

Original article:

Role of sentinel lymph node biopsy in avoiding axillary lymph node dissection in early breast carcinoma

¹DR. SINGHAL S, ²DR. TIWARY BN, ³DR. ARORA PK, ⁴DR. PUSHKAR, ⁵DR. CHADHA S, ⁶DR. MALIK P, ⁷DR GOEL A, ⁸DR ZAMRE V.

¹Additional Chief Health Director and Head Of the Department-Surgery/NRCH

^{2,3,5}Senior Divisional Medical Officer(SG) and Head of Unit/ Surgery/NRCH

⁴DNB Resident/ Surgery

⁶Divisional Medical Officer and Head of Unit/ Surgery/NRCH

^{7,8} Consultant Onco-Surgeon/ NRCH and Max Vaishali

Name of the Institute/college: Northern Railway Central Hospital

Corresponding author: DR Bishwanath Tiwary

Abstract

Introduction- Axillary lymph node dissection (ALND) is the preferred treatment for management of axilla in breast cancer. However, the morbidity of ALND and its questionable utility in early breast cancer has necessitated the search for a less extensive method of predicting axillary lymph node involvement. Sentinel lymph node biopsy (SLNB) has emerged as such a modality. It is ideally performed using identification with radio-isotope and blue dye and evaluation by frozen section. However, facilities for the same are not universally available.

Aims- To assess SLNB evaluated by imprint cytology in SLN identified using blue dye alone, as a predictor of Axillary Lymph node status.

Materials and Methods- This observational prospective study was conducted on 35 patients of early breast carcinoma with clinically node negative axilla. All patients underwent modified radical mastectomy (MRM). SLN isolation was done using Methylene blue dye (2.5% solution) injected 10-15 minutes pre-operatively peri-lesionally. SLNB evaluated by imprint cytology and completion ALND was done in all cases.

Observation and Results- Sentinel node was localized in 94.29%. and it accurately predicted axillary lymph node status in 94.26%. False negative rate was 18.18%, sensitivity was 81.18% and the specificity was 100% with diagnostic accuracy of 94.29%. There were 2 false negatives, both in post-chemotherapy patients.

Conclusion - SLNB using localization by blue dye and evaluation by imprint cytology is a safe and effective predictor of axillary lymph node involvement. Patients of early breast cancer with negative SLNB may avoid ALND.

Keywords: Axillary lymph node dissection, Sentinel lymph node biopsy, Early breast cancer, imprint cytology.

INTRODUCTION

Carcinoma of breast continues to be one of the most frequent cancers in women all over the world. In Indian women, it is second only to carcinoma of cervix with annual incidence of 17/10000 population. In the past radical mastectomy has been the cornerstone of management of Ca. breast. For the last few decades, a controversy is raging about the extent of excision and for last 10 years role of axillary lymph node dissection (ALND) has been

questioned in early breast cancer. Axillary lymph node dissection has been considered to be the gold standard for management of the axillary lymph nodes. However, Axillary lymph node dissection may be associated with significant morbidities such as post-operative numbness in inner side of arm, local wound complications, seroma formation, infection, limitation of shoulder movements, chronic pain syndrome and lymphedema which can lead to lymphosarcoma in many cases.⁽¹⁻³⁾

In addition, with increasing awareness and better screening more number early breast carcinomas are being detected. The benefit of ALND is being questioned in these early breast carcinoma patients because these rarely have metastasis and should therefore not be subjected to the potential of complications of ALND.^(4,5)

Various methods of predicting axillary lymph node status has been described including clinical assessment, radiological and operative procedures. Thus there is a need of a procedure which can detect axillary lymph node status as accurately as ALND and is free from its attendant complications.

Based on the concept that the lymph from the primary tumor drains into the first regional group of lymph node/nodes defined as Sentinel Lymph Node (SLN), the concept of intra-operative lymph node mapping and sentinel lymph node biopsy (SLNB) was developed to identify lymph node metastasis from primary cutaneous melanoma.⁽⁶⁾ This technique has false negative rate of only 1% in melanoma. The same technique was adopted by Giuliano et al. to identify the axillary lymph node metastasis in breast carcinoma. In this study, the sentinel lymph node was identified in 114 of 174 patients and accurately predicted axillary status in 109 of these 114 patients with false negative rate of 5%.^(7,8) Flett et al using a similar technique successfully identified sentinel lymph node in 56 (82%) of 68 patients. There were only 3 false negative (5%). The sensitivity and the specificity of SLND was 83% and 100% respectively.⁽⁹⁾

Another method of detection of the sentinel node involves use of filtered technetium labeled sulfur colloid and technetium labeled human serum albumin. In western world, due to easy availability of better facilities and wide coverage under health insurance they can use facilities of sentinel node biopsy using both radioactive colloid and blue dye. In an Indian study by Chintamani et al sentinel lymph node biopsy showed sentinel node identification of 100%, sensitivity of 86.6% and accuracy of 93.3%.⁽¹⁰⁾ The purpose of our study is to determine the role of sentinel lymph node biopsy in predicting the axillary lymph node status of patients with early invasive breast cancer using 2.5% Methylene Blue dye alone. The best method of identification of sentinel lymph node is using both dye and radioactive colloid but such facilities are available only few centers in our country. Results using blue dye alone are also promising but the sufficient studies not available in our country. The study is being continued in our institution so that we can generalize our results in the future to avoid axillary dissection on basis of imprint cytology of sentinel lymph node identified using dye alone.

