ORIGINAL ARTICLE

SENTINEL LYMPH NODE SCINTIGRAPHY IN BREAST CARCINOMA - COMPARISON OF TWO VERSUS FOUR-INJECTION TECHNIQUE

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Abstract

Purpose: Sentinel lymph node (SLN) is the first regional node that drains lymph from the primary tumour and receives seeding of metastatic cells. Axillary node dissection remains the most reliable predictor of disease outcome. Controversies still exist about several aspects of lymphatic mapping and SLN biopsy for breast cancer, including number of radioisotope injection. The purpose of this study is to evaluate the success rate of different number of injection sites in the detection of SLN in breast cancer.

Materials and Methods: A total of 120 consecutive breast cancer patients were divided into two groups. Group A (60 patients) received four intradermal periareolar (ID-PA) injections. Group B (60 patients) received two ID-PA injections. Imaging was carried out at 45 min post-injection. A gamma probe was used to explore the SLNs during surgery.

Results: In Group A, 60 females with the mean age of 50.77 years were included in the study. 34 (56%) patients had single SLN. 25 (41.7%) had SLN with the second tier. 1 (1.7%) was negative. Group B included 60 patients (59 females and 1 male) with the mean age of 51.9 years. In 30 (50%) patients, single SLN was detected. 29 (48.3%) had SLN with the second tier. 1 (1.7%) was negative.

Conclusion: SLN mapping with two periareolar ID injections carries less radiation dose and less pain as compared to the four injections with equal sensitivity for the visualization of SLNs.

Key words: Breast cancer, intradermal injection, sentinel lymph node, Tc^{99} human serum albumin

Introduction

Breast cancer is the most common malignancy of females all over the world and the second leading cause of death due to cancer among females. Approximately one in every nine Pakistani women is likely to suffer from breast cancer. This is one of the highest incidence rates in Asia.[1]

Sentinel lymph node (SLN) is the first regional lymph node that drains the lymph from the primary tumour.[2] It is potentially the first node to receive the seeding of lymph-borne metastatic cells. Axillary lymph node dissection remains one of the mainstays of breast cancer because clinical, imaging or laboratory methods are insufficient to define nodal status, the most reliable predictor of disease outcome.[3] SLN biopsy is a standard practice in most centres.

The morbidity associated with an axillary procedure includes arm swelling, sensory disturbance, infection, shoulder stiffness and impaired shoulder movement.[4] The ideal situation, therefore, would be to stage the axilla with no or minimal intervention. SLN scintigraphy allows the surgeon to easily identify and biopsy the SLN, and it can be performed under local anaesthesia in an attempt to reduce the risks of general anaesthetics. At present, detection of SLN is highly accurate in the context of carcinoma breast and there is rapidly increasing database population. SLN mapping (SLNM) is a technique in which a radioactive tracer is injected into the breast and a molecular imaging scan is performed to provide a 'road map' of lymphatic drainage from the

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tumour.[5] However, there are still ongoing controversies about several aspects of lymphatic mapping and SLN biopsy for breast cancer, including number of injection sites of radioisotope.[6] This study aims to evaluate the success rate of different number of the intradermal periareolar (ID-PA) injection sites in the detection of SLN in breast cancer. No such study has been carried out in the Pakistani population.

Materials and Methods

Retrospective data collection was done over a period of 6 months from October 2013 to March 2014. 120 consecutive patients were enrolled. Patients of any gender and any age with biopsy-proven breast carcinoma and no clinically palpable axillary lymph nodes were included in the study.

Patients with primary tumour >5 cm, local recurrence and pre-operative chemotherapy/radiotherapy were excluded from the study.

Breast lymphoscintigraphy for SLN localization was performed in the evening before surgery. Radiopharmaceutical used was 99mTc-labelled human albumin colloid particles (99mTc-HSA nanocolloids) 20 MBq/injection site, in a volume of 0.2 ml. The patients were divided into two groups by simple random sampling. Aseptic technique was used for injection. Group A (60 patients) received four ID-PA injections at 3, 6, 9 and 12'0 clock positions. Group B (60 patients) received two ID-PA injections at 6 and 12'0 clock positions. Scintigraphic images were acquired 45 min and 16 h post-injection (p.i.) by a gamma camera (Infinia; GE Medical Systems, Milwaukee, WI, USA) equipped with a low-energy general purpose collimator with energy window set at 140 KeV. Static left/right anterior, oblique (30°) and lateral views were performed (128 × 128 matrix, zoom 1.0) on a time-based (2 min each view) study. Delayed imaging was done next morning before surgery, but not later than 18 h post-injection. The first lymph node to be visualized on gamma camera scan is referred to as SLN. The node receiving radiotracer from other node is referred to as the second tier node. A surgical gamma probe was used to explore the SLNs during surgery along with blue dye injection intraoperatively.

Statistical analysis

All data were entered and assessed using computer-based Statistical Package for the Social Sciences version 19. The mean ± SD was calculated for quantitative variables like age. Qualitative variables such as gender and detection of SLN are presented in percentages and frequency.

Chi-square test was used to compare the detection of SLN in both groups. $P \leq 0.05$ was considered as statistically significant.

Results

Demographic parameters

Group A

In Group A, a total of 60 patients were included in the study. All of them were females with the mean age of 50.77 years and the age range was 31–80 years (SD ± 11.8).

Group B

Group B included total of 60 patients, of which only 1 (1.6%) was male while the remaining 59 (98.4%) were females. Mean age was 51.90 years and the age range was 30–80 years (SD ± 10.3).

