

Using Methylene Blue Spray during Thyroidectomy for Preserving Recurrent Laryngeal Nerve

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Abstract

Background: The main postoperative complication of thyroidectomy is recurrent laryngeal nerve (RLN) injury. RLN is identified by its relationships with inferior thyroid artery, tracheoesophageal groove and ligament of Berry. This method may not be always accurate due to anatomical variations. Different adjuvant methods have been used to aid in the identification of the nerve. Nerve fibre staining with methylene blue (MB) is a known method during parotid surgery.

Aim of Study: This study aimed to evaluate the value of using methylene blue spray during thyroidectomy to properly identify and preserve RLN during surgery to improve outcomes following thyroidectomy.

Patients and Methods: This study was a prospective study done on sixty two patients with benign and malignant goiter disorders who were admitted at Ain Shams University Hospital and underwent total thyroidectomy in the period from January 2021 to December 2021 at endocrine surgery unit. Patients with reoperative surgery, presence of preoperative cord dysfunction were excluded from study. Patients were randomized into two groups with an equal number of candidates (n=31) using the lottery method. 31 patients underwent thyroidectomy as study group with methylene blue spray and other 31 patients were operated without methylene blue spray as control group. During the surgery, after ligation of superior pole of thyroid and the thyroid lobe could be deviated medially, One ml of 1% methylene blue solution (10mg) was sprayed over the thyroid bed and perithyroidal tissue. This area includes the parathyroid glands, inferior thyroid artery, veins and recurrent laryngeal nerve. The entire area was irrigated by normal saline solution to rinse the MB out of the surrounding tissue. After 10min, the thyroid bed was inspected for areas in which the blue color was rapidly absorbed. Comparisons between studied groups were collected.

Results: Intraoperatively, recurrent laryngeal nerve was not stained and remained white in all cases while all other tissues were stained blue. RLN could be identified in all the patient, as an unstained structure in the tracheoesophageal groove. Four to seven minutes later the parathyroid glands washed out the blue stain and regain their original yellow color. It took nearly 15 minutes for the thyroid tissue to wash out the stain in all cases.

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Conclusion: Intra-operative RLN identification by MB staining is safe, cheap and readily available method and could make thyroidectomy dissection less stressful.

Key Words: *Thyroidectomy – Methylene blue spray – Recurrent laryngeal nerve.*

Introduction

THYROIDECTOMY is one of the most frequent operations performed in iodine-deficient regions [1].

Recurrent laryngeal nerve (RLN) injury and hypoparathyroidism are the main postoperative complications of thyroidectomy [2].

The surgeon's in experience, reoperation for completion, thyroid gland volume and the extent of resection are risk factors for morbidity of thyroid surgery. Meticulous dissection is a key factor in minimizing the development of complications [3].

Although the overall incidence of nerve palsy is low, when it occurs, nerve palsy is a devastating life-long handicap [4].

Most surgeons identify the RLN intraoperatively via its anatomic relationships with the inferior thyroid artery, tracheoesophageal groove, and ligament of Berry as anatomical landmarks. However, because of the numerous variations of this neurovascular relationship altered also by pathologic conditions of the gland, identification of the inferior thyroid artery does not assure accurate identification and preservation of the recurrent laryngeal nerve [3].

To help identify the RLN and measure its function immediately before thyroid resection, various medical devices have been developed since 1987 for intraoperative use. Several methods have been described for RLN monitoring intraoperative such

as: Finger palpation of the cricoarytenoid muscle during nerve stimulation, vocal cord observation by fiberoptic or direct laryngoscopy and the use of intramuscular vocal cord electrodes [5].

Methylene blue dye is readily available and used medically, but not without its probable complications, especially if injected intravenously. Several publications report complications ranging from blue staining of the skin and fat necrosis [6].

The dye is inexpensive, it can be easily and safely applied, unless by an inexperienced surgeon.

In this study, we tried a novel method of identification of RLN intraoperatively, by spraying methylene blue dye in the tracheoesophageal groove area, after ligation of superior pole during dissection of the thyroid. Identification of RLN at this stage will help the surgeon to take adequate measures to preserve the nerve and avoid damage during dissection.

