Sentinel lymph node detection by intranipple injection of patent blue dye in breast cancer: a preliminary report of a feasibility study

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Summary

Sentinel lymph node (SLN) biopsy is a well established option for assessing axillary lymph node status in breast cancer. Several techniques have been applied so far (superficial or deeper ones). Based on anatomical features of the lymphatic drainage in the breast, we assessed the feasibility of an intranipple approach for SLN mapping. Our data support the feasibility of SLN detection by our technique, with a high rate of SLN identification, which could be used in clinical practice as an alternative to the peri-areolar approach.

Key words: Sentinel lymph node detection; Breast cancer; Patent blue; Intranipple injection; Techniques for SNL identification.

Introduction

Sentinel lymph node (SLN) evaluation can accurately predict the regional nodal status [1], and hence, there is a growing trend for SLN biopsy to replace axillary dissection in clinically node-negative cases. Although considered routine, several techniques are applied regarding the site of injection of the tracer. Nearly all anatomic boundaries of the external superficial anatomy have been used as sites of injection (dermis, dermo-areolar boundary, areola). However, no report has identified the intranipple route as an alternative so far. Herein, we present a multicentric pilot study regarding intranipple administration of a blue tracer as an alternative approach of SLN detection in an effort to investigate if such a technique is feasible and simple to perform.

Material and Methods

The study was approved by the Ethics Committees of the four participating institutes: Lito Maternity Hospital of Athens (Greece), Rea Maternity Hospital of Athens (Greece), University Hospital of Ioannina (Greece), and Saint Joseph University of Beirut (Lebanon).

Sixty-seven patients with breast cancer and non-palpable axillary nodes (N_0) were enrolled in the study. All patients were informed about treatment options and opted for axillary lymph node dissection. After the management plan had been established, the patients were informed about the current research protocol and gave their written informed consent. The mean age of the participants was 50.7 (SD = 10.19) years, ranging from 26 to 80 years. SLN detection was performed intraoperatively. An intranipple injection (via major mammary ducts) of 2 ml of patent blue solution was administered, followed by a gentle massage of the breast for 3-5 min (Figure 1). Fifteen minutes post-administration, a standard axillary lymph node dissection was performed. Any node marked as blue was removed separately and sent for pathology evaluation. The rest of the lymph nodes as well as the breast specimen followed.

Results

At least one SLN was detected in 62 out of the 67 patients enrolled (SLN detection rate: 92.5%). The overall mean number of SLNs colored was 1.86 (SD = 1.2). By omitting the five cases where no SLN was detected, the mean number of SLNs colored was 2.0 (SD = 1.1) which did not differ significantly ($p = 0.5$) from the mean number of SLNs in the total number of patients.

Taking into account that the lymphatic system of the breast is vast (comprising a network over the entire surface of the chest, neck, and abdomen with increased density under the axilla), it could be suggested that the proportion of patients in whom lymph nodes were colored (92.5%) is the sensitivity of the method in terms of its capability to color lymph nodes [1]. In cases of no SLN coloration, we proceeded to axillary lymphadenectomy (with negative nodes in all cases). Taking into account the negative results for cancer cases after axillary lymph node dissection (56 cases) and negative results for cancer SLN cases (50), the negative predictive value (NPV) of the method was 89.3%.

In three patients, although our method showed a colored negative SLN for cancer, after axillary lymphadenectomy, it was proven that the axillary nodes were positive for cancer. This could be explained as a "skip" phenomenon or as a false-negative result of our method.

Even if we assume that all of these three cases (from a total of 62 colored cases) were false-negatives, the sensitivity of the method is high (95%) in terms of its capability to correctly identify the "true" sentinel nodes.

Revised manuscript accepted for publication January 16, 2012

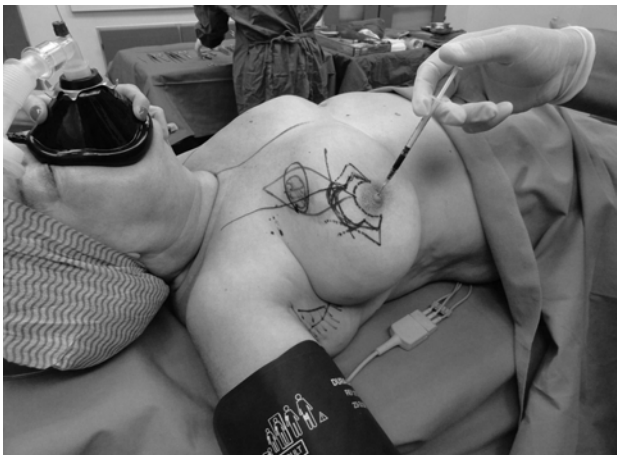

Figure 1. — Intranipple injection before batwing procedure.

No local infection or wound complications from the nipple were observed, underlying the safety of the procedure. Similarly, patient satisfaction was very good and not even minimal morbidity was related to the method.

Discussion

In the past, lymphatic mapping in breast cancer, performed solely by intraparenchymal injections of blue dye, remained an accepted method of identifying sentinel nodes, largely because of its simplicity. However, the technique was associated with a marked learning curve, variable identification rates of sentinel nodes, and high false-negative rates. Later on, dye injections into the subareolar plexus demonstrated a high sentinel node identification rate, low false-negative rate, and rapid learning curve.

The concept of the intranipple administration of a tracer is based on certain anatomic characteristics of the breast: following the galactophore ducts, each periductal lymphatic plexus converges into Sappey's subareolar plexus which is the major anatomic site where lymph from different breast sites is mostly drained [2]. The lymph from the nipple also drains into Sappey's subareolar plexus [3], and then to axillary nodes, whereas a small lymph portion is directed to the internal mammary glands and other adjacent lymph node groups [2, 4]. It was also shown that breast dermis lymphatics are concentrated in the nipple-areolar area [5]. By combining these together, it can be hypothesized that the tracer can mostly be accumulated in an axillary lymph group that should be the sentinel node.

The major advantages of this technique are:

a) easiness to perform,

b) short learning curve and

c) standardization of injection site.

Finally, as mentioned above, wound complications were not observed with our technique, in contrast with peritumoral injection (discoloration of the skin for many months) [6, 7].

The blue dye used has been considered as biologically inert and, as such, it has been allowed to be injected for SLN detection. However, several objections could rise regarding potential harm in the breast parenchyma, although no serious (or mild) adverse effects have been observed in our patients.

Pressure-induced damage due to the dye could also be hypothesized. However, both galactography and ductoscopy so far (both increasing parenchyma pressure) have not been reported as harmful procedures. Finally, possible iatrogenic infections due to a major mammary duct approach are unlikely by applying a good antiseptic technique.

A previous study by Kern *et al*. with smaller samples concluded definitely that: "on the basis of these findings, we propose that injections into the subareolar lymphatic plexus are the optimal way to perform dye-only lymphatic mapping of the breast" [8].

Taking into account that in the cases of no SLN colorization we proceeded to axillary lymphadenectomy (with negative nodes in all cases), our method "retains" its safety. This approach (if no blue nodes are detected; a standard axillary dissection is performed) is the usual practice published in previous studies [9]. However, in the previous studies, although a greater number of patients were included, the percentage of no colored nodes with blue dye - 18% (47 out of 260) was much higher compared to our data.

Conclusion

Although we believe that our results almost prove that the "intranipple injection" approach is feasible in detecting the SLN of the breast and that this technique could be used in clinical practice as an alternative to the periareolar or subcutaneous approach, the technique needs to be validated in larger studies.

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