ORIGINAL ARTICLE

Evaluation of Sentinel Lymph Node Biopsy with Methylene Blue Dye in Early Carcinoma Breast

AHMAD SOHAIL, MUHAMMAD SOHAIL, MUHAMMAD ASIM, *JAVED SHAKIR, KHALID M. DURRANI.*

ABSTRACT

Aim: To determine the accuracy and feasibility of this procedure to incorporate the sentinel node biopsy in future surgical practice.
Design: Prospective and experimental.
Patients and Methods: Between July 2001 and August 2002, 30 female patients, diagnosed as carcinoma breast on fine needle aspiration cytology with clinical stage T1-2, N0, M0 were recruited for study. Under general anesthesia 1ml 1% methylene blue sterilized dye was injected in subareolar region of breast in all patients and gently massaged the breast for 1-2 minutes to disperse the dye in the lymphatics. Then the blue stained sentinel node was detected and biopsied from the axilla. Later all patients underwent routine mastectomy with axillary clearance.
Results: Over all sentinel node identification rate was 93.4% (28 of 30 patients) and false negative rate was 7.1% (2 of 28 patients). Sensitivity and specificity were (85.7%) and (71.4%) respectively with positive and negative predictive values were (75.0%) and (83.3%) respectively.
Conclusion: The findings of the study support the hypothesis that sentinel node is a true representative and predictor of the axillary nodal status in early carcinoma breast and the procedure can be performed safely with cheaper and feasible methylene blue dye with confidence.
Key words: Sentinel Nodes, Breast Biopsy, Lympho Scintigraphy.

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 United States and 1 in 12 women in England and wales who are expected to get this disease in their life time.[1] Incidence in Pakistan is about 24.4%[2] and due to poor screening program 1/3rd of patients present with locally advanced disease and 17% present with distant metastasis at the time of there initial diagnosis[3].

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[4]. 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 conservation" surgery. The same transformation is now occurring with regard to the axilla where operations evolved from complete axillary node dissection (CAND) to sentinel lymph node (SLN) biopsy[5] 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 like chemoradiotherapy and hormonal therapies, there is no survival difference found between immediate removal of nodes or removal later when the nodes are clinically evident[6]. So by doing routine axillary clearance in all those early stage disease, render 63-69% patients to un-necessary axillary dissections.[7] Causing prolonged hospital stay and the complications like numbness, arm odema, brachial plexopathy and seroma formation[8].

Current methods available to assess the axillary nodal status include clinical, radiological, node sampling and frozen section etc but none of the method has proven its efficacy with full confidence[9].

Recent studies show that the sentinel lymph node (SLN) biopsy is a newer, reliable and minimally invasive diagnostic method to determine the regional nodal status in breast cancer[10] and provides accurate staging alternative to complete axillary dissection in clinically node negative patients[11]. Sentinel lymph node (SLN) is that first lymph node in the route of the lymphatic channels to the axilla which is infiltrated by the tumour and can predict the status of other nodes in the axillary basin and can be detected by injecting the dye, radioactive material or both into the breast lymphatics.

PATIENTS AND METHODS

This prospective study was conducted at the Department of Surgery, Unit I Shaikh Zayed Federal Postgraduate Medical Institute Lahore from July 2001 to August 2002 after the approval of Hospital Ethical

Department of Surgery, Federal Post Graduate Medical Institute, Shaikh Zayed Hospital Lahore.
Correspondence to Dr. Ahmad Sohail, E25/6 B Al-Noor Town, Walton Road, Lahore Cantt. email: drsilu@hotmail.com

Committee. A total number of 30 patients were included in the study, all with fine needle aspiration cytology (FNAC) proven carcinoma breast, presented through out patient clinics and were scheduled for modified radical mastectomy. Clinical stage of all pre, peri and post menopausal patients was T1-2, N0, M0 and all were willing for modified radical mastectomy as their surgical treatment. Patients with metastatic, inoperable disease, previous surgery for benign lesions, clinically palpable nodes, larger tumour size or those who were not willing for the procedure were excluded from the study.

At the operation table, prophylactic antibiotics were given at the time of induction to all the patients and after draping 1ml sterilized 1% methylene blue dye was infiltrated with a 23G needle attached to a syringe in the subdermal region of the areola of the diseased breast. Gentle massage of breast done for 1-2 minutes and then with in 5-10 minutes a 3-4cm transverse incision was made just below the hair line in the axilla and by blunt dissection with curved haemostat the blue coloured lymphatic channels were followed which lead to the blue stained node called sentinel lymph node (SLN), the node was identified and carefully dissected out, any other stained node if found in vicinity was also removed.