AIMS AND OBJECTIVES

1. To localize sentinel node by injecting 2.5% Methylene blue dye around the primary tumor.
2. To assess the reliability of technique in predicting axillary lymph node status.
3. To study the incidence and prevalence positive axillary lymph nodes in Indian population.

MATERIALS AND METHODS

This observational prospective study was conducted in the department of Surgery, Northern Railways Central Hospital (NRCH), New Delhi, from July 2016 to October 2018.

INCLUSION CRITERIA:

Patients with early proven carcinoma breast with clinically negative axillary node

EXCLUSION CRITERIA:

1. Patient with clinically multifocal lesion
2. Prior axillary surgery
3. Inflammatory carcinoma breast
4. Recurrent carcinoma following previous surgery
5. Patient with clinically positive axillary lymph nodes.

Sample size & Sample Technique:

Assuming the accuracy to be 83% with a margin of error of 14% and the 5% level of significance. The minimum required sample size is 28 patients.

We have taken 35 patients who fulfilled the inclusion and exclusion criteria, in all these patients, thorough history was taken and detailed clinical examination was performed along with the relevant investigations according to the study proforma. After preliminary investigations, confirmation of diagnosis and pre-anesthetic checkup, patients were taken up for modified radical mastectomy (MRM).

Study Method:-

After above investigations clinical staging of disease was done. Patient belonging to stage I (T1 N0 M0) and Stage II (T2 N0 M0, T3 N0 M0) and patient with neo-adjuvant chemotherapy who were included in lymph node negative group were selected for MRM and sentinel lymph node biopsy and ALND.

After preliminary investigations, confirmation of diagnosis and pre-anesthetic checkup, patients were taken up for MRM with SLNB and ALND. .

1. 3-5 ml of sterilized Methylene blue dye (2.5% solution) was injected 10-15 minutes before surgery into the breast tissue surrounding the primary tumor after cleaning and draping the patient.
2. Standard incision for MRM was made and inferior and superior skin flaps dissected.
3. Then axilla was explored after 10-20 minutes and sentinel lymph node was detected by its blue color and by tracing the afferent lymphatic vessel and was removed. Modified Radical Mastectomy was completed and whole of the breast tissue along with axillary contents labeled as L1, L2, L3 were sent for histopathology along with sentinel lymph node in a separate container.
4. Result of sentinel lymph node biopsy were correlated with histopathology of other axillary lymph nodes.

OBSERVATION AND ANALYSIS

In this study a total no of 35 patients with carcinoma breast diagnosed with Core (Trucut) needle biopsy and having clinically node negative axilla were included. Out of these 35 patients, maximum were between age groups 46-55 (42.86%) and 56-65 age group (31.43%). Most patients in our study were postmenopausal (94.29%) and most attained menopause in age group 45-50 years (69.7%).

Most of our patients attained menarche between 13-15 years of age (51.43%) and 42.86% before 13 years of age. In our study age at first birth was between 19-22 years in maximum no. of patients (62.86%) and only 5.71% has first child above 26 years. Most patients had ≥ 3 children (68.57%), and only 28.57% had 2 children. Maximum no. of patients breastfed their children for an average period of 6-12 months (82.86%), and 11.43% for < 6 months. Most of our patients presented with painless lump (97.14%), and only 5.71% presented with pain in breast and, 2.85% presented with nipple discharge. Maximum no. of patients presented with a lump in outer quadrant of breast 57.14% and 20% in upper inner quadrant. The size of lump on presentation was between 2-5 cm in 94.29% of patients and 5.71% presented with breast lump size of < 2 cm.

Most patients were in clinical staging T2N0M0 (51.43%) and 42.86% in clinical stage T3N0M0.

In our study, sentinel lymph node was positive in 22.86% of patients, and was negative in 71.43% of patients. In 5.71% patients (n=2), sentinel lymph node was not visualized. The sentinel node localization rate was 94.29%.

The sentinel lymph node was positive in 9 patients and other axillary nodes were positive in 11 patients with sensitivity of 81.8%, specificity of 100% with diagnostic accuracy of 94.29%. p-value of test is < 0.001 using Fisher's exact test and kappa value of test is 81.8%, with false negative rate of 18.18%. The other axillary nodes beside sentinel lymph nodes were also positive in all cases where sentinel lymph node were positive. There are 2 cases [post NACT] where sentinel lymph node was negative, but other axillary nodes were positive. In cases in stage T1-T2, sentinel lymph node biopsy sensitivity, specificity and accuracy is 100%

DISCUSSION

The status of axillary lymph node remains the most important predictor of survival in women with invasive breast cancer and this status is used for enrollment in adjuvant protocol and to make treatment decision.

