Conventional surgical techniques versus intraoperative methylene blue spraying for safe total thyroidectomy

Abd-Elradi Abd-Elsalam Farghaly, Mostafa T. Ahmed, Mohamed B. M. Kotb, Ibrahim A. Ibrahim

Department of General Surgery, Faculty of Medicine, Assiut University, Assiut, Egypt

Correspondence to Ibrahim A. Ibrahim, Msc, Department of General Surgery, Faculty of Medicine, Assiut University, Assiut Abnoub Gomhoria St., Assiut, Egypt
Zib Code: 71514; Tel: 01113089781;
e-mail: Dr.hima2020@gmail.com

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Background
Thyroidectomy is one of the most surgical interventions in endocrine surgery. When the operation is performed in respective surgical centers, the operation is safe with low morbidity and ~0% mortality.

Patients and methods
The study was a quasi-experimental study carried out at Assiut University Hospital. One hundred patients with benign and malignant goiter disorders underwent primary (not recurrent) total thyroidectomy. The patients were assigned into two groups: group 1 (interventional group) included 50 cases operated upon with methylene blue spraying technique and group 2 (control group) 50 cases established with the conventional technique. Methylene blue was sprayed over the thyroid lobe and perilober area. Parathyroides and recurrent laryngeal nerve were identified and evaluated.

Results
Recurrent laryngeal nerve was not stained and remained white in all cases while all other tissues were stained blue. Three minutes later the parathyroid glands washed out the blue stain and regain their original yellow color. Thyroid gland wash-out time was ~15 min.

Conclusion
Methylene blue spraying is a new technique that allows identification of both parathyroid glands and recurrent laryngeal nerves. This technique is safe, effective, and technically feasible.

Keywords:
intraoperative, methylene blue, safe, spraying, thyroidectomy

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Background

Thyroidectomy is one of the most surgical interventions in endocrine surgery. When the operation is performed in respective surgical centers, the operation is safe with low morbidity and ~0% mortality [1]. Complications of thyroid surgery are directly correlated to the extent of resection and are inversely proportional to the experience of the surgeon [1,2]. Therefore, the cornerstones of safe and effective thyroid surgery are adequate training, the understanding of the anatomy and pathology, and choosing a meticulous dissection technique.

The meticulous dissection technique can be achieved by proper exposure of all fine anatomic structures in a bloodless dry surgical field. Furthermore, the dissection must be based on a perfect knowledge of the three-dimensional topographic anatomy, typical landmarks, and possible anatomic variations.

Patients and methods

Study design

This was a quasi-experimental study carried out at Assiut University Hospital. Ethical Review Board in Assiut Faculty of Medicine approved the study, and a consent was taken from all patients who were included in the study. The hospital is a main teaching hospital for Assiut University Faculty of Medicine. The study was conducted between May 2016 and February 2017. Informed consent was obtained from all patients.

Study participants

One hundred patients with benign and malignant goiter disorders underwent total thyroidectomy. Those with reoperative surgery, presence of preoperative vocal cord dysfunction, and impaired mental state were excluded. The patients were assigned into two groups: group 1 (interventional group) included 50 cases operated upon with methylene blue spraying technique and group 2 (control group) included 50 cases established with the conventional technique.

All patients were subjected to:

Serum T_3, T_4, and TSH levels estimation, vocal cord examination by direct laryngoscope, serum calcium level determination (total and ionized), neck ultrasound, and fine-needle aspiration cytology.

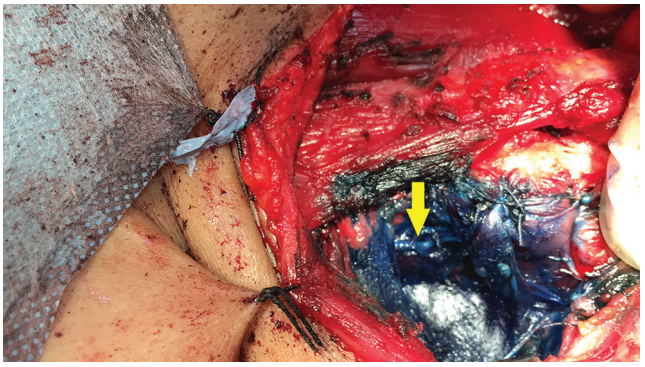
Follow-up was offered to all patients particularly those who developed hypoparathyroidism and monitoring of calcium level was done every week until serum calcium level returned to normal.