Following that, in all patients the routine mastectomy with axillary clearance was performed and the harvested node (SLN) and mastectomy with axillary clearance specimen were sent to the histology laboratory fixed in formaline in two separate containers labeled “A” and “B” respectively.

The histology report with thin sliced H & E staining study of both specimen was the end point of the procedure and the results of study were analyzed statistically nominal variables were reported as frequency and percentage numerical data was reported as mean±SD and analysis was performed by utilizing SPSS version 10.

RESULTS

All 30 patients underwent modified radical mastectomy with level II axillary clearance and all primary tumours turned out to be infiltrating ductal carcinomas on histologic examination, mean age of patients was 45±13.48 years with range of (20-70) years and the mean tumour size was 3.7cm with range of (1.5-5cm). Sentinel lymph node (SLN) was detected in 28 out of 30 (93.4%) patients and among those 28 patients total of 32 SLN were detected with mean of 1.14 SLN in each patient. The most frequent location of tumour was upper and outer quadrant 19 of 30- (63.33%).

In 2 of 30 patients the SLN was not detected and the identification rate was 93.4% and among 28 patients with detected SLN, 2 patients who had negative SLN for tumour metastasis showed axillary nodes positive for tumour so false negative rate was (7.1%). Similarly in 4 out of 28 patients (14.2%) the SLN was the only site of metastasis showing the false positive results. Sensitivity and specificity of the method were 85.7% and 71.4% respectively. Similarly the positive and negative predictive values came out to be 75% and 83.33% respectively.

Table: Percentage of various parameters in the study

Identification rate of sentinel lymph nodes.	93.4%
False negative rate	7.1%
Sensitivity	85.7%
Specificity	71.4%
Negative predictive value	83.3%
Positive predictive value	75%

DISCUSSION

In the present study the methylene blue dye alone was used for lymphatic mapping and retrieved the identification rate of SLN 93.4% (28 out of 30 patients). Literature reveals identification with blue dye alone in the range of 66-98% and slightly improved rates with combination of both radioactive colloid and blue dye[12]. In an other study Guenther et al[13] has reported 71% identification rate in series of 145 patients using blue dye alone. However in recent studies Edward et al[14] and Zerwes et al[15] has even shown 100% identification rates.

In the present study we found better results than Giuilliano et al[16] Guenther et al and what Kanwal et al[17] (83%) has described in the literature. The proposed reasons for lower identification rate in different studies may be the initial experience of the surgeon, high body mass index of patients, the blockage of lymphatics by tumour infiltration or the skip metastasis to other nodes like in level III of axilla, which has 3.5-5% reported incidence in literature[18,19].

Lucci et al[20] has also described the presence of SLN even in internal mammary chain rather than axilla especially for inner quadrant tumours but has very low incidence.

False negative rate in our study was calculated by dividing the false negative SLN by the total number of patients in which the (SLN) was detected and that came out to be 7.1% which was comparable to the rates reported elsewhere. In the literature the false negative rate varies among surgeons between (0-15)[21].

The reason for this variation may be the extensive tumour infiltration causing re-routing of the lymph fluid to the non-sentinel nodes or still the initial experience of the surgeon as the Guilliano et al[12] in 1994 with 174 patients experience showed (65%) identification and (12%) false negative rates, but later the same group in next series in 1997[16] published (93%) identification and (0%) false negative rates showing the better understanding of the procedure.

The sensitivity in different series reported in the range of 85-92%[22] and the present study revealed 85.7% which was in accordance with the literature. Similarly positive and negative predictive values in literature range from (40-65%) and (88-100%) respectively and our data revealed (75%) and (83.3%) respectively.

The considerable variations in the results are always present in the different series shows the initial experience of the surgeons to learn the procedure and the studies show that this technique has a definite but a short learning curve which can be attained by experience and ultimately achieves more improved identification and lower false -ve rates[23].

Moreover it is found that there is no standardization in this procedure so far seen among different surgeons and there is variability in using the dose, materials and choosing the sites for lymphatic mapping, and inspite of the all those methods it does give results. In this study the methylene blue dye was used because it was cheaper, safe, readily available and did not need any hand held gamma camera to detect the radiation. The site of injection peritumoural versus sub-areoler does not make any difference in mapping because breast and the overlying skin, embryologically share the same lymphatics[24], however the subareolar route is considered better in case of non palpable and multifocal breast tumours.

CONCLUSION

In this study the use of subareolar methylene blue dye was found cheaper and safe for the sentinel lymph node biopsy and the procedure reliably predicts the axillary lymph node status in early breast cancer, and the findings were comparable with the literature and the procedure can be used with confidence in surgical practice after achieving the short learning curve.

