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Original Article

Sentinel Lymph Node Biopsy For Breast Cancer Using Methylene Blue

Dr.Rama mani.L Dr.Manohar pai, Dr. U. Anand kini.

Surgery, KMC Mangalore, MANIPAL UNIVERSITY/INDIA

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ABSTRACT

Aims & objectives : Carcinoma breast is the most common malignancy in females and is the leading cause of the death in their middle age. 1/3rd of patients present with locally advanced disease with distant metastasis at the time of their initial diagnosis. Sentinel lymph node (SLN) biopsy is a reliable and minimally invasive diagnostic method to determine the regional nodal status in breast cancer and provides accurate staging. This study to assess sentinel lymph node biopsy (SLNB) using dye alone (methylene blue) method and complications of using methylene blue such as anaphylaxis, allergic reactions, delayed wound healing, urine discoloration were studied. **Methods:** 96 patients with breast cancer were subjected to SLNB (using methylene blue dye) followed by complete axillary lymph node dissection and the lymph node with positive dye was identified. The dye was injected 30 minutes prior to surgery and the stained lymph nodes were identified during dissection. The hemodynamics of the patient was assessed during and after the procedure. Patients followed up in post operative period and complications such as wound healing and urine discoloration were assessed. **Results:** Of 96 patients with dye injected, 69 of 96 (71.87%) patients showed stained lymph node for dye. Of 69 patients with positive stain 47 patients showed evidence of malignancy. No patients had anaphylaxis or allergic reactions. 7 of 96 (7.29%) patients had delayed wound healing in post operative period requiring dressings and local treatment measures and 45 of 96 (46.87%) patients had discoloration of urine. **Conclusion :** In our study with this method we observed there were no dye related complications and results were reliable as confirmed with intraoperative findings. SLNB can be considered in breast carcinoma as reliable cost effective and safe method for lymph node status.

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1. Introduction

Modern screening methods and increased self awareness about breast cancer has made it possible to diagnose breast cancer in early stage. Axillary lymph node status is the most important prognostic indicators in breast cancer. Routine axillary dissection does not benefit the 70–80% of early breast cancer patients who are clinically node negative [1]. Also axillary lymphadenectomy results in significant morbidity like chronic lymph edema of ipsilateral extremity (3–12%), [2, 3] frozen shoulder syndrome and long term sensory abnormalities [4, 5]. A promising alternative to assess axillary lymph node status in early breast cancer patients is Sentinel Lymph Node Biopsy (SLNB). The Sentinel Lymph Node (SLN) concept represents a biological model that assumes the presence of a specific afferent lymphatic drainage pathway from a

primary tumor to a principal, “Sentinel”, lymph node in the regional lymphatic basin [6,7]. The definition of SLN in breast carcinoma is the node most likely harbor metastases if they are present. The assumption is that if SLN is negative, all other axillary lymph nodes will be negative. Thus the technique of SLNB was developed to provide surgeons with information that allows axillary dissection to be avoided if SLN is negative, which is less invasive and with least morbidity. We have performed SLNB study using methylene blue dye in early breast cancer patients. We have used methylene blue dye in our study as it is more readily available, safe, less expensive and equally effective [8–13]. In the following article we want to share our experience of validity of SLNB in early breast cancer using methylene blue in Indian patients.

2. Materials and methods

With written informed consent, all patients with pathologically proven carcinoma breast, were included in our study (inclusion criteria). Prior clearance from ethical board of our institution was taken for the study. Fine Needle Aspiration

* Corresponding Author : **Dr.Rama mani.L**

Cytology (FNAC) was done in most of the cases for the diagnosis of carcinoma breast. Total number of patients were 96 from January 2012 till September 2013 who underwent SLNB followed by axillary lymphadenectomy only, if SLNB was positive for metastases. Patients of carcinoma breast with presence of systemic metastasis, patients with multicentric and multifocal tumors and with h/o previous radiotherapy and/ chemotherapy were excluded.

After induction of anesthesia, 5 cc of 1% methylene blue for injection is infiltrated into the subareolar tissue and peritumoral tissue (yields higher identification rate with blue dye than other sites). In either case, special care must be taken to avoid injection into the skin or submammary connective tissue and muscle. The breast is then massaged for 5 minutes. Mastectomy is the definitive procedure, the surgeon goes for the sentinel node after creating the superior flap. All blue nodes and any node receiving a blue lymphatic channel are sentinel nodes. After removal of sentinel nodes, adjacent tissue is palpated and any additional hard or large nodes are also removed. Total number of nodes removed should usually not exceed three. Intraoperatively, SLN was searched after raising upper flap (in cases of mastectomy). Axillary tissue is gently dissected until a blue lymphatic is identified which is traced proximally and distally to identify all SLNs. Blue stained nodes were excised and sent for final HPE in a separately labelled bottle. All patients underwent complete axillary dissection subsequently. Sensitivity, specificity, positive predictive value and negative predictive value of the sentinel lymph node biopsy was analyzed after final histopathology report was available in comparison with rest of the axillary lymph nodal status.

