hypocalcaemia ***Otolaryngol Head Neck Surg.*** 1988; 114: 168–174.
3. Sommerey S, Al Arabi N, Ladurner R, et al: Intraoperative optical coherence tomography imaging to identify parathyroid glands. ***Surg Endosc.*** 2015; 29: 2698–2704.
4. Yan Huang H, Li H, jian Lin S, et al: Fine-needle aspiration with measurement of parathyroid hormone levels in thyroidectomy [Article in Chinese] https://pubmed.ncbi.nlm.nih.***gov/24444640/ Zhonghua Er Bi Yan Hou Tou Jing Wai Ke Za Zhi.*** 2013;48:934–938.
5. Evangelos B, Devang K: Methylene Blue, National center of biochemistry. 2023; 23(4): 270-4.
6. Gillman PK: Methylene blue implicated in potentially fatal serotonin toxicity. ***Anaesthesia.*** 2006; 61: 1013–1014.
7. Sari E, Aysan E, Muslumanoglu M, et al: Safe thyroidectomy with intraoperative methylene blue spraying. ***Thyroid Research.*** 2012; 5(1): 15.
8. Sherif M, Abdullah M, Mohamed IA: Methylene blue spray for identification of parathyroid glands during thyroidectomy. ***Cureus.*** 2020; 12(11).