Bassi et al used combined technique of iso-sulphan blue and Tc 99 sulfur colloid for mapping SLN in 40 patients of early breast cancer. The study showed localization in 98%, with accuracy of 92%.⁽¹¹⁾ Parmar V et al performed low axillary sampling in clinically node negative operable breast cancer. Their study showed validation of 100% with sensitivity of 95% with false negative rate of 8.8%.⁽¹²⁾ Rama et al did a study on 96 patients with early breast cancer which demonstrated a sensitivity 85.5% and accuracy of 68.8% by using methylene blue dye.⁽¹³⁾ A review of the National Cancer Data Base (NCDB) data from 1998 to 2005 revealed that there were no difference seen in axillary recurrence rates or survival for patients who had sentinel node surgery only versus those who underwent ALND.⁽¹⁴⁾

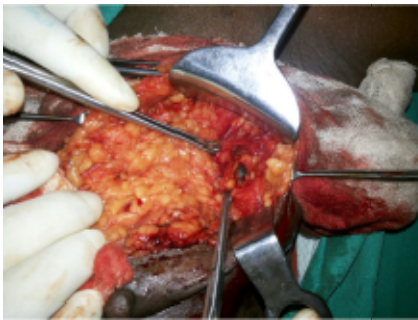
In our study, 35 patients of carcinoma breast underwent sentinel lymph node biopsy after injecting 2.5% Blue dye at the periphery of lesion before starting the procedure. Sentinel node was localized in 33 patients (94.29%). There were two false negative. So localization of sentinel lymph node is 94.29% (33/35) and it accurately predicted axillary lymph node status in 94.26%. In this study false negative rate for sentinel lymph node biopsy is 18.18%. The sensitivity of the sentinel lymph node biopsy is 81.18% and the specificity is 100% with diagnostic accuracy of 94.29%. The p value of the study using Fischer's Exact Test is < 0.001 which is statically significant.

CONCLUSION

SLNB is a safe and effective predictor of axillary lymph node involvement and in patients of early breast cancer with negative SLNB axillary dissection can be omitted.



1. Infiltration of blue dye peri-lesionally



2. Localization of Sentinel Lymph Node in Axilla

BIBLIOGRAPHY

1. Engel J, Kerr J, Schlesinger-Raab A. Axilla surgery severely affects quality of life; results of a five year prospective study in breast cancer patients. *Breast cancer Res treat* 2003; 79: 47-57.
2. Kissin MW, Quercideela, Rovere G, Easton D. Risk of lymphedema following the treatment of breast cancer. *Br J Surg* 1986; 73: 280-4.
3. Ivens D, Hoe AL, Podd TJ. Assessment of morbidity from complete axillary dissection. *Br J Cancer* 1992; 66: 136-8.
4. Hughes RJ, John C, Holland PA, Gateley CA. Prediction of axillary node metastases by size and grade of tumor – An aid for the discussion of the axillary surgery in patients with operable disease. *Eur J Cancer Suppl* 2007; 5: 21.
5. Fisher B, Wolmark N, Bauer M. The accuracy of clinical nodal staging and of limited axillary dissection as a determinant of histologic nodal status in carcinoma of breast. *SurgGynecolObstet* 1981; 152: 765-72.
6. Morton D, Wen D, Conchran A. Management of early melanoma by intraoperative lymphatic mapping and selective lymphadenectomy: an alternative to routine elective lymphadenectomy or watch and wait. *SurgOncolClin N Am* 1: 247-259,1992.

7. Guiliano AE, Kirgan PM, Guenther JM, Morton D. Lymphatic mapping and sentinel lymphadenectomy of breast cancer. *Ann Surg* 220: 391-401,1994.
8. Guiliano AE, Dale PS, Turner RR et al. Improved axillary staging of breast cancer with sentinel lymphadenectomy. *Ann Surge* 222: 394-401,1995.
9. Flett MM, Gling JJ, Stanton PD, Cooke TG. Sentinel node localisation in patient with breast cancer. *Br J Surg* 85: 991-1003,1998.
10. Chintamani ,Megha Tendon , Ashwani Mishra , UshaAgrawal , SunitaSaxena. Sentinel lymph node biopsy using dye alone method is reliable and accurate even after neoadjuvant chemotherapy in locally advanced Breast cancer – a prospective study. *World J SurgOncol.* 9:19,2011.
11. Bassi KK, Seenu V, Ballehaninna UK, Parshad R, Chumber S, Dhar A, *et al.* Second echelon node predicts metastatic involvement of additional axillary nodes following sentinel node biopsy in early breast cancer. *Indian J Cancer*43: 103-9, 2006.
12. Parmar V, Hawaldar R, Nadkarni MS, Badwe RA. Low axillary sampling in clinically node-negative operable breast cancer. *Natl Med J India* 22: 234-6, 2009.
13. Rama M, Manohar P, Anand UK. Sentinel lymph node biopsy in breast cancer with methylene blue. *Int J Biol Med Res.* 5(1): 3793-3796, 2014.
14. Kim T,Guiliano AE, Lyman GH: Lymphatic mapping and sentinel lymph node biopsy in early breast carcinoma: A meta-analysis.*Cancer* 106:4-16,2006.