3.RESULTS

Between January 2012 and September 2013, 96 consecutive patients underwent SLNB followed by axillary lymphadenectomy using methylene blue, the results of analysis of 96 patients are included here. The average age of patients was 54 years (range 29-85). 36 patients were premenopausal and 60 were postmenopausal. Table 1 shows various tumor characteristics.

Table 1 Tumor characteristics

Breast carcinoma	No of cases
Side	
Right sided tumors	30
Left sided tumors	66
Location	
Outer quadrant tumors	58
Inner quadrant tumors	26
Central quadrant tumors	12
Histology	
Invasive ductal carcinoma	89
Invasive lobular carcinoma	7
(all unilateral)	

Table - 2.

SLN Characteristics	No of cases
Sentinel node identified	69
a) Total no of cases with positive axillary nodes	47
b) Total no of cases with negative other nodes and negative SLN	41

Table - 2.

	HPE		Total
	Positive	Negative	
STAINED/NOT STAINED	47	22	69
	68.1%	31.9%	100.0%
	85.5%	53.7%	71.9%
Not stained	8	19	27
	29.6%	70.4%	100.0%
	14.5%	46.3%	28.1%
Total	55	41	96
	57.3%	42.7%	100.0%
	100.0%	100.0%	100.0%

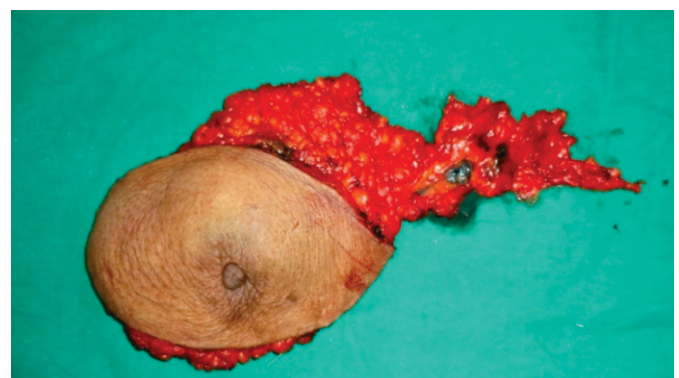
$$X^2=11.748, p=.001, HS$$

Sensitivity	Specificity	PPV	NPV	Accuracy/agreement
85.5	46.3	68.1	70.4	68.8%

$$X^2=.049, p=.976, NS$$

Table 2 shows the salient features of SLN. Sentinel Lymph Node was identified in 69 cases (72%). The mean number of sentinel lymph nodes detected was 2 and mean number of axillary nodes dissected was 12. Total number of cases with positive axillary nodes was 47, both SLN and rest of the axilla also being positive for metastases, and SLN was negative for metastases in 8 cases (false negative rate of 14.5%). Total number of cases with negative axillary nodes was 41. With above mentioned results, the overall sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of SLNB in predicting axillary node status was 85.5%, 46.3%, 68.1% and 70.4% respectively. The overall accuracy was 69%.

Fig-Blue staining of lymph nodes



4.DISCUSSION

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The histological status of axillary lymph nodes is one of the most important prognostic factors in patients with breast carcinoma. The main premise of SLNB is that patients with negative nodes can be identified as accurately as with an axillary dissection while surgical morbidity can be decreased. We conducted the study of SLNB in breast cancer patients using methylene blue dye alone method. Methylene blue dye demonstrated poor lymphatic uptake in initial studies but recent work shows that it can be substituted for isosulfan blue. We are using methylene blue dye to identify SLNs and also it is less expensive and more readily available. In our study we found that it readily reaches SLN and stains the node deeply blue.

Various sites of injection of the mapping agent are peritumoral, intratumoral, intradermal over the tumor site and subareolar. Intradermal or subareolar injection appear to increase the identification rate when compared to peritumoral injection in most studies [14–16], although the two methods have been found equivalent in other studies [17, 18]. 1.6% of patients experienced allergic reactions due to use of isosulphan blue in an large MSKCC study [19]. None of our patients had any of the above reactions proving safety value of the methylene blue dye [16]. The administration of isosulfan blue dye has been shown to artificially decrease the intraoperative pulse-oxymetric readings without any associated ill effects or changes in arterial oxygen tension [20, 21]. In our series none of the patients had any interference during intraoperative monitoring.

Skin lesions at the site of injection of methylene blue is seen in 2% of patients [22]. There is no blue tattooing effect on skin. Fat necrosis at the injection site has also been described following use of methylene blue dye [23]. None of our patients had any fat necrosis.

SLN identification was higher when combination was used (86–98%) [25, 26, 27–29, 30–33] rather than when dye alone was used (74–94%). [25, 29] False negative rates varied between 0–19%, higher when radiocolloid was not used. In our study SLN localization rate is 72% and false negative rate is 14.5%

5.Conclusions

Sentinel lymph node biopsy using methylene blue dye can stage the axilla with high accuracy and low risk of false negativity in breast cancer patients. Methylene blue dye is an effective and safe blue dye for SLNB. SLNB with methylene blue is effective in Indian set of patient population. A very good coordination between members of multidisciplinary team including surgeons, and pathologists is required for a successful SLNB

6. References

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