

Original Research Article

A study on the feasibility of axillary reverse mapping with blue dye only in breast cancer patients

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ABSTRACT

Background: Axillary reverse mapping is (ARM) the concept of visualization of the nodes in axilla that drain the arm and preserving them. Literature describes this procedure being done with blue dye (methylene blue) and 99mTC technetium sulphur colloid. This study was undertaken to look for the feasibility of axillary reverse mapping using blue dye alone as there is lack of availability of the radio colloid in many centres in India.

Methods: 30 breast cancer patients who underwent axillary dissection as part of their surgery were included in the study. 2.5–5 ml of methylene blue was injected in the medial upper arm in the intermuscular groove region. The number of blue nodes identified, their location, pathological status and procedure related complications were analysed.

Results: The ARM blue node was identified only in 7 out of the 30 patients (sensitivity– 23%) and none had a pathologically positive blue node. In those 7 patients, only 1 blue node was identified. All the nodes were in level 1 and the largest node measured 2cm in largest dimension. The complications associated with the procedure included pain, pigmentation, induration and skin necrosis. 16 (53.3%) had pain, 10 (33.3%) had induration, 6 (20%) had pigmentation and 1 (3.33%) had skin necrosis.

Conclusions: The feasibility of ARM being done using blue dye alone needs to be questioned in view of its poor sensitivity. Added to this, the complication rates are higher. However, larger studies are needed to validate the same or otherwise.

Keywords: Axillary reverse mapping, Blue dye, Lymphedema, Complications

INTRODUCTION

Axillary nodal status is the most important predictor of prognosis in breast cancers.¹ Surgical treatment of axillary dissection results in lymphedema invariably. Lymphedema is by far the most commonly published complication associated with axillary dissection. The incidence of lymphedema after axillary dissection varies between 7–77% in various literatures.² There is a lymphedema incidence of approximately 7% even after sentinel node biopsy. Axillary reverse mapping (ARM) is a relatively newer concept and is the technique of injecting a dye and mapping the lymphatics of the arm

which lie in the axilla and preservation of the lymphatics or lymph nodes of the upper limb and thereby trying to reduce the incidence of lymphedema post axillary dissection. It can be considered as an opposite of sentinel lymph node biopsy. The arm lymphatics have crossovers with the breast lymphatics and hence can get involved by malignant cells.³ Therefore the oncological safety of axillary reverse mapping needs to be evaluated. There are very limited literatures with regard to the oncological safety of axillary reverse mapping. This concept of axillary reverse mapping is also supported by the anatomical descriptions of the lymphatics of arm by various authors.

The procedure for axillary reverse mapping includes injecting radio colloid or blue dye or a combination of both in various locations of arm (web spaces, medial upper arm) and looking for the hot or blue nodes and preserving them. The blue dye that is used is methylene blue in most centres. The radio colloid material differs in various centres though the most common used is Tc99m sulphur colloid.

The success of any procedure depends on its simplicity and the availability of materials. Though ARM is a simple procedure, in view of widespread non-availability of radio colloid and a gamma probe (nuclear medicine department), we fixed the aims and objectives of this study as to assess the feasibility of axillary reverse mapping using blue dye only and to evaluate the oncological safety of the procedure.

METHODS

Among the patients who attended the surgical oncology outpatient department in our hospital between October 2018 to December 2018, 30 biopsy proven breast cancer patients were included in the study. These patients underwent axillary dissection as part of their surgical management. The patients were selected irrespective of the stage of their disease, as the primary aim of the study is to look for the feasibility of ARM with blue dye and not evaluation of ARM in reducing lymphedema. Patients who had completed neoadjuvant chemotherapy were also included. Those who had a known allergy to the drug alone were excluded.

After the patient is positioned in table for the surgery and just after induction of anaesthesia, 2.5–5 ml of methylene blue was injected subcutaneously under strict aseptic precautions in the medial upper arm in the intermuscular groove region. This has been the preferred site as per literature for the reason that, there is fast reach of the dye into axilla if injected at this site. The injection site was massaged for 5 min. The blue nodes were looked for during axillary dissection. The time interval between injecting and axillary dissection had a range of 15-35 min. All the blue nodes were removed and their number, their location and pathological status (from postoperative histopathology report) was analysed. Postoperative injection associated complications were also noted. Descriptive statistical method such as range and median were used in analysis.

Institutional Ethical committee clearance was obtained before the start of the study and consent was obtained prior to surgery from all patients.

RESULTS

The 30 patients who underwent ARM were analysed for their baseline characteristics (Table 1). The average age of the patients was 50 (range: 31-67). Majority of the patients had a T2N1 disease (stage 2). 15 patients (50%)

were in stage 2 whereas 14 patients (46%) were in stage 3. Locally advanced breast cancer patients were also included after their neoadjuvant chemotherapy. 1 patient (4%) was in stage 1 and none were in stage 4. 12 patients (40%) had been given neoadjuvant chemotherapy. 11 patients (36%) had tumor in upper outer quadrant.

Table 1: Patient baseline characteristics (n=30).

Characteristics	N (%)
Age of the patients	Range: 31–67 years; Median: 50
Stage of the disease	
I	1 (4)
II	15 (50)
III	14 (46)
IV	0
Neoadjuvant therapy	
Yes	12 (40)
No	18 (60)
Quadrant of tumor	
Upper outer	11 (36)
Upper inner	6 (20)
Lower outer	8 (26)
Lower inner	5 (16)

Table 2: Outcome of the study.