Procedure

Surgeons of Assiut General Surgery Department performed operations and we used general anesthesia.

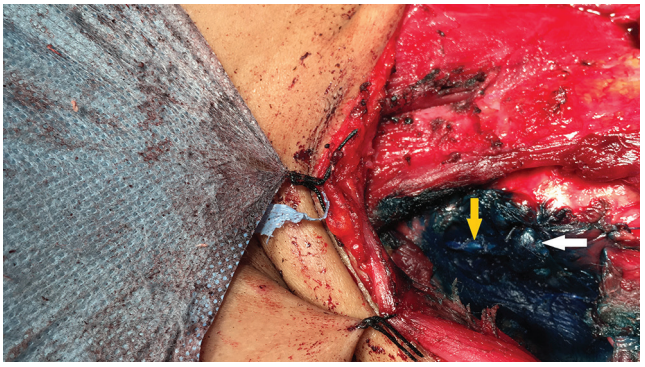
Collar incision was made in the skin, the subcutaneous tissue, and platysma muscle. And the strap muscles separated vertically in the midline and retracted laterally, the middle thyroid vein ligated, and the superior pole of the thyroid dissected. Division of the superior vessels enables us to medially rotate and anteriorly mobilize the gland, which results in optimal exposure of the important structures in this site. Methylene blue was sprayed [in ampules of 4 ml (0.1%) concentration] over the thyroid lobe and perilober area. The parathyroid glands and recurrent laryngeal nerve can be injured in this area. We observed that the wash-out time of the parathyroid glands was less than 3 min but for thyroid glands it was more than 15 min. The recurrent laryngeal nerve (RLN), however, did not take the stain at all (Figs. 1–3). The parathyroid glands were identified and an attempt was made to leave each with an adequate blood supply while moving the gland off the thyroid lobe. Care was taken to avoid injury of the recurrent laryngeal nerve all along its course. The nerve is gently protected from the surrounding tissue, with care taken to avoid trauma to it. Once the nerve and parathyroid glands have been identified and preserved, we ligate the inferior pole removing it from its tracheal attachments.

Figure 1



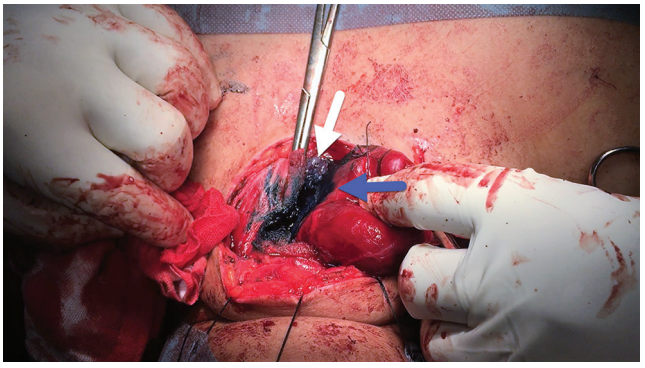
Recurrent laryngeal nerve identification, the nerve does not take the stain (yellow arrow).

Figure 2



Recurrent laryngeal nerve (yellow arrow) and parathyroid gland (white arrow) identification.

Figure 3



Wash out the stain from parathyroid gland (white arrow) and thyroid gland still blue (blue arrow).

Results

This study was conducted on 100 cases of total thyroidectomy (200 thyroid sides); 87 women and 13 men; the patients were assigned into two groups; group 1 included (the interventional group) 50 cases operated with methylene blue spraying technique and group 2 (control group) included 50 cases established with the conventional technique.

The mean age for the study groups is 49.52 ± 13.97 for group 1 and 45.38 ± 9.30 for group 2 (Table 1).

In group 1, there were 45 (90%) cases with simple noduler goiter (SNG), two (4%) cases with malignant nodule, two (4%) cases with primary toxic goiter, and one (2%) case with secondary toxic goiter. In group 2, there were 46 (92%) cases with SNG, 0 case with malignant nodule, two (4%) cases with primary toxic goiter, and two (4%) cases with primary toxic goiter (Table 2).

All patients in the study had mobile vocal cords by preoperative vocal cord examination.

One case developed postoperative transient bilateral vocal cord paralysis in group 2 and no vocal cord affection was noticed in group 1 (Table 3).

When we compared calcium level preoperatively and postoperatively, we found that in group 1 all the cases (50 patients) had normal Ca++ level (100%).