Sentinel node localization in Groups A and B

Group A

In 34 (56%) patients, single SLN was detected, and in 25 (41.7%), SLN with the second tier was visualized. In 1 patient (1.7%), no SLN was visualized [Figure 1].

Group B

In 30 (50%) patients, single SLN was detected, and in 29 (48.3%), SLN with the second tier was visualized. In 1 patient (1.7%), no SLN was visualized [Figure 1].

Comparison of sentinel node localization in Groups A and B

There was no statistically significant difference between the results of two-injection techniques ($P = 0.761$).

Discussion

Breast cancer is the most common malignancy among females and the second leading cause of cancer-related deaths. Pakistan has one of the highest incident rates in Asia with every ninth women likely to suffer from

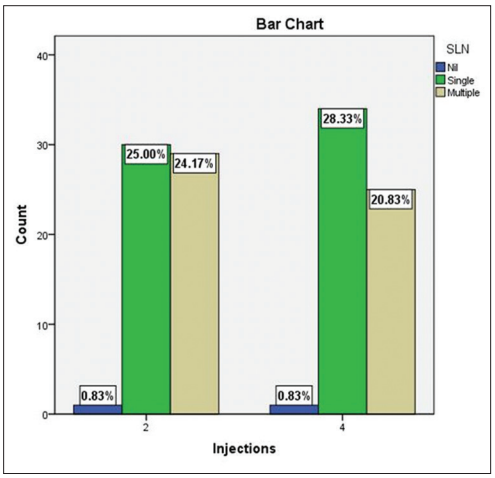

Figure 1: Results of sentinel node visualization in Groups A and B

breast cancer.[1] The first lymph node in the lymphatic basin draining the primary tumour is called the SLN.[7] It reflects the histological characteristics of the rest of the nodes in the chain. The metastases to lymph node are not a random phenomenon and can be determined by identifying the lymph flow from tumour to primary lymph draining node.

Satisfactory results are obtained with SLNB despite significant variations in the methodology. Some centres use blue dye only, others use radiocolloid (Tc^{99} sulphur colloid), only but most of the centre use combination of two for the detection of SLNB. All three methods had reliable results in experienced hands. Many authors demonstrated best results with combination techniques proving that this hypothesis is true. Of 39 studies, using radioisotopes (16 studies) or blue dye (11 studies) or a combination of both (12 studies) identified SLN in 92%, 81% and 93%, respectively.[8]

Different injection techniques are applied for the injection of radiotracer and blue dye in patients with primary breast lesion for SLNB. Peritumoural or intratumoural injection technique was used in initial studies of SLNB for following reasons; first, the lymphatic drainage of the skin of the breast and glandular tissue was thought to be different, and second, the injection distant from tumour may not represent true SLN.[9,10] Many recent studies use ID, subdermal (SD) and subareolar (SA).[11-13] Several authors demonstrated that visualization of axillary lymph nodes by ID or SA injection is faster than with peritumoural PT injection.[13-16] Most of the studies reported, SLN identification >95% in appropriately selected patients.[17-20] The detection rate in both the groups of this study is 98.33% which is in line with the meta-analysis of previous literature.[17-20] Also noted is the fact that there is no significant difference ($P = 0.546$) in the frequency of detection of SLNs in both groups with different number of radiotracer injections. Hence, the frequency of the detection of SLN using two-injection technique is comparable four-injection technique in patients with breast carcinoma. Furthermore, more number of the second tier nodes is identified in the two-injection technique as compared to the four injections, which signifies that the visualization of the second tier nodes is not related to the number of injection sites. However, it is of clinical importance that the radiation dose as well as the pain is less in case of two injections (Group B) as opposed to four injections (Group A).

Many factors can affect visualization of the sentinel node during lymphoscintigraphy. In advanced breast cancer, lymphatics become progressively infiltrated with tumour cells and do not allow the passage of radionuclides.[21] Cancerous involvement of the lymphatic system may influence the drainage pattern.

Completely invaded nodes may lead to unsuccessful axillary node detection due to a lack of ability of tracer uptake in the leading node. Heuser *et al*. reported five cases in which no axillary SN could be detected and consecutive axillary surgery revealed a positive nodal status in four of these patients with unsuccessful mapping.[22] The two patients in our study with negative sentinel scan underwent surgery after blue dye labelling. One out of these patients had nodal involvement by the tumour while the other had nodes negative for malignancy.

It has previously been reported that the age of the patient and tumour size may influence sentinel node detection rates.[23] Furthermore, the radiopharmaceutical used, the dose of the pharmaceutical, the particle size of the pharmaceutical and the injection-to-imaging time may all influence visualization of the sentinel node during lymphoscintigraphy.[24] The site of pharmaceutical injection (whether intratumoural vs. extratumoural, ID vs. SD or lateral vs. medial to a previous breast scar) can also affect visualization of the sentinel node during lymphoscintigraphy.[25]

Limitations

There are few limitations and possible biases in our study.

- As in any other cross-sectional study, we could not exclude the possibility of referral bias that influenced our study.
- The study was conducted over a short period of time. Further studies with larger sample size may be conducted.
- Difference in expertise level of injecting physician may also be a cause of variability in results.

Conclusion

Sentinel lymph node mapping with two periareolar intradermal injections carries less radiation dose and less pain as compared to the four injections with equal sensitivity for the visualization of sentinel lymph nodes.

Conflict of Interest

The authors declare that they have no conflict of interest.

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