Material and Methods

Study design:

This is prospective study included patients with benign and malignant goiter disorders who were admitted at Ain Shams University Hospital underwent primary (not recurrent) total thyroidectomy in the period from January 2021 to December 2021. This study was ethically approved from Ain Shams University Hospital Surgical Department Ethics Committee prior to commencing the study.

Ethical considerations:

Patients involved in the study were informed by simple explanation of the study. Written informed consent was obtained from them. Approval from Ethical Committee Department of Ain Shams University was taken.

Study subjects:

Sixty two patients with thyroid disease, scheduled for total thyroidectomy, were included within this study. 31 patients chosen at random underwent total thyroidectomy as study group with methylene blue spray and other 31 patients were operated without methylene blue spray as control group. Patients aged less than 18 years or preoperative thyroid surgery or preoperative vocal cord paresis or patients unwilling to take part in the study were excluded. All patients underwent laryngoscopy to assess vocal folds mobility preoperatively.

Surgical work:

Under general anesthesia operations were performed by experienced endocrine surgeons in en-

docrine unit at Ain Shams University. In each patient, both before and after surgery indirect laryngoscopic examination were performed to evaluate vocal cord motility.

After a standard Kocher incision, total thyroidectomy was performed. Following the elevation of flaps, middle thyroid vein ligation and dissection of thyroid lobes were done. To allow the gland to be rotated medially and facilitate access to the recurrent laryngeal nerve (RLN) and parathyroid glands, the upper and lower poles were freed and their vessels were ligated as follow:

The superior pole was ligated and cut. Normally, at this stage, the identification of RLN or the parathyroid is difficult.

Once the vessels were safely controlled, the gland was mobilized inferiorly and medially. The lower pole veins were divided and ligated close to the gland.

Once the upper and lower poles were controlled and dissected, the gland was rotated medially, allowing access to its posterolateral surface as Fig. (1). In the area where the RLN was suspected to loop to enter the trachea-esophageal groove, cautious dissection was done layer by layer parallel to the suspected RLN course.

At this point in the surgery, neither the parathyroid glands nor RLN could be easily identified.

The thyroid lobe was deviated medially and One ml of 1% methylene blue solution (10mg) was sprayed over the thyroid bed and perithyroidal tissue as Fig. (2). This area includes the parathyroid glands, inferior thyroid artery, veins and recurrent laryngeal nerve. The entire area was irrigated by normal saline solution to rinse the MB out of the surrounding tissue.

After 10min, the thyroid bed was inspected for areas in which the blue color was rapidly absorbed. Thyroid gland was still stained blue, RLN was unstained at all. Four to seven minutes later the parathyroid glands washed out the blue stain and regain their original yellow color. It took nearly 15 minutes for the thyroid tissue to wash out the stain in all cases. Tissues were identified and evaluated, especially the recurrent laryngeal nerve as Fig. (3).

The other 31 patients were operated without methylene blue spray like tradition technique. The patients received standard post-operative care. The post-operative complications and duration of hospital stay were recorded. A repeat indirect laryn-

goscopic examination was carried out to assess vocal cord mobility postoperatively.

Data was entered, cleaned and analyzed, using the statistical package for social sciences, SPSS version 26 (SPSS Inc., Chicago, Illinois, USA) Results will be considered significant when p -value is less than 0.05.



Fig. (1): Thyroid gland rotated medially, before applying of methylene blue.



Fig. (2): Thyroid gland rotated medially, immediate after applying of methylene blue.

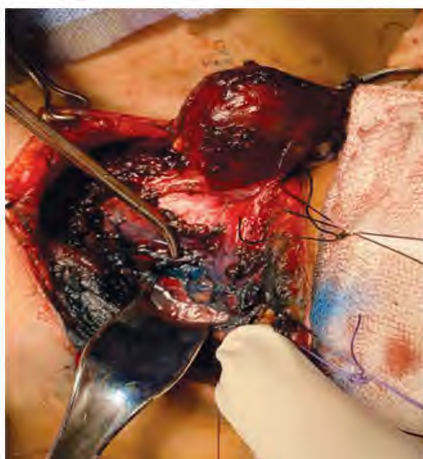


Fig. (3): (10 min) after applying of methylene blue spray, tip of artery instrument pointing to RLN unstained.