Results	N (%)
No. of patients in whom blue node was identified	7 (23.3)
Post neoadjuvant chemotherapy	3 (42.8)
Upfront surgery	4 (57.1)
No. of patients with pathologically positive blue nodes	0
Levels of lymph nodes identified	
Level 1	7 (100)
Level 2	0
Level 3	0
No. of patients whom had complications	21 (70)

The results are tabulated in Table 2. The blue node was identified only in 7 patients (23.8%). 3 patients (42.8%) out of the 7 had undergone neoadjuvant chemotherapy. In all the patients, the nodes were identified in the level 1. The most common location was lateral to latissimus dorsi vascular pedicle. None of the nodes showed metastatic deposits histopathologically. The average time of identification of the node was 25 minutes (range: 15–35 min). The average size of the node was 1.42 cm (range: 1–2 cm).

Patients had various complications as tabulated in Table 3. Nine (30%) patients did not have any complication. Most common complication was pain at the injection site postoperatively and was seen in 16 patients (53.3%) which got settled with routine analgesics. The duration of

pain varied between 2 to 18 days. 10 patients (33.3%) had induration at the injection site along with pain. The induration started to resolve after 2 weeks and completely resolved during the 1st month follow up. 6 patients (20%) had persistent pigmentation beyond 1 week and during follow up. 1 patient (3.3%) had skin necrosis which was managed conservatively with antibiotics and wound care. All patients had complications graded by clavien dindo as grade 1.

Table 3: Complications.

Complication	N (%)
Pain	16 (53.3)
Induration	10 (33.3)
Pigmentation	6 (20)
Skin necrosis	1 (3.33)
None	9 (30)

DISCUSSION

Axillary reverse mapping is a procedure employed to identify and preserve nodes in the axilla that drain the arm and thereby reducing the incidence of lymphedema. This procedure can be performed with radiocolloid injection or blue dye injection.⁴ In our study, the sensitivity of the blue dye in identifying the arm nodes in axilla was only 23.8%. Also, there were significant complications with blue dye injections. Probable explanations for non-localization of the blue nodes in majority of patients could be inherent decreased sensitivity of the blue dye, decreased time interval between injection and surgery, debatable existence of ARM nodes itself. This decreased time interval between injection for the blue dye and looking for them in axilla, tells us that the lymphatic flow of arm is relatively slower than that of the breast. In a study by Nos et al. blue dye of very small volume (0.5 ml) was used with an aim of reducing the skin changes that it produces but the detection rate was very poor.⁵ Subsequently, they opted for radio colloid injection which gave a detection rate of 91%. In another study by Thompson et al, 61% detection rate was given with blue dye technique.⁶ In another study by Suzanne klimberg also, the detection rate was 61% but the dye used was isosulphan blue dye and not methylene blue.⁷ In Gandhi et al, the feasibility of lymphoscintigraphy was established with a detection rate of 94%.⁸

The locations of the nodes were also recorded with all the 7 nodes found in level 1 of axillary nodes in our study. In the study by Gandhi et al, the nodes were commonly found lateral to subscapular pedicle, above the 2nd intercostobrachial nerve and below the axillary vein. In the study by Shivakumar et al, the most common location was lateral to the subscapular pedicle.⁹ Though the location of the node was not so significant clinically, this parameter helps us to look for the nodes in the same location in subsequent cases. In the study by Nos et al,

the nodes were seen above and below the intercostal nerves and in relation to the subscapular pedicle.⁵

The oncological safety of the procedure was also assessed by the histopathological examination of the blue nodes. None of the blue nodes showed metastatic foci histopathologically. The crossover of lymphatics between those that drain the arm and the breast is responsible for the involvement of arm lymphatics. Noguchi et al had already demonstrated the presence of metastasis in axillary nodes identified by ARM.¹⁰ In Nos et al, 14% metastatic involvement was reported in all patients who had a pN3 disease.⁵ Most other studies were not taken into account as they had only N0 disease in their studies. Also intraoperative gross examination of the nodes could help in identifying the possibility of metastatic deposits. This would include, size (>2 cm), rounded, consistency (hard), location (central group), However, in our study none of these factors were contributory. The small sample size and the low sensitivity of the technique make it insufficient to draw any conclusions. In a study by Shivakumar et al, intraoperative FNAC was used to detect metastatic ARM nodes.⁹ It was concluded that nodes that are reported benign by intraoperative FNAC could be preserved safely to reduce lymphedema.

The complications due to the procedure were not recorded in many of the studies except for a few. In the study by Shivakumar et al, the complications described included pain, itching, induration, pigmentation, cellulitis.⁹ There are not much literature describing about the complications of ARM as most studies included radiocolloid and in studies where both are used, the dose of the dye injected was very less and intradermal. Injecting high volume intradermally will again result in overlying skin morbidity and hence the injections were given subcutaneously. In our study, the complications recorded includes, pain, pigmentation, induration, cellulitis and skin necrosis. These complications in addition to the decreased sensitivity of the blue dye in detecting ARM node doubt the feasibility of the procedure with blue dye alone. Though these complications amount to only short term morbidity of the patient, long term follow up data are lacking.

CONCLUSION

Axillary reverse mapping has been described in literature as a procedure that helps in reducing the incidence of lymphedema of arm. The Sensitivity of blue dye in identifying the ARM nodes appears to be very poor and the procedure related complication rates are high. Hence, the feasibility of ARM using blue dye only needs to be questioned and larger studies are needed to validate the oncological safety.

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