But in group 2, four (8%) patients had hypocalcemia with significant difference between calcium level preoperatively and postoperatively (Table 4).

The four patients who developed hypocalcemia were managed with oral supplementation of calcium and vitamin D and recovery occurred within a period of 1 week to 1 month.

Table 1 Personal data of the studied groups

	Group 1 (*n*=50) [*n* (%)]	Group 2 (*n*=50) [*n* (%)]
Sex		
Male	9 (18.0)	4 (8.0)
Female	41 (82.0)	46 (92.0)
Age (years)		
Mean±SD	49.52±13.97	45.38±9.30
Range	25.0-85.0	26.0-62.0

Table 2 Clinical diagnosis

	Group 1 (*n*=50) [*n* (%)]	Group 2 (*n*=50) [*n* (%)]
Clinical diagnosis		
SNG	45 (90.0)	46 (92.0)
Malignant nodule	2 (4.0)	0 (0.0)
Primary toxic	2 (4.0)	2 (4.0)
Secondary toxic	1 (2.0)	2 (4.0)

Table 3 Vocal cords examination preoperatively and postoperatively

Vocal cords examination	Group 1 (*n*=50) [*n* (%)]	Group 2 (*n*=50) [*n* (%)]	*P*
Preoperative			
Mobile	50 (100.0)	50 (100.0)	-
Postoperative			
Mobile	50 (100.0)	49 (98.0)	1.000
Immobile	0 (0.0)	1 (2.0)	

Table 4 Calcium level preoperatively and postoperatively

Ca++ level	Group 1 (*n*=50)	Group 2 (*n*=50)	*P*[1]
Preoperative			
Mean±SD	8.69±0.21	8.73±0.56	0.961
Range	8.5-9.1	8.1-9.5	
Postoperative			
Mean±SD	8.60±0.17	8.30±0.82	0.013*
Range	8.3-9.1	5.2-9.0	
P[2]	0.256	0.019*	

*Means statistically significant.

Discussion

Disorders of the thyroid gland constitute the second most common endocrine disease following diabetes mellitus in Assiut University Hospital. The need to find an efficient, safe, and affordable method for thyroidectomy provided the basis for this study.

The wash-out time of the parathyroid glands was less than 3 min but for thyroid glands it was more than 15 min while RLN did not take the stain at all.

The differences in time are due to the lympho-vascular pattern of the tissues. The lympho-vascular structure of the parathyroid glands is affluence. Unstaining of the recurrent laryngeal nerve is due to it is covered by a Schwann sheath.

Assessment of postoperative hypoparathyroidism

Postoperative hypoparathyroidism is a major concern and may lead to prolonged hospital stay and eventually increased expenses. There is a clear distinction between the two study arms in postoperative hypocalcemia. In group 1 (with methylene blue spraying technique), there were no cases detected in comparison with the other group (with the conventional technique), where four (8%) cases developed transient hypocalcemia. The incidence of transient hypoparathyroidism ranged from 6.9 to 46% while a rate of 0.4–3.3% has been reported for permanent hypoparathyroidism. Falk *et al.* [3] mentioned that transient hypoparathyroidism occurred in 27.8% manifested mostly as transient hypocalcemia, and easily managed with oral vitamin D and Ca.

All research concerning thyroid surgery and staining of parathyroid glands was performed through intravenous and/or intra-arterial methylene blue injections. Dudley used an intravenous infusion technique on 17 patients. Only one or more of the parathyroid glands have been proved with histological confirmation. Elias *et al.* used the same technique on 59 patients undergoing thyroidectomy. Localization of the glands was possible in 87%. The intravascular (intravenous and/or intra-arterial) techniques mentioned above ensure only parathyroid gland visualization and, accordingly, it simplifies the prevention of hypoparathyroidism only. In our study, localization and identification of the glands was possible in 96% [4–6].

Sari and colleagues studied 56 patients who had undergone primary (nonrecurrent) thyroid surgery for a variety of thyroid diseases by methylene blue spraying technique. No operative mortality occurred and the incidence of transient hypoparathyroidism was 5%. Three cases had transient hypocalcemia, for a maximum of 3 days. Hypoparathyroidism improved with oral calcium supplementation with subsequent normal serum parathyroid hormone levels [7].

Assessment of postoperative RLN injury

Another major complication of thyroid surgery is recurrent laryngeal nerve palsy [8]. This results in significant impairment of the quality of life and profoundly affects job performance [9–11]. Erbil *et al*. [12] reported that recurrent laryngeal nerve palsy occurred in 1.8% of their cases. Anatomic and functional preservation of RLN is the gold standard in thyroid surgery. Visual identification of RLN has decreased the rate of permanent RLN palsy during thyroid operations. However, unexpected RLN palsy still occurs.

In group 1 (with methylene blue spraying technique) in our study, there were no cases of RLN injury in comparison to group 2, where one case suffered from bilateral vocal cord affection.

To help identify the RLN and measure its function before thyroid resection, various medical devices have been established over the past few decades for intraoperative use. Several methods have been described for RLN monitoring including the use of intramuscular vocal cord electrodes, finger palpation of the cricoarytenoid muscle during nerve stimulation, and vocal cord observation by direct or fiberoptic laryngoscopy [13].

Intraoperative nerve monitoring (IONM) is nowadays widely used for identifying the RLN, especially in specialized centers, and allows identification and functional assessment of the RLN in the operative field. Application of IONM in thyroid surgeries was initially proposed by Shedd in 1966 and by Flisberg in 1970 [1].

Randolph and colleagues tested the laryngeal palpation technique using RLN stimulation in 449 thyroid and parathyroid surgeries. In a group of patients, laryngeal palpation and laryngeal Electromyography (EMG) recordings were compared during intraoperative RLN stimulation. In this study, there was no permanent RLN paralysis. There was one case of temporary RLN paralysis due to neural stretch that improved 6 weeks postoperatively (temporary paralysis rate: 0.2% of patients) [14].

Calò and colleagues studied between June 2007 and December 2012, 2034 consecutive patients who underwent thyroidectomy. They compared patients who had IONM and patients who had surgery with nerve visualization alone. Nine hundred and ninety-three patients were operated with IONM, while that with nerve visualization alone were included, 1041 patients. In patients with IONM, 28 (2.82%) recurrent laryngeal nerve injuries were observed, 21 (2.11%) transient and seven (0.7%) permanent. In patients with RLN visualization alone, 23 (2.21%) recurrent laryngeal nerve injuries were observed, in 17 (1.63%) cases transient and in six (0.58%) permanent. Differences were not statistically significant. Therefore, visual nerve identification remains the gold standard for recurrent laryngeal nerve identification in thyroid surgery. Nevertheless, IONM helped to identify the nerve, particularly in difficult cases, but, according to Calo's study, it did not decrease nerve injuries compared with visualization alone [15].

Gremillion and colleagues conducted a retrospective chart review, analysis of surgery, time with and without IONM, analysis of postoperative vocal cord function, and review of the literature. They reach that IONM did not reduce the operative time during either lobectomy or total thyroidectomies in 119 surgeries. Use of IONM increased the cost of each surgery by $387, without significant decrease in the number of injured nerves [16].

Strengths of the study

The current study entails identifying not only the parathyroid glands but also recurrent laryngeal nerves. We aimed to visualize the RLN and parathyroid and confirm it by staining with methylene blue. The intravascular techniques ensure only parathyroid gland visualization.

The current study adds no additional cost on the patient unlike the technique of IONM. We did not use any expensive device. Only the dye and our vision were used. Methylene blue dye is inexpensive; and is readily prepared in the bacteriology unit in the Clinical Pathology Department in Assiut University Hospital, where it is packed in ampules at 4 ml (0.1%) concentration and sterilized.

Study limitations

The number of cases was limited and many surgeons perform thyroidectomy without trial to identify the RLN and parathyroid in anticipation of their injury.

New studies with larger numbers of cases, together with application of the technique by different surgeons are important to confirm the reliability and effectiveness of this technique.

Conclusion

During thyroidectomy, all surgeons desired to preserve the nerves and parathyroid glands from potential risks. Some surgeons do not prefer to identify the RLN and parathyroid because they consider identification is

related to increased risk of injury. Others see that the sooner the nerve and parathyroid glands are identified, the lower the surgeon's level of stress. Methylene blue spraying technique is safe, effective, and technically feasible.

We demonstrated the effectiveness of the spraying technique plus the lack of necessity of intravascular injection, along with its potential risks, for identification of the RLN and parathyroid. New studies with larger numbers of cases and also application of the technique by different surgeons are important to confirm the reliability and effectiveness of this technique.

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Nil.

Conflicts of interest
There are no conflicts of interest.

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