Results

All 62 patients underwent total thyroidectomy for goitrous thyroid enlargement. RLN could be identified in all the patients with methylene blue spray, as an unstained structure in the tracheoesophageal groove Fig. (3).

With MB staining, recurrent laryngeal nerve was not stained at all cases of patient group. RLN remain white while all other tissues stained blue. The nerve could be identified easily at tracheoesophageal groove. Four to seven minutes later the parathyroid glands washed out the blue stain and regain their original yellow color. It took nearly 15 minutes for the thyroid tissue to wash out the stain in all cases. No vocal cord palsy detected postoperatively.

Comparisons between studied group regarding demographic data, timing of operations and complications were carried out.

A total of 62 patients participated in this study, nineteen were male (30.6%) and 43 of whom were female (69.4%). The average age was 40.5 years old (ranging from 25 to 51 years old). There was statistically non-significant difference between the studied groups regarding demographic data. Table (1).

Duration of thyroidectomy among studied groups was calculated per minute. Timing started after separation of the strap muscles in the midline to the end of thyroidectomy. The mean thyroidectomy duration (started after separation of the strap muscles in the midline to the end of thyroidectomy) with RLN visual identification alone was 46.7 ± 2.2 min, while it was 51.4 ± 2.3 min with MB application, with statistically significant difference. Table (2).

Hospital stay ranged from one to three days (1.5 ± 0.7), during which time patients underwent clinical assessments, calcium level monitoring and treatment for hypocalcaemia.

No permanent postoperative vocal cord palsy was reported among studied groups. Only three cases (9%) had biochemical hypocalcaemia in the control group in early postoperative period and improved after 2 weeks. No other complications were reported during a follow-up period of 6 months.

Statistical methods:

The data was organized and statistically analyzed using the Statistical Package for Social

Sciences (SPSS) Statistics version 26 (IBM Corp., Armonk, NY, USA). For quantitative data, the mean, standard deviation (SD), and range were calculated. For interpretation of the results of significance tests, *p*-values were considered significant at *p*<0.05.

Table (1): Comparison between the studied groups regarding demographic data.

Parameters	Groups		Test
	(Study group) with MB spray. N=31	(Control group) without MB spray. N=31	<i>p</i>
<i>Age (year):</i>			
Mean ± SD	42.29±7.161	38.42±5.130	0.172
Range	25-51	31-50	
<i>Gender:</i>			
Female	26 (41.9%)	17 (27.4%)	
Male	5 (8%)	14 (22.7%)	
<i>BMI:</i>			
Mean ± SD	26.52±3.075	26.48±3.032	0.575
Range	21-32	21-32	

p-value-MB: Methylene blue.

BMI: Body mass index-SD standard deviation.

***p*≤0.05 is statistically significant.

Table (2): Comparison between the studied groups regarding timing of operation between studied groups.

Parameters	Groups		Test
	(Study group) with MB spray. N=31	(Control group) without MB spray. N=31	<i>p</i>
<i>Timing (min):</i>			
Mean ± SD	51.4±2.306	46.7±2.241	<0.0001
Range	47-56	43-50	

Discussion

The most important and serious complications following thyroidectomy are RLN injury and parathyroid insufficiency, when they occur, they cause catastrophic lifelong handicap [7].

In a recent multicenter trial of 16,448 thyroidectomies, Dralle H. et al., concluded that visual nerve identification, in respect to RLN treatment, emerged as the “gold standard” of care [8].

In the present study, we aimed to investigate whether methylene blue spraying technique during total thyroidectomy will allow us to safely identify RLN.

Intra-operative RLN identification with MB in thyroidectomy is almost costless. It gives the sur-

geons more confirmation of the anatomically suspected nerve with less stress and clearer field that helps the surgeons to identify and protect the RLN without adding more risk. MB staining can be combined with other techniques such as identification of the anatomical landmarks or use of nerve detection devices.

