

Comparative study of role of bupivacaine instillation into the operative bed for post-operative pain analgesia in modified radical mastectomy

¹Dr.Kiran Kumar Nayak S, ²Dr.Srilakshmi N,³Dr.Vinay G,⁴Dr.Abhilash

¹Assistant Professor, Department of General Surgery, Chamarajanagar Institute of Medical Sciences, Chamarajanagar, Karnataka, India

²Senior Resident, Department of General Surgery, KIMS, Hubli, Karnataka, India

³Senior Resident, Department of General Surgery, Chamarajanagar Institute Of Medical Sciences, Chamarajanagar

⁴Senior Resident, Department of General Surgery, BLDE (Deemed to be University), Shri B M Patil Medical College, Vijayapura, Karnataka, India

Corresponding Author: Dr. Abhilash

Abstract

Surgery still has a pivotal role in the management of breast cancer, even though recent advances in oncology are trending towards more conservative techniques followed by chemotherapy. The consensus development conference on the treatment of breast cancer in 1979 stated that modified radical mastectomy was the standard of treatment for stage 1 and 2 disease. 60 patients of either sex between age group 30 to 60 years undergoing elective Modified Radical Mastectomy were divided into two groups of 30 patients each randomly who fulfilled the inclusion and exclusion criteria. In this study, when we look closer, we could see that, despite of being statistically significant, the VAS and VRS scores at initial intervals (1hr, 4hrs) were low in group A when compared to group B. At 8 hours and, there was a marked increase in VAS and VRS score in group B and thereafter it was akin in two groups.

Keywords: Bupivacaine instillation, post-operative pain analgesia, modified radical mastectomy

Introduction

Breast cancer is a major public health problem for women throughout the world. Breast cancer remains the most frequent cancer in women and the second most frequent cause of cancer death.

In 2017, it was estimated there were 255,180 new cases of breast cancer, with 41,070 deaths. Worldwide, breast cancer is the most frequently diagnosed cancer and the leading cause of cancer death among females, accounting for 25% of cancer cases and 15% of the cancer deaths, although there is a 4-fold variation in mortality rates and over 10-fold variation in incidence rates between high-incidence areas such as the United States and Western Europe and low-incidence areas such as Africa and Asia^[1, 2].

Surgery still has a pivotal role in the management of breast cancer, even though recent advances in oncology are trending towards more conservative techniques followed by chemotherapy.

The consensus development conference on the treatment of breast cancer in 1979 stated that modified radical mastectomy was the standard of treatment for stage 1 and 2 disease.

Pain is derived from the word 'poine' - the Greek goddess of revenge, a certitude not lost on us, at times it feels like a divine vengeance^[3].

According to Indian Association for Study of Pain (IASP), pain is defined as an "unpleasant

sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage”.

Recently it has evolved into a multidimensional entity involving sensory, cognitive, motivational and affective qualities. Despite centuries of theoretical and scientific inquiry, perioperative analgesia with minimal side effects is a major concern.

Poorly managed pain following surgery can produce pathophysiologic process in both peripheral and central nervous system which have the potential to produce chronicity^[4].

Mastectomy is one among the surgical procedures that can be associated with chronic painful condition. Various strategies like NSAIDs, opioids, peripheral nerve blocks, wound infiltration with local anaesthetics were found to have significantly improved postoperative pain relief.

Optimal acute postoperative pain relief after major breast surgery is still a matter of controversy.

Surgical wound infiltration with a local anaesthetic solution is currently performed in many surgical procedures. Paravertebral blocks and brachial plexus blocks have been practiced from long back for pain relief^[5,6].

When compared to breast conserving surgery, Modified Radical Mastectomy is considerably painful. Local anesthetics are speculated to reduce postoperative pain when placed at surgical operative bed.

Methodology

60 adult patients between age group 30 to 60 years undergoing elective Modified Radical Mastectomy were divided into two groups of 30 patients each randomly.

All patients underwent similar general anesthetic procedure.

Group (A): Study Group: Patients received 20 ml of 0.5% bupivacaine instilled intraoperatively into operative bed.

Group (B): Placebo Group: Patients received 20 ml of normal saline intraoperatively at the same location.

The elective Modified Radical Mastectomy procedure was done in standard fashion.

Patients in group A (Study group) received intraoperatively instillation of 0.5% bupivacaine into operative bed at the end of surgery.

Patients in group B (Placebo group) received intraoperative instillation of normal saline into the operative bed at the end of surgery position.

Approval from the ethical committee of the institution was obtained.

All the patients were explained about the basis of the study and informed consent were obtained.

Study design: Randomized clinical trial.