REFERENCES

1. Greenlee RT, Hill-Harmon MB, Murray T. Cancer statistics 2001. J Clin 2001; 51: 15-36.
2. Rasool MI, Malik MI, Luqman M, Khalilullah. The clinicopathological study of carcinoma breast. Pak J Med Res 1987; 6: 135-6.
3. Malik IA. Clinicopathological features of breast cancer in Pakistan. J Pak Med Assoc 2002; 52: 100-4.
4. Halsted WS. A clinical and histological study of certain adenocarcinoma of breast. A brief consideration of results of operation of carcinoma breast from 1889-98 at John Hopkin's Hospital. Ann Surg 1898; 28: 557-76.
5. Shahab F, Emmanuel E, Manju P, Willium B, Lisa D, Micheal T et al. Predictors of positive axillary nodes after sentinel node biopsy in breast carcinoma. Am J Surg 2000; 182: 316-20.
6. Gajdos C, Tartter PI, Bleiweiss TT. Lymphatic invasion, tumour size and age are independent predictors of axillary lymph node metastasis in T1 brast cancer. Ann Surg 1999; 230: 692-6.
7. Lindhl T, Engel G, Alilgren J. Can axillary dissection be avoided by improved molecular diagnosis. Acta Oncol 2000; 39: 319-26.
8. Sohail A, Asim M, Sohail M. Morbidity of axillary dissections in carcinoma breast. J Fatima Jinnah Med Coll 2008; 2: 99-101.
9. Herrada J, Lyer RA, Atkinson EN, Sneige N, Buzdar AU, Hortobagyi GN. Relative value of physical examination, mammography and sonography in evaluating the size of primary tumour and regional nodes metastasis in patients with locally advanced breast carcinoma. Clinical Cancer Res 1997; 3: 1565
10. Krag DN, Wener DL, Alex JC. Surgical resection and radiolocallization of sentinel node in breast cancer using gamma probe. Surg Oncol 1993; 2: 335-40.
11. Veronesi U, Paganelli G, Galimberti V, Sentinel node biopsy to avoid axillary dissection in breast cancer with clinically negative nodes. Lancet 1997; 349: 1864-7.
12. Giulliano AE, Kirgan DM, Guenther JM. Lymphatic mapping and sentinel lymphadenectomy for breast cancer. Ann Surg 1994; 220: 391-401.
13. Guenther JM, Krishnamoorthy M, Tan LR. Sentinel lymph adenectomy for breast cancer in a community managed care setting. Cancer J Sci Am 1997; 3: 336.
14. Edward J. Sentinel node imaging and biopsy in breast cancer patients. Am J Surg 2001; 182: 426-8.
15. Zerwes FP, Frasson AL, Gutfilen B, Barbosada Fonseca LM. Identification of sentinel node in breast cancer. J Exp Clin Cancer Res 2002; 21: 155-8.
16. Giuliano AE, Jones RC, Brennan M, Statman R. Sentinel lymph adenectomy in breast cancer. J clin Oncol 1997; 15: 2345-50.
17. Kanwal S, Hussain R. Sentinel lymph node biopsy in early carcinoma breast with blue dye. J Coll Physicians Surg Pak 2005; 15: 515-6.
18. Manbel RE, Cunnick GH. Analysis of potential risk for failed localization of axillary sentinel node in breast cancer. Breast cancer research treatment special issue 24th Annual Sanantonia Breast Cancer Symposium 2001; 69: 217-8.
19. Eary JF, Mankoff DA, Dunnwold LD. Sentinel node mapping for breast cancer in diverse patient group. Radiology 1999; 213: 526-9.
20. Lucci A. Unresolved issues in sentinel node dissection for breast cancer in minisymposium, what new in breast surgery? Breast cancer research treatment special issue 24th Annual Sanantonia Breast Cancer Symposium 2001; 69: 88-9.
21. O'Hea BJ, Hill AD, El-shirbiny AM. Sentinel node biopsy in breast cancer. Innitial experience at memorial sloan-kettering cancer center. J Am Coll Surg 1998; 186: 423-7.
22. Tse Jia Liu. Selective sentinel lymph node dissection in breast cancer, experience from Taiwan. Surg Clin N Am 2000; 80: 1779-85.
23. Tafra L. The learning curve and sentinel node biopsy. Am J Surg 2001; 82: 347-50.
24. Borgstein PJ, Meijer RJ, Vondiest PJ. Functional lymphatic anatomy of sentinel node biopsy in breast cancer and echos from the past and the periareolar blue dye method. Ann Surg 2000; 232: 81-9.