In 2012, Sari S. et al., studied the effects of methylene blue spraying in identification of RLN and performing safe thyroidectomy. They observed that dye did not stain the RLN while all other tissues stained blue. Further, it was noted that although the parathyroid glands were stained, they washed out the color in three minutes and was visible in their original yellow color [3].

We obtained similar results in our study also. In all 31 patients, the RLN was visible as an unstained white structure in the blue stained background and could be easily identified. Regarding parathyroid glands, four to seven minutes later the parathyroid glands washed out the blue stain and regain their original yellow color. It took nearly 15 minutes for the thyroid tissue to wash out the stain in all cases.

A.A.F. Nofal, 2016, studied application of MB in 46 patients to assess RLN identification and preservation during total thyroidectomy by intra-operative RLN staining with MB in one side and compare it with visual identification alone in the other side in same patient. The mean lobectomy time (started after separation of the strap muscles in the midline to the end of lobectomy) between both sides has statistically significant difference like our results [9].

In current study, transient biochemical hypocalcaemia was detected in three cases (9%) in the control group in early postoperative period with no reported clinical or permanent cases. This incidence is near to the lowest rates detected in the literatures for transient hypoparathyroidism (6.9-46%) and permanent hypoparathyroidism (0.4-3.3%) [10].

No complications from MB use were reported in the current study ensuring the safety of MB staining.

The limitation of present study was the small sample size. There is a need for a study with a larger sample size for strengthening the results.

The results of this study can be applied in order to help to identify the parathyroid gland during thyroidectomy and may decrease post-operative hypocalcemia.

Conclusion:

Intra-operative RLN identification by MB staining is safe, cheap and readily available method and could make thyroidectomy dissection less stressful.

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استخدام رش الميثيلين الأزرق أثناء استئصال الغدة الدرقية للحفاظ على العصب الحنجري الراجع

استئصال الغدة الدرقية هي واحدة من أكثر العمليات المتكررة التي تتم في المناطق التي تعاني من نقص اليود. المضاعفات الرئيسية بعد العملية الجراحية لاستئصال الغدة الدرقية هي شلل العصب الحنجري الراجع ونقص افراز الغدة جار الدرقية.

على الرغم من أن معدل الإصابة بالشلل العصبى منخفض، إلا أنه عند حدوثه، يكون الشلل العصبى عائقاً مدمراً مدى الحياة.

يتعرف معظم الجراحين على مكان العصب الحنجري أثناء الجراحة من خلال علاقته التشريحية مع الشريان الدرقي السفلى والأخدود الرغامى المريئى ورباط بيرى باعتبارها معالم تشريحية. ومع ذلك، وبسبب الاختلافات العديدة في هذه العلاقة العصبية الوعائية التي تغيرت أيضاً بسبب الظروف المرضية للغدة، فإن تحديد الشريان الدرقي السفلى لا يضمن التحديد الدقيق للعصب الحنجري الراجع والحفاظ عليه.

تم تطوير العديد من الأجهزة الطبية منذ عام ١٩٨٧ للاستخدام أثناء الجراحة للمساعدة في تحديد العصب الحنجري الراجع وتم وصف عدة طرق لمراقبة العصب الحنجري أثناء العملية مثل ملاسة الأصابع للعضلة الحلقية أثناء تحفيز العصب، ومراقبة الحبل الصوتى عن طريق التنظير الليفي أو التنظير المباشر للحنجرة واستخدام أقطاب الحبل الصوتى العضلى.

صبغة الميثيلين الزرقاء متاحة بسهولة وتستخدم طبيياً، ولكن ليس بدون مضاعفاتها المحتملة، خاصة إذا تم حقنها عن طريق الوريد. تشير العديد من المنشورات إلى حدوث مضاعفات تتراوح بين تلطخ الجلد باللون الأزرق ونخر الدهون. الصبغة غير مكلفة، ويمكن تطبيقها بسهولة وأمان، ما لم يكن من قبل جراح غير متمرس.

في هذه الدراسة، جربنا طريقة جديدة لتحديد العصب الحنجري الراجع أثناء الجراحة، عن طريق رش صبغة الميثيلين الزرقاء في منطقة الأخدود الرغامى.