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Original Article

Role of Subareolar Injection of Methylene Blue in Carcinoma Breast

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Abstract

Introduction: Carcinoma breast is the most common disease of adult females and is the leading cause of the death in their middle age. Self-awareness about breast cancer has increased and diagnosing breast cancer in an early stage is possible by the modern screening methods. The axillary lymph node status is the most important prognostic indicator for carcinoma breast. The procedure sentinel lymph node (SLN) dissection provides the operating surgeon with information to do or not to do an axillary dissection. Methylene blue dye was used in this study because of its easy availability, less expensive, safety, and its effectiveness.

Aim: The aim of this study was to study the uptake of blue dye in SLN following subareolar injection, the presence of lymph node metastasis among early breast cancer patients, the incidence of skip metastasis among these early carcinoma breast cancer patients.

Materials and Methods: All carcinoma breast patients with tumor size <5 cm and with clinically non-palpable nodes were included in this study. Fine-needle aspiration cytology was done in all the cases for the diagnosis of carcinoma breast. They were subjected to injection of methylene blue dye in the subaerolar region to identify sentinel node positivity.

Results: The results shows that the simplified technique of identifying the sentinel nodes by using subareolar injection of methylene blue has sufficiently high technique success rate of 93.3%, methylene blue dye positive SLN were observed in 56 patients (93.3%), but histopathological tumour positive was in 85% and negative in 9 patients accounting for 15% of the total. Sentinel node positive patients also had the positivity of the other axillary node while negative patients had negativity of other axillary node.

Conclusion: Our results show that the simplified technique of identifying sentinel nodes by using subareolar methylene blue has sufficiently high identification rate of 93.3%. Out of 60 patients, SLN was successfully identified in 56 patients. The study showed that high sensitivity of SLNB in this study is 85%.

Key words: Carcinoma breast, Methylene blue, Sentinel lymph mode

INTRODUCTION

Carcinoma breast is the most common disease of adult females and is the leading cause of the death in their middle age. There is an incidence of 1 in 8 women in the United States and 1 in 12 women in England and Wales who are expected to get this disease in their lifetime.[1] Self-awareness about breast cancer has increased and diagnosing breast cancer in an early stage is possible by the modern screening methods. The axillary lymph node status is the most important prognostic indicator for carcinoma breast. Since 19th century, Halsted first proposed the importance of lymph nodes, which determine the stage and guide the adjuvant treatment in the carcinoma of breast.[2] In the recent years, the surgical treatment of the disease is getting more and more limited from radical mastectomies (Halsted) to the modified radical mastectomy and even the "breast

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conservation" surgery. The same transformation is now occurring with regard to the axilla where operations evolved from complete axillary node dissection to sentinel lymph node (SLN) biopsy[3] might be referred as "axillary conservation." As the incidence of axillary nodal involvement in clinical Stage I and II breast cancer is only 4-37% and with the emergence of better adjuvant treatments such as chemoradiotherapy and hormonal therapies; there is no survival difference found between immediate removal of nodes or removal later when the nodes are clinically evident.[4] Hence, by doing routine axillary clearance in all those early stage disease, render 63-69% patients to unnecessary axillary dissections.[5] Among the early breast cancer patients who are clinically node negative, 70-80% of are not benefitted by routine axillary dissection. Although axillary lymph node dissection (ALND) came with substantial morbidity and most of the ALND patients were node negative, the presence of a specific afferent lymphatic drainage pathway from a primary tumor to a principal SLN represents the SLN concept. The procedure SLN dissection provides the operating surgeon with information to do or not to do an axillary dissection. Methylene blue dye was used in this study because of its easy availability, less expensive, safety, and its effectiveness.

Aim of the Study

- To study the uptake of blue dye in SLN following subareolar injection
- To study the presence of lymph node metastasis among early breast cancer patients
- To study the incidence of skip metastasis among these early carcinoma breast cancer patients.

MATERIALS AND METHODS

This prospective study was conducted in Tirunelveli Medical College Hospital, Tirunelveli, and Ethical Committee approval was obtained.

Inclusion Criteria

Patients with carcinoma breast of tumor size <5 cm and with clinically non-palpable nodes were included in the study.

Exclusion Criteria

- Breast carcinoma patients with palpable axillary lymph nodes
- Prior major breast surgery or axillary operations
- Patients of carcinoma breast who have received preoperative chemotherapy or radiotherapy
- Patients with multifocal breast cancer
- Patients hypersensitivity to methylene blue dye.

Patients with established diagnosis of breast carcinoma and clinically negative axillary lymph nodes were selected for this study. Fine-needle aspiration cytology was done in all the cases for the diagnosis of carcinoma breast.

They were subjected to injection of methylene blue dye in the subareolar region to identify sentinel node positivity.

RESULTS

This study was conducted in Tirunelveli Medical College Hospital in the Department of General Surgery. The patients attending the outpatient department were screened for any lump in the breast with non-palpable lymph nodes. Those patients were admitted based on the inclusion criteria and they were submitted for the procedure. The following observations were noted in our study.

