

Sentinel Lymph Node Biopsy Using Methylene Blue Dye in Carcinoma of the Breast; in Resource-Limited Settings: A Prospective Study

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Abstract

Objective: To evaluate the effectiveness and safety of methylene blue dye as a single tracer for sentinel lymph node identification in patients with breast cancer.

Methods: This prospective study was conducted in the Department of General Surgery, Jawaharlal Nehru Medical College, Aligarh Muslim University, from 2018 to 2020. Thirty patients with stage I to III breast cancer were included; patients with a history of dye allergy were excluded. After induction of anesthesia, 2–5 ml of 1% methylene blue dye was injected peri areolar and the breast was massaged for 10 minutes. Blue-stained lymph nodes were identified as sentinel lymph nodes and excised, followed by standard axillary lymph node dissection (ALND). Histopathology of sentinel nodes was compared with that of the axillary nodes. Detection rate, sensitivity, specificity, accuracy and complications were analyzed.

Results: The mean age of the 30 patients was 47.83 ± 10.37 years. Sentinel lymph nodes were identified in 28 of 30 patients (detection rate 93.33%). Sensitivity, specificity and overall accuracy were 88.23%, 100% and 92.86%, respectively, with a false-negative rate of 11.76%. The mean number of sentinel nodes retrieved was 1.42. No allergic reactions occurred; one patient had transient blue discoloration of urine.

Conclusion: Sentinel lymph node biopsy using methylene blue dye alone is a safe, simple and cost-effective technique for axillary staging in breast cancer, with acceptable diagnostic accuracy. It may be particularly useful where radioisotope facilities are unavailable.

Keywords: Breast neoplasms; Sentinel lymph node biopsy; Methylene blue; Axillary staging; Resource-limited settings

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I. Introduction

Breast cancer is the most common malignancy among women worldwide and remains a leading cause of cancer-related mortality. Its incidence is rising rapidly in low- and middle-income countries because of improved awareness, increased life expectancy and changing lifestyle factors.

Assessment of axillary lymph node status is crucial for determining prognosis and planning treatment. Traditionally, axillary lymph node dissection (ALND) was the standard method of axillary staging, but it is associated with significant morbidity, including lymphedema, shoulder stiffness and sensory neuropathy.

Sentinel lymph node biopsy (SLNB) has replaced routine ALND in clinically node-negative breast cancer because it provides accurate staging with significantly reduced morbidity.[1–6]

In developed countries, SLNB is usually performed with a dual-tracer technique combining a radioactive tracer, detected with a gamma probe, and a blue dye.[7,8] However, radioisotope facilities are often unavailable in hospitals in developing countries because of cost and the lack of nuclear medicine infrastructure.

Methylene blue dye is inexpensive, widely available and associated with a low incidence of allergic reactions, and may therefore serve as an alternative for sentinel node identification in resource-limited settings.[9–11]

This study was conducted to evaluate the feasibility, effectiveness and safety of methylene blue dye alone for SLNB in patients with breast cancer.

II. Methods

Study design and setting. This prospective study was conducted in the Department of General Surgery, Jawaharlal Nehru Medical College, Aligarh Muslim University, Aligarh, India, between 2018 and 2020. Ethical approval was obtained from the Institutional Ethics Committee, and written informed consent was obtained from all participants.

Participants. Thirty patients with histologically diagnosed stage I to III breast cancer were included. Patients with a known history of allergy to methylene blue dye were excluded. The small sample size was mainly due to interruption of surgical services during the COVID-19 pandemic, when the hospital was designated a Level II and Level III COVID care facility.

Surgical technique. After induction of general anesthesia, 2–5 ml of 1% methylene blue dye was injected periareolar [12,13] and the breast was gently massaged to facilitate lymphatic uptake. Blue-stained lymphatic channels were followed to identify the sentinel lymph nodes; nodes that were stained blue or connected to blue lymphatic channels were considered sentinel nodes. These nodes were excised and sent for histopathological examination. Standard ALND was then performed, and all axillary nodes were sent for histopathological evaluation. The histopathological findings of the sentinel nodes were compared with the status of the axillary nodes.

Outcome measures. Detection rate, sensitivity, specificity, accuracy, false-negative rate and complications.

Statistical analysis. Data were analyzed using SPSS version 20. Sensitivity, specificity and accuracy were calculated, with ALND histopathology as the reference standard, and receiver operating characteristic (ROC) curves were generated.

III. Results

Thirty patients were included, with a mean age of 47.83 ± 10.37 years. Seven patients (23.33%) had received neoadjuvant chemotherapy (Table 1).

Sentinel lymph nodes were successfully identified in 28 of 30 patients, giving a detection rate of 93.33%. The mean number of sentinel nodes identified was 1.42. Of the 28 patients in whom a sentinel node was identified, 15 had a positive sentinel node, all of whom had positive axillary nodes (no false positives). Of the 13 patients with a negative sentinel node, 2 had metastasis in the axillary nodes (false negatives) and 11 were true negatives (Table 2).

The sensitivity, specificity and accuracy of SLNB were 88.23%, 100% and 92.86%, respectively, with a false-negative rate of 11.76% (Table 3).

No allergic reaction was observed. One patient had transient blue discoloration of urine, which resolved spontaneously.

Table 1. Patient characteristics

Variable	Value
Total patients	30
Mean age (years)	47.83 ± 10.37
Stage I	[n (%) – to be completed]
Stage II	[n (%) – to be completed]
Stage III	[n (%) – to be completed]
Neoadjuvant chemotherapy	7 (23.33%)

Table 2. Sentinel lymph node status compared with axillary lymph node dissection (n = 28)

Sentinel node status	Axillary node positive	Axillary node negative	Total
Positive	15 (true positive)	0 (false positive)	15
Negative	2 (false negative)	11 (true negative)	13
Total	17	11	28

Table 3. Diagnostic performance of methylene blue SLNB

Parameter	Value
Detection rate	93.33% (28/30)
Sensitivity	88.23% (15/17)
Specificity	100% (11/11)
Accuracy	92.86% (26/28)
False-negative rate	11.76% (2/17)

Positive predictive value 100% (15/15)

Negative predictive value 84.62% (11/13)

IV. Discussion

SLNB has become an important component of breast cancer management. In developed countries, radioisotope-guided SLNB using a dual-tracer technique is the standard method of axillary staging,[7,8] but the lack of nuclear medicine facilities in many developing countries limits its use. Alternative techniques such as methylene blue dye have therefore gained attention.[9–11]

In the present study the sentinel node identification rate was 93.33%, which is comparable with the 85% to 96% reported in previous studies using methylene blue alone.[9–11,14,15] The sensitivity, specificity and accuracy were likewise comparable with those reported in other studies evaluating methylene blue for SLNB.

The mean number of sentinel nodes identified (1.42) was lower than in some studies. This may be attributed to the inclusion of patients with those who had received neoadjuvant chemotherapy.

Although the identification rate was satisfactory, the false-negative rate of 11.76% remains a concern. Surgeons experience, patient selection and careful pathological evaluation of sentinel nodes may help reduce it.

Limitations. The study has a small sample size and a single-center design. Larger multicenter studies are needed to validate the effectiveness of methylene blue dye for SLNB in resource-limited settings.

V. Conclusion

SLNB using methylene blue dye is a safe, simple and cost-effective technique for axillary staging in breast cancer, with acceptable diagnostic accuracy and minimal complications. It may be particularly useful in resource-limited settings where radioisotope facilities are not available.

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