Sample size: 60 patients of either sex between age group 30 to 60 years undergoing elective Modified Radical Mastectomy were divided into two groups of 30 patients each randomly who fulfilled the inclusion and exclusion criteria.

Inclusion criteria

Patients of either sex between 30 and 60 years, with carcinoma of breast who is posted for elective Modified Radical Mastectomy and who give consent for the study.

Exclusion criteria

1. Patient below 30 and above 60 years
2. Patient with underlying respiratory, renal, neurologic, psychiatric and cardiac abnormalities

3. Patient who do not understand the visual analogue score
4. Patients who undergo any additional procedure
5. Patients with a history of chronic analgesic drug usage
6. Patients with major blood loss and unpredictable action of drugs such as continuous excessive blood collection
7. Patient who do not give consent for the study.

Results

Table 1: Age distribution

Age groups	Group A	%	Group B	%
31-40yrs	9	30.00	3	10.00
41-50yrs	12	40.00	14	46.67
51-60yrs	9	30.00	13	43.33
Total	30	100.00	30	100.00
Chi-square=3.881 P = 0.144 (Not significant)				

In our study we compared the age wise distribution in the two groups. In the group A, 30% were in the age group between 31-40 years, 40% were in the age group 41 to 50 years and 30% were in the age group 51 to 60 years.

In group B, 10% were in the age group between 31-40 years, 46.6% were in the age group 41 to 50 years and 43.3% were in the age group 51 to 60 years. There was no significant difference in age distribution between two groups.

Table 2: VAS scores at different time points

VAS scores at	Group A		Group B		P-value
	Mean	SD	Mean	SD	
1hr	1.53	0.82	2.73	0.45	<0.001
4hrs	2.76	1.49	4.67	1.27	<0.001
8hrs	3.47	1.48	5.70	1.68	<0.001
24hrs	2.53	0.51	2.83	0.38	0.0120

In group A, mean VAS score at 1 hr, 4 hrs, 8 hrs and 24 hrs is 1.53, 2.76, 3.47 and 2.53 respectively. In group B mean VAS score at 1hr, 4hrs, 8hrs and 24hrs is 2.73, 4.67, 5.70 and 2.83 respectively.

There is significant difference in p value in both groups at 1hr, 4hrs and 8hrs. p Value at 24 hours is insignificant.

Table 3: VRS scores at different time points

VRS scores at	Group A		Group B		P-value
	Mean	SD	Mean	SD	
1hr	0.60	0.72	1.63	0.56	<0.001
4hrs	1.53	0.73	2.27	0.45	<0.001
8hrs	2.10	0.48	2.60	0.50	<0.001
24hrs	1.73	0.52	1.97	0.41	0.0596

Mean VRS Score in Group A at 1hr, 4 hrs, 8 hrs and at 24hrs is 0.60, 1.53, 2.10 and 1.73 respectively. Whereas VRS score in Group B at 1hr, 4 hrs, 8 hrs and at 24hrs is 1.63, 2.27, 2.60 and 1.97 respectively.

There is significant changes in p value at 1hr, 4 hrs and at 8 hrs.

Table 4: Rescue analgesia

Rescue analgesia	Group A	%	Group B	%
No	24	80.00	6	20.00
Yes	6	20.00	24	80.00
Total	30	100.00	30	100.00
Chi-square= 21.600 P = 0.0001 shows significant				

*p<0.05

Rescue analgesia requirement were studied and compared between the two groups at 1hr, 4hrs, 8hrs and 24hrs.

In our study 80% of the patients in group A had a VAS Score of <4 and VRS Score of <3 and does not require any rescue analgesia, whereas in group B only 20% of the patients had a VAS score of <4 and VRS Score of <3.

In our study, 20% of patients in group A had VAS score of more than 4 and VRS score of >3 and thereby requiring rescue analgesia, whereas in group B 80% of patients had VAS score of >4 and VRS score of >3 thereby requiring rescue analgesia. So rescue analgesia in the form of Inj. Diclofenac 75mg i.m were given to them.

At 1 hour none of the patients in group A and B required rescue analgesia, whereas in group A 2 patients i.e. 6.66% of patients at 4 hrs and 6 patients 19.98% of patients at 8 hrs required rescue analgesia.

In group B 24 patients at 4 hours and 8 hours required rescue analgesia that is 80% of the patients required analgesia. We found that the maximum analgesic effect after wound instillation was up to 8hrs in our study groups.

Also in our study, the p value for VAS score at 8 hours was 0.0001 and hence was statistically significant.

The VAS score and VRS score was high in group B when compared to group A at 8 hours indicating more pain in group B requiring rescue analgesia.

In this study, when we look closer, we could see that, despite of being statistically significant, the VAS and VRS scores at initial intervals (1hr, 4hrs) were low in group A when compared to group B. At 8 hours and there was a marked increase in VAS and VRS score in group B and thereafter it was akin in two groups.