- The results shows that the simplified technique of identifying the sentinel nodes using subareolar injection of methylene blue has sufficiently high technique success rate of 93.3%
- Majority of the patients are in the age group of 51-60 years - 22 patients - 37% (Table 1)
- Our study revealed that on histological basis intraductal, carcinoma was more -55, patients - 92%, and lobular carcinoma in 5 patients - 8%
- According to the lump size, lesions <2 cm were seen in 46 patients (77%), more than 2 cm seen (2-4 cm) in 14 patients (23%) (Table 2)
- 55 patients had intraductal carcinoma, 5 patients had lobular carcinoma (Table 3)
- 15 patients were in T1N0M0 stage, 45 patients were in T2N0M0 stage (Table 4)
- Methylene blue dye positive SLN were observed in 56 patients (93.3%), but histopathological tumour positive was in 85% and negative in 9 patients accounting for 15% of the total (Table 5)
- Sentinel node positive patients also had the positivity of the other axillary nodes while negative patients had negativity of other axillary node.

DISCUSSION

The observations in the present study in which SLN was positive in 93.3% was lower with those reported by Golshan and Nakhlis[6] of 96.5% and they have added that 24% herbored metastatic disease, but no such metastasis was identified in the present study. Mathelin *et al.*[7] have stated that out of 100 patients, SLN was found in 65% by methylene blue dye which was lower than the present study. Soni *et al.*[8] has stated that the success rate with methylene blue was 96.7%. Zakaria *et al.*[9] have stated that the technical success of SLN mapping with methylene

Table 1: Age-wise distribution of study group

Age group (years)	Number of patients	Percentage of SLN positive
<40	9	15
40-50	20	33
50-60	22	37
>61	9	15

SLN: Sentinel lymph node

Table 2: Distribution based on lump size

Lump size (cm)	No. of patients (%)
<2	14 (23)
2-4	46 (77)

Table 3: Classification based on histology of breast carcinoma

Histology	No. of patients (%)
Intraductal carcinoma	55 (92)
Lobular carcinoma	5 (8)

Table 4: TNM classification

Classification stage	No. of patients	Percentage of SLN+ve (%)
T1N0M0	15	25
T2N0M0	45	75

TNM: Tumor, node, and metastasis, SLN: Sentinel lymph node

Table 5: Relation between HPE report and staining

Staining	SLN HPE report	
	Positive (%)	Negative (%)
Yes	51 (78.4)	5 (8.3)
No	0 (0)	4 (6.6)
P value	<0.0001*	

*Fisher's exact test. SLN: Sentinel lymph node, HPE: Histopathological examination

blue dye was lowest in group receiving full strength in a peritumoral location and highest in the group received very dilute methylene blue dye (1.25 mg/ml) in the subareolar location. Straddling *et al.*[10] have stated that 21% developed skin lesion at the injection site of methylene blue, but no such adverse effect was observed in the present study. Salhab *et al.*[11] have reported a rare case of skin and fat necrosis following methylene blue dye injection followed by dry gangrene of the skin in a patient with breast cancer, but similar effect was not observed in the present study. Kern[12] reported identification rate of 98.4% and false negative of 100%. Veronesi *et al.*[13] achieved an accuracy rate of 100% for tumour size <1.5 cm compared with 97% for larger tumors. Furthermore, our observation supports the functional concept of the breast lymphatic system. The concept suggests that the mammary gland and its overlying skin share a common lymphatic pathway due to the common embryonic origin. Hence, such a concept supports the need to inject the labeling the reagent in the subareolar region. The diseased status of the axillary lymph node is the most significant prognostic factor for patients with early stage breast cancer. Predictors of node metastasis include tumor size, lymphovascular invasion, tumor grade, and patient's age. Receptor status, DNA content, tumor location, method of detection, and presence of calcification on mammography have some predictive value. However, no combination of predictors have replaced surgical resection and histopathological examination of lymph nodes. SLN biopsy has been widely accepted as a minimally invasive alternative to axillary dissection for nodal staging of breast cancer. The identification rate of 85% in our study is comparable with the studies of McMasters *et al.*[14] Among patients <40 years of age, there were 9 patients that forms 15% of positive lymph node sampling, 41-50 age group 20 patients were there forming 33%, 51-60 age group 22 patients were there contributing to 37% and >61 years were there 9 patients forming 15% of positive lymph node sampling. In our study, the tumour was located in the upper outer quadrant in 36 patients (60%) inner quadrant, in 16 patients (27%) central quadrant 8 patients (13%) but Mani *et al.*[15] have reported that out of 96 patients, tumour was located in outer quadrant in 58, inner quadrant in 26 and central quadrant in 12 patients.

CONCLUSION

Our results show that the simplified technique of identifying sentinel nodes using subareolar methylene blue has sufficiently high identification rate of 93.3%. Out of 60 patients, SLN was successfully identified in 56 patients. The study showed that high sensitivity of SLNB in this study is 85. This technique eliminates painful preoperative injection of 99 mTc colloid. As this procedure is performed by the surgeon in the operating room unnecessary radiation exposure are avoided. SLN biopsy using methylene blue can stage axilla with high accuracy and low risk of false negativity in breast cancer patients. Using methylene blue dye has lesser adverse effects compared to other methods of identifying the sentinel nodes.

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