Discussion

The advances in breast cancer surgery in the last few decades were not associated with similar advancement in the acute or the chronic pain control.

In this prospective, randomised controlled study, the results showed that patients, who received instillation with 0.5% bupivacaine into operative bed following MRM procedure experienced a good postoperative analgesia as compared with patients who received normal saline similarly.

Cumulative rescue analgesic consumption and number of demands for analgesia in the first 24 h, when the pain score was ≥ 4 [7] was significantly lower in the bupivacaine group compared with the saline group and control groups ($P = 0.00$).

Local anaesthetic drugs have become increasingly popular because of their analgesic properties, and lack of opioid-induced adverse effects for treating postoperative surgical pain.

In many of the plastic reconstructive breast procedures, irrigation of the pocket created for the insertion of the prosthesis with local anaesthetics is reported with high levels of satisfaction regarding postoperative pain and have recommended this technique of analgesia for all the cosmetic breast surgery.

Various regional and systemic techniques such as local wound infiltration, wound instillation, thoracic epidural, thoracic paravertebral block, NSAIDs, opioids, and more recently ultrasound guided fascial plane blocks have been used to provide analgesia in breast

surgeries. Despite the availability of wide variety of options for Pain management, satisfactory pain relief remains elusive.

Arunakul and Ruksa^[7] found that single injection of paravertebral block (PVB) reduced pain scores and opioid consumption in MRM. However, these techniques are laborious and technically challenging.

Infiltration of local anaesthetic along the suture line also provides analgesia but, for malignant lesions this method may not be recommended because of fear of needle track seedlings and cutaneous spread of malignancy.

Sidiropoulou and his colleagues^[8] in their study compared analgesic effect of single injection of PVB with ropivacaine and continuous irrigation of wound with ropivacaine through two dedicated multi-lumen catheters placed subcutaneously at the end of the procedure following mastectomy for 24 h. They found that early postoperative analgesia (4 h) was good with PVB and late postoperative analgesia was good with continuous irrigation and concluded that continuous wound irrigation is as effective as PVB with low pain scores and good patient satisfaction.

In our study the technique of drug instillation into operative bed is technically simple, and operation theatre time is also not a constraint because it takes very little time to instill the drug into operative bed.

The technique of instillation of the drug through drains is well established in surgical procedures like laparoscopic cholecystectomy, abdominal hysterectomy where the results have shown some positive impact on postoperative analgesia. Moreover, this is well accepted by the patient and the surgeons.

But in a study by Fredman *et al.*^[9] it was seen that after major abdominal surgery repeated wound instillation of 0.25% bupivacaine solution via an electronic patient-controlled analgesia (PCA) device and a double-catheter system did not decrease postoperative pain or opioid requirements. Here the authors opined that the lack of uniform distribution or rather spread of the drug was unpredictable, and also the dose of the local anaesthetic was insufficient. However, there is sparse literature regarding its use in the MRM procedure.

In a study by Legeby *et al.*^[10] following breast reconstruction surgery, levobupivacaine injected locally every 3rd h as a supplement to paracetamol orally, and morphine given by PCA resulted in improved pain relief at rest and during mobilization compared with placebo.

Talbot *et al.*^[11] in their study to determine the effect of local anaesthetic irrigation of axillary drains on postoperative pain following a modified Patey mastectomy felt it did not appear to offer any contribution for postoperative analgesia in some of their patients. They opined that this could be because of malpositioned drain, blockade of some holes of the drain or unequal distribution of the local anaesthetic due to gravity and concluded that further refinement in the technique was needed.

In our randomized control study, the results showed that patients, who received instillation with 0.5% bupivacaine into operative bed following MRM, experienced a better post-operative pain control compared with patients of control group who had received saline. Cumulative rescue analgesic consumption and number of demands for analgesia in the first 24 h were significantly lower in Bupivacaine group compared with the saline group so as the use of injection Diclofenac is also less in Bupivacaine group and their VAS and VRS scores were significantly higher as compared to the patients who received saline. Assessment of pain was done using VAS and VRS score. Our study showed that VAS and VRS score increases significantly early in Group B than Group A. When VAS score reached >4, rescue analgesia in the form of intramuscular Diclofenac 75mg was administered.

This finding is in concordance with the study of Jonnavithula *et al.* who studied the analgesic effect of instillation of 0.25% of bupivacaine versus 0.9% normal saline and control group with no instillation, in cases of modified radical mastectomy through surgical drains.

Our study was in contrast to the study of Talbot *et al.* who in their study determined the effect of irrigation of axillary drains with local anesthetic on post-operative pain following modified

Patey mastectomy. They noted that it did not appear to offer any beneficial for post-operative analgesia in some of their patients nor were there any differences in antiemetic or supplemental analgesic consumption. They opined that this could be because of malpositioned drain, blockade of some holes of the drain, or unequal distribution of the local anesthetic due to gravity and concluded that further refinement in the technique was needed. Hence, to overcome this limitation, we have instilled directly into operative bed. This could have resulted in more uniform distribution of the drug, thereby improving the efficacy of the technique, and the patients were pain free in the post-operative period.

In our study, there was no case of local anesthetic toxicity observed which was in concordance with the study of Jonnavithula *et al.*^[12] and Talbot *et al.*^[11]

Conclusion

Wound instillation with local anaesthetics is a simple, effective and inexpensive means of providing good analgesia for patients following the MRM procedure without any major side-effects.

Wound infection and healing do not appear to be a major concern. Local anaesthetics are generally well tolerated, provided they are used correctly and in the correct doses. This technique of providing postoperative analgesia can be included in the armamentarium of multimodal analgesia.

Here we conclude that wound instillation of bupivacaine in modified radical mastectomy.

References

1. Howlader N, Noone AM, Krapcho M, Garshell J, Neyman N, Altekruse SF *et al.* Cancer Statistics Review, 1975-2010. Bethesda, MD: National Cancer Institute, 2012. Available from: http://www.seer.cancer.gov/csr/1975_2010/ Based on November 2012 SEER data submission, posted to the SEER web site.
2. Fayman M, Beeton A, Potgieter E, Becker PJ. Comparative analysis of bupivacaine and ropivacaine for infiltration analgesia for bilateral breast surgery. *Aesthetic Plast Surg.* 2003;27:100-3.
3. Lu L, Fine NA. The efficacy of continuous local anesthetic infiltration in breast surgery: Reduction mammoplasty and reconstruction. *Plast Reconstr Surg.* 2005;115:1927-34.
4. Uematsu T, Kasami M. Risk of needle tract seeding of breast cancer: Cytological results derived from core wash material. *Breast Cancer Res Treat.* 2008;110:51-5.
5. Dr. Aarushi Kataria, Dr. Naveen Nandal and Dr. Ritika Malik, Shahnaz Husain -A Successful Indian Woman Entrepreneur, *International Journal of Disaster Recovery and Business Continuity* Vol.11, No. 2, (2020), pp. 88–93
6. Malik, R., Nandal, Naveen and Gupta, Prakhar. (2021), The Impact of online shoppers to price and quality: a survey study in Delhi-NCR, *Efflatounia*, 5 (2), pp. 376 – 389.
7. Chanrachakul B, Likittanasombut P, O-Prasertsawat P, Herabutya Y. Lidocaine versus plain saline for pain relief in fractional curettage: A randomized controlled trial. *Obstet Gynecol.* 2001;98:592-5.
8. Jonnavithula N, Durga P, Madduri V, Ramachandran G, Nuvvula R, Srikanth R *et al.* Efficacy of palatal block for analgesia following palatoplasty in children with cleft palate. *Paediatr Anaesth.* 2010;20:727-33.
9. Arunakul P, Ruksa A. General anesthesia with thoracic paravertebral block for modified radical mastectomy. *J Med Assoc Thai.* 2010;93(7):S149-53.
10. Sidiropoulou T, Buonomo O, Fabbi E, Silvi MB, Kostopanagiotou G, Sabato AF *et al.* A prospective comparison of continuous wound infiltration with ropivacaine versus single-injection paravertebral block after modified radical mastectomy. *Anesth Analg.* 2008;106:997-1001.
11. Fredman B, Zohar E, Tarabykin A, Shapiro A, Mayo A, Klein E *et al.* Bupivacaine wound instillation via an electronic patient-controlled analgesia device and a double-catheter

- system does not decrease postoperative pain or opioid requirements after major abdominal surgery. *AnesthAnalg.* 2001;92:189-93.
12. Legeby M, Jurell G, Beausang-Linder M, Olofsson C. Placebo-controlled trial of local anaesthesia for treatment of pain after breast reconstruction. *Scand J Plast. Reconstr. Surg. Hand Surg.* 2009;43:315-9.
 13. Talbot H, Hutchinson SP, Edbrooke DL, Wrench I, Kohlhardt SR. Evaluation of a local anaesthesia regimen following mastectomy. *Anaesthesia.* 2004;59:664-7.
 14. Jonnavithula N, Pisapati MV, Durga P, Krishnamurthy V, Chilumu R, Reddy B. Efficacy of peritubal local anesthetic infiltration in alleviating postoperative pain in percutaneous nephrolithotomy. *J Endourol.* 2